Differences between capillary and venous blood counts in children—A data mining approach

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Abstract

Background: Capillary sampling of blood counts is a well-established alternative to venipuncture in paediatrics. However, the sampling method has to be considered when interpreting test results, as measurements differ. Ethical and practical considerations prevent simultaneous venous and capillary sample acquisition in comprehensive paediatric cohorts that span all ages for the purpose of a direct method comparison, resulting in uncertainty regarding the interpretation of capillary test results.

Methods: We applied a data mining method to calculate the differences between capillary and venous blood count analytes using laboratory data collected during patient care. We examined 486,401 blood counts performed between 2010 and 2017 in two German paediatric tertiary care centers in children from birth to 18 years analysed on SYSMEX XE-2100 and SYSMEX XE-5000 devices, and analysed the differences between capillary and venous test results in 15,218 paired samples performed within 24 h.

Results: We identified the mean systematic differences between capillary and venous (capillary–venous) test results for haemoglobin (+6.5 g/L), haematocrit (+2.38%), platelet count (–7.01 x 10^9/L), red cell count (+0.18 x 10^12/L), white cell count (–0.64 x 10^9/L), mean corpuscular cell volume (+2.07 fl), mean corpuscular haemoglobin (+0.33 pg), mean corpuscular haemoglobin concentration (–4.4 g/L) and red cell distribution width (+0.40%). The effect of age on these mean deltas is negligible, while the levels of test results influence the difference between capillary and venous test results in most analytes.

Conclusions: Our results improve guidance regarding the interpretation of capillary test results for children of all ages and in both physiological and pathological ranges.

KEYWORDS
capillary blood counts, data mining, paediatric haematology

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1 | INTRODUCTION

Basic hematologic tests are among the most commonly performed laboratory tests, with diagnostic and therapeutic implications for many diseases and traits during all periods of life. The blood samples necessary for analysis are most commonly obtained using venipuncture. However, in paediatric laboratory medicine, capillary blood sampling is well established as a complement or alternative to venous sampling for the analysis of haematological and biochemical analytes.

Capillary blood sampling is performed most often in paediatric patient groups where laboratory testing is performed frequently (e.g. paediatric haematology/oncology) or where difficult venous access would otherwise oppose sample acquisition (e.g. pre-term neonates and children with chronic diseases). Benefits of capillary sampling include a reduction of children's stress and pain, more rapid sample acquisition, and reduced need for operator training. However, when laboratory test results are used to guide clinical decisions, the reference limits and decision limits used as cut-offs are usually based on examinations of venous test results. Previous research consistently showed differences between capillary and venous samples in haematology analytes: Haemoglobin (HB), haematocrit (HCT), red cell count (RBC) and white cell count (WBC) are significantly higher when measured in capillary blood, while the platelet count (PLT) is reported to be lower (Table 1). Measurements in red cell indices (mean corpuscular haemoglobin, MCH, mean corpuscular haemoglobin concentration, MCHC, and mean corpuscular volume, MCV) also differ, however, the reported deltas between sampling techniques are inconsistent between studies. Different physiological mechanisms have been proposed to explain the differences between capillary and venous blood counts; leakage of plasma out of capillaries, arterioles, and venules results in a relative hemoconcentration in capillary blood, "enrichment" of larger cells (i.e. leukocytes and red cells) due to laminar flow in capillaries with "displacement" of platelets to the vessel wall, and release of active substances (e.g. thromboplastin) due to sampling-induced tissue injury with consecutive changes in cell activity and concentration. This demonstrates the importance of differentiating between capillary and venous peripheral blood to avoid misinterpretation of test results. While optimum guidance of clinical decisions would theoretically require separate decision limits for venous and capillary samples, this is not feasible in clinical practice. Instead, addition or subtraction terms (i.e. "deltas") for capillary test results are favoured, which would allow "conversion" of capillary test results to venous test results. However, the determination of these "delta values" is challenging: while blood count test results in the majority of individuals are within age-specific reference limits (which also need to be adjusted according to sampling method), clinical decision limits are most often especially important outside the range of physiological test results (e.g. when to perform red cell or platelet transfusions in haemat-oncological patients). Conversion deltas therefore need to be established both in the physiological and the pathological range. Specific to children, age-dependent differences in body composition require inclusion of patients from all paediatric age groups in such studies. While a variety of studies cover paediatric age groups, none covers children from birth to 18 years (Table 1). A major challenge when setting up these studies in children is the fact that both capillary and venous blood sampling are associated with pain, blood loss and physical injury, albeit minimal. Acquisition of an additional sample, that is not required for patient care (or acquisition of both a venous and a capillary sample in the case of healthy children) to determine "delta values" is therefore ethically challenging and has limited the number of samples analysed in previous studies.

