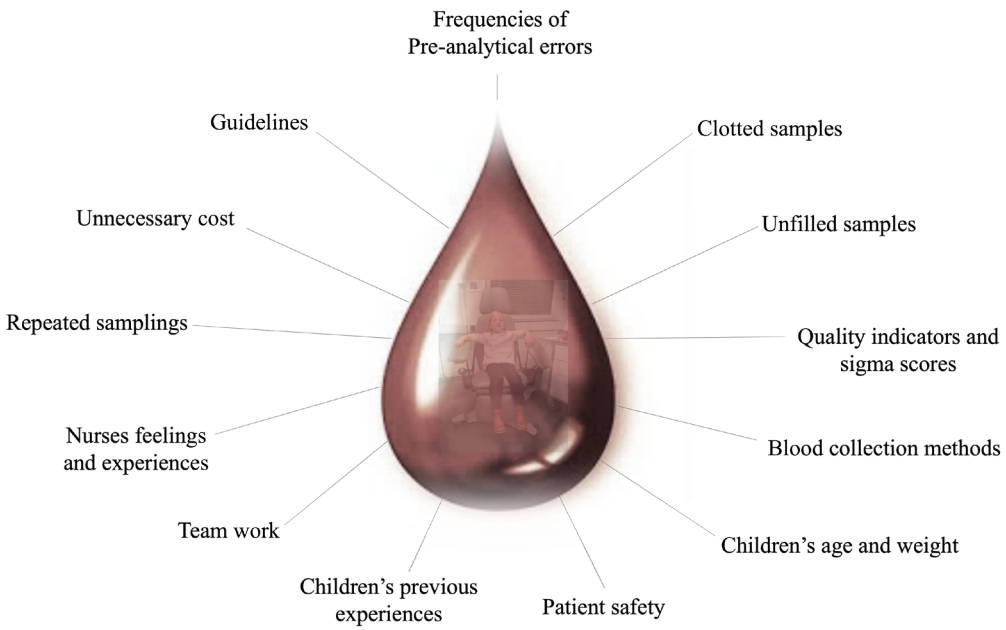
Thesis for doctoral degree (Ph.D.)
2022

Pre-analytical errors in blood sampling procedures in paediatric hospital care



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THESIS FOR DOCTORAL DEGREE (PhD)

By

Henrik Hjelmgren

The thesis will be defended in public at Karolinska University Hospital in Solna, the hall of Birger & Margareta Blombäck J3:11, February 4, 2022, at 13:00.

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To Betty and August, and for all those children and families who were affected by failed blood sampling in paediatric hospital care.

/ Henrik Hjelmgren

‘Every age has its turn, every branch of the tree has to learn.
Learn to grow, find its way, make the best of this short-lived stay’.

- José Gonzales

POPULAR SCIENCE SUMMARY OF THE THESIS

Blood sampling is one of the most common procedures conducted in any modern hospital. Blood tests are needed to correctly diagnose and treat patients. If the blood sampling procedure fails, it can lead to repeated sampling and increased costs for the healthcare organisation. These failures, called pre-analytical errors (PAE), often occur in the phase before the blood sample reaches the laboratory, referred to as the pre-analytical phase. Children often find blood sampling and other needle-related procedures to be stressful. Further, nurses may feel stress when they need to repeatedly execute blood samplings on children, which can be associated with difficulties in following blood sampling guidelines.

Thus, the overall research aim of this doctoral thesis was to investigate the frequency and consequences of PAE in paediatric hospital care.

The results show that from a total 1,148,716 blood analyses taken between 2013 and 2014 at Astrid Lindgren's Children's Hospital in Stockholm, Sweden, the PAE frequency was 5.4 percent. Coagulated samples represented 50 percent of all the observed PAE. Capillary blood sampling, which involves puncturing a finger or the side of the heel, was found to have double the risk of PAE compared to venous blood sampling, in which veins are punctured directly or blood is drawn from intravenous lines. The cost due to PAE was calculated at 84,000 euros annually. The highest expense was personnel cost, amounting to 55,000 euros annually, representing approximately 60 percent of the total incurred PAE costs.

Three focus group interviews with nurses working in paediatric hospital care were conducted and analysed. Paediatric blood sampling was identified as a major challenge for the nurses. The participants felt frustrated regarding when, why and how PAE would occur. The nurses stated that they wanted more education and knowledge about how to avoid PAE and not have to repeat failed blood sampling procedures.

This doctoral thesis addresses the frequency of PAE, which amounted to 5.4 percent over two years. It found that clotted blood samples were by far the most frequent type of PAE in paediatric hospital care. Further, capillary blood sampling was presented double the risk of PAE compared to venous blood sampling. The annual hospital costs due to PAE were also substantial, and the interviews with nurses revealed that they need both theoretical and practical training on how to avoid PAE when conducting capillary and venous sampling. Future studies should focus on interventions targeted at decreasing the frequency of PAE in paediatric hospital care.

Svensk populärvetenskaplig sammanfattning

Blodprovstagning är en av de vanligaste procedurerna på alla moderna sjukhus. Blodprovsanalyserna är en viktig del för att ställa rätt diagnos och behandling. Om blodprovstagningen misslyckas kan det leda till upprepade provtagningar och ökade kostnader för hälso- och sjukvården. Dessa misslyckanden, som kallas preanalytiska fel, inträffar i fasen innan blodprovet når laboratoriet, den så kallade preanalytiska fasen. Vidare upplever barn ofta att blodprovstagning är stressande. Även sjuksköterskor kan uppleva stress när de behöver utföra blodprovstagning på barn, vilket kan göra att de får svårigheter att följa riktlinjer för blodprovstagning som omfattar hur man förebygger felprover.

Det övergripande syftet med denna doktorsavhandling var att undersöka frekvensen och konsekvenserna av preanalytiska fel.

Frekvensen av preanalytiska fel var i genomsnitt 5,4 procent av totalt 1,148,716 blodanalyser på Astrid Lindgrens Barnsjukhus under åren 2013 och 2014. Koagulerade prover representerade 50 procent av alla observerade preanalytiska fel. Kapillär blodprovstagning, som involverar stick i ett finger eller vid sidan av hälen, visade sig vara dubbelt så stor risk för preanalytiska fel jämfört med venös blodprovstagning, där

venpunktion utförs direkt eller dras från befintliga intravenösa infarter. Kostnaden för preanalytiska fel beräknades till ca 84,000 euro årligen. Den högsta kostnaden var personalkostnader som uppgick till 55,000 euro. Detta representerade cirka 60 procent av alla kostnader uppkomna på grund av preanalytiska fel.

Intervjuer med sjuksköterskor som arbetar inom barnsjukvården visade att dom upplevde att blodprovstagning var en stor utmaning. Deltagarna kände frustration över när, varför och hur preanalytiska fel kunde uppstå. Sjuksköterskorna uppgav att de ville ha mer utbildning och kunskap om hur man undviker preanalytiska fel för att slippa behöva upprepa blodprovsprocedurer som misslyckas.

Denna avhandling visade att frekvensen av preanalytiska fel uppgift till 5.4 procent under två år och att koagulerade blodprover var det vanligaste preanalytiska felet inom barnsjukvården. Kapillär blodprovstagning visade sig innebära dubbelt så stor risk för preanalytiska fel jämfört med venös blodprovstagning. De årliga sjukhuskostnaderna för preanalytiska fel var av betydande andel av de totala kostnaderna för blodprovstagning. Intervjuer med sjuksköterskor visade att sjuksköterskor behöver både teoretisk och praktisk utbildning i hur man undviker preanalytiska fel vid kapillär- och venös provtagning. Framtida studier bör inriktas på åtgärder som syftar till att minska frekvensen av preanalytiska fel inom barnsjukvården.

ABSTRACT

Introduction

Blood tests are important for diagnosing and treating children who are hospitalised with illnesses. The blood test process follows the specific phases of pre-analysis, analysis and post-analysis. Most blood test errors occur in the pre-analytical phase. Such pre-analytical errors (PAE) can affect children's safety due to delayed clinical decision-making support or discomfort related to repeated blood sampling.

Aim

The overall research aim of this doctoral thesis was to investigate the frequency and consequences of PAE in paediatric hospital care. In specific, the following research questions were set out to be answered:

- How frequent is PAE?
- Which type of blood sampling methods, capillary or venous, is most affected by PAE?
- What are the annual costs associated with blood tests affected by PAE?
- What are nurses' experiences with blood sampling procedures and related PAE?

Methods

Information about how frequently PAE occurs was retrieved from the laboratory information system FlexLab™, which contained data from blood analyses ordered from Astrid Lindgren Children's Hospital from 2013 to 2014. Information on the type of blood sampling method and associated PAE factors was retrieved from a blood sampling survey and the medical record Take Care™. The costs associated with blood tests affected by PAE

were calculated using hospital information from combined data sources and supply systems (Flexlab™, Tableau software© and Medicarrier AB). Clinical observations were also used to estimate the time healthcare personnel spend on the blood sampling process. A qualitative approach was used to explore the participating nurses' views and experiences with PAE and with the blood sampling process.

Results

The frequency of PAE was 61,656 (5.4%) of 1,148,716 blood analyses sent to the laboratory from Astrid Lindgren Children's Hospital (2013-2014). Clotting represented 31,605 (51.3%) of all PAE. Based on 951 blood samples from two paediatric inward departments, the capillary sampling method had a significantly higher risk of PAE than venous blood sampling, at 72 (20%) of 354 vs 56 (9.4%) of 597, p = 0.001, adj-OR 2.88 (CI 1.79-4.64). The annual cost of PAE was estimated at approximately 84,000 euros. The highest expense was personnel cost (65%), which amounted to 55,000 euros annually. Focus group interviews demonstrated that blood sampling was a challenge for nurses, revealing that they need more information about how to reduce PAE.

Conclusion

The results of this thesis demonstrate that the high frequency of PAE is primarily related to clotting. Capillary blood sampling carries a higher risk of PAE than venous blood sampling. The consequences of PAE include substantial annual costs to paediatric hospital care. Nurses need both theoretical and practical training on how to avoid PAE when conducting capillary and venous sampling.

LIST OF SCIENTIFIC PAPERS

This thesis is based on the following four scientific papers, which are referred to in the text with roman numerals.

I. **Hjelmgren H**, Nilsson A, Andersson, N, Ritzmo C, Ygge B-M, Nordlund B. Retrospective study showed that blood sampling errors risked children's wellbeing and safety in a Swedish paediatric tertiary care. Acta Paediatr. 2019 Mar;108(3):522-528.

II. **Hjelmgren H**, Nilsson A, Myrberg I-H, Andersson N, Ygge B-M, Nordlund B. Capillary blood sampling increases the risk of preanalytical errors in pediatric hospital care: Observational clinical study. J Spec Pediatr Nurs. 2021 May 7:e12337.

III. **Hjelmgren H**, Heintz E, Ygge B-M , Andersson N, Nordlund B. *Cost analysis of failed blood samples in paediatric hospital care* [manuscript in preparation].

IV. **Hjelmgren H**, Ygge B-M, Nordlund B, Andersson N. Nurses' experiences of blood sample collection from children: A qualitative study from Swedish paediatric hospital care. BMC Nursing. 2021. Under review.

CONTENTS

LIST OF ABBREVIATIONS

ALCH	Astrid Lindgren Children Hospital
CI	Confidence interval
CLSI	Clinical and Laboratory Standards Institute
CVL	Central venous lines
DPM	Defects per million
EDTA	Ethylenediaminetetraacetic acid
EFLM	European Federation of Clinical Chemistry and Laboratory Medicine
ESR	Erythrocyte sedimentation rate
OR	Odds ratio
PAE	Pre-analytical error
PIC	Peripheral intravenous catheter
QI	Quality indicators
TA	Thematic analysis
WHO	World Health Organization

1 INTRODUCTION

In paediatric hospital care, there are a wide range of procedures for diagnosing and treating hospitalised children. Blood sampling is one of the most common procedures (1). Laboratory blood tests provide clinicians with important information needed to make correct clinical decisions concerning prevention, treatment, diagnosis and disease management (2, 3); as such, these blood tests demonstrate the vital importance of having reliable test results. Errors occur in all fields of medicine and can lead to potential risks for patients (4). In laboratory medicine, error rates are low compared to other medicine fields. High volumes of tests, however, mean that even low rates can have a significant impact on patient safety (5). The general frequency of blood sampling errors in paediatric hospital care is largely unknown, as are the underlying reasons for the problem. These blood sampling errors often lead to delayed test results and repeated blood sampling, which can be stressful for hospitalised children.

1.1 Pre-analytical errors

Blood sampling errors in laboratory medicine can occur in the pre-, intra- and post-analytical phases. Most testing errors occur in the pre-analytical phase, accounting for approximately 70 percent of all errors in laboratory medicine (**Figure 1**) (6, 7).

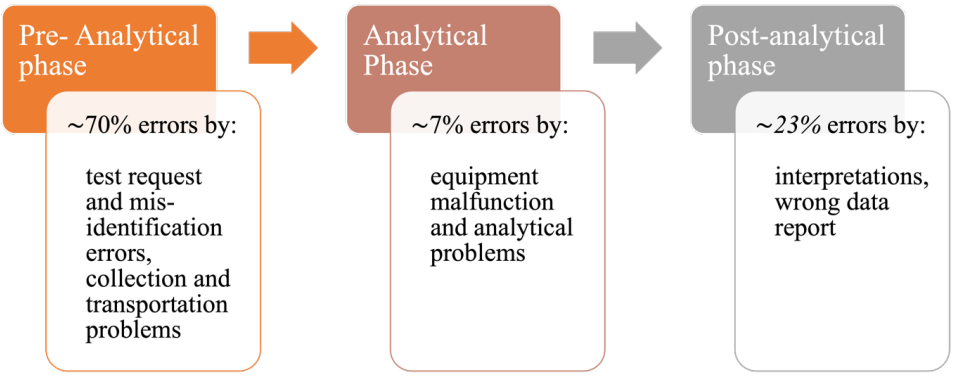


Figure 1. Total analytical process and reported rate errors (Plebani, 2006; Lippi et al., 2011).

The pre-analytical phase begins with the prescription of a blood sample test. Next comes identification of the patient and the specimen, followed by blood sample collection. The phase ends when the blood specimen arrives at the laboratory (**Figure 2**) (8).

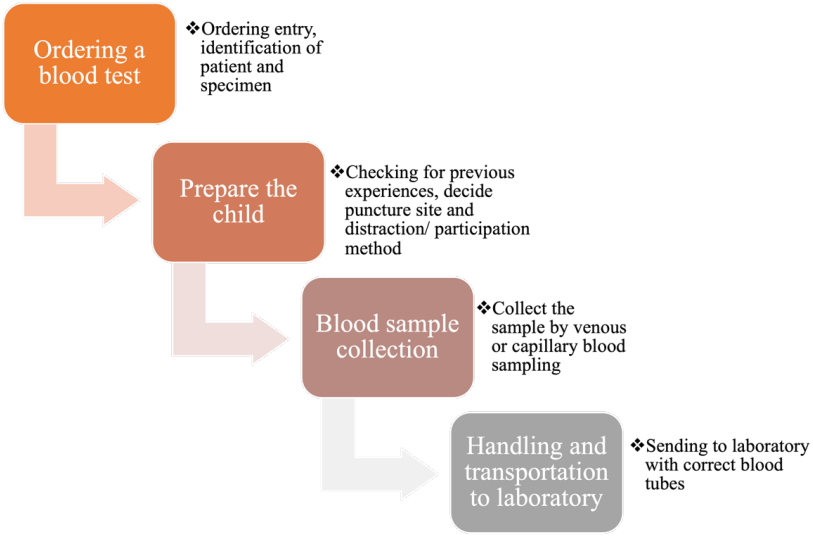


Figure 2. Different actions in the pre-analytical phase.

When this procedure fails because of pre-analytical errors (PAE), the blood sampling is bound to be repeated (9). This is time consuming for healthcare workers and potentially harmful to the patient (10). When PAE occur, they can lead to inappropriate treatment or even misdiagnosis or delayed care (6, 8, 11). PAE cause blood samples to be rejected by the laboratory due to such errors as haemolysis, clotting, unfilled or wrong tubes, missing samples or other handling problems (6). Several clinical laboratory studies from recent decades report on PAE frequency between 8-14 percent, which demonstrates a growing interest in this research field (11-13).

