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Stability and comparison of complete blood count parameters between capillary and venous blood samples

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Abstract

Introduction: This study assessed the comparability of complete blood count (CBC) parameters between capillary and venous samples, and extended previous research by examining the influence of different storage temperatures on CBC stability up to 7 days after sample collection.

Methods: Venous and capillary blood samples were collected from 93 adult patients. Hemoglobin (Hb), hematocrit (Ht), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), mean platelet volume (MPV), leukocytes, lymphocytes, basophils, eosinophils, erythrocytes, red cell distribution width (RDW), immature granulocytes (IG), immature reticulocyte fraction (IRF), monocytes, neutrophils, platelets, and reticulocytes were measured. Deming regression and mean relative differences between venous and capillary measurements were contrasted with desirable total allowable error (TEa). Stability was assessed in 20–27 venous blood samples stored at 4, 21–22, or 30°C, and analyzed at 0, 24, 48, 72, 96, 120, 144, and 168 h. Mean relative change with respect to baseline measurements was compared to the desirable TEa to determine acceptable stability.

Results: Deming regression demonstrated strong linear correlations and acceptable variation between venous and capillary measurements. Erythrocytes, Hb, Ht, MCH, MCV, RDW, reticulocytes, and platelets showed acceptable stability for at least 96 h at 4°C. Mean relative change exceeded desirable TEa after 24 h at 30°C for all parameters, except erythrocytes, Hb, leukocytes, and MCH.

Conclusion: Clinical laboratory specialists and clinicians should be aware of potential differences between venous and capillary measurements, and the influence of storage conditions. Clinical validity of delayed CBC analysis depends on the clinical situation and required precision of the result.

KEYWORDS
analytical variation, clinical laboratory techniques, complete blood count, hematology, storage temperature

1 | INTRODUCTION

The complete blood count (CBC) is among the most frequently performed diagnostic assays in clinical laboratories. CBC analysis consists of a count of the total number of erythrocytes, leukocytes and platelets, a measurement of the hemoglobin concentration, and determination of average cell size and size distributions in blood. These hematological parameters are used in diagnosis and monitoring of many acute and chronic conditions. Therefore, accurate measurement of these parameters is crucial for patient care. The standard procedure for blood collection with regard to CBC is through venipuncture. Unfortunately, venipunctures are associated with a number of disadvantages, including the requirement of a trained phlebotomist and patient discomfort, especially when frequent monitoring is necessary.

In contrast, capillary blood sampling offers a less invasive sampling method, making it more suitable for patients with poor venous access or anxiety regarding blood sample collection.[1] Research regarding blood sampling methods and patient preferences has so far indicated that the majority of patients prefer capillary blood sampling over venipunctures.[2–5] Moreover, capillary blood sampling can be performed by patients themselves or their caregivers and may therefore be suitable for remote or at-home blood sample collection, especially in pediatric populations.[4,6,7] Since laboratory monitoring is an indispensable part of patient care, the possibility to remotely collect blood samples is essential to fully realize remote healthcare. Moreover, the laboratory results are monitored and interpreted by clinical laboratory specialists and the quality of the CBC results can be guaranteed.

Previous research regarding venous and capillary blood sampling to measure CBC parameters has primarily focused on comparability of results and, to a lesser extent, on short-term stability (up to 24–72 h).[8–16] Data on comparability, longer term stability, and influence of sample storage conditions for current generations of hematology analyzers is limited. Therefore, in order to determine which CBC parameters are potentially suitable for remote or at-home capillary sampling with delayed analysis, the evaluation of venous and capillary comparability and long-term stability is highly valuable. The aim of this study is to assess the comparability of CBC parameters between capillary and venous samples, and to extend previous research by examining the influence of different storage temperatures on CBC parameter stability up to 7 days after blood sample collection.

2 | MATERIALS AND METHODS

2.1 | Subjects

Capillary and venous CBC parameters were compared using samples from 93 patients presenting to the outpatient clinic of the Central Diagnostic Laboratory at the University Medical Center Utrecht (UMCU, Utrecht, The Netherlands). All adult patients (≥18 years) for whom routine CBC assays were requested by their treating physician were eligible for this study and were asked to participate. After patients provided written informed consent, a capillary sample was collected for analysis in addition to the venous blood sample required for standard care. An overview of the total study population is presented in Table 1.

TABLE 1 Overview of study population characteristics.

	Capillary versus venous measurements	Stability of parameters
Number of total patients	93	136
Age (years), median (IQR)	62 (51–69)	60 (47–70)
Female, *n* (%)	43 (46)	61 (45)

Abbreviation: IQR, interquartile range.