To address these challenges, both large multicenter studies and data mining approaches have been proposed. While multicenter studies reduce hospital-dependent bias and result in a diverse patient group, the ethical challenges specified above remain. Conversely, data mining approaches use data obtained during patient care to gain clinically and scientifically relevant insights. This bypasses ethical obstacles to (repetitive) blood sampling in children, and the large amount of laboratory test results stored in hospital and laboratory information systems allows data-mining studies to access large datasets.

In this study, we examined capillary and venous blood counts from two large paediatric tertiary care centers to systematically calculate the deltas between venous and capillary sampling methods in children from birth to adulthood and in both physiological and pathological ranges.

2 | PATIENTS AND METHODS

2.1 | Patients

We analysed 295 918 blood samples (73 730 capillary blood counts and 222 188 venous blood counts) from 5794 children aged 0–18 years performed during clinical care in the Department of Paediatrics and Adolescent Medicine, University Hospital Erlangen, Germany between 2010 and 2017. Additionally, we analysed 190 483 samples (22 770 capillary blood counts and 167 713 venous blood counts) from the Department of Paediatrics and Adolescent Medicine, University Hospital Ulm, Germany. Venous and capillary samples from all patients (in- and outpatients) and all units (including specialty units caring for severely sick children, e.g. neonatal and paediatric intensive care units and haematology/oncology units) were analysed. Use of pseudonymized paediatric patient datasets obtained during patient care without patients' explicit consent is in accordance with the applicable German/Bavarian regulations and has been approved by the Ethical Review Boards of the University Hospital Erlangen, reference number 97_17 Bc.