Laboratories that use monitoring systems in the pre-analytical stage can influence the prevention of errors (14). A promising strategy for improving the pre-analytical phase has been to use the quality instrument six sigma metric (15). This instrument is a basic measurement that identifies defects in a process (16). The six sigma metric system of measurement ranges from zero to six. The minimum level of acceptable quality in a process is three, which equates to 66,807 defects per million. The highest quality level, a performance of six, has only 3.4 defects per million or a 99.99 percent success rate (17). Other advances in technology and quality control systems have led lower laboratory error rates in recent decades (18).

The frequency of PAE and sample rejection rates in paediatric clinics are not yet fully understood compared to PAE in adult departments. In a study from Italy, which examined PAE frequency in coagulation tests the paediatric patients had much higher rates of PAE than adult patients (10.1% vs 5.4%), suggesting that the blood sampling process is more affected by PAE in paediatric clinics (13).

1.2 Blood sampling collection methods

Different methods exist for blood sampling. Blood can be drawn via venous, capillary or

arterially sampling, as well as intraosseous collection. In paediatric departments, the most common procedures are capillary and venous blood sampling (**Figure 3**).

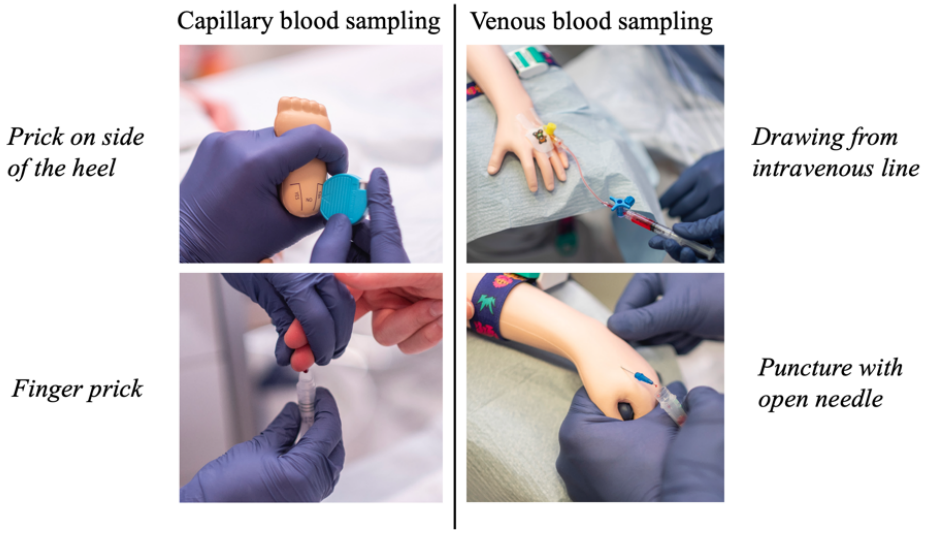


Figure 3. Common blood sampling methods in paediatric hospital care.

Capillary blood sampling (CBS) is a procedure that involves making a small puncture in the finger, heel, toe or earlobe. CBS is preferable when a small amount of blood or a quick result are needed (19). CBS is also considered less invasive and easy for health professionals to learn (20). CBS is common in neonatal units, but it can be problematic and cause distress for the child. Further, the samples can result in clotted or haemolysed specimens (21). One way to mediate these risks is to warm the hand before performing the finger puncture to increase blood flow and reduce the number of punctures required (22).

Venous blood sampling (VBS) can be executed through venepuncture in almost any visible vein, but most sampling occurs in the bend of the arm, back of the hand, foot or the scalp in small neonates. Blood can also be drawn from existing venous lines using a peripheral intravenous catheter (PIC), which makes the blood sampling procedure easier and does not require further needle insertions, thereby minimising pain (23, 24). Obtaining VBS through

central venous lines (CVL) requires special attention to hygiene and materials (25). Errors occurring from sampling via the CVL often relate to contamination or not having discarded enough blood (26). The poor mixture of tubes can be another error during the blood sampling procedure (27).

The existing literature does not contain much information on the associated factors of PAE in paediatric hospital care. One conference paper showed an increased risk of haemolysed frequency in VBS compared to CBS in the paediatric population (28). Another possible paediatric factor is the child's age. Small veins, small samples and infant blood characteristics can all increase the risk of haemolysis (29). The previously mentioned conference paper found PAE to be more frequent in patients under two years old than in older children (28). Several blood sampling techniques are widely used in paediatric clinics, yet few guidelines or recommendations exist on when, why and how to choose one method over another to avoid PAE in the hospitalised child. Thus, studies are needed to elucidate best practices for blood sampling to reduce the number of PAE in paediatric patients.

1.3 Health economic impact of PAE

To help decision-makers prioritise and improve healthcare, it is important to compare and measure economic burdens related to health issues (30). For hospital organisations, laboratory costs represents approximately five percent of the total budget (31). Diagnostics are ever important because they influence many medical decisions (3). Repetitive and excessive blood sampling due to PAE can lead to increased costs but also anaemia and potential trauma for the patient (31, 32). Previous studies of healthcare costs due to PAE report various cost issues (31, 33-35). Recollection costs and patient treatments where the most costly expenses (31) and material cost (34) as well as personnel and analytical cost (33). Understanding which costs associate with PAE in paediatric care is important to be able to allocate more resources for conducting targeted interventions reducing PAE.

1.4 Blood sampling, nurses' knowledge and children's experiences

Tertiary paediatric hospital care covers several diagnoses and conditions, from advanced surgery to all specialities within medicine. At Swedish hospitals, inward blood sampling is mainly performed by nurses and nurse assistants. Previous research has shown that nurses generally lack knowledge about PAE and their causes, as well as the impact these errors have on laboratory test results (36). An interview study on nurses' experiences with adult phlebotomy showed that an educational intervention program may improve knowledge on VBS and therefore increase patient safety (37).

In children's hospitals, the paediatric nurse needs to have a special interaction with the child and their parents to be able to reduce suffering during stressful procedures like blood sampling (38). Paediatric patients often have difficulties complying with blood sampling collection because of the pain and stress involved (39, 40). Their own perspective on illness is important to understand because it concerns the child's integrity and the quality of healthcare that can be provided in a hospital context (41, 42). Further, blood sample collection is a more complicated procedure for children than for adults, requiring extra attention from hospital staff so that good patient care and good quality blood sampling can be achieved (9, 39). The blood sampling procedure is also a painful procedure and needs to be treated with both pharmacology and behavioural means to avoid negative long- and short-term effects (43, 44). Simple means such as skin-to-skin contact, oral glucose administration, swaddling, and warming can be effective for pain relief in small children (45-47), as well as topical local anaesthetics and soap bubbles during VBS (48).

This emphasises that healthcare providers in paediatric hospitals require skill and competence concerning blood sampling procedures to be able to avoid PAE and the unnecessary pain and stress that come with repeated samplings. Nurses' experiences with PAE and the blood sampling process in a paediatric hospital setting was largely unknown

when this doctoral project was designed. Exploring such experiences could yield insights to help design and tailor specific interventions to reduce PAE.

2 AIMS

The overall research aim of this doctoral thesis is to investigate the frequency and consequences of blood tests affected by PAE in paediatric hospital care.

The research questions of this thesis are as follows:

1 What is the frequency of PAE in blood analyses in paediatric hospital care, and what are the corresponding measured quality indicators? (**Paper I)**

2 What type of blood sampling methods, capillary or venous, are most affected by PAE, and what factors are associated with PAE? (**Paper II**)

3 What are the average cost, both annually and by 10,000 blood sampling associated with blood tests affected by PAE in paediatric hospital care? (**Paper III**)

4 What are nurses' experiences with blood sampling procedures and related PAE? (**Paper IV**)

3 MATERIALS AND METHODS

3.1 Study designs and data sources

The different data sources and study designs used in this thesis are shown in **Figure 4**.

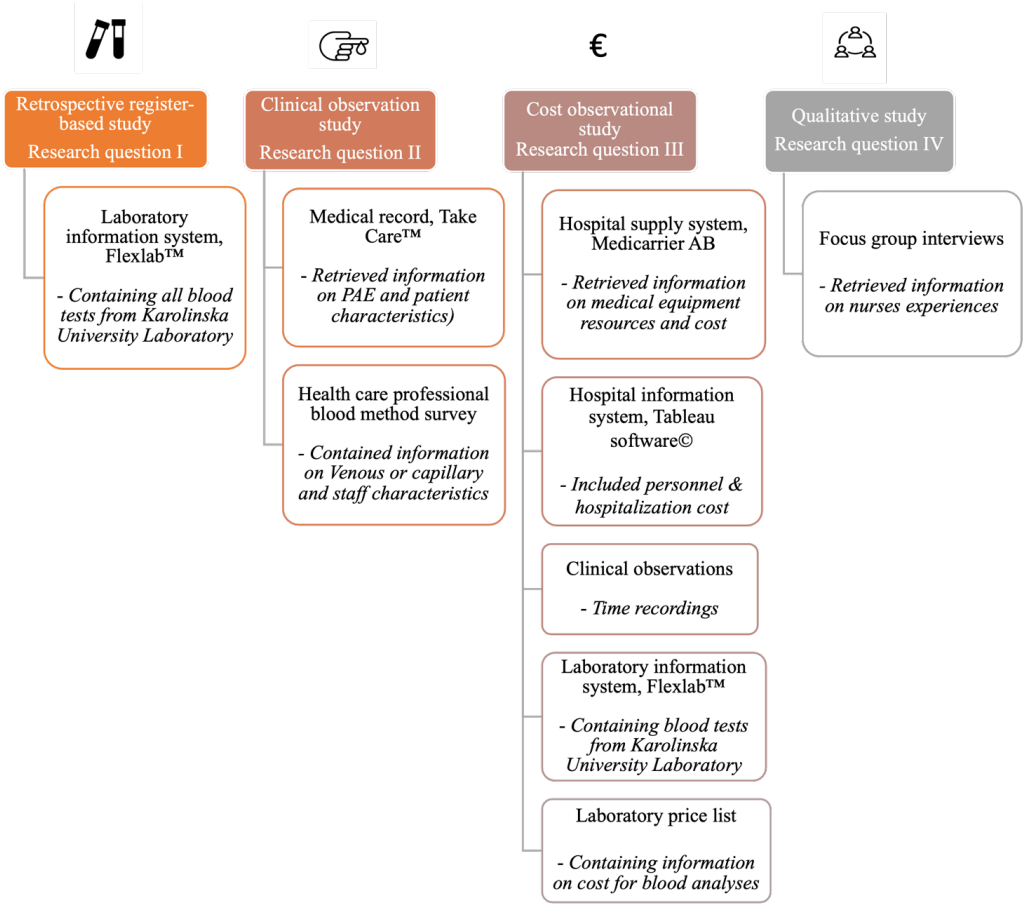


Figure 4. Data sources and study design used in this thesis.

Information about the frequency of PAE was retrieved from the Karolinska University Hospital laboratory information system, FlexLab™ between 2013 and 2014. The data was used retrospectively in a register-based study to answer research question 1. The data

contained information about blood analyses sent to the hospital laboratory's section of haematology, coagulation and chemistry. The samples were from children hospitalised at Astrid Lindgren Children's Hospital (ALCH) including the emergency department, medicine and surgical wards, as well as homebased care and neonatal care.

A clinical observation study was performed on two inward departments to answer research question 2. Data on the type of blood sampling used and associated factors of PAE were retrieved from a blood sampling survey and the Take Care™ system of medical records.

A pragmatic bottom-up approach cost analysis study analysed the direct costs of blood samples affected by PAE to answer research question 3. The costs associated with blood tests affected by PAE were gathered from combined data sources, which consisted of hospital information from Tableau software©, FlexLab™, laboratory price list, and Medicarrier AB and clinical observations. These data sources contained information on healthcare personnel salaries, material costs, laboratory chargeable price, hospitalisation costs and the time health personnel spend in different phases of the blood sampling process. The hospital laboratory information system, FlexLab™, was used to gather information on PAE outcomes.

A qualitative study explored the nurses' views and experiences of PAE and the blood sampling process. Interview data were collected from nurses in three focus groups to address research question 4.

3.2 Participants and settings

The research in this thesis was mainly carried out at the ALCH, which is a tertiary university hospital serving a local population of approximately 220,000 children and adolescents from birth to 18 years of age living in the Region of Stockholm, Sweden. ALCH also provides national and specialist care in some areas of surgery and medicine.

Concerning PAE among VBS and CBS methods, the study population consisted of all child patients whose blood sampling information was complete, according to the healthcare professionals blood method survey. The patients were hospitalised at one of two paediatric emergency wards at ALCH between January 27, 2014 and October 1, 2016. A total of 645 unique patients were included, with 951 blood samplings occasions (Research question 2).

During the study period, 9,500 unique children were treated in the wards (Hospital information system, Tableau software©). The wards treated children aged 0 to 18 years within general paediatric medicine for approximately two to three days, mostly for infectious diseases.

The qualitative research included 19 participants (nurses), both experienced and inexperienced. The nurses worked in ALCH and Sachsska Children's Hospital, both tertiary hospitals in the Stockholm Region (**Table 1**). Sachsska Children's Hospital has two medical wards and an emergency ward, as well as outpatient clinics (Research question 4).

Table 1. Demographics of nurse participants in the focus group interviews

Interviews	Participants (n)	Age (mean)	Workplace	Nursing degree	Length of work experience (mean)
Focus Group 1	9	26	4 wards (ALCH)	RN	10.6 months
Focus Group 2	6	33	2 wards (ALCH)	MSN	6.7 years
Focus Group 3	4	28	2 wards (SCH)	RN	7 months

ALCH = Astrid Lindgren Children's Hospital, SCH = Sachsska Children's Hospital

RN = Registered Nurses, MSN = Master Degree Nurses

3.3 Data collection and definitions

3.3.1 PAE

Information about the frequency of PAE was retrieved from the laboratory information system (Flexlab™) and medical record (Take Care) at Karolinska University Hospital, Astrid Lindgren Children's Hospital. PAE were harmonised under the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC-LM) model with quality indicators (QI), explained and defined in **Table 2**, to enable comparisons with previous studies (15). Blood analyses that ended in PAE were calculated as one PAE, so one blood sampling collection could include several PAE for the analysis of research question 1.

Table 2. List of Pre-analytical errors (PAE) harmonised in Quality Indicators (QI) after IFCC-LM* model

Types of PAE at Karolinska University Hospital	**Explanation**	**Quality Indicator**
- Unmarked sample - Wrong patient	Misidentified samples Misidentified patients Unlabelled samples	Misidentification error
- Wrong analyses - Not calculated**	Requests with erroneous data entry (test name, missed test, added test)	Test transcription errors
- Unfilled sample - Wrong collection method	Inappropriate sample-anticoagulant volume ratio with insufficient sample volume	Incorrect fill level
- Wrong tubes - Not executed	Wrong container Inappropriate sample type	Incorrect sample type
- Haemolysed errors	Rupturing of red blood cells	Analyse haemolysed
- Clotted errors	Blood coagulated	Clotted analyse
- Wrecked sample - Old sample - Sample missing	Damage during transportation Under inappropriate temperature condition and/or time Lost-not received Not properly stored	Unsuitable sample for transportation and storage

* The International Federation of Clinical Chemistry and Laboratory Medicine

** Request of additional analysis not possible

3.3.2 Six sigma and quality performance

The quality performance of blood sampling at ALCH was assessed using the six sigma method. The outcome of quality performance in the pre-analytical phase, related to PAE, was defined by defects per million (DPM) (16). The DPM rate was converted to a six sigma score based on standard tables available online (49). The six sigma score quality control enabled generic comparisons between the pre-analytical blood sampling process and the quality performance of other processes, based on the existing literature (11, 50, 51).

3.3.3 Survey of PAE associated blood sampling methods and factors

Data regarding blood sampling methods were retrieved from a survey (Appendix 1), which nurses and nurse assistants anonymously filled in after each blood sample was collected during the years 2014 to 2016. The survey contained data about sampling methods, the staff's professional academic level, puncture location, needle size and number of punctures, as such information could not be collected from the hospital laboratory information system (Research question 2).

The patient information from each survey was used to collect data about each child's age, gender, weight, diagnosis, symptoms, PAE and number of tubes in the electronic medical record. Comparisons of CBS and VBS included several blood analyses. When evaluating the rate of PAE across different methods of blood sampling, a sample was recorded as a PAE if one blood analysis in the collection ended in error. This meant that one blood sample could include several PAEs but was still calculated as one PAE (Research question 2).