Stability of CBC parameters was assessed in anonymous residual blood of venous whole blood samples of 20–27 patients for each parameter, which were stored at different temperatures and durations prior to analysis. For studying stability at day 1–4, 7 and days 5–6 two independent sets of samples were used. In addition, all samples were analyzed at baseline. Patients agreed that residual material of their anonymized blood sample could be used for medical research.

This study was conducted in accordance with the Declaration of Helsinki (2013, revised version) and guidelines for Good Clinical Practice. The study protocol was approved by the Institutional Review Board at the UMCU (20-676/C and 22-800/DB).

2.2 | Sample collection

Venous blood sampling at the outpatient clinic was performed by a trained phlebotomist via venipuncture with the BD Vacutainer® blood collection system (Becton Dickinson, NJ), at the cubital fossa. Subsequently, blood was collected in an EDTA tube (K2EDTA, 2 mL, Vacutainer®, Becton Dickinson, Plymouth UK) [Correction added on 03 July 2023, after first online publication: product details have been updated in this version.]. In addition to the venipuncture, a capillary blood sample was obtained by fingerprick. Prior to the fingerprick, the puncture site was cleaned with isopropyl alcohol 70% and allowed to air dry. The skin was punctured using a BD Microtainer® contact activated lancet (Becton Dickinson, New Jersey) to a depth of 2.0 mm and the first drop of blood was wiped off. Subsequent blood drops were collected into EDTA microtubes (K2EDTA, 0.5 mL, Microtainer® MAP, Becton Dickinson, New Jersey) [Correction added on 03 July 2023, after first online publication: product details have been updated in this version.]. After collection, tubes were capped and inverted eight times prior to analysis.

2.3 | CBC measurements

All CBC measurements were performed at the ISO15189 accredited Central Diagnostic Laboratory of the UMCU using the Abbott

ALINITY hq hematology analyzer (Abbott Diagnostics, Santa Clara, CA). The analyzer was maintained according the recommendations of the manufacturer and results were guaranteed by a rigorous quality control program using internal and external qc schemes. hemoglobin concentration (Hb), hematocrit (Ht), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin

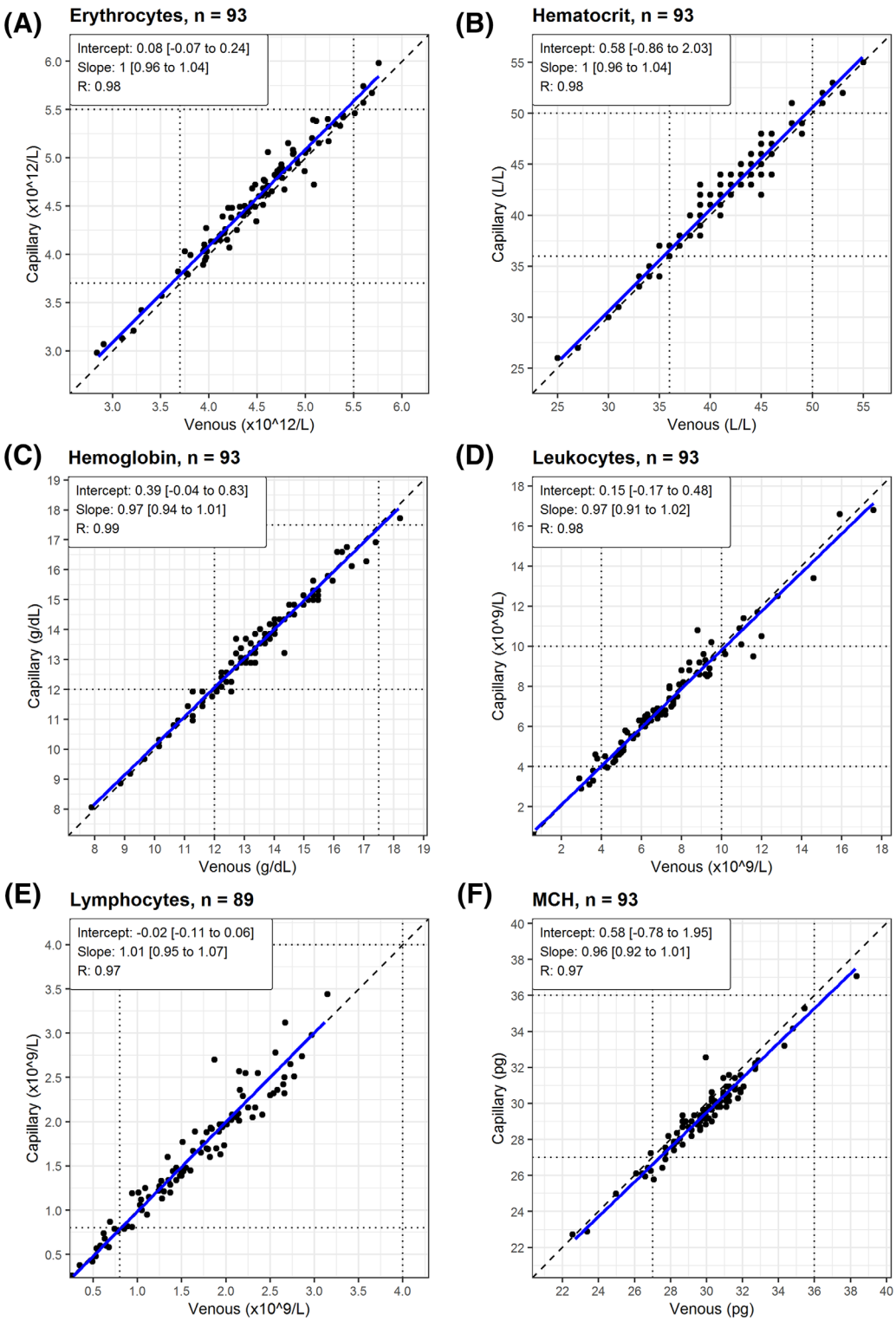

FIGURE 1 (A)–(J) Scatter plots of venous (x-axis) and capillary (y-axis) measurements with Deming regression (solid blue line), line of equality (dashed line), and reference values (horizontal and vertical dotted lines). Slope and intercept of the Deming regression are presented with 95% confidence intervals between brackets. Correlation coefficient between venous and capillary measurements is denoted by R. Outliers removed from the analysis are presented in red. MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume.