2.2 | Blood sampling

Capillary blood sampling was performed by skin puncture at the fingertip or heel. Venous samples were collected using different forms of blood sampling (e.g. venipuncture, samples taken during placement of
| Study                  | Year | Patients | Age               | Path* | n  | ΔHB (g/L) | ΔRBC (10^{12}/L) | ΔMCV (fl) | ΔPLT (×10^9/L) | ΔWBC (×10^9/L) | ΔRDW (%) | ΔHCT (%) | ΔMCH (pg) | ΔMCHC (g/L) |
|-----------------------|------|----------|-------------------|-------|----|-----------|------------------|----------|----------------|----------------|----------|----------|-----------|-------------|
| Feusner et al. [3]    | 1979 | 29       | Young adults      | No    | 29 | -32.80    |                  |           |                |                |          |          |           |             |
| Peevy et al. [2]      | 1982 | 30       | 1 day             | No    | 30 |           | +16.0            |           |                |                |          |          |           |             |
|                       |      |          | 2 days            | No    | 30 | +8.0      |                  |           |                |                |          |          |           |             |
| Rivera et al. [1]     | 1982 | 29       | 4–6 weeks         | No    | 29 | +7.0–10.0 |                  |           |                |                |          |          | +2.1–3.7  |             |
|                       |      |          | 15                | No    | 15 | +4.0–6.0  |                  |           |                |                |          |          | +1.0–1.4  |             |
| Bellamy et al. [1]    | 1988 | 33       | 6 months–14 years | Yes   | 70 | +4.0      | +0.15            | -7.0     | +0.50          |                |          |          | +1.40     |             |
|                       |      |          | 10 Adults         | No    | 10 | +5.0      | +0.10            | -12.0    | +0.20          |                |          |          | +0.90     |             |
| Daae et al. [3]       | 1988 | 43       | 22–62 years       | No    | 40 | +3.2      | +0.10            | +0.57    | -22.00         | +0.58          |          |          | +1.20     | -0.05–2.4 |
| Lee et al. [1]        | 1989 | 50       | Adults            | No    | 50 | +2.9      | +0.09            | -5.40    | -10.85         | -1.08          |          |          | -3.38     | -0.11–17.9|
| Daae et al. [2]       | 1991 | 16       | 3 months–14 years | Yes   | 16 | +2.9      | +0.07            | -3.00    | +1.60          |                |          |          | +1.00     |             |
| Dreyer et al. [1]     | 1994 | 60       | Adults            | Yes   | 60 |          |                  |          |                |                |          |          |           |             |
|                       |      |          | 18 Adults         | No    | 18 |          |                  |          |                |                |          |          |           |             |
| Hinchcliffe et al. [1]| 1996 | 188      | 6 months–17 years | Yes   | 188| +3.5      |                  |          |                |                |          |          |           |             |
| Özbek et al. [2]      | 2000 | 95       | 1 day             | No    | 95 | +2.3      | +0.60            | -0.21    | -39.45         | +3.10          | -0.15    | +6.57     | +0.17     | +3.7        |
| Yang et al. [4]       | 2001 | 24       | 20–22 years       | No    | 72 | -1.0      | +0.01            | -2.00    | +0.60          |                |          |          | +0.40     |             |
| Neufeld et al. [5]    | 2002 | 72       | 6 months–15 years | Yes   | 72 | +6.0      |                  |          |                |                |          |          |           |             |
|                       |      |          | 72 Adults         | No    | 72 | +4.0      |                  |          |                |                |          |          |           |             |
| Kayiran et al. [3]    | 2003 | 141      | 7 days            | No    | 38 | +9.5      | +0.18            | -0.32    | -55.34         | +1.10          | -0.48    | +1.72     | +0.33     | -4.8        |
|                       |      |          | 14 days           | No    | 35 | +10.6     | +0.28            | -0.16    | -58.20         | +2.60          | -0.03    | +2.70     | +0.15     | +2.1        |
|                       |      |          | 21 days           | No    | 32 | +7.0      | +0.20            | -0.19    | -61.03         | +1.70          | -0.00    | +1.93     | +0.02     | +0.2        |
|                       |      |          | 28 days           | No    | 36 | +9.9      | +0.32            | -0.07    | -31.17         | +1.90          | -0.05    | +2.97     | 0.00      | -2.2        |
| Schalk et al. [3]     | 2007 | 428      | 18–82 years       | Both  | 463| +3.0      | +0.10            | +3.10    | -1.00          | +0.20          |          | +2.00     | +0.01     | -6.0        |
| Eslemi et al. [2]     | 2012 | 1600     | 1–28 days         | No    | 1600| +26.2     |                  |          |                |                |          |          |           |             |
| Herrera-Rojas et al. [10] | 2015 | 92       | 18–91 years       | Yes   | 92 | +2.0      | +0.10            | -0.70    | -4.90          | +0.60          | ±0.00    | ±0.50     | ±0.00     | ±3.0        |
| This report           | 2021 | 5794     | 1 day–18 years    | Both  | 486401| +6.5      | +0.18            | +2.07    | -7.01          | -0.64          | +0.40    | +2.38     | +0.33     | -4.4        |

*Inclusion of subjects with pathologies.