VBS was defined as a blood sample obtained from a vein via the blood collection system Vacutainer® Becton Dickson (BD), butterfly collection set (BD), open needle (BD or Sarstedt) or a direct draw from a PIC or CVL. CBS was defined as a blood sample obtained

from a finger, BD Microtainer®, contact-activated lancet or heel (BD Quickheel™). BD Microtainer® sample tubes were used to collect CBS samples (Research question 2).

3.3.4 Defining costs

Cost estimations were defined by the average costs of blood sample collections and PAE, both annually and per 10,000 blood samples (Research question 3). Per the present analysis, PAE lead to the need for recollected samples and affect the cost of the total testing process, which consists of three phases: pre-analytical, analytical and post-analytical (**Figure 5**). Clinical observations were made during May 2021 to estimate personnel and material resource uses and costs.

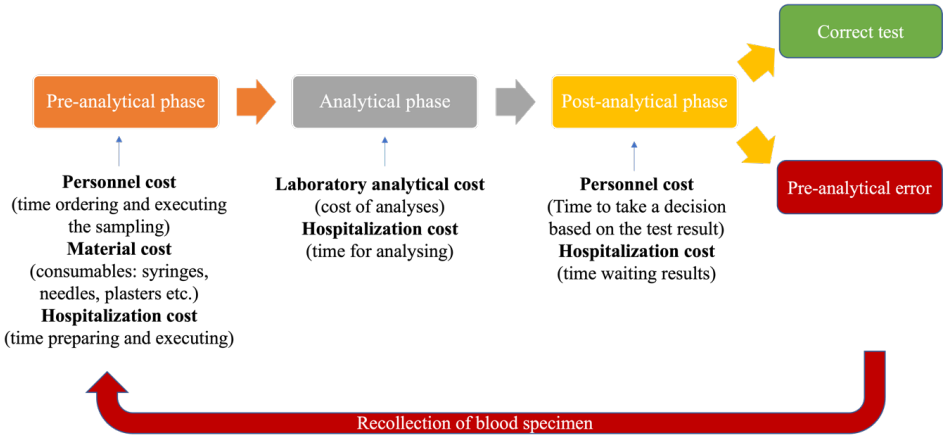


Figure 5: Outline of the costs of resources related to blood specimen collection.

3.3.4.1 Personnel costs

Personnel costs were defined as the time healthcare personnel (medical doctors, nurses and nurse assistants) spend on blood sample collection. The allocated time for each procedure

was documented and observed in relation to each healthcare profession and multiplied by the average hourly salary. Data on average salary per hour for doctors, nurses and nurse assistants were gathered from the hospital's economic information system, Tableau software©.

3.3.4.2 Material costs

Material costs were defined as the materials used during blood sampling and the average cost of the consumables related to VBS and CBS. Unit costs for consumables were collected from the hospital supply system and price lists for the year 2020, per Medicarrier AB in Stockholm, Sweden (Appendix 2).

3.3.4.3 Laboratory costs

Laboratory costs were defined as the average laboratory costs for the most common blood sample analyses in the biochemistry laboratory at Karolinska University Hospital, Sweden. The laboratory costs were collected from the hospital laboratory price list for 2019 (Appendix 3). The average analytical cost of blood samples was estimated by dividing the total cost of all blood analyses by the total number of blood analyses.

3.3.4.4 Hospitalisation costs

Hospitalisation costs were defined as the hospitalisation time that covered the whole blood sampling procedure, from preparation of the sample to the receipt of laboratory test results by clinicians (**Figure 5**). Costs for hospitalisation during blood sampling were based on the hospitalisation cost of 112.7 euros per patient per day (including facilitating costs with a two percent overhead) in general and neonatal wards. These costs were analysed using the hospital's economic information system, Tableau software©.

3.3.5 Data collection of participants (nurses) for focus group interviews

A purposeful sampling was used to find participants who could ensure rich informative data and in-depth information about the studied phenomena (52). The participants were approached by email or face-to-face. A letter containing the background and aim of the study was sent to the responsible healthcare administrators to get approval for further contact. An interview guide was made, and the interviews started with open-ended questions and followed by probing questions to elicit more elaborative answers (52). The interviews lasted between 39 and 58 minutes and were audio recorded. The interviews were carried out between September and December 2019 and conducted in comfortably spaced conference rooms close to the clinic to create a relaxed environment (Research question 4).

3.4 Data analyses

3.4.1 Frequency of PAE

The main statistical analyses regarding PAE frequency were presented using descriptive statistics with Stata/14MP (StataCorp LLC, Texas, USA). The data were calculated as numbers and percentages with a 95 percent confidence interval (95% CI). The differences in PAE across the various years, specialities, laboratory sections and work shifts were analysed using chi-square tests and p values of < 0.05, which rejected the null hypothesis of no significant difference (Research question 1).

3.4.2 PAE associated blood sampling methods and factors

The proportions of PAE in children with different characteristics, such as gender and age, were calculated separately for CBS and VBS. Mixed effect logistic regression was used with PAE as an outcome variable and a random intercept per patient to account for the dependencies of samples from the same patient. Differences between CBS and VBS in odds ratios (OR) or adjusted OR (adj-OR), adjusting for the weight and number of collected

tubes, were evaluated by adding an interaction term between the puncture type and the variable of interest (i.e. weight and number of tubes) (Research question 2).

3.4.3 Cost analysis

Estimations of the resources related to blood sampling, annual costs, by 10,000 samplings and with and without association to PAE were identified, quantified and valued using unit costs (30, 53). The direct costs of personnel, material, laboratory analyses and hospitalisations were summarised and separately calculated. A one-way sensitivity analysis was made to illustrate costs per 10,000 blood samples related to one percentage change in the frequency of PAE. Swedish kronor were converted to euros at 1 SEK = 0.0945 EURO, the average exchange rate for 2019 (Research question 3).

3.4.4 Qualitative analysis of interviews

Thematic analysis (TA) was used as a theoretical framework for data analysis of the transcribed interviews. There existed only fragmented knowledge concerning the research question, so the researchers converged the TA with an 'inductive' approach, as described by Clark and Braun in 2006 (54) and recently clarified and discussed by the same authors (55). Data organisation went through six described phases, including transcribing, making notes, coding and creating themes composed from code patterns and data meanings (56). Microsoft Excel and Microsoft Word were used to organise the data. The initial patterns and coding were discussed after familiarising with the data. The analysing process went back and forth as themes were discussed, and a thematic map was created, revised and refined throughout the process (Research question 4).

3.5 Ethical considerations

The four papers included in this thesis were prior to the collection of data approved by the ethical regional committee of Stockholm (Registration number: 2015/206-31/4). The research followed the principles of the Declaration of Helsinki to ensure the safety of the study subjects and to consider the protection of vulnerable groups (57). Children in hospitals are a vulnerable population that needs special and ethical considerations (58). All blood sampling collections included in this thesis were taken during ordinary patient care and not for the purpose of this thesis research. All the participating nurses were asked to voluntarily fill in the surveys after blood sampling was done. All data concerning the blood samples were unidentified, and the nurses were anonymised. The cost analysis was not included in the original study plan, so an amendment was sent to the ethical review board. The ethical review board judged the study not to need any ethical approval as no sensitive data regarding study subjects were included (Registration number: 2021-00846).

4 RESULTS

4.1 Frequency of PAE and quality indicators

In the investigated paediatric hospital care settings, the frequency of PAE was 61,656 (5.4%, CI 5.3-5.4) between 2013 and 2014, as presented in **Table 3**. There were differences in PAE between paediatric clinics at ALCH, ranging from the highest at 9.4 percent (CI 7.2-11.9) in obstetric wards to the lowest at 1.9 percent (CI 1.9-2.0) in the oncology ward**.**

Table 3. Frequency of PAE in different clinics at Astrid Lindgren Children's Hospital (2013–2014).

Paediatric clinic	**Number of blood analyses n**	**Number of PAE n, %, (95% CI*)**		
Emergency department	345,977	20,849	6.0	(5.9–6.1)
Intensive care	214,649	6,767	3.1	(3.1–3.2)
Medicine	207,796	12,543	6.0	(5.9–6.1)
Oncology	150,829	2,900	1.9	(1.9–2.0)
Neonatal	147,380	12,175	8.3	(8.1–8.4)
Surgical and orthopaedic	69,115	5,685	8.2	(8.0–8.4)
Advanced homecare	12,329	677	5.5	(5.1–5.9)
Obstetric	641	60	9.4	(7.2–11.9)
Total	1,148,716	61,656	5.4	(5.3–5.4)

*Confidence Interval

The frequency of PAE decreased in all clinics, except the intensive care and oncology wards, from 2013 to 2014. In total at ALCH, PAE decreased from 5.6 percent (CI 5.5-5.6) in 2013 to 5.2 percent (CI 5.1-5.2) in 2014 (**Figure 6**).

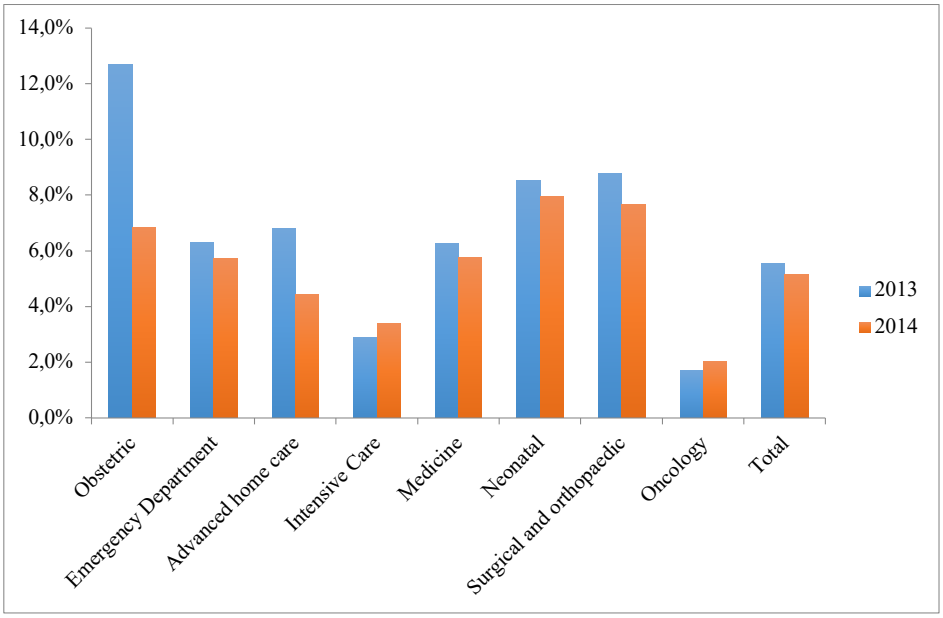


Figure 6. The frequency of PAE in the paediatric clinics

The frequency of PAE at ALCH (2013–2014) within the different sampling hours showed significant differences between the day, evening and night shifts, at 6.0 percent (CI 5.9-6.1), 5.7 percent (CI 5.6-5.8) and 4.3 percent (CI 4.3-4.4), respectively.

The specific ordered blood analyses of PAE frequency varied significantly. The top five blood analyses with the highest frequency of PAE were the Prothrombin complex (INR)-capillary (26.7%), Erythrocyte sedimentation rate (ESR) (19.3%), ESR capillary (16.3%), P- Glucose (13.5%) and P- Lactate Dehydrogenase (LD) (10.9%), **Table 4**.

Table 4. The frequency of the most affected blood analyses with PAE during 2013–2014 in laboratory sections of haematology, coagulation and chemistry.

Blood analyses	No of PAE	Total N	No of PAE%
kB- Prothrombin complex (INR), capillary	323	1211	26,7%
B- Erythrocyte sedimentation rate (ESR)	453	2379	19,0%
kB- ESR(Micro), capillary	301	1849	16,3%
P- Glucose	438	3239	13,5%
P- Lactate Dehydrogenase (LD)	928	8544	10,9%
P- Lactate	120	1225	9,8%
P- Troponin T	266	2896	9,2%
B- Reticulocytes	322	3649	8,8%
P- Lead	82	1100	7,5%
P- Bilirubin conjugated	1084	15029	7,2%
B- Standard bicarbonate	100	1479	6,8%
B- Haemoglobin	4932	73953	6,7%
B- Thrombocytes	4855	72338	6,7%
B- Leukocytes	4928	73512	6,7%
P- Prothrombin complex INR	1074	15920	6,7%

*P= Plasma, kB= Capillary, B= Whole Blood

The frequency of PAE varied across the three investigated sections of the clinical laboratory (haematology, coagulation and chemistry). Blood analyses that experienced clotting were high in the haematology and coagulation sections of the laboratory, at 72 and 28 percent, respectively. Incorrectly filled samples were a frequent problem in all three sections but foremost in coagulation and chemistry, as shown in **Figure 7**.

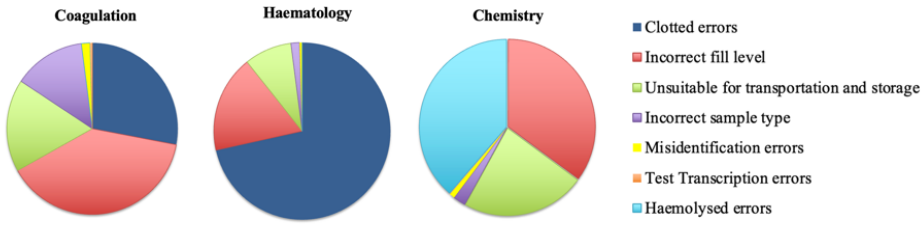


Figure 7. PAE distributed by the analyses of haematology, coagulation and chemistry.

The most frequent type of PAE was clotted samples 31,605 (51.3%), followed by incorrectly filled samples 14,389 (23.3%), together representing approximately 75 percent of all PAE. These PAE, which had the lowest respective six sigma scores of 3.5 (clotting) and 3.8 (incorrectly filled), are presented in **Table 5**.

Table 5. PAE harmonised by Quality Indicators at Astrid Lindgren Children's Hospital (2013–2014), according to six sigma metric scores.

PAE by quality Indicators	Number of PAE	% of all PAE (95% CI)	Sigma metric score*
Clotted samples	31605	51.3 (50.9 – 51.7)	3.5
Incorrect filled level	14389	23.3 (23.0 – 23.7)	3.8
Unsuitable for transportation/storage	8443	13.7 (13.4 – 14.0)	4.0
Haemolysed	4948	8.0 (7.8 – 8.2)	4.2
Incorrect sample type	1771	2.9 (2.7 – 3.0)	4.5
Misidentification errors	350	0.57 (0.51 – 0.63)	5.0
Test transcription errors	150	0.24 (0.21 – 0.29)	5.2

*Very good: ≥ 5.0 sigma; Good: 4.0-4.9 sigma; Acceptable: 3.0-3.9 sigma; Unacceptable: <3.0 sigma.

4.2 Blood collection methods and PAE

The PAE were investigated according to blood collection method (CBS or VBS) among 951 blood samples. PAE were significantly higher with CBS at 72 (20%) out of 354 samples, compared with VBS at 56 (9.4%) out of 597 samples, OR 2.56 (1.69–3.88).

Table 6 illustrates that the risk of PAE was significantly higher in neonates and toddlers compared with adolescents, at OR 2.76 (1.45–5.3) and OR 1.97 (1.11–3.51), respectively. Low weight of the child was another factor that significantly increased the risk of PAE, at OR 2.05 (1.35–3.10). Blood sample collections that required more than one tube also

significantly increased the risk of PAE, OR 2.14 (1.32–3.47). No significant difference could be seen in PAE frequency between genders or the two included wards.