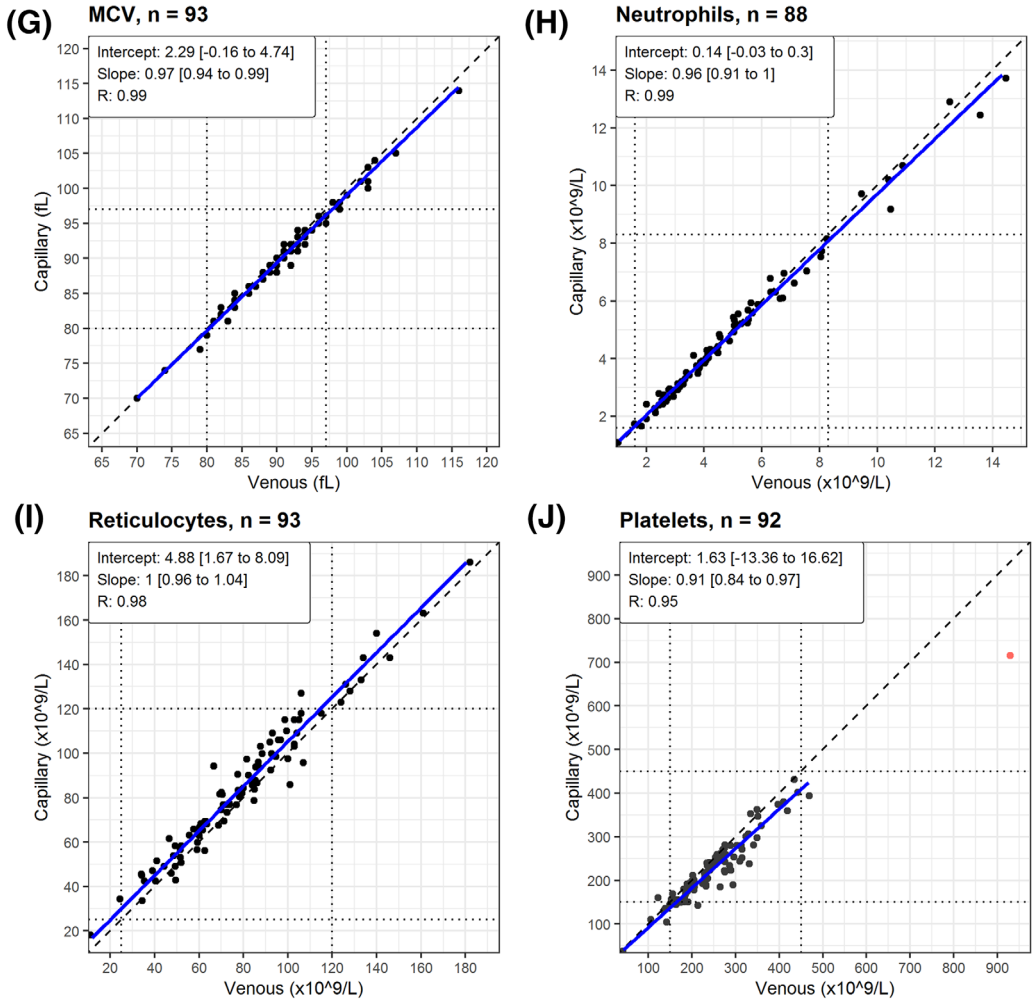

FIGURE 1 (Continued)

concentration (MCHC), mean platelet volume (MPV), leukocytes, lymphocytes, basophils, eosinophils, erythrocytes, red cell distribution width (RDW), immature granulocytes (IG), immature reticulocyte fraction (IRF), monocytes, neutrophils, platelets, and reticulocytes were determined. Capillary and venous blood tubes designated for method comparison were analyzed within 3 h after collection.

Stability of CBC parameters was assessed by randomly dividing residual venous whole blood samples into three different groups. All samples were analyzed at baseline (within 4 h after collection). Thereafter, primary sample tubes were stored at 4°C, room temperature (21–22°C), or 30°C and analyzed at $t = 24$, 48, 72, 96, 120, 144, and 168 h. Blood samples designated to assess the stability of CBC parameters were independently collected from samples used for method comparison.

2.4 | Statistical analysis

For direct method comparison between capillary and venous samples, Deming regression and mean difference with 95% confidence intervals (CI) were calculated. For each of the CBC parameters, mean differences between capillary and venous samples were compared to the desirable total allowable error (TEa) derived from the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) database.[17] The TEa consists of the within subject coefficient of variation (CV_i) and between subject coefficient of variation (CV_g) and can be calculated according to the formula: $0.25 \times \left(CV_i^2 + CV_g^2\right)^{0.5} + 1.65 \times 0.5 \times CV_i$. Outliers in the data were identified by visual inspection using histograms. One extreme platelet count (930×10^9/L) was identified as outlier and subsequently removed from the Deming regression analysis and calculation of mean difference. Stability of CBC parameters in different storage conditions was assessed by calculating the mean relative change (with 95% CI) compared to the baseline measurement at each time point, contrasted with the desirable TEa for each specific parameter, respectively. CBC measurements classified as invalid by the Abbott Alinity hq hematology analyzer were excluded from all analyses. All data were analyzed using R version 4.0.3. (R Foundation for Statistical Computing, Vienna, Austria) with p-values <0.05 considered as statistically significant.

TABLE 2 Mean difference (%) with 95% confidence interval between capillary and venous measurements contrasted with desirable total allowable error (TEa).

Parameter	Mean relative difference % [95% CI]	TEa (%)	Within TEa?
Erythrocytes	2.0 [1.5 to 2.5]	3.9	Yes
Hematocrit	1.5 [0.9 to 2.0]	3.9	Yes
Hemoglobin	0.3 [−0.2 to 0.7]	3.8	Yes
Leukocytes	−0.7 [−2.2 to 0.7]	13.8	Yes
Lymphocytes	0 [−2.2 to 2.3]	15.2	Yes
MCH	−1.6 [−2.0 to −1.2]	1.8	No
MCV	−0.7 [−0.9 to −0.5]	1.6	Yes
Neutrophils	−0.9 [−2.0 to 0.3]	18.4	Yes
Reticulocytes	8.4 [6.0 to 10.8]	15.2	Yes
Platelets	−8.1 [−10.1 to −6.1]	11.3	Yes

Abbreviations: CI, confidence interval; MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume.

3 | RESULTS

3.1 | Regression analysis

Deming regression slope and intercept for erythrocytes, hematocrit, hemoglobin, leukocytes, lymphocytes, MCH, and MCV did not significantly deviate from equality, as demonstrated by their respective 95% CI (Figure 1). Although differences were small, capillary measurements resulted on average in systematically higher reticulocyte counts (Figure 1I). In contrast, platelet measurements were slightly lower in capillary samples with increasing platelet counts, although the regression intercept did not significantly deviate from 0 (Figure 1J). Correlation coefficients demonstrated a very strong linear correlation between capillary and venous measurements for CBC parameters presented in Figure 1. A small trend from equality of the regression slope (with 95% CI) was observed for neutrophil counts, indicating a small proportional difference between capillary and venous measurements, more apparent at higher values (Figure 1H). High linear correlations were observed for IRF, monocyte, MPV, and RDW measurements (Supplementary Figure S1D,F–H) while weaker correlations were found for basophils, eosinophils, IG, and MCHC measurements (Supplementary Figure S1A–C,E).