bNot all analytes were included in all blood counts.
2.3 Analytical procedures

We measured Haemoglobin (HB), Haematocrit (HCT), Platelet Count (PLT), Red Blood Cell Count (RBC), White Blood Cell Count (WBC), mean corpuscular volume (MCV), mean corpuscular haemoglobin (MCH), and mean corpuscular haemoglobin concentration (MCHC). Samples from Erlangen also included red cell distribution width (RDW) test results. Measurements in the University Hospital Erlangen were performed on SYSMEX XE-2100 devices, while samples in the University Hospital Ulm were measured using SYSMEX XE-5000. Both systems require the same minimal sample volume (200 μl closed mode, 130 μl open mode, 40 μl capillary mode),\(^{25,26}\) and the comparability of test results from both centers (and therefore implicitly analyzers) has been shown in a related publication of our group.\(^{27}\) Capillary samples were almost exclusively measured directly after sample acquisition (point-of-care testing), while venous samples were analysed promptly (mostly within 2 h), resulting in negligible bias due to procedural delay.\(^{28,29}\)

2.4 Identification of capillary/venous pairs

For each of the nine analytes we identified all pairs of venous and capillary test results from the same individual taken within 24 h. Each record therefore contained a venous test result, the corresponding capillary test result, the time difference between the two samples and the patient’s age and sex. Specifically, one venous measurement resulted in as many value pairs as capillary samples were taken within 24 h before and after the venous sample. For haemoglobin 15 216 capillary-venous records were extracted from the database of 96 498 capillary and 389 184 venous blood samples (Table 2). To investigate whether differences are due to methodological differences or medical interventions and pathophysiological processes between venous and capillary sampling timepoints, we additionally analysed shorter time ranges (samples taken within 8 and 16 h, with the larger timespan[s] also containing capillary-venous differences within the narrower timespan[s]).

2.5 Testing for significant differences between venous and capillary test results

To confirm that significant differences between venous and capillary test results exist (and therefore to confirm the need for this study) we performed the Wilcoxon-Rank-Sum-Test on all pairs of venous and capillary test results. This test was performed as the Kolmogorov-Smirnov-Test showed no normal distribution neither for venous and capillary samples nor for calculated delta values. The resulting p-values indicate significant differences between venous and capillary test results (p < 0.001) in all analytes. Additionally, we tested for significant differences between venous and capillary test results depending on the time delta between both samples (≤ 1 h, ≤ 2 h, …, to ≤ 24 h), the resulting p-values also indicate significant differences between venous and capillary test results (p < 0.001) in all analytes, except for WBC in blood samples taken within a time interval equal or

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**TABLE 2** Differences between capillary and venous test results and comparison to specifications for total error

| Maximum Δt | Center | Paired test results\(^a\) | HB (g/L) | RBC (×10^12/L) | MCV (fl) | PLT (×10^9/L) | WBC (×10^9/L) | RDW (%) | HCT (%) | MCH (pg) | MCHC (g/L) |
|------------|--------|-------------------------|---------|----------------|---------|-------------|-------------|---------|---------|----------|-------------|
| 8 h        | Erlangen | 3972 | +5.8 | +0.15 | +2.16 | −10.38 | −0.58 | +0.47 | +2.24 | +0.29 | −5.1 |
|            | Ulm     | 949  | +7.5 | +0.26 | +2.15 | −22.13 | +0.18 | N/A | −2.85 | −0.01 | −8.4 |
|            | Both    | 4921 | +6.1 | +0.17 | +2.16 | −12.68 | −0.44 | +0.47 | +2.36 | +0.24 | −5.8 |
| 16 h       | Erlangen | 6973 | +6.3 | +0.16 | +2.10 | −8.39 | −0.89 | +0.43 | +2.33 | +0.35 | −4.3 |
|            | Ulm     | 1369 | +6.5 | +0.22 | +2.05 | −17.94 | −0.07 | N/A | −2.56 | +0.00 | −8.0 |
|            | Both    | 8342 | +6.4 | +0.17 | +2.09 | −9.98 | −0.76 | +0.43 | +2.37 | +0.29 | −4.9 |
| 24 h       | Erlangen | 12 393 | +6.6 | +0.17 | +2.10 | −6.17 | −0.80 | +0.40 | +2.35 | +0.40 | −3.7 |
|            | Ulm     | 2823 | +6.3 | +0.22 | +1.90 | −10.63 | +0.06 | N/A | −2.50 | +0.01 | −7.3 |
|            | Both    | 15 216 | +6.5 | +0.18 | +2.07 | −7.01 | −0.64 | +0.40 | +2.38 | +0.33 | −4.4 |
| EFLM Specification for Total Error (Desirable), absolute\(^b\) | ±5.0 | ±0.18 | ±1.30 | ±27.6 | ±0.92 | ±0.33 | ±1.50 | ±0.36 | ±4.5 |