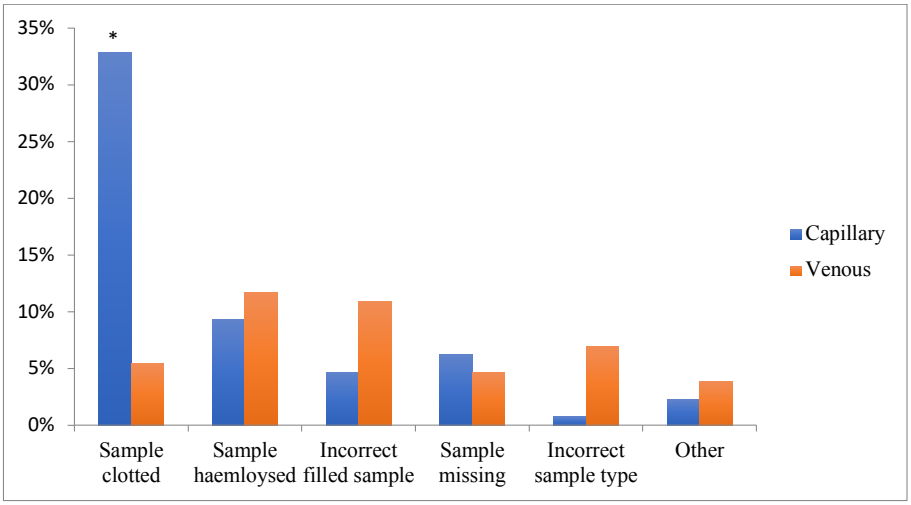
Table 6. Factors associated with PAE in 951 blood sample collections. A logistic regression analysis with univariable and multivariable associations.

Variables	Blood sample collections n (%)	PAE n (%)	Crude odds ratio (95% CI)	P-value >0.05	Adjusted** odds ratios (95% CI)
Blood sampling					
Venous	597 (63)	56 (9.4)	1	1	
Capillary	354 (37)	72 (20)	2.56 (1.69–3.88)	< 0.001	2.88 (1.79-4.64)
Blood amount					
One tube	350 (37)	31 (8.9)	1	1	
Two or more tubes	601 (63)	97 (16)	2.14 (1.32–3.47)	0.002	3.12 (1.84-5.31)
Gender					
Boys	516 (54)	73 (14)	1	1	
Girls	435 (46)	55 (13)	0.87 (0.58–1.30)	0.503	
Age					
Adolescents (10-18years)	253 (27)	23 (9.1)	1	1	
Childhoods (6-9years)	166 (17)	21 (13)	1.44 (0.77–2.71)	0.247	
Pre-schoolers (3-5years)	162 (17)	19 (12)	1.32 (0.70–2.52)	0.386	
Toddlers (1-2years)	188 (20)	31 (16)	1.97 (1.11–3.51)	0.021	
Infants (3-11months)	85 (8·9)	13 (15)	1.81 (0.87–3.75)	0.113	
Neonates (0-2months)	97 (10)	21 (22)	2.76 (1.45–5.3)	0.002	
Weight					
≥11 kg	695 (73)	77 (11)	1	1	
0–10 kg	256 (27)	51 (20)	2.05 (1.35–3.10)	<0.001	
Weight* (ln kg)			0.64 (0.51–0.82)	< 0.001	0.66 (0.50–0.86)

*Weight transformed using the natural logarithm to limit the influence of outliers and better fit the regression models

**The model analysed independent factors that were significantly associated with PAE in the crude analysis: type of blood sampling collection (capillary vs venous). Weight was treated as a continuous variable and transformed using the natural logarithm to limit the influence of outliers and to provide a better fit for the regression models. The number of collected blood sample tubes was analysed as two or more vs one.

When stratifying the distribution of PAE by CBS and VBS, clotting was significantly higher in CBS (33%) than in VBS (5.5%) ($p < 0.001$). Clotting was found to be the most common type of PAE at 49 (38%) of the total 128 PAE (**Figure 8**).



Other: Sample damaged, thrombocytes aggregated, or sample analysis not executed
* P-value < 0.001

Figure 8: The proportion of PAE by venous and capillary samplings.

Stratified analyses of CBS and VBS demonstrated a reducing risk of PAE per increasing weight (kg) of the child for VBS, adj-OR 0.52 (0.38–0.72), but not for CBS, adj-OR 1.08 (0.76–1.55). The stratified analyses for collecting more than one tube showed increased risk of PAE for both VBS and CBS, at OR 2.74 (1.21–6.21) and OR 3.00 (1.57–5.71), respectively (**Figure 9**).

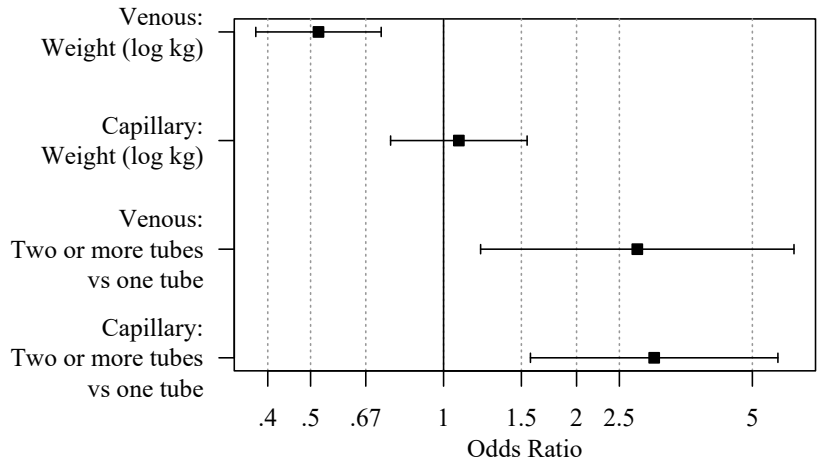


Figure 9. Odds ratios and 95% confidence intervals for PAE for increasing weight and number of blood tubes, for venous and capillary blood sampling, respectively.

4.3 Cost of blood sampling and PAE

The cost analysis demonstrated that the estimated annual cost of PAE in a paediatric hospital was 84,000 euros. The personnel cost at 55,000 euros per year represented 65 percent of all PAE related cost (**Table 7**). The cost due to PAE per 10,000 samples was estimated to be 15,500 euros, whereas the total cost without PAE was 290,000 euros (**Table 7**).

Table 7. Direct costs of PAE, including cost per sampling, annual costs and cost per 10,000 samplings.

Resources	**Annual cost per 54,040 samplings**	**Annual cost due to PAE (frequency 5.4%*)**	**Cost per 10,000 samplings**	**Cost per 10,000 samplings due to PAE (frequency 5.4%*)**	**Cost proportion (%)**
Personnel cost	1,016,492€	54,891€	188,150€	10,160€	65.4
Material cost	78,898€	4,261€	14,648€	791€	5.1
Laboratory analytical cost	111,322€	6,011€	20,790€	1,123€	7.2
Hospitalisation cost	346,937€	18,735€	64,200€	3,467€	22.3
Total cost	1,553,650€	83,897€	287,787€	15,541€	100

*Based on FlexLab data between 2013–2014.

Table 8. Costs of personnel, materials, laboratory analyses and hospitalisation for blood sample collection (venous and capillary)

Resource		**Unit cost (€)**	**Total cost per blood sample (€)**
Personnel costs	**Time per sampling**		
Doctor	5min	39.22/h	3.27
Registered nurse	30min	22.77/h	11.39
Nurse assistant	15min	16.63/h	4.16
Summary of personnel			18.81
Material costs	**Percentage of all sampling procedures***		
Venous sampling by open needle	2.6%	4.17	0.11
Venous sampling by PIC** draw when new insertion	11.3%	4.58	0.52
Venous sampling by PIC draw	23.7%	0.87	0.21
Venous sampling by butterfly needle	3.1%	4.07	0.13
Venous sampling by straight needle Vacutainer	1.6%	3.55	0.06
Venous sampling by drawing from CVL***	20.6%	1.41	0.29
Capillary sampling by finger prick	35.3%	0.38	0.14
Capillary sampling by side of heel	1.89%	1.42	0.03
Summary of material			1.46
Laboratory cost	**Analyses per sampling**		
Blood analysis	1	2.06	2.06
Hospitalisation cost	**Time from pre-analytics to post analytics**		
Paediatric wards	82.7min	112.7	6.42
Total resources cost			**€28.75**

*Refers to the frequency of different blood sampling methods and based on clinical surveys and observations, by Hjelmgren et al., 2021.
** *Periphery vein catheter*
*** *Central Venous Line*

The findings of the cost analysis showed that the average direct cost per blood sample was 28.8 euros, divided by costs for personnel (€19), materials (€1.5), laboratory analysis (€2.1) and hospitalisation of the patient (€6.5), shown in **Table 8**. Thus, the annual average cost was approximately 1.5 million euros for 54,040 blood samplings (288,000 euro per 10,000samplings).

Table 9 demonstrates the sensitivity analysis of costs related to each percentage change in the frequency of PAE from the rate of 5.4 percent. For each percentage change in the frequency of PAE increases or decreases the cost with 2,879 euros per 10,000 blood samples.

Table 9. Costs of one percentage change in the frequency of PAE per 10,000 blood samples.

Rate difference	PAE frequency	Cost of PAE (10,000 samplings)	Cost difference
- 1 %	4.4 %	12,662.6€	- 2,878.9 (↓ 18.5 %)
± 0	5.4%	15,541.5€	-
+ 1 %	6.4%	18,418.4€	+ 2,876.9€ (↑ 18.5 %)

4.4 Nurses' experiences of blood sampling and PAE

Three focus group interviews were conducted with nurses from different clinics and different experiences levels. The transcribed data from the three focus group interviews were analysed and the findings condensed into five themes (**Figure 10**).

Figure 10: Thematic map of the results of focus group interviews.

The main theme identified in the focus groups was ***Paediatric blood sampling is a challenge for the nurses***. In general, the blood sampling procedure was experienced as a huge challenge, being more complex than with adults. Notably, the entire procedure was mentioned as complicated, not only performing the puncture itself. The procedure could last for a whole day.

'Yes, there's a huge difference when you're working on adults but with a child it could be a process that takes a whole morning just to get near them'. (Nurses Group 2)

A consequence of PAE was the subtheme ***Nurses have feelings of frustration with unsuccessful samplings***. This theme identified feelings of frustration and sometimes even

anger among the nurses. It often occurred when nurses thought a procedure went well and was correctly performed and thus could not understand why a PAE occurred.

'And then on occasion, when I've taken the same sample from a child three times and all three have coagulated each time, and when I really know I turned everything and warmed it up and did everything, that from here on, now there's something strange – something spooky about it'. (Nurses Group 3)

Another subtheme generated was ***Nurses believe in teamwork***. The nurses believed it was easier to conduct procedures successfully when they had good communication and a supportive team. Management and distraction methods also went more smoothly when working with a team.

'...better if there's more of you, not just for distraction but also so you have someone who can hand you things, stand and turn tubes'. (Nurses Group 3)

When the nurses backed each other up and when the parents were included in the process, it tended to work better.

'But they (the parents) are really important in it going well. Because if they start getting stressed about things or say stuff that has nothing to do with it or whatever, it can go belly up because of it'. (Nurses Group 2)

A third subtheme was ***Venous blood sampling was experienced as the best option.*** The nurses experienced that VBS tended to increase the chance of greater blood volume extraction, which increased their chances of not having to repeat the sampling.

'If you've learnt venous it's easier than capillary, has better flow and it increases the chances of getting good samples'. (Nurses Group 1)

The nurses described that they lacked knowledge of paediatric care. ***Nurses' thoughts and needs regarding skills development in paediatric blood sampling*** were often discussed in

the focus groups. They reported that differences between paediatric and adult blood sampling procedures had not been taught during their university studies. The nurses felt that learning by doing and observing colleagues were the main ways to gain the necessary knowledge. They described uncertainty about choosing correct preparations and blood sampling methods.

'The thinking around sampling and perhaps a bit more on which ones I can actually take from capillaries and which ones have to be venous, so that's what I wish I had in my training'. (Nurses Group 3).

5 DISCUSSION

The overall aim of this thesis was to investigate the frequency and consequences of blood sampling errors in paediatric hospital care. The main findings demonstrate that laboratory-reported PAE among blood analyses over a two-year period amounted to 5.4 percent. Clotting was the most frequent type of PAE (51.3%). The risk of PAE increased with CBS compared to VBS. Further, a lower weight of the child and a higher number of sampling tubes were both associated with PAE. The consequences of PAE included considerable annual costs due to PAE (84,000 euros); there were primarily related to personnel and hospitalisation costs. Focus group interviews revealed that the blood sampling procedure was challenging, creating feelings of stress and frustration. The nurses felt they lacked knowledge concerning PAE and stated that they needed additional training on how to avoid PAE.

5.1 Frequency of PAE

Over two years, the average frequency of PAE was 5.4 percent, decreasing significantly from 5.6 percent in 2013 to 5.2 percent in 2014. The literature reports different frequencies of PAE. In 2015, Dikmen et al. reported a total PAE frequency of 5.9 percent for the year 2013, including both paediatric and adult blood samples (59), which is in the same range as our findings. In contrast, a retrospective paediatric study from Turkey in year 2017, showed a very low PAE frequency of 0.78 percent in 565,409 samples over a one-year period (60). This discrepancy may be related to methodological variation as different methods of counting PAE were used between the studies. Obstetric and neonatal wards reported highest frequency of PAE compared to other clinics in this thesis. This was consistent with a report from United States, where the neonatal intensive care unit also had the highest PAE frequency (61). The reason for high PAE in this population group could be due to small blood volume in new-

borns and premature babies resulting in having high haematocrit, erythrocyte and haemoglobin concentration, which may affect the sensitivity to PAE haemolysis and clotting (62).

5.2 Type of PAE

More than half of all PAE in the observed paediatric hospital setting resulted in clots (51.3%), indicating that clotting is one of the major unmet problems related to blood sampling errors among children. A paediatric laboratory study reported that up to 70 percent of all PAE were clotted and over 20 percent were insufficient samples (60). This is higher than the present study's results for clotting (51.3%) but lower for unfilled samples (23.3%). In previous laboratory medicine reports, PAE reporting has mostly focused on haemolysed samples in adult care (63-65). A study that retrospectively collected information about PAE observed differences in clotting frequency between adult and paediatric care, with eight percent in the adult ward versus 63 percent in the paediatric ward (13). In 2017, Rooper et al. confirmed such variations of PAE frequency. They found that 10 hospital departments represented 85 percent of all rejected blood specimens; further they reported that the neonatal intensive care units had troubles with clotted samples. The adult wards reported high rates of haemolysis (61). To the best of the author's knowledge, the present thesis is the first to focus solely on the paediatric hospital care setting that includes a wide range of clinics, bringing novelty and unique information in addition to other studies that mix different contexts.

5.3 Process evaluation

The performance quality model featuring a six sigma evaluating system and the QI proved to be effective at improving quality in the pre-analytical process (15). The analysis results

in our study setting indicated a barely acceptable process, which could be due to the study's unique focus on children and neonates. Not all of the previous studies clearly reported what kind of patients were included, as they often focused on laboratory performance (9, 15, 60). In 2015, Plebani et al. conducted a meta-analysis of the sigma scores that several laboratories worldwide had reported in a four-year period (15). They discovered an average sigma score of 4.3 for clotted samples compared with the present results of 3.5. Also in 2015, Salinas et al. recorded PAE in urine, chemistry, coagulation and haematology samples over a 10-year period at their university hospital laboratory in Spain, which consisted of a 350-bed hospital and several primary care centres (66). They reported a total score of 3.8, which is higher than the present thesis results of 3.2; in terms of PAE frequency, their process performance was better than the present paediatric pre-analytical process (66). In 2018, Kulkarni et al. reported a well-controlled process with a six sigma score of >4 for both insufficient and clotted samples (67). One recent study from United States that focused on elderly people in an outpatient laboratory, found that PAE haemolysis had a prominent number of errors, with a six sigma score of 4.7. Whereas the PAE clot had a six sigma score of 4.9. This study elucidated the importance of following Qis over time, as the errors decreased from 1.4 percent to 0.14 percent in seven years, despite the number of tests increasing by 290 percent (68).

5.4 Comparing blood sampling methods

In this thesis, the risk of PAE was significantly higher with CBS than with VBS. This is a novel result, as no other study has reported different rates of PAE between blood sample methods. This finding highlights that implementing more VBS could reduce PAE. Using CBS could be a good supplement for point-of-care testing, but it should not be recommended when the analysis requires added anticoagulant or higher numbers of analyses and tubes.

Point-of-care testing has also been associated with increased PAE in a neonatal unit compared to sending samples to the hospital laboratory (69). The Swedish national handbook of care include guidelines, which provides instructions on CBS and VBS (70), but adherence to these guidelines has shown to be low in adult contexts (71, 72). Further, the guidelines provide no paediatric-specific situations and lack structured information on how to avoid PAE, which can cause uncertainty among staff. The official recommendation regarding CBS is to remove the first drop of blood, because the first drop can contain skin tissue and dirt. It is also recommended a secure, gentle pressing of surrounding tissue when the puncture is done to prevent haemolysis (73). A gentle mixing of the blood with an anticoagulant can prevent clotting (19), but staff can easily forget or miss these steps when they are under stress or when they are trying to distract the child during or after the sampling. As standards and guidelines have numerous steps, they can be hard to remember, and they can be unintentionally missed (72). Implementation of a VBS checklist may be a promising strategy for to enhance quality and reduce PAE (74).