3.2 | Bias analysis

Relative mean differences and their 95% confidence intervals were within desirable TEa for erythrocytes, hematocrit, hemoglobin, leukocytes, lymphocytes, MCV, monocytes, MPV, neutrophils, platelets and reticulocytes (Table 2 and Supplementary Table S1).

Relative mean differences of MCH (−1.6% [95% CI −2.0 to −1.2]) and MCHC (−0.9% [95% CI −1.4 to −0.5]) measurements did not significantly exceed desirable TEa. Nevertheless, 95% confidence intervals were not within desirable TEa limits of 1.8% and 1.3%, respectively (Table 2 and Supplementary Table S1). A positive relative mean difference was observed for basophils (49.0% [95% CI 17.6 to 80.5]) and eosinophils (52.2% [95% CI 5.5 to 99.0]), indicating increased values for capillary measurements when compared to venous measurements (Supplementary Table S1).

Bias plots of relative and absolute differences plotted against venous measurements are presented in Supplementary Figures S2 and S3, respectively.

3.3 | Stability

To assess stability of CBC over time (up to 7 days after collection), mean relative change (with 95% confidence interval) compared to baseline measurements was assessed for each sample at each time point and contrasted with desirable TEa (Table 3, Supplementary Table S2, Supplementary Figure S4).

Confidence interval limits for erythrocyte counts, hematocrit, hemoglobin, MCH, MCV, reticulocyte and platelet counts did not exceed desirable TEa for at least 4 days (96 h) when stored at 4°C. At room temperature (21–22°C), hematocrit and MCV exceeded desirable TEa within 24 and 48 h, respectively. Erythrocyte and platelet counts, hemoglobin, and MCH were relatively stable up to 7 days (168 h). At 30°C, hematocrit, MCV, reticulocyte and platelet counts exceeded TEa within 24 h while MCH and erythrocyte counts were stable for up to 5 days (120 h) after collection.

Leukocyte and differential leukocyte counts were generally less stable, regardless of storage temperature. Although lymphocyte counts appeared to be within desirable TEa up to 7 days (168 h) after blood sample collection, the proportion of invalid measurements identified by the analyzer increased over time (Supplementary Table S3).

Overall, cell counts were most stable at room temperature, while cell size and distribution parameters, such as MCV, MCH, MPV, and RDW, were most stable at a storage temperature of 4°C. Trajectories of individual sample measurements over time are presented in Supplementary Figure S5.

4 | DISCUSSION

Previous research on CBC measurements has primarily focused on comparability between venous and capillary results and short-term stability up to 72 h. In this study, we assessed the comparability of

TABLE 3 Mean change (%) with 95% confidence interval of complete blood count measurements compared to baseline up to 7 days at 4, 21–22°C (room temperature), and 30°C. Stable column presents maximum hours where mean change (%) and 95% confidence intervals were within desirable TEa. Validity is expressed as maximum storage hours where at least 100% or 90% of measurements were classified as valid by the analyzer.