Relative (%): 3.8 3.9 1.6 9.7 13.8 2.6 3.9 1.3 1.3

Note: Positive values indicate higher test results in capillary samples. The highlighted row indicates the sample set selected for final analysis.

Abbreviations: HB, haemoglobin; HCT, haematocrit; MCH, mean corpuscular haemoglobin; MCHC, mean corpuscular haemoglobin concentration; MCV, mean corpuscular volume; PLT, platelet count; RBC, red blood cell count; RDW, red cell distribution width; WBC, white blood cell count.

\(^a\)Not all analytes were included in all blood counts, the number of paired capillary and venous haemoglobin test results is shown.

\(^b\)Calculated using an exemplary 10-year-old girl’s normal blood count, that is all values 50th percentile (HB 132 g/L, HCT 38.5%, PLT 285 × 10^9/L, RBC 4.72 × 10^12/L, WBC 6.7 × 10^9/L, MCV 81 fl, MCH 28 pg, MCHC 345 g/L, RDW 12.8%).
shorter than 6 h (p = 0.0042 to p = 0.50). To illustrate the clinical significance of capillary-venous differences in relation to an established comparator, we used the EFLM Specification for Total Error, which was calculated using an exemplary 10-year-old girl’s normal blood count, i.e. all values 50th percentile (HB 132 g/L, HCT 38.5%, PLT 285 × 10^9/L, RBC 4.72 × 10^{12}/L, WBC 6.7 × 10^9/L, MCV 81 fl, MCH 28 pg, MCHC 345 g/L, RDW 12.8%).

2.6 | Graphical and statistical evaluation

Due to small quantity of outliers in all capillary and venous samples, the capillary-venous delta for each analyte was calculated as mean value of the delta values calculated for every value pair. We examined the impact of three major influencing factors on these delta values between capillary and venous test results: the time interval between the acquisition of venous and capillary samples (and implicitly the order, i.e. whether the venous or capillary sample was taken first), the influence of the test result itself (by analysing the influence of the venous test results) and the impact of children’s ages. The effect of the time difference between venous and capillary samples was assessed using a linear model (time interval vs. mean capillary–venous delta) and its 95% confidence interval. To this end, we performed graphical and statistical evaluations using Python (https://www.python.org/) and R (https://www.r-project.org/).

3 | RESULTS

The differences between capillary and venous test results are shown in Table 2. Different maximum time intervals between venous and capillary measurements (±8, ±16, and ± 24 h) resulted in comparable (no clinically relevant differences) delta values between both measurement methods in both centers (except for platelet count and white cell count). We therefore used the 24-h-interval for further analyses, as this resulted in the largest dataset, minimizing bias and statistical uncertainty. Indicators of red cell count and red cell volume (haemoglobin, haematocrit, red cell count, MCV, and MCH) are higher in capillary than venous blood (6.5 g/L, 2.38%, 0.18 × 10^{12}/L, 2.07 fl, 0.33 pg), while white cell count, platelet count, and MCHC are lower (0.64 × 10^9/L, 7.01 × 10^9/L, 4.4 g/L). Platelet count differences are less pronounced with an increasing time interval between venous and capillary samples and the magnitude differ by center, while white cell count differences show no clear trends by center and time interval. When comparing the differences between capillary and venous test results to EFLM (European Federation of Clinical Chemistry and Laboratory Medicine) specifications for Total Error, only haemoglobin, haematocrit, MCV, and RDW exceed these.