The high risk of unsuccessful blood sampling when using CBS is a major justification for choosing VBS. Another reason to use VBS is because it is less painful than CBS for neonates and babies (75, 76). Further, samples can be drawn from existing venous lines without the risk of PAE and pain for the child (23). Low body weight in children has not previously been associated with PAE, nor has having to take two or more tubes in a blood sample. When stratified for both CBS and VBS, a tube number greater than one remains as a high risk for both CBS and VBS. Stratified analyses regarding increasing weight only reduces risk in VBS. When taking more than one tube, it is crucial to be aware of that the order of blood draw is different between VBS and CBS. One reason for the increased clotting in capillary samplings may be that EDTA (Ethylenediaminetetraacetic acid) sample tubes are not prioritized as the first collection tube because this differs from venous sampling (19, 77).

5.5 Cost of PAE

The costs associated with PAE in this thesis largely involve personnel and hospitalisation. The annual hospital costs of PAE were 84,000 euros, or 15,500 euros per 10,000 blood samples in the observed hospital setting. Studies from Italy (34) and Canada (78) reported lower PAE-related costs, presenting results of approximately 1,200 euros and 3,300 euros per 10,000 samples, respectively. However, the present results of this thesis were lower than those of a German study, which reported costs ranging from 34,000 – 61,000 euros (33).

Comparing the results of this thesis to the literature was complicated due to the different contexts and aims of these past studies. For example, the Canadian study only investigated blood coagulation tests (Prothrombin complex INR), which could explain the low costs it found (78). Similarly, the Italian and German studies only investigated the cost of haemolysis and not other related PAE (33, 34).

The present study found that the personnel time needed for nurses to conduct paediatric blood sampling was approximately 30 minutes. In the studies from Italy (34) and Germany (33, 34), the mean time for nurses to execute an adult venepuncture was 2.5 and 10 minutes, respectively, which is very short in relation to the present observation concerning paediatric samplings. Further the studies from Italy (34), Canada (78) and Germany (33) did not include the cost of doctors and nurse assistants which could result in higher costs in the context of paediatric blood sampling.

The reviewed prior studies also did not include hospitalisation costs. These costs are important to estimate when considering PAE because PAE can lead to delayed treatment and diagnosis (79). Paediatric hospital care is generally more costly than regular general hospital care due to more high-cost hospitalisations and a more complex population (80).

The one-way sensitive analysis of this cost analysis illustrated that just a 1 percent change in PAE frequency for 10,000 samples could affect the PAE cost by almost 19%. This indicates that small measures to reduce the frequency of PAE may have large impact on the overall costs. In this thesis, the total cost of blood sampling represented approximately 0.8 percent of children's hospital 2019 budget of 195,00,000 euros (hospital's economic information system, Tableau software©).

5.6 Nurses' experiences of PAE and paediatric blood sampling

This thesis explored nurses' experiences with paediatric blood sampling and PAE. The main theme, *Paediatric blood sampling is a challenge for nurses*, was generated from the interview data. A survey study from the United States supports this finding. Here, the phlebotomists identified coping with children's and parents' anxieties as the foremost challenge in paediatric sampling (81). Other factors that nurses have reported as affecting their morale and stress levels include having to restrain children and using pain alleviators during needle-related procedures (39). Blood sampling procedures are complex, so health organisations must recognise that extra time and personnel are needed. Previous research has demonstrated that advanced paediatric care requires a high level of clinical competence and resources (82).

Four subthemes were revealed in the present study's analysis. *Nurses' feelings of frustration with unsuccessful samplings* describes that unsuccessful sampling, including PAE, occurs frequently. Consequently, nurses experience feelings of anger, stress and frustration. Some nurses described incidents in which they could not understand why the PAE occurred. This might reflect the knowledge gap concerning biochemistry theory among nurses in Sweden. In 2018, Watson et al. described challenges and future recommendations regarding the roles that laboratory medicine and stakeholders can play to

help manage knowledge gaps in a collaborative healthcare system. For example, the specialist in laboratory medicine could support the patients and clinicians with valuable tools and help interpret the results of growing field of laboratory testing (83). Nurses must cope not only with applying technical skills to perform blood sampling correctly to avoid PAE but also with the stress of the situation itself and the anxieties of the children and their family members. Further, children's rights became law in Sweden in 2020, meaning that the rights of the child must be considered in all deliberations and assessments. This emphasises the magnitude of the role that paediatric nurses play working in Swedish paediatric hospitals; they must have knowledge, skills and specific competencies concerning blood sampling procedures, and these must be individualised for each child (38, 84).

The second subtheme was *Venous blood sampling was experienced as the best option.* A Canadian study described the same finding, reporting that the VBS process was seen as less time consuming, less painful for the infant and an easier method for blood collection than CBS (75). Current guidelines for blood sampling procedures in paediatric hospital care do not clarify different processes for diverse ages and situations. Venous guidelines from the Swedish Handbook of Healthcare (70) and the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) (85), as well as recommendations in the American Clinical and Laboratory Standards Institute (CLSI) (73, 86), focus largely on adult care. Blood sampling guidelines from the World Health Organization (WHO) (87) include some child-specific recommendations, but nothing on how to approach children's developmental stages, anatomical challenges and PAE avoidance. Updating these guidelines would be of great help to personnel working with blood sampling in paediatric hospital care.

The third subtheme was *Nurses' thoughts and needs regarding skills development in paediatric blood sampling*. The participating nurses described that they gained knowledge from learning by doing or by observing other nurses. By themselves, they lacked

knowledge on how to avoid PAE. Thus, providing standardised training and education about PAE may lead to fewer failed samplings (88). It is important to note that these nurses wanted to be competent and to feel secure in the quality of the care they delivered. The absence of comprehensive guidelines and educational activities creates stress and uncertainty, and if not addressed properly, it will likely lead to more stress and turnover among paediatric hospital care staff (89).

5.7 Methodological considerations

This thesis included different data sources that contained both quantitative and qualitative research approaches. Having a mixed method design creates valuable insights by integrating different approaches to gain new knowledge (90).

Generalisability refers to the degree to which the results of a study can be applied in other settings. There should be a balance between internal and external validity (91). The results of this thesis that refer to PAE, such as frequency, associated sampling methods, costs and nurse experiences with blood sampling, may be applied to paediatric tertiary care in Sweden and other countries with similar healthcare resources and contexts.

Cis were used when presenting the proportions of PAE. Cis show the variability of statistics; a wide CI indicates low precision, and a narrow CI indicates high precision (92). A strength of this study was that it used a large sample size when investigating PAE frequency, which resulted in a narrow CI of over one million during the two-year retrospective research period. The laboratory information system, FlexLab, made it possible to retrospectively study the frequency of the different sources of PAE but had the limitation that some detailed information of e.g. sampling methods were missing. The missing information also concerned the size of the sample tubes, namely that it was not recorded whether microtainers or normal size sample tubes were used during blood sample

collections. Sample tube size may influence PAE frequency, as microtubes are more difficult to handle both for laboratory staff and clinicians.

When comparing VBS and CBS using the blood method survey, the sample size at two inward departments was smaller and therefore the CI wider, which may indicate statistical uncertainty. A limitation was that the staff sometimes forgot to fill in the surveys after completing blood samplings, which led to long inclusion periods and low answering frequency. More frequent reminders of the study in the wards may have increased the sample size and resulted in a more representative population sample.

Blood taken via CBS and VBS can be directly analysed bedside using various equipment items. This is called point of care testing and is widely used in Swedish hospitals. Such tests were not included in this thesis, however, so the PAE frequency for these tests in a paediatric hospital care setting is still unknown.

Child age and weight were both found to closely associate with PAE. Weight showed the strongest association to PAE and was therefore included in the model. Age was excluded from the adjusted model to avoid over-adjustment.

Descriptive studies show that limited information biases may be present in this kind of research. Information biases occur if the data collected deviates from the true information (93). In the present study, this may have occurred if classifications of PAE were wrong or miss reported. For example, the cost analyses for personnel and hospitalisation were based on time observations. The collected data may have deviated due to the conscious or subconscious mindset of the observer (93). To mitigate information biases, an observation protocol and documented memos were used, so the results were adequately informed professional guesses. Adding a blind observer to the exposed status may reduce the incidence of differential information errors, but this was not possible due to practical reasons in the scope of the present thesis. Also, during cost analysis, an opportunity was

missed to obtain new data on PAE frequency from the hospital laboratory for several reasons. The main reason was laboratory reorganisation and its focus on handling the COVID-19 pandemic, largely through increased testing and workloads across the whole hospital organisation. Because of these complications, we used retrospective data already published by a register-based study, which may have altered the results.

In qualitative research, transferability is prioritised over the generalising of findings (94). In such cases, it is the reader rather than the author who defines the transferability of the study's results to other contexts (94). The trustworthiness of qualitative data is confirmed through several actions. This thesis' findings and interpretations were illustrated by rich quotes to add transparency and trustworthiness to the data (95). Purposive sampling added credibility because the participants were from different backgrounds and work settings, which diversified the study sample (52). Purposive sampling refers to choosing participants who have experience and can provide informed data on the phenomenon being studied (96). A strength of using focus group interviews is that the method can generate group effects via participant interactions, which leads to learning moments that are not possible in individual interviews (97, 98). For example, several participants from the present study stated that they gained new knowledge during the interviews.

Confirmability refers to the transparency of the authors' pre-understanding of the studied phenomenon. A researcher's subjectivity is seen as a resource in TA rather than something negative, as it strengthens engagement with the interpretation of data and theory (55). In this thesis, three researchers conducted the focus group interviews, but only one (Nina Andersson) was present in all of them because some of the participants were colleagues to the authors (Henrik Hjelmgren). Self-awareness of the researcher is important to sustain credibility (99).

A limitation of this thesis' qualitative data was that the original plan included interviews with other healthcare professionals, such as nurse assistants, but this was later scaled down to interviewing only nurses for consistency.

Another limitation of this thesis was that the evaluating process with QI did not consider patient satisfaction. Low PAE frequency is good for patient health and safety. If children have poor experiences with the blood sampling procedure, they may carry that fear and trauma with them further in life (100). Paediatric patients have previously described needle-related procedures as a negative experience (101, 102). Addressing children's rights and their participation in their own care is needed to avoid restraining and painful actions. Venepunctures and intravenous accesses cause distress; one child expressed it as 'someone stabs you' (101). If a child has a negative experience, it can lead to challenges the next time the child needs a medical visit (103).

6 CONCLUSIONS

The overall finding of this thesis is that the frequency and consequences of PAE in paediatric tertiary hospital care is substantial. Future research should focus on interventions targeted at decreasing the frequency of PAE. In answer to the specific research questions set out at the start, the following conclusions and interpretations were drawn:

- Laboratory-reported PAE among blood analyses in a two-year period (2013-2014) amounted to 5.4 percent.
- The six sigma score for the total pre-analytic process was 3.2, which is a barely acceptable level and indicates the need for continuous monitoring and acting on the process.
- Clotting was the most frequent type of PAE (51.3%).
- The risk of PAE increased with capillary blood sampling compared to venous blood sampling.
- A lower weight of the child and higher number of sampling tubes were both associated with PAE frequency.
- The annual direct costs due to PAE were approximately 84,000 euros or 15,500 euros per 10,000 blood samples (65% personnel costs and 22% hospitalisation costs). Material and laboratory costs represented five percent and seven percent, respectively.
- Nurses felt that the paediatric blood sampling procedure were challenging and could create stress and frustration. They also elucidated their lack of knowledge concerning PAE, wishing for both theoretical and practical training to avoid PAE.

7 POINTS OF PERSPECTIVE

7.1 Implications for clinical practice

The findings of this thesis should encourage healthcare providers and laboratory personnel to work together to reduce PAE in paediatric hospital care. To improve the blood sampling process and understand why PAE occurs in paediatric hospitals, it is essential to analyse, evaluate and monitor the process in a standardised way. With modern technical solutions and systems, the process for monitoring PAE frequency with included six sigma scores could easily be presented at each hospital unit on a regular basis. This could increase staff awareness of PAE, which itself may lead to better understandings and consequently, improved patient safety. Visualising and presenting PAE frequency in clinics has had promising results in the past (104).

The quantitative data gathered for this thesis provides a cross-sectional picture of the situation, which may be used to create tailored interventions for each clinic. Such interventions could include educational activities that teach healthcare workers in paediatric hospitals how to reduce clotting, improve day shift sampling procedures and reduce errors in the types of analysis most at risk for PAE. The blood sampling process also needs to be improved by establishing VBS as the preferred sampling method over CBS. Poor outcomes and frequent PAE clotting associated with CBS show that staff could benefit from receiving repeated clinical training programs on how to avoid clotting.

The cost analysis presented in this thesis will hopefully be of use to healthcare organisations and lead to allocating more resources towards reducing PAE frequency and improving patient safety. The collected qualitative data about the nurses' experiences indicate a strong need to improve guidelines and increase nurses' skills and knowledge concerning PAE through empowering, educational interventions. Such interventions would

help nurses increase their competence as well as understand why sampling procedures fail and how this can be avoided.

7.2 Future research

There is a need for further investigation about PAE and how to avoid them in paediatric hospital care. Future studies should focus on intervention strategies to promote less repeated sampling due to PAE, combined with standardised child satisfaction strategies. As health organisations and blood sampling procedures are complicated, a structured implementation method should be put in place to address complex interventions.

Newly updated Medical Research Council guidance provides useful structures on how to plan, evaluate and implement complex interventions (105). According to this guidance, future solutions may include multicomponent intervention packages, such as web-based learning, practical training through simulations and case-based learning as well as technical innovations like digital information applications for patients and personnel. Combined with visual monitoring, such solutions could be a promising strategy to reduce PAE frequency.

To gain an even deeper understanding of the problem, it would be interesting to investigate other health professionals' experiences with PAE. What do paediatricians think when they have to reorder samples due to PAE? How much do nurse assistants know about PAE? Would self-assessments during the different steps of the procedure reveal which types of errors nurses feel are more problematic? What are children's thoughts on the sampling procedure? Can they add valuable information?

Further, children's rights and participation must be considered in future research. Without adequate information and pain relief provided by pharmacological and non-pharmacological methods, punctures and blood sampling are bound to fail. Thus, skilled personnel are needed to handle the blood sampling process and reduce the risk of PAE.

These skilled personnel should be able to accommodate children's rights and provide adequate information, preparation and child-centred care.

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9 APPENDICES

Appendix 1: Blood sampling survey

Q80 2015-09-01

Studie: Pre-analytiskt avvikande blodprover och patientsäkerhet inom Barnsjukvården

1. Blodprovet är taget:

Ifall kapillärt:	Via…	Häl	☐
		Finger	☐
		Tår	☐
	Med…	Rosa-lancett	☐
		Blå- lancett	☐
		Lila- lancett	☐
		Häl- lancett	☐

Ifall venöst:	Vid PVK-sättning	☐ strl____
	Draget ur befintlig pvk	☐ strl____
	Draget ur SVP	☐
	Draget ur CVK	☐
	Via öppen nål (grön/blå)	☐ _____
	Via butterfly (grön/blå)	☐ _____
	Via Vaccutainer	☐

2. Antal stickförsök: ____st

3. Jag är: ☐ USK ☐ BSK ☐ SSK ☐ Spec-SSK

4. RID-numret på blodprovet:

Klistra kopia på RID-numret och personnumret här!