Parameter	Temp	Day 1 (24 h)	Day 2 (48 h)	Day 3 (72 h)	Day 4 (96 h)	Day 5 (120 h)	Day 6 (144 h)	Day 7 (168 h)	TEa (%)	Stable (h)	100% valid (h)	>90% valid (h)
Erythrocytes	4	−0.4 [−0.7, 0]	−0.6 [−1, −0.2]	−0.4 [−0.7, −0.1]	−0.7 [−1.1, −0.4]	2.1 [1.5, 2.8]	1.5 [0.9, 2.1]	0.1 [−0.4, 0.5]	3.9	168	168	168
	RT	0.7 [0.3, 1]	0.5 [0.1, 0.8]	0.4 [0, 0.9]	1.1 [0.5, 1.6]	1 [0.5, 1.6]	0.5 [0.1, 0.9]	2.2 [1.8, 2.7]	3.9	168	168	168
	30	0 [−0.3, 0.3]	0.6 [0.3, 0.9]	0.2 [0, 0.5]	0.3 [−0.1, 0.7]	2.5 [1.9, 3]	−3.5 [−5.8, −1.2]	−1 [−1.8, −0.2]	3.9	120	168	168
Hematocrit	4	−1 [−1.4, −0.6]	−0.7 [−1.1, −0.2]	−0.3 [−0.8, 0.1]	−0.1 [−0.6, 0.3]	3 [2.1, 3.9]	2.4 [1.7, 3.2]	0.9 [0.3, 1.4]	3.9	96	168	168
	RT	2.3 [1.9, 2.8]	4.4 [3.8, 5.1]	5.3 [4.5, 6.1]	6.1 [5.2, 7]	5.1 [4.1, 6.1]	4.3 [3.4, 5.2]	5.9 [4.8, 7]	3.9	24	168	168
	30	4 [3.5, 4.6]	5.4 [4.6, 6.3]	4.3 [3.5, 5]	3.1 [2.2, 3.9]	4.9 [4, 5.7]	−2.3 [−4.7, 0.1]	1.3 [0, 2.6]	3.9	<24	168	168
Hemoglobin	4	0 [−0.3, 0.4]	0.1 [−0.2, 0.4]	0 [−0.4, 0.4]	0.2 [−0.1, 0.5]	1 [0.5, 1.6]	0.7 [0.3, 1.1]	−3.5 [−8.9, 1.9]	3.8	144	<24	168
	RT	0.6 [0.3, 0.9]	0.5 [0, 0.9]	0.4 [−0.1, 0.8]	1.1 [0.7, 1.5]	0.5 [0.1, 0.9]	0.9 [0.4, 1.3]	1.5 [1.2, 1.9]	3.8	168	24	168
	30	0.4 [0.1, 0.7]	0.9 [0.6, 1.2]	0.7 [0.4, 1]	0.6 [0.3, 0.9]	1.5 [0.9, 2.1]	1.7 [1.3, 2]	0.9 [0.4, 1.3]	3.8	168	96	120
Leukocytes	4	−2.8 [−5, −0.6]	−2.9 [−7.7, 2]	−12.1 [−16.7, −7.6]	−18.7 [−24.3, −13]	−15.8 [−25.3, −6.4]	−45.6 [−55.9, −35.3]	−25.5 [−35.2, −15.8]	13.8	48	72	96
	RT	−1.7 [−2.9, −0.5]	−4.8 [−6.4, −3.2]	−8.4 [−11, −5.7]	−11.2 [−14.3, −8.2]	−18.3 [−24.2, −12.5]	−17.2 [−22.3, −12]	−12.8 [−17, −8.6]	13.8	72	96	120
	30	−4.9 [−6.3, −3.6]	−8.2 [−10.2, −6.2]	−14 [−16.6, −11.4]	−19.3 [−22.1, −16.6]	−18 [−21.4, −14.6]	−11.7 [−22.5, −0.9]	37.9 [NA, NA]	13.8	48	48	48
Lymphocytes	4	−13.9 [−23.9, −3.9]	0.3 [−21.3, 21.9]	53.1 [−82.7, 188.9]	56.6 [−87.6, 200.9]	−12.5 [−23.8, −1.3]	−13.9 [−20.1, −7.6]	335.1 [−287.6, 957.8]	15.2	<24	<24	24
	RT	0.5 [−2.9, 4]	5.4 [−1, 11.8]	0.5 [−9, 9.9]	−7 [−12.6, −1.3]	−8.1 [−14.1, −2]	−6.5 [−13.9, 1]	−4.9 [−13.7, 3.9]	15.2	168	<24	24
	30	1.4 [−3.6, 6.3]	14.9 [6.7, 23.2]	9.9 [−6, 25.7]	−13.6 [−27.9, 0.6]	−3.8 [−19.5, 11.9]	−3.2 [−20, 13.5]	−42.3 [NA, NA]	15.2	24	<24	48
MCH	4	0.3 [−0.1, 0.8]	0.9 [0.3, 1.5]	0.6 [0.2, 1]	1 [0.6, 1.3]	−0.9 [−1.5, −0.4]	−0.7 [−1.4, 0]	0.4 [0, 0.9]	1.8	168	<24	168
	RT	−0.1 [−0.5, 0.4]	0 [−0.5, 0.5]	−0.2 [−0.8, 0.4]	−0.1 [−0.6, 0.5]	−0.5 [−0.9, 0]	0.4 [−0.1, 1]	−0.8 [−1.3, −0.3]	1.8	168	24	168
	30	0.5 [0.1, 0.8]	0.4 [0, 0.9]	0.6 [0.2, 1]	0.5 [0, 0.9]	−1 [−1.6, −0.3]	7.5 [−0.8, 15.7]	2 [1, 2.9]	1.8	120	96	120
MCV	4	−0.7 [−0.9, −0.5]	−0.2 [−0.4, 0]	0.3 [0, 0.5]	0.6 [0.3, 0.8]	0.9 [0.5, 1.4]	1 [0.6, 1.5]	0.8 [0.4, 1.1]	1.6	168	168	168
	RT	1.7 [1.3, 2]	3.9 [3.3, 4.6]	4.8 [4.1, 5.6]	5 [4.2, 5.8]	4 [3.2, 4.8]	3.9 [2.9, 4.8]	3.5 [2.6, 4.4]	1.6	<24	168	168
	30	4 [3.5, 4.6]	4.8 [4.1, 5.5]	4 [3.3, 4.8]	2.7 [1.9, 3.5]	2.4 [1.8, 3]	1.2 [0.3, 2.1]	2.3 [1.3, 3.4]	1.6	<24	168	168
Neutrophils	4	−4.6 [−9.3, 0.1]	−8.7 [−14.3, −3.2]	−19.7 [−27.7, −11.6]	−26.6 [−34.7, −18.5]	4.9 [−27.1, 37]	−60.2 [−77.3, −43]	−40.5 [−56.2, −24.9]	18.4	48	<24	24
	RT	−1 [−2.6, 0.6]	−3.2 [−5.5, −0.9]	−6.3 [−8.6, −3.9]	−5.7 [−8.3, −3]	−13.7 [−21.6, −5.8]	−14.7 [−20.9, −8.6]	−14.7 [−19.7, −9.7]	18.4	96	<24	24
	30	−6.9 [−12.1, −1.7]	−12.3 [−21, −3.5]	−23.7 [−37.6, −9.9]	−18.7 [−31.2, −6.3]	−16.5 [−26.4, −6.6]	−5.3 [−24, 13.4]	88.1 [NA, NA]	18.4	24	<24	48
Reticulocytes	4	1 [−1.2, 3.2]	2 [0.1, 3.9]	3.3 [0.9, 5.8]	3.9 [1.6, 6.2]	4.8 [1.7, 7.9]	5.1 [2.5, 7.7]	7.2 [4.7, 9.7]	15.2	168	<24	168
	RT	−1.4 [−3.4, 0.5]	−4.7 [−6.5, −2.9]	0.6 [−2.7, 3.9]	10.1 [5.6, 14.7]	22.5 [13.2, 31.7]	37.1 [18.4, 55.8]	54.8 [38.2, 71.5]	15.2	96	24	168
	30	−5 [−7.4, −2.6]	14.5 [9.1, 19.8]	31.5 [17.3, 45.7]	84.7 [57.2, 112.2]	203.9 [151.4, 256.5]	193.9 [131.8, 256]	114.6 [80.4, 148.9]	15.2	24	168	168