The associations between venous test results and capillary test results are shown in Figure 1A and Figure S1A. Although the correlation between venous and capillary test results is strong, a substantial number of measurements differ with a clinically relevant extent between both methods. Importantly, the deviation from a hypothetical perfect correlation is asymmetrical, indicating a systematic shift due to methodological differences.

A detailed analysis of the time interval between capillary and venous measurements is shown in Figures 1B and 2, and in Figures S1A and S2. Although there is a significant effect of the time interval on capillary-venous delta values in haemoglobin, haematocrit, and platelet count, this effect is negligible in comparison to the extent of the capillary-venous delta. In comparison, the influence of the time interval between measurements is much more pronounced in red blood cells and white blood cells. For red cell indices (MCH, MCHC, MCV) and RDW there is no substantial effect of the time interval. The number of samples per time interval is highest at approximately 24 h, reflecting “daily” blood samples in clinical practice.

Figure 3 shows the effect of the absolute venous haemoglobin level on the capillary-venous delta, and Figure S3 shows this effect in other blood count analytes. In the clinically important haemoglobin

![Figure 1](https://www.python.org/)

Association between venous and capillary haemoglobin test results (A) and influence of the time interval between both samples (B)
range 70–110 g/L, the difference between capillary and venous haemoglobin test results is stable at the average reported difference (+6.5 g/L). The mean difference is less pronounced ($\Delta \text{HB} < +5 \text{ g/L}$) above this range (venous values $\geq 112 \text{ g/L}$ and $\leq 148 \text{ g/L}$), and more pronounced ($\Delta \text{HB} > +15 \text{ g/L}$) below (venous values $\leq 68 \text{ g/L}$), although a reduced sample count makes clear guidance below 70 g/L challenging. Capillary platelet test results are generally lower, but our analysis shows higher capillary measurements in very low platelet counts ($<50,000/\mu l$). Similarly, white cell counts are generally lower in capillary samples, with a more pronounced difference in higher white
cell counts. Differences between MCH, MCV, and RDW are relatively independent of the absolute value, while MCHC differences decline with increasing absolute value.

3.1 Influence of age

To analyse the effect of age on capillary-venous deltas, we examined differences separately for each year-based age group (Figure 4, Figure S4). This analysis shows relatively stable differences for all age groups, although notable differences in the first years of life exist. These differences are most pronounced in haemoglobin, haematocrit, red cell count, and white cell count in children aged 1–3 years, and in MCHC and MCV in the first year of life.

4 DISCUSSION

Capillary blood counts are an important part of diagnostic decision making in paediatric laboratory medicine. However, reference intervals and decision limits are established mainly on venous blood, resulting in uncertainty when capillary test results are used to guide clinical decisions, and previous studies allow only limited guidance (Table 1). We used blood counts performed during routine paediatric clinical care to determine the systematic differences between capillary and venous haematology test results (Table 2). This approach enabled the inclusion of children of all ages and analysis of a wide range of physiological and pathological test results, in contrast to the majority of published studies, which focus on specific age ranges in healthy children or children with certain diseases.

Our results show higher haemoglobin, haematocrit, and MCV values in capillary blood counts (+6.5 g/L, +2.38%, and +2 fl) than in venous samples, while the platelet count is lower in capillary samples (−7 × 10^9/L). For the remaining analytes, the differences between capillary and venous samples are so small that they should not affect clinical decision making in most cases. Comparison of the calculated differences to EFLM specifications for Desirable Total Error (Table 2) confirms this. Additionally, our findings for haemoglobin, haematocrit, and platelet count are in line with results from previous studies, while results for red cell indices except MCV, white cell count and RDW are inconsistent in-between previous studies and our report (Table 1). The latter finding therefore supports our conclusion that differences in sampling methods in red cell count, MCH, MCHC, white cell count and RDW should not affect clinical decisions.