Stort TACK för din medverkan!
Henrik Hjelmgren, Vid frågor maila mig:
henrik.hjelmgren@karolinska.se

Appendix Table 2. Material consumables costs at Astrid Lindgren's Children's Hospital in 2020

Consumables	Reference	Cost per unit (SEK)	Resource use
Venous micro needle	Sarstetd AB	7.50	50/package
Venous periphery vein catheter (24G)	BD neoflon	10.50	50/ package
Syringe 5ml	Omnifix	0.49	100/ package
Venous central lines			
Vacuum holder + vacuum cannula	BD Vacutainer	0.15 + 0.80? (Hittar inte vaccumkanylen I varukatalogen)	200/ package
Venous butterfly	BD Vacutainer	6.46	100/ package
Venous vaccutainer	BD Vacutainer		
Vacuum holder+ cannula		0.15 + 0.80	200/ + 480/ package
EMLA(lidokain/prilokain) 5g cream	Aspen Pharma	79	1/ package
Film dressing (4.4x4.4cm)	Tegaderm	1.81	400/package
Capillary lancet finger	BD Microtainer	0.79	200/ package
Capillary lancet heel	Medicarrier Sarstedt Safety-Heel	11.75	200/ package
Plaster	DermaPlast Kids	0.16	4000/ package
Skin antiseptic (5x5cm)	Yibon	0.02	13500/ package
Surgical tape	Micropore	2.99	240/ package
Micro tube MAP 0.5ml	BD EDTA MAP	4.20	200/ package
Micro tube (0.5ml)	BD Li-hep	1.89	200/ package
Vacuum Tube (3–5ml).	BD EDTA	0.75	100/ package
Injection membrane	Bionector	4.75	2400/ package
Infusion connector (3 way)	Sendal	4.64	200/ package

Appendix Table 3: Costs of blood analyses of blood ordered and analysed to the chemistry, haematology and coagulation sections at Astrid Children's Lindgren's Hospital in 2019

Section	Analyses	Cost per unit/SEK	Total number of analyses	Total cost per year /SEK
Chemistry	P-CRP	11.13	38 030	423 382.23
	P-Kreatinin	5.56	35 924	199 788.24
	P-Natrium	5.56	22 964	127 711.51
	P-Kalium	5.56	22 563	125 481.69
	P-Albumin	5.56	23 071	128 307.05
	P-Bilirubin	5.56	18 583	103 346.99
	P-ASAT	5.56	22 009	122 404.48
	P-ALAT	5.56	25 143	139 836.33
	P-Fosfat	5.56	15 605	86 783.49

	P -Magnesium	11.13	13 885	154 580.99
	P-Calcium	5.56	14 606	81 228.49
	P-Bilirubin, konj	5.56	8 612	47 891.92
	P-Urea	5.56	8 630	47 992.29
	P-GT	5.56	10 197	56 709.78
	P-LD	5.56	5 683	31 602.63
	fP-Triglycerid	5.56	3 706	20 610.93
	P-Klorid	30.57	2 351	71 858.62
	P-Urat	5.56	3 874	21 544.80
	P-ALP (Alk fosfatas)	5.56	2 118	11 779.99
	P-Glukos	5.56	4 542	25 263.07
	P-Troponin, högkänsligt	79.12	1 789	141 542.38
	P-Pankreasamylas	41.01	4 396	180 277.45
	P-Cystatin C	24.15	5 537	133 739.80
	P-NT-proBNP	233.10	1 218	283 911.24
	P-Järn	5.56	2 568	14 283.29
	P-Methotrexat	869.64	1 123	976 601.50
	S-Procalcitonin	244.86	5 363	1 313 169.59
	S-Ferritin (ModE)	44.52	4 755	211 677.51
Haematology	B-Blodstatus	18.97	58 813	1 115 920.48
	B-Celler	24.15	35 923	867 602.19
	B-Retikulocyter	36.89	4 260	157 142.97
	B-SR	22.92	6 126	140 403.37
	B-Standardbikarbonat	66.83	1 273	85 080.20
Coagulation	P-PK(INR)	33.38	11 734	391 629.89
	P-APT-tid	55.64	8 044	447 557.43
	P-Fibrinogen (koag)	74.80	6 234	466 302.28
	P-Fibrin-D-dimer	151.20	2 192	331 421.74
	P-Antitrombin (enz)	129.10	2 786	359 659.06
	P FIBRIN, LÖSLIGT	284.74	2 003	570 337.98
Total cost per analyses:		21.8	468 233	10 216 365

Cost per analyses: 10216365sek / 468233 analyses = 21.8 SEK/analyses = 2.06 euros

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REGULAR ARTICLE

Retrospective study showed that blood sampling errors risked children's well-being and safety in a Swedish paediatric tertiary care

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ABSTRACT

Aim: Blood analyses containing preanalytical errors (PAEs) are hazardous for patients. This study investigated the frequency of PAEs in blood analysis and the corresponding quality indicators of the sampling process in Swedish paediatric tertiary care.

Methods: Data were retrieved from the laboratory at Astrid Lindgren Children's Hospital between 2013 and 2014. Preanalytical blood sampling performance was analysed according to the Six Sigma scale, ranging from 0 to 6 (933 137–3.4 defects per million [DPM]).

Results: Of the 1 148 716 analyses, 61 656 (5.4%) were rejected due to PAEs. The PAEs ranged between hospital specialities from 1.9 to 9.4% ($p < 0.001$) and work shift times, from 6.0% in the day to 5.7% in the evening and 4.3% at night (p values <0.001). Clotting was the most prominent error (51.3%), affecting mostly haematology and coagulation analyses. Incorrectly filled samples represented almost 25% of all PAEs, with effects on chemistry, haematology and coagulation analyses. The sigma score for the overall preanalytical phase (3.2) corresponded to 44 565 DPM.

Conclusion: Samples with PAEs were frequently clotted and insufficiently filled, and the distribution of errors varied within working shifts and specific analyses. The overall quality control in paediatric blood sampling was barely acceptable.

INTRODUCTION

It is claimed that about 70% of all clinical health decisions are based on laboratory test results (1). Paediatric health care depends on well-established blood sampling procedures and results to manage and diagnose children with medical conditions. When a blood analysis fails, it leads to missing results that hamper important medical decisions (2–4). In laboratory testing, errors occur in the preanalytical, intra-analytical and postanalytical phases. The preanalytical phase involves test requests, patient preparations, blood sample drawing and delivering the samples to the laboratory. Knowledge on blood samples with diagnostic errors has increased in recent decades, but 60–70% of all these errors occur in the preanalytical phase (4).

Preanalytical errors (PAEs) in blood sampling result in specimens being rejected from the laboratory due to different types of errors, such as clotting, haemolysis, unfilled tubes and mislabelling (4). The International Federation of Clinical Chemistry and Laboratory Medicine has categorised different types of PAEs into quality indicators (QIs), such as misidentification errors, test transcription errors, incorrect fill levels, incorrect sample types, unsuitable samples for transportation and storage, haemolysed samples, clotted samples and contaminated samples (5). Regularly monitoring QIs with a quality instrument, such as the Six Sigma metric, has been determined as a promising strategy for improving the preanalytical phase in blood sampling (5). The Six Sigma metric is a generic

Abbreviations
DPM, Defects per million; ESR, Erythrocyte sedimentation rate; PAE, Preanalytical error; QI, Quality indicators.

Key notes

- Blood analyses containing preanalytical errors (PAEs) are hazardous for patients, and this study investigated the frequency of PAEs in Swedish paediatric tertiary care.
- Preanalytical errors occurred in 5.4% of the 1 148 716 analyses samples analysed and varied between specialities (1.9–9.4%) and the shift when they were taken (4.3–6.0%).
- Clots were the most common errors, and the results indicated that blood sampling procedures were not acceptable and risked children's safety and well-being.

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measurement that identifies defects and improves the quality of a process (6). The standard table of the Six Sigma metric ranges from 0 to 6, where three, which equates to 66 807 defects per million (DPM), is considered the minimum level of acceptable quality for the process performance and six is seen as the top-class quality level, with as little as 3.4 DPM or a 99.99% success rate (7).

To our knowledge, the frequency of PAEs and blood specimen rejection rates in a paediatric hospital setting has not yet been fully elucidated. Collecting paediatric blood samples is more challenging, because children have small blood vessels and microtainers are used for collecting small blood volumes. Coagulation tests in paediatric departments seem to have much higher rates of PAEs than adult departments (8). The overall rate of PAEs in paediatric hospital care is still unknown. Moreover, there is a lack of information about why PAEs and rejected blood tests occur. The aim of this study was to investigate the frequency of PAEs in blood analyses and identify corresponding QIs in a paediatric tertiary hospital care.

MATERIALS AND METHODS

Study design

This was a retrospective, register-based study that collected information about PAEs in a Swedish tertiary paediatric university hospital.

Study population

The study was carried out at the Astrid Lindgren Children's Hospital, which serves a local population of approximately 220 000 children and adolescents from birth to 17 years of age living in the area covered by Stockholm County Council. It also provides national and specialist care in some areas of medicine and even accepts a limited number of international patients. The study cohort included all children admitted to the hospital as well as children connected to home-based care. The data covered all blood specimens collected from these patients and sent to the Department of Clinical Chemistry Laboratory in 2013 and 2014. The children were hospitalised in the following departments: medicine, orthopaedic and general surgery, oncology, neonatal, obstetric and intensive care. The study was approved by the Regional Ethical Review Board in Stockholm (Registration number: 2015/206-31/4).

Blood sampling

Blood samples were collected in vacuum tubes and microtainers using capillary, venous and arterial sampling methods. The samples were sent to the laboratory in a mailing tube system and, after their arrival, they were sorted by a robot to different sections of the laboratory. The biomedical scientific staff then distributed the specimens to the correct machines. The samples were analysed in six laboratories within the Stockholm County Council area. Samples were taken and analysed 24 hours per day. The sampling time points were categorised as follows: day shift (7.01am–3.00 pm), evening shift (3.01 pm–9.30 pm) and night shift (9.31 pm–7.00am). Information about all analysed blood samples and PAEs was derived from the hospital's FlexLab laboratory information system (FlexLab™; Tieto, Helsingfors, Finland).

Assessment of PAEs

The vacuum tubes were automatically loaded on to the automated machines that detected PAEs in the haematology, coagulation and chemistry laboratory sections. The different instruments provided alerts for clots, haemolyses or incorrect filling, and the laboratory personnel reported the errors in the patients' journals using the laboratory's information system. The microtainer samples were manually loaded onto the instruments by personnel to detect errors. The laboratories used included the Karolinska University Hospital and all complied with the ISO standard 15189:2012.

Table 1 outlines the types of PAEs listed according to the QIs presented by the International Federation of Clinical Chemistry and Laboratory Medicine (9). However, contaminated samples were not reported to the laboratory information system, nor were structured information about the PAEs from the transfusion and microbiology laboratories. As a result, they were not included in the analysis. In addition, all 51 870 nonblood specimens were excluded from the analysis.

Data and statistical analysis

Descriptive statistics using Stata/14MP (StataCorp LLC, College Station, TX, USA) were used to analyse the data. The data were calculated as numbers and percentages with a 95% confidence interval (95% CI). The differences in PAEs in the various years, specialities and work shifts were analysed using chi-square tests, and p values of <0.05 rejected the null hypothesis of no significant difference.

We used the Six Sigma method to measure the quality performance of blood sampling in the preanalytical phase, where we calculated DPM (6). Like previous studies, we converted the DPM rate to a Six Sigma score based on standard tables available online at westgard.com, to enable us to carry out the quality control of the preanalytical process in comparison with the existing literature (3,10,11). The Six Sigma metric corresponds to the following levels of quality control: a 3.0 sigma or less is unacceptable, a 3.0–4.0 sigma is acceptable, a 4.0–5.0 sigma is good, and a sigma value of 5.0 or above is very good (11).

RESULTS

The frequency of PAEs was 61 656 (5.4%) of the 1 148 716 blood analyses that were taken in tertiary paediatric care in 2013 and 2014 (Table 2). In 2013, the PAE rate was 5.6%, which decreased to 5.2% the following year ($p < 0.001$). The different paediatric specialities had a wide range of rejected samples, from 1.9% in oncology to 9.4% in the obstetric clinic. The PAE rate was higher in the blood specimens taken during the day shift (6.0%) and decreased by the evening shift (5.7%) and night shift (4.3%; Table 2).

Table 1 List of preanalytical errors at the Karolinska University Hospital Laboratory, harmonised with quality indicators using the International Federation of Clinical Chemistry and Laboratory Medicine Model

Types of PAEs at Karolinska University Hospital	Explanation	Quality indicator
Unmarked sample Wrong patient	Misidentified samples Misidentified patients Unlabelled samples	Misidentification error
Wrong analyses Not calculated*	Requests with erroneous data entry (test name, missed test, added test)	Test transcription error
Unfilled sample Wrong collection method	Inappropriate sample – anticoagulant volume ratio with insufficient sample volume	Incorrect fill level
Wrong tubes Not executed	Wrong container Inappropriate sample type	Incorrect sample type
Haemolysed analyses		Haemolysed error
Clotted sample		Clotted error
Damaged sample Old sample Missing sample	Damaged during transportation under inappropriate temperature conditions and, or, time. Lost, as not received Not properly stored	Unsuitable sample for transportation and storage

PAE = Preanalytical errors.
*The request for added tests was not handled by the laboratory due to erroneous data entry.

Table 2 Prevalence of blood samples and preanalytical errors at Astrid Lindgren Children's Hospital

	Number of blood analyses	Number of preanalytical errors		
	n	n	%	95% CI
Year:				
2013	564 408	31 390	5.6	5.5–5.6
2014	584 308	30 266	5.2	5.1–5.2
Total	1 148 716	61 656	5.4	5.3–5.4
Speciality:				
Medicine	207 796	12 543	6.0	5.9–6.1
Surgical and orthopaedic	69 115	5685	8.2	8.0–8.4
Oncology	150 829	2900	1.9	1.9–2.0
Emergency department	345 977	20 849	6.0	5.9–6.1
Intensive care	214 649	6767	3.1	3.1–3.2
Obstetric	641	60	9.4	7.2–11.9
Advanced homecare	12 329	677	5.5	5.1–5.9
Neonatal	147 380	12 175	8.3	8.1–8.4
Sampling hours:				
Day shift	495 542	29 667	6.0	5.9–6.1
Evening shift	267 315	15 301	5.7	5.6–5.8
Night shift	385 859	16 688	4.3	4.3–4.4

Table 3 shows that clotting was the most common type of PAE in 2013 and 2014 (51.3%), followed by incorrectly filled samples (23.3%). The PAE rate of incorrect filling decreased from 25.9 to 20.7%, ($p < 0.001$) in 2014, while the frequency of haemolysed analyses increased. Unsuitable samples for transportation and storage problems corresponded to 13.7%, and the majority of PAEs in this category pertained to samples that never arrived at the laboratory (12.2%). The error rate due to haemolysed samples was 8.0% and misidentification accounted for 0.57% and test transcription errors represented for 0.24%.

Six Sigma scores were applied to quantify the quality of the preanalytical process in relation to specific QIs. The total score for overall paediatric tertiary care was 3.2 (acceptable), and the lowest and highest scores of 3.5 and 5.2 were due to clotted samples and test transcription errors, respectively (Table 3).

The rate of PAEs among the blood analyses that were tested more frequently than 1000 times during the study period is shown in Table 4. A PAE frequency of over 10% was found in the capillary analyses of erythrocyte sedimentation rate (16.3%) and prothrombin complex-international normalised ratio (26.7%) and by venous analyses of the erythrocyte sedimentation rate (19.6%), glucose (13.5%) and lactate dehydrogenase (10.9%), as shown in Table 4.

Figure 1 demonstrates that the errors among the analyses of haematology and coagulation were mostly clotted, at 72 and 28%, respectively. Incorrect filling was equally distributed among all the laboratory sections. PAEs within chemistry analyses were affected by haemolyses (39%) and incorrect filling (35%; Fig. 1).

DISCUSSION

According to our analysis of more than one million blood samples, PAEs were a common occurrence and they were distributed differently within specialities, working shifts and types of analyses. The errors mostly occurred due to clots and the incorrect filling of the blood, which affected haematology, coagulation and chemistry analysis. The quantified functionality of paediatric blood sampling and the overall preanalytical process were estimated by the Six Sigma score to be at a barely acceptable level.

The year 2014 showed a significantly lower PAE rate than 2013. The PAE of incorrectly filled test tubes was the only specific QI that significantly decreased between the two years, and it only decreased in haematology analyses. A new ethylenediaminetetraacetic acid microtainer tube was introduced in 2014 with more easily distinguished markers for filling with the required volumes. This made it easier for staff to handle and fill containers to the acceptable levels.