TABLE 3 (Continued)

Parameter	Temp	Day 1 (24 h)	Day 2 (48 h)	Day 3 (72 h)	Day 4 (96 h)	Day 5 (120 h)	Day 6 (144 h)	Day 7 (168 h)	TEa (%)	Stable (h)	100% valid (h)	>90% valid (h)
Platelets	4	0.5 [−4.8, 5.8]	−0.9 [−5.5, 3.6]	0.3 [−8.3, 9]	−1.8 [−7.6, 4]	−7.7 [−13.3, −2.1]	−4.1 [−7.3, −0.9]	−1.7 [−9.3, 5.9]	11.3	96	72	96
	RT	−5.9 [−7.5, −4.4]	−6.5 [−8.1, −4.9]	−6.5 [−8.4, −4.7]	−6.5 [−8.2, −4.8]	−3.5 [−5.4, −1.7]	−3.7 [−5.6, −1.8]	−8.1 [−11.2, −5.1]	11.3	168	<24	120
	30	−9.2 [−12.1, −6.2]	−13.1 [−15.8, −10.4]	−14.3 [−17.5, −11]	−16.8 [−20.3, −13.3]	−12.7 [−15.7, −9.8]	−4.1 [−25.9, 17.7]	−50.5 [−55.3, −45.7]	11.3	<24	<24	48

Abbreviations: h, hours; MCH, mean corpuscular hemoglobin; MCV, mean corpuscular volume; RT, room temperature; TEa, total allowable error.

venous and capillary CBC from simultaneously collected samples and evaluated long-term stability of CBC parameters at different temperatures up to 7 days after sample collection.