A major strength of our study is that we analysed a large number of children of all ages (i.e. 5794 children between birth and 18 years) and included children with normal blood counts as well as children with severe pathologies (e.g. paediatric haematology and oncology patients). This is especially important as differences between sampling methods are of minor importance in healthy children (i.e. in children with test results mostly within reference intervals) in comparison to children with substantial disease. For example, capillary test results in hemato-oncological paediatric patients are often used as the basis for the indication for red cell or platelet transfusions, with established decision limits between 70 and 80 g/L or 10 000–50 000/μl, depending on the particular circumstances. In this regard, our results allow clear guidance (Figure 3 and Figure S3): differences between

**FIGURE 4** Association between venous and capillary haemoglobin test results for different age groups (top) and number of samples (bottom)
capillary and venous haemoglobin test results between 70 and 100 g/L (venous) are stable and not substantially different from the overall mean difference (±6.5 g/L). In contrast, there are substantial differences in capillary and venous platelet counts in children when the (venous) platelet count is below 100 000/µl (Figure S3), a venous sample should therefore be obtained if exact results are required (which depends on the clinical situation and might only seldom be the case).

When examining the effect of children’s ages on differences in test results, our study offers reassuring findings: for most analytes, the impact of age is negligible in comparison to the overall differences (Figure 4, Figure S4). While the effect of age is considerable for red cell count and white cell count, the capillary-venous delta in these analytes is negligible. For haemoglobin, probably the most important analyte in this context, a less pronounced difference between capillary and venous test results exists in the second and third year of life, while the tendency (capillary test results tend to be higher) is identical. From a practical point-of-view, we would therefore not handle capillary test results in children aged 1–2 differently.

This study’s major limitation is the fact that we analysed paired test results performed during clinical care of children within 24 h rather than simultaneous measurements performed in a well-defined study setting. Therefore, there is a high likelihood of interventions between the two samples, which include fluid replacement and transfusions, in addition to physiological and pathological changes due to biological variation and underlying diseases. Additionally, a relative overrepresentation of severely sick children and hematopoietic patients (especially those with blood counts close to transfusion thresholds) has to be suspected, as in these children more frequent blood sampling is indicated on clinical grounds. While this approach has major advantages (most importantly it avoids the ethical and practical dilemma of obtaining 15 000 paired paediatric capillary and venous blood samples) and allowed us to include children of all ages with a comprehensive range of test results (i.e. both normal and abnormal test results), assignment of differences between capillary and venous test results to the sampling method is challenging. To examine the effect of interventions and (patho-)physiological dynamics on the calculated deltas, we investigated the influence of the time interval (and implicitly the order) of venous and capillary samples (Table 2, Figures 1B, 2 and Figures S1B, S2). Our analyses show that the results for haemoglobin, haematocrit, platelet count, red cell indices (MCH, MCHC, and MCV) and RDW are not substantially influenced by the order or timing between both samples. In contrast, the delta between capillary and venous test results drastically changes in red cell count and white cell count. This suggests that the majority of calculated deltas (ΔHB, ΔHCT, ΔPLT, differences in red cell indices, and ΔRDW) are due to the sampling method, while ΔWBC and ΔRBC represent intrinsic and extrinsic changes rather than sampling method differences.10,19

In conclusion, we used a data mining approach to investigate the differences between capillary and venous blood counts in children of all ages both in physiological and pathological ranges. The dataset examined is therefore the largest of its kind, containing 15 218 paired samples from 5794 patients, and allows guidance on the interpretation of capillary test results for the complete paediatric age range and different ranges of test results.

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CONFLICT OF INTEREST
The authors declare have no conflict of interest.

AUTHOR CONTRIBUTIONS
Mathias Becker and Jakob Zierk designed the study, analysed the data, interpreted the results, and wrote the manuscript. Thomas Gscheidmeier, Hans-Jürgen Groß, Holger Cario, and Joachim Woelfle analysed the data and interpreted the results. Manfred Rauh, and Markus Metzler designed the study, analysed the data, and interpreted the results. All authors read and approved the final manuscript.

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

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Additional supporting information may be found in the online version of the article at the publisher’s website.

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