Surgical, orthopaedic, obstetric and neonatal specialties had the highest rates of PAEs, while oncology and intensive care specialities showed very low rates of PAEs. The latter often collect blood samples by drawing blood from central

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Table 3 Preanalytical errors in blood specimens according to the Six Sigma metric score and harmonised with quality indicators at Astrid Lindgren Children's Hospital during 2013 and 2014

Quality indicators of PAEs	Year	Number of preanalytical errors	% of all PAEs (95% confidence interval)	DPM	Sigma metric score*
Clotted errors	2013	15 896	50.6 (50.1–51.2)	28 164	3.5
	2014	15 709	51.9 (51.3–52.5)	26 885	3.5
	Total	31 605	51.3 (50.9–51.7)	27 513	3.5
Incorrectly filled level	2013	8122	25.9 (25.4–26.4)	14 390	3.7
	2014	6267	20.7 (20.3–21.2)	10 726	3.8
	Total	14 389	23.3 (23.0–23.7)	12 526	3.8
Unsuitable for transportation and storage	2013	4210	13.4 (13.0–13.8)	7459	4.0
	2014	4233	14.0 (13.6–14.4)	7244	4.0
	Total	8443	13.7 (13.4–14.0)	7350	4.0
Haemolysed errors	2013	2114	6.7 (6.5–7.0)	3746	4.2
	2014	2834	9.4 (9.0–9.7)	4850	4.1
	Total	4948	8.0 (7.8–8.2)	4307	4.2
Incorrect sample type	2013	830	2.6 (2.5–2.8)	1471	4.5
	2014	941	3.1 (2.9–3.3)	1610	4.5
	Total	1771	2.9 (2.7–3.0)	1542	4.5
Misidentification errors	2013	152	0.48 (0.41–0.57)	269	5.0
	2014	198	0.65 (0.57–0.75)	339	4.9
	Total	350	0.57 (0.51–0.63)	305	5.0
Test transcription errors	2013	66	0.21 (0.16–0.27)	117	5.2
	2014	84	0.28 (0.22–0.34)	144	5.2
	Total	150	0.24 (0.21–0.29)	131	5.2
Sum of all PAE indicators	2013	31 390	5.6 (5.5–5.6)	55 616	3.1
	2014	30 266	5.2 (5.1–5.2)	51 798	3.2
	Total	61 656	5.4 (5.3–5.4)	53 674	3.2

DPM = Defects per million; PAE = Preanalytical errors.
*Very good: ≥5.0 sigma; Good: 4.0–4.9 sigma; Acceptable: 3.0–3.9 sigma; Unacceptable: <3.0 sigma.

venous lines, which may suggest that PAEs decrease with this method.

The reason for the significant differences in PAE rates during working hours may be because more experienced staff work during the night shift. This indicates that educational level and work experience have an impact on PAEs but more research is needed into this. Another reason for PAE differences during working hours could be that mornings are probably a stressful time for nurses and laboratory staff to handle all the requested samples. Organising the samples according to staffing, and also spreading the collection more evenly during the hours of the day, could have an effect on PAEs.

The most common PAEs were clotted samples and insufficiently filled sample tubes, which together accounted for three-quarters of all PAEs. Clotted and incorrectly filled samples are strongly related to the preanalytical process and can probably be avoided with simple preparations, such as preparing the puncture site by warming it and mentally preparing the child and parents (12). To avoid clots, mixing blood samples correctly is important (13). In contrast to other analytical phases, the preanalytical phase is mainly a set of different manual processes and includes personnel competence with variations in education level and skills (14). Misidentification errors were low in our study, showing a high Six Sigma score. This QI is probably underestimated in the retrieved database, because when laboratories receive unlabelled samples, the samples cannot be registered in the system. It might be more appropriate to investigate this QI using observational methods (15).

The high frequency of PAEs in clotted samples and incorrectly filled samples may be due to the frequent use of capillary sampling in our hospital. Capillary sampling is considered an easy and quick method, but it would be valuable to investigate whether an increased use of venous samples could reduce the number of PAEs. Not all analyses in our study were labelled as capillary in the laboratory information system, but those that were labelled had high PAE frequency. This indicates that venous sampling is a more reliable method in paediatric hospital-based care, but more research is needed to prove this. Incorrectly filled samples were the second most common reason for PAEs in this study, which demonstrates the difficulties of receiving the correct amount of blood for analyses of children. On the other hand, the risk of anaemia is present if too much blood is collected and discharged through venous sampling (16). This can make it difficult for health personnel to balance those two factors.

The frequency of PAEs among the analyses in this study was highest for erythrocyte sedimentation rate and glucose. For the glucose analysis, a high frequency of QIs was unsuitable due to transport and storage problems, which in this case led to the sample not being received by the

Table 4 The rate of PAEs among the blood analyses that were tested more frequently than 1000 times during the study period, at Astrid Lindgren Children's Hospital

	No. of PAE	Total N	No. of PAE%
Haematology (EDTA tube)			
B-Leucocytes	4928	73 512	6.7
B-Neutrophil granulocytes	3028	45 077	6.7
B-Basophile granulocytes	1335	22 128	6.0
B-Eosinophilia-leukaemic	1335	22 128	6.0
B-Lymphocytes	1335	22 128	6.0
B-Monocytes	1335	22 127	6.0
B-Metamyelocytes	44	1434	3.1
B-Myelocytes	44	1336	3.3
B-Erythrocytes	3310	56 552	5.9
B-Reticulocytes	322	3649	8.8
B-Haemoglobin	4932	73 953	6.7
B-Erythrocyte volume fraction EVF	4781	69 869	6.8
Erc(B)-Mean corpuscular haemoglobin (MCH)	3304	56 263	5.9
Erc(B)-Mean corpuscular volume (MCV)	3304	56 152	5.9
Erc(B)-Mean corpuscular haemoglobin concentration (MCHC)	3303	56 120	5.9
B-Thrombocytes	4855	72 338	6.7
B-Erythrocyte sedimentation rate (ESR)	453	2379	19.0
kB-ESR (Micro), capillary	301	1849	16.3
B-Standard bicarbonate	100	1479	6.8
Coagulation (Sodium citrate tube)			
P-Prothrombin complex INR	1074	15 920	6.7
P-Activated partial thromboplastin time (APTT)	676	13 156	5.1
P-Fibrinogen	400	9393	4.3
P-Fibrin D-dimer	343	8643	4.0
P-Antithrombin	297	8184	3.6
kB-Prothrombin complex (INR), capillary	323	1211	26.7
General chemistry/immunochemistry/miscellaneous (FC-mixture tube, lithium heparin tubes, sodium fluoride/K-oxalate tube)			
P-C-reactive protein (CRP)	1311	51 408	2.6
P-Creatinine	550	39 205	1.4
P-Sodium	526	29 139	1.8
P-Potassium	936	29 087	3.2
P-Albumin	380	24 558	1.5
P-Bilirubin	998	23 409	4.3
P-Alanine aminotransferase (ALT)	461	22 539	2.0
P-Aspartate aminotransferase (AST)	1134	21 825	5.2
P-Phosphate	448	18 082	2.5
P-Magnesium	580	16 780	3.5
P-Calcium	254	15 825	1.6
P-Bilirubin conjugated	1084	15 029	7.2
P-Urea	267	14 883	1.8
P-Gamma glutamyl transferase	363	9607	3.8
P-Lactate dehydrogenase (LD)	928	8544	10.9
fP-Triglyceride	109	4385	2.5
P-Chloride	153	3844	4.0
P-Uric acid	55	3697	1.5
P-Fibrin, loose	37	3635	1.0
P-Alkaline phosphatase (ALP)	46	3614	1.3
P-Glucose	438	3239	13.5
P-Troponin T	266	2896	9.2
P-Pancreas amylase	50	2692	1.9
P-Cystatine C	30	2232	1.3
P-NT-proBNP	55	1422	3.9
P-Myoglobin	26	1394	1.9
P-Amylase	49	1291	3.8
P-Haptoglobin	28	1233	2.3
P-Lactate	120	1225	9.8
P-Lead	82	1100	7.5
P-Methotrexate	3	1497	0.2
S-Procalcitonin	154	9079	1.7
S-Ferritin (Dxl)	148	2367	6.3
S-Osmolality	14	1064	1.3

B = Whole blood; fP = Lenten plasma sample; kB = Capillary; P = Plasma; PAE = Preanalytical errors; S = Serum.

laboratory. The analysis of glucose was requested and sent in the electronic journal system, but the sample was never sent to the laboratory. The reason for this might be that the wards use glucose meters to measure blood sugar. A more standardised method of using a new request system has shown significant results for minimising these PAEs (17). Although we did not get high PAE results in the coagulation tests, a study conducted in Italy reported almost twice the amount. The PAE rate was 10.1% in their paediatric department, and 60% of those PAEs were related to clotting (8). Compared to our PAE frequency of 5.4%, clotting represented only 30% of PAEs and incorrect filling represented 42%.

Plebani et al. reported QIs based on sigma scores from laboratories worldwide. Compared with the results in their study, our QIs had lower sigma scores for clotted and incorrect fill levels, which indicates a higher rejection of blood samples in paediatric tertiary hospitals (5). Our total sigma score of 3.2 was somewhat lower than that reported by Salinas et al. (18), but can probably be explained by the fact that only children, including neonates, and adolescents were included in our study. The QIs of clotted and incorrectly filled samples had sigma scores of 3.5 and 3.8, respectively, which indicates that these QIs were at a minimum acceptable range. This helps us to target the factors that affect the total preanalytical process. A five-year study from Spain presented a sigma score of 3.7 for clotted samples and 4.2 for insufficiently filled samples. This study also showed a remarkably low sigma score of 2.9 for haemolysed samples (3). It has been reported that, when a large number of tests are conducting using the Six Sigma method, even small rates of error can cause an unacceptably large number of errors and lead to severe adverse events (7,10). As modern laboratories test large numbers of samples, this can be an issue.

Several studies have reported different practical interventions for reducing PAEs, such as introducing a

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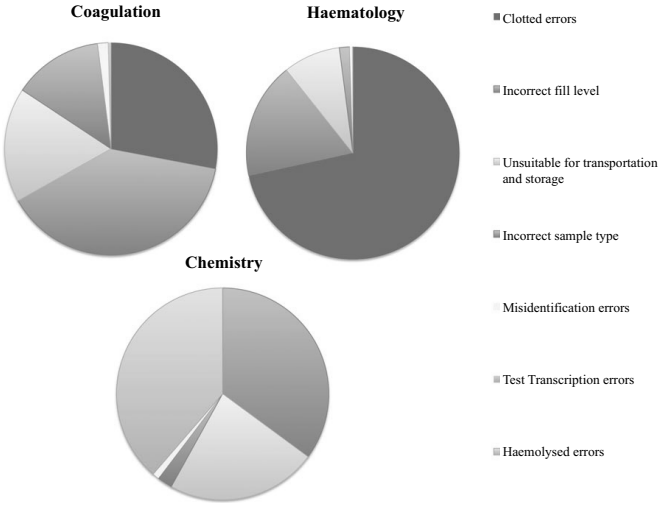

Figure 1 Preanalytical errors distributed by the analyses of haematology, coagulation and chemistry.

collection module and introducing educational training programmes for staff. These interventions have had effects on reducing PAEs in the studied departments (17,19,20). Dorotic et al. investigated whether nurses were aware of PAEs, such as haemolysis, and found that many of them lack knowledge on the causes of PAEs and the impact that PAEs have on laboratory test results (21). Staff who do not follow guidelines could also have a lack of experience and competence, as well as stress. High personnel turnover, and a lack of structured education, may harm the quality of the collected blood samples (22). Repeated blood sampling is stressful and can be traumatising for children and their families. It is also clear that blood sample collection is a more complicated procedure for children than adults. The procedure requires extra attention so that good patient care and good quality blood sampling can be achieved (23,24). Repeated sampling is also time-consuming and costly for healthcare providers (25).

One limitation of this study was that data were lacking in the laboratory information system on the number of blood specimens that were collected using arterial, capillary and venous blood sampling. There was also missing information about how many PAEs from blood samples were taken from central venous lines, and this could have created false lows or highs due to a poor flush technique. For example, if drugs or other residues are left in the central venous line, they can affect a blood sample without creating clotting or haemolysis. A strength of this study was the large number of observations, of over one million, collected during the long two-year study. To our knowledge, this is the first study in this area that has just focused on paediatric patients.

Implementing these findings in paediatric health care may help us understand the problems caused by commonly occurring PAEs. Using quality control management, such as the Six Sigma metric, can help us identify the QIs in the preanalytical phase that needs to be improved. More research is needed to improve the quality of the preanalytical phase and to improve paediatric patient safety.

CONCLUSION

This study determined that the prevalence of PAEs during blood sample analyses was common in tertiary paediatric care in Sweden. The prevalence of PAEs varied between years, hospital specialities, work shift times and different analysis types. Haematology, coagulation and chemistry analyses were commonly affected by PAEs, mostly due to clots (51.3%) and incorrect filling (23.3%). The Six Sigma score for the total preanalytic process was 3.2, which was a barely acceptable level and indicates the need for improvement. Our results should encourage healthcare providers and laboratory personnel to work together to reduce the number of PAEs by focusing on learning improved methods of blood sampling. This study turns the spotlight on to patient safety and minimising repeated blood sampling procedures, which are painful and stressful events for children in paediatric health care.

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CONFLICT OF INTERESTS

The authors have no conflict of interests to declare.

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ORIGINAL ARTICLE

WILEY

Capillary blood sampling increases the risk of preanalytical errors in pediatric hospital care: Observational clinical study

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Abstract

Purpose: The blood sampling procedure is complex and prone to failure, as reflected by preanalytical errors in pediatric hospital care. The primary aim was to evaluate if the risk of preanalytical errors was higher with capillary blood sampling than with venous blood sampling, and secondary, explore specific factors associated with preanalytical errors, both overall and stratified by capillary and venous blood sampling.

Design and Methods: This observational pediatric hospital study collected outcomes from medical records and blood sampling surveys from year 2014 to 2016. The risk of preanalytical errors was analyzed with adjusted-odds ratio (adj-OR) by multivariable logistic regression with 95% confidence intervals (CIs).

Results: Overall, 128 (13%) preanalytical errors were identified among 951 blood samples. The proportion and adj-OR of errors was significantly higher in capillary compared with venous blood samples, 72 (20%) of 354 versus 56 (9.4%) of 597, $p = .001$, adj-OR 2.88 (CI 1.79–4.64). Blood collection with multiple sample tubes was significantly associated with increased risk of preanalytical errors ($n = 97$ of 601, 16%), while log weight (kg) significantly decreased the risk of preanalytical errors adj-OR 0.66 (CI 0.50–0.86), indicating a protective effect of increasing weight. However, stratified analyses indicated a protective effect of increasing log weight for venous blood sampling adj-OR 0.52 (CI 0.38–0.72), but not capillary blood sampling, adj-OR 1.08 (CI 0.76–1.55).

Conclusion: This study indicates that capillary blood sampling collection increases the risk of preanalytical errors. Further, a child's increasing body weight reduced the risk of preanalytical errors, while multiple sample tube collections significantly increased the risk of preanalytical errors.

Practice Implications: This new information may help nurses improve their knowledge concerning blood sampling collection in pediatrics. Altogether, this study also indicates that implementing more venous blood sampling and improve the cases of capillary sampling could reduce the number of preanalytical errors in pediatric hospitals.

KEYWORDS
blood sampling collection, capillary blood sampling, children, nursing, pediatric hospital care, preanalytical errors, risk factors, venous blood sampling

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1 | INTRODUCTION

Blood sampling is one of the most common diagnostic methods for the treatment and assessment of pediatric diseases and conditions (Plebani, 2006). In addition, children may find blood sampling to be the most anxiety-causing procedure experienced during their hospital stay (Hands et al., 2010). The success of blood sampling strongly depends on the technical, psychological, and pedagogical skills of the nurses and laboratory assistants and knowledge of preanalytical pitfalls and guidelines (Harnik & Moreiras, 2014).

This study was executed in a pediatric tertiary hospital in Sweden, but the results may be of interest to nurses and other professionals working with blood sampling collection in other countries.

1.1 | Background

The process of the total laboratory testing can be defined according to the preanalytical, analytical, and postanalytical phases. The preanalytical phase involves submitting electronic requests for the analyses, preparing the patient, sampling the blood, and delivering the samples to the laboratory. Errors in the preanalytical phase account for approximately 60%–70% of all blood sampling errors (Carraro & Plebani, 2007; Lippi et al., 2011). Preanalytical errors (PAE) often lead to rejected samples due to clotting, hemolysis, and unfilled tubes (Lippi et al., 2011). Regarding PAE and associated factors including patient characteristics of age, body weight, underlying medical condition, and nurse and phlebotomist academic education are not well established. In general, avoiding PAE is crucial for sustaining blood sample quality and preventing effects on lab results that will lead to wrong diagnoses and treatments, stressful recollection, as well as economic burdens for hospitals and society (Green, 2013; Lippi et al., 2018).

Previous studies, not stratified to adults and children, have shown that hemolysis is the most common cause of blood sample error (Simundic et al., 2010, 2019). Two-fold higher rates of PAE were reported in pediatric wards compared with adult wards (Salvagno et al., 2008). Collection using capillary blood sampling (CBS) seems particularly problematic in neonatal units due to a high rejection rate of clotting and hemolysis (Phillips et al., 2011). CBS is accomplished by puncturing a finger, heel, toe, or earlobe (Krleza et al., 2015). Intuitively, CBS is a quick and easy method of choice; however, it cannot be recommended for sampling blood volumes larger than 1 ml (Folk, 2007). The success of CBS depends on securing the blood flow and circulation, usually by warming the puncture area (Becht & Anderson, 1996). We have published data from a laboratory register and found high numbers of PAE, mainly related to clotting, in Swedish pediatric hospitals (Hjelmgren et al., 2019). While the register lacks detailed information of methods used for blood sample collection, we decided to test our hypothesis that clotting errors are associated with CBS due to low blood flow and volumes. Therefore, we designed a clinical investigation comparing PAE between capillary- and venous blood sampling (VBS), as well as in detail evaluate factors affecting the risk of PAE in children treated inward for medical conditions.

1.2 | The study

1.2.1 | Aims

The primary aim of this study was to evaluate if the risk of PAE was higher with CBS compared with VBS, and secondary, explore specific factors with influence on PAE, both overall and stratified by CBS and VBS in pediatric hospital care.

2 | METHODS

2.1 | Study design

This was an open clinical observation study that prospectively combined information on blood sampling from a health professional survey with information of the main outcome of PAE from the medical record.

2.2 | Participants

The study population consisted of all available children with complete information on blood sampling during hospital stays in two pediatric emergency wards in Stockholm Sweden, from January 27, 2014 to October 1, 2016.

2.3 | Data collection and analysis

While VBS and CBS were routinely collected by nurses with bachelor's or master's degrees, CBS could regularly be taken by nurse assistants. VBS was retrieved using Microtainer (0.5 ml) or regularly vacuum tubes (4 ml max volume), while CBS was retrieved only by Microtainers. Data regarding blood sampling were retrieved from healthcare professionals who had filled in a survey when the sample was collected. The survey contained information about sampling methods, the sampler's professional academic level, and the puncture location, needle size, and a number of punctures. The information from each survey was used to collect information about each child's age, gender, weight, diagnosis/symptoms, PAE, and number of tubes in the electronic medical record (Take Care™ system). All blood samples analyzed at Astrid Lindgren's Children's Hospital are registered in the medical record by the Karolinska University Hospital Laboratory, which complies with ISO standard 15189:2012.

In total, 9500 unique children (ward 1: 4866 and ward 2: 4634) at Astrid Lindgren's Children's Hospital were treated during the study period, according to data extracted from the hospital information register. The wards treated children aged 0–18 years within general pediatric medicine for approximately 2–3 days, mostly for infectious diseases. Regarding the external validity, the annual number of blood samples collected during the year 2014 was 11,590 at Astrid Lindgren's Children's Hospital. Based on data from 2014 and lack of annual

data from 2016 to 2017, we estimate that approximately 32,000 blood samples were collected during the study period.

2.4 | Definition of outcomes

The primary outcome PAE was defined by the laboratory due to any of the following specific types of errors: clotting, hemolysis, incorrect filling level, missing sample, or erroneously labeled sample tube as described elsewhere (Hjelmgren et al., 2019). Uncommon PAE represented in the study were defined as "other," and included damaged samples, samples with thrombocyte aggregation, and sample analyses that were not executed. VBS was defined as a blood sample obtained from a vein by a blood collection system (Becton Dickson [BD] Vacutainer®, butterfly collection set, open needle, or a direct draw from a peripheral intravenous catheter [PVC], or central venous line [CVL]). CBS was defined as a blood sample obtained through a finger (BD Microtainer®, contact-activated lancet) or heel (BD Quickheel™). The BD Microtainers sample tubes were used to collect CBS. The child's medical condition was classified based on a review of the medical record and defined accordingly as fever, respiratory, gastroenteritis, oncology, surgical, and other (i.e., pain, infectious disease, possible renal and liver diseases, neurological diseases, metabolic diseases, skin disorders, and eating disorders).

2.5 | Statistics

Power estimation was based on analysis of 708 collected blood samples, with a PAE rate of 20% in CBS and 9% in VBS. Attainment of 80% power for detecting a statistically significant difference between CBS and VBS in risk of PAE at a 5% significance level required at least 160 CBS and 160 VBS. The data from the surveys and medical records were compiled in a Microsoft Excel spreadsheet, and the patient identification number was replaced and coded in the statistical data analysis using STATA MP14 (StataCorp LLC). Proportions of children in different categories, for example, female, male, were calculated separately for CBS and VBS, including 95% confidence intervals (CIs). The distribution of weight was evaluated with a histogram and transformed using the natural logarithm (ln) to limit the influence of outliers and provide a better fit for the regression models.

Mixed-effects logistic regression was used with PAE as an outcome variable, with a random intercept per patient, to take into account the dependencies of samples from the same patient. p values of less than .05 were considered to allow for rejection of the null hypothesis of no significant difference. Differences between CBS and VBS in odds ratios (OR) or adjusted OR (adj-OR), adjusting for weight and number of collected tubes, were evaluated by adding an interaction term between the puncture type and the variable of interest (i.e., weight and number of tubes). Weight and age were both closely associated with PAE. To avoid overadjustment in the multivariable model, only weight, the variable showing the strongest correlation with PAE, was included in the model. Since the linearity assumption of the association between weight (kg) and log-odds was violated, the shape of the association between weight (kg) and the probability of PAE was investigated by fitting logistic regression models, with weight transformed using restricted cubic splines (RCS) with four knots, separately for CBS and VBS. RCS is a method for relaxing the linearity assumption in regression models, thereby enabling alternative shapes of the association between an explanatory variable and an outcome variable. The function *rcspline.plot* in the R package *rms* in R version 3.6.0 was used (Harrell, 2019).

2.6 | Ethical considerations

The study was approved by the Regional Ethical Review Board in Stockholm (Registration number: 2015/206-31/4). Independently of this study, all blood sampling was performed due to child's health condition.

3 | RESULTS

A sample of 1020 surveys was collected with information about blood collection during the study period. Of these 1020 surveys, 69 contained incomplete information due to duplications, missing information, and missing patient IDs. Among the final sample of 951 complete surveys were 645 unique patients identified. The discordant number of filled in surveys and patients was related to repeated blood sampling in some patients during the time of hospitalization.

Table S1 shows detailed information about the 951 blood sample collections across 354 (37%) CBS and 597 (63%) VBS. For laboratory tests requiring one sample tube, a significantly higher proportion was collected using CBS (51% [95% CI, 46–56]) than VBS (29% [95% CI, 25–32]), whereas the proportion of VBS samples was greater for laboratory analyses requiring three or more sample tubes. In children with fever, respiratory symptoms, or other medical conditions according to the study definition, was CBS used more frequently than VBS. Children with oncological conditions were less common in the CBS group. The ways that CBS and VBS were executed are described in Table S2.

The proportional distributions of categorized PAE across CBS and VBS are presented in Figure 1. The overall number of PAE was

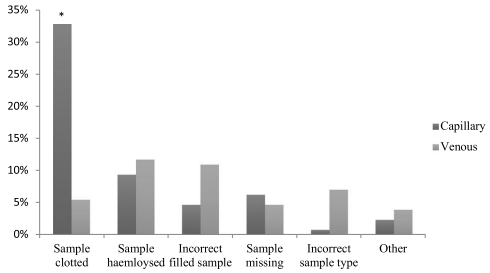

FIGURE 1 Proportional distribution of preanalytical errors (PAE) across capillary and venous blood sample collections. Of the 951 registered blood samples collected at two pediatric emergency wards, 128 were defined as PAE

128 (13%) of the 951 investigated blood samples. The most frequent cause of PAE was clotting, at 38% ($n = 49$), and the proportion was significantly higher in CBS (33%) than in VBS (5.5%) ($p < .001$).

Figure S1 provides proportions of PAE between CBS and VBS in age groups from neonates to adolescents.

Binary logistic regression analyses are presented in Table 1. The distribution of PAE was significantly higher in CBS compared with VBS (OR 2.56 [1.69–3.88]). Neither the study site nor the child's gender was statistically significantly associated with PAE. Toddlers and neonates had significantly higher PAE risk than adolescents. Weight less than 11 kg was another factor increasing the risk of PAE (OR 2.05 [1.35–3.10]). Blood sampling requests for two or more sample tubes compared with one tube were associated with PAE (OR: 2.14 [1.32–3.47]).

A multivariable logistic regression model showed that CBS and a requirement for two or more sample tubes significantly increased

TABLE 1 Univariable logistic regression analysis of factors associated with preanalytical blood sample errors, $n = 951$

	Blood samples	Preanalytical errors		Odds ratio
	n (%)	*n* (%)	*p* value	95% CI
Wards				
Ward 1	447 (47)	70 (16)	1	1
Ward 2	504 (53)	58 (12)	.070	0.69 (0.47–1.03)
Gender				
Boys	516 (54)	73 (14)	1	1
Girls	435 (46)	55 (13)	.503	0.87 (0.58–1.30)
Age				
Adolescents (10–18 years)	253 (27)	23 (9.1)	1	1
Childhoods (6–9 years)	166 (17)	21 (13)	.247	1.44 (0.77–2.71)
Pre-schoolers (3–5 years)	162 (17)	19 (12)	.386	1.32 (0.70–2.52)
Toddlers (1–2 years)	188 (20)	31 (16)	**.021**	1.97 (1.11–3.51)
Infants (3–11 months)	85 (8·9)	13 (15)	.113	1.81 (0.87–3.75)
Neonates (0–2 months)	97 (10)	21 (22)	**.002**	2.76 (1.45–5.3)
Weight				
≥ 11 kg	695 (73)	77 (11)	1	1
0–10 kg	256 (27)	51 (20)	**<.001**	2.05 (1.35–3.10)
Weight[a] (ln kg)			**<.001**	0.64 (0.51–0.82)
Blood sampling				
Venous	597 (63)	56 (9.4)	1	1
Capillary	354 (37)	72 (20)	**<.001**	2.56 (1.69–3.88)
- Capillary ward 1	221 (23)	49 (22)	**.001**	2.95 (1.58–5.52)
- Capillary ward 2	133 (14)	23 (17)	**.016**	2.01 (1.14–3.54)
Blood amount				
One tube	350 (37)	31 (8.9)	1	1
Two or more tubes	601 (63)	97 (16)	**.002**	2.14 (1.32–3.47)
Staff–academic level				
Nurse Assistant, capillary samples	130 (37)	29 (22)	1	1
Nurse Bachelor, capillary samples	152 (43)	31 (20)	.680	0.88 (0.49–1.60)
Nurse Master Degree, capillary samples	72 (20)	12 (17)	.353	0.70 (0.32–1.50)

Abbreviation: CI, confidence interval.

[a]Weight transformed by using the natural logarithm to limit the influence of outliers and better fit the regression models.

TABLE 2 Multivariable logistic regression analysis estimating adjusted odds ratios (adj-OR) of factors associated with PAE, *n* = 951

	Adj-OR (95% confidence interval)	Std. Err	*p* value
Capillary blood sampling	2.88 (1.79–4.64)	0.70	**<.001**
Weight in kg	0.66 (0.50–0.86)	0.09	**.002**
Two or more sample tubes	3.12 (1.84–5.31)	0.85	**<.001**

Note: The model analyzed independent factors that were significantly associated with PAE in the crude analysis: type of blood sampling collection (capillary vs. venous). Weight was treated as a continuous variable and transformed using the natural logarithm to limit the influence of outliers and to provide a better fit for the regression models. The number of collected blood sample tubes was analyzed as two or more versus one.

Abbreviation: PAE, preanalytical errors.

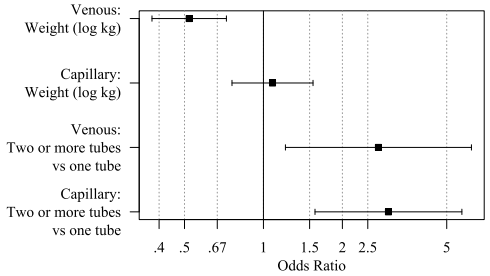

FIGURE 2 Odds ratios and 95% confidence intervals for preanalytical errors for increasing weight and number of blood tubes, for venous- and capillary blood sampling, respectively

the risk of PAE (adj-OR: 2.88 [1.79–4.64] and 3.12 [1.84–5.31], respectively) (Table 2). Weight, following natural logarithm transformation, significantly decreased the adj-OR of PAE (0.66 [0.50–0.86]), indicating a protective effect of increasing body weight.

Stratified analyses of VBS and CBS are shown in Figure 2. Increasing logarithmic weight is protective against PAE in the VBS group, but not in the CBS group (OR: 0.52 [0.38–0.72; *p* value < .0001] and OR: 1.08 [0.76–1.55; *p* value < .66], respectively, *p* value for interaction weight x type of blood sampling method 0.003). A requirement for two or more sample tubes increased the risk of PAE for both VBS and CBS groups (OR 2.74 [1.21–6.21, *p* value = .015] and OR 3.00 [1.57–5.71, *p* value = .001], respectively).

Figure 3 panel plot ABC describes the shape of the association between children's body weight and PAE probability. A high risk of PAE was strongly correlated with low body weight in the total sampling (Figure 3a) and VBS (Figure 3c), but not for CBS (Figure 3b).

4 | DISCUSSION

This pediatric study identified that the risk of PAE was significantly higher with CBS than with VBS. PAE was also associated with blood analysis requiring multiple sample tubes and low body weight. Furthermore, the use of body weight as a continuous variable, indicated that increases in the child's body weight reduced the risk of PAE in the VBS group but not in the CBS group. This study indicates that denser introduction of VBS may prevent clotting. The community of pediatric healthcare needs to improve the blood sampling procedure to achieve best clinical practice and secure patient safety.

In this study, clotting was the most frequent cause of PAE, consistent with other reports (Hjelmgren et al., 2019; Rooper et al., 2017; Salvagno et al., 2008). However, to the best of our knowledge, PAE have never been analyzed between CBS and VBS

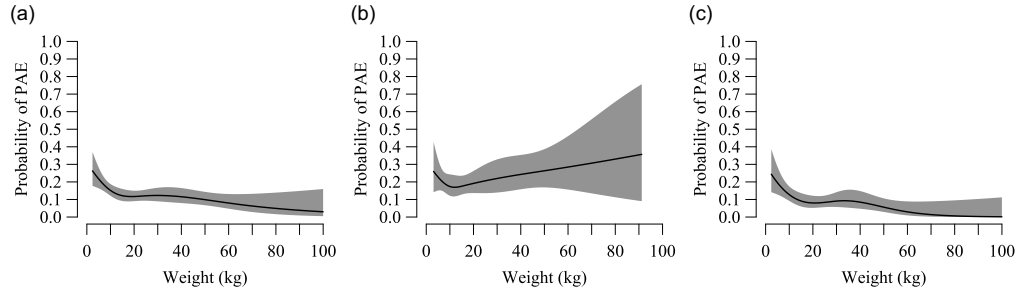

FIGURE 3 Association between weight (kg) and preanalytical errors probability of total samples (a), and stratified by capillary- (b), and venous blood sampling (c)

in a pediatric hospital context. Possible reasons reducing the apparent association between clotting and CBS is deletion of the first drop of blood, mixing of the sample during and after sampling, and gentle pressing of surrounding tissue are prerequisites for a capillary sample without clots and hemolysis. Healthcare professionals have previously been reported to have difficulties in complying with the guidelines in blood sampling procedures (Simundic et al., 2015). To improve the outcome of CBS in pediatric healthcare, the establishment of detailed guidelines, repeated clinical training programs supporting staff, and avoiding the risk factor of clotting will be important.

Low body weight in children has not previously been associated with PAE. Interestingly, the stratified analysis indicated that increasing weight was only protective in the VBS group. This finding highlight implementation of more VBS could reduce the events of PAE. The existing worldwide guidelines on blood sampling procedures have not noticed