Deming regression analyses demonstrated no significant proportional or systematic differences between venous and capillary measurements for erythrocytes, hematocrit, hemoglobin, leukocytes, lymphocytes, MCH, MCV, neutrophils, monocytes and RDW. A small proportional difference was observed with increasing platelet counts and MPV. Bias analysis indicated acceptable variation between capillary and venous measurements for the majority of CBC parameters when desirable TEa was selected as a decision threshold. Our results on comparability between venous and capillary measurements are in line with results of previous studies.[8,11,13,15,18]

To determine whether CBC parameters are potentially suitable for remote sampling and delayed analysis, we aimed to extend previous research and assess long-term CBC stability. Red cell indices, such as erythrocyte counts, hematocrit, hemoglobin, MCH, MCV, MPV, RDW, and platelet counts were generally most stable (up to 168 h) when stored at 4°C, in agreement with previous studies on stability up to 72 h.[10,16,19] Hematocrit, MCV, and RDW measurements gradually increased over time at room temperature (21–22°C) and 30°C. These results are consistent with previous studies, which also observed notable decreased stability of these parameters at higher temperatures.[10,16,20]

Mean relative difference for leukocyte counts was within desirable TEa up to 48 or 72 h when stored at 4°C or room temperature, respectively. Previous studies have concluded similar stability, albeit with different stability criteria.[10,14]

For differential leukocyte counts, a rapid increase of the number of invalid measurements over time was observed, especially beyond 72 h of storage at 4 and 30°C (Supplementary Table S3). Previous studies on differential leukocyte counts have reported acceptable stability between 48 and 72 h at 4°C or room temperature.[10,14,21–23] Differences between these reports and our results may be attributable to the number of samples with differential leukocyte counts outside the reference range in our study, which remained less stable over time compared to differential counts within the reference range (Supplementary Figure S5). Furthermore, selected stability criteria and instruments can also partly explain differences in conclusions between our and other studies.[10,14] In addition, stability of leukocyte and differential counts may have been affected by using the primary sample tube for all measurements over time, thus temporarily reheating samples stored at 4°C at each time point.

There are several limitations to this study. First of all, the majority of measurements were within respective reference ranges of the CBC parameters. Although comparability between venous and capillary measurements was similar between normal and abnormal values for the majority of parameters (Figure 1, Supplementary Figure S1, Supplementary Table S4), larger sample sizes of abnormal values and specific study populations are required to reach definitive conclusions. Depending on the situation and required precision, the best approach may be to also obtain a venous measurement at or below important clinical thresholds. Furthermore, measurements identified as invalid

were excluded from analyses, in accordance with clinical practice. This further limited the number of samples contributing to the results. In addition, low eosinophilic, basophilic, and immature granulocyte cell counts were observed in the majority of samples included in the comparability and stability experiments. Thus, conclusions regarding these parameters should be interpreted with caution. Even though the Abbott Alinity hq is one of the most recent automated hematology analyzers with good analytical performance and comparability with other analyzers,[22,23] we were only able to evaluate one type of analyzer. Finally, we used desirable TEa from the EFLM database to determine acceptable stability of CBC.[17] Although this criterion incorporates components of biological variation, one could argue that it would be better to select stability criteria based on clinical relevant outcomes. Since this approach would result in different stability criteria across diseases and patient populations, it was not feasible within this study. Future efforts will focus on increasing the sample size at each time point and further assess the effect of transport conditions on diagnostic laboratory measurements. In addition to laboratory validation, it is also important to examine the clinical feasibility of remote capillary sampling in different patient populations to determine which laboratory measurements are potentially suitable for remote or at-home blood sample collection.

In conclusion, overall comparability between capillary and venous CBC measurements was excellent, as demonstrated by Deming regression and bias analysis. The feasibility and clinical validity of delayed blood sample analysis depends on the clinical situation and required precision of the result. Although statistical significant changes of CBC measurements were observed within 24 h after sample collection, the majority of CBC parameters remained within desirable TEa up to 72 h at 4°C or room temperature (21–22°C). Clinical laboratory specialists and clinicians should be aware of possible differences in venous and capillary measurements, and increased probability of invalid measurements with delayed analysis or storage temperatures exceeding room temperature. Our research extends previous studies that investigated CBC stability up to 72 h and may aid with the interpretation of delayed and capillary CBC measurements.

AUTHOR CONTRIBUTIONS

All authors made substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work, contributed to drafting the work or revised it critically for important intellectual content, provided final approval of the version to be published, and agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

PATIENT CONSENT STATEMENT

All participants where additional samples were prospectively collected provided informed consent.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article. [Correction added on 18 May 2023, after first online publication: The supplementary Figures S3 and S4 were corrected in this version.]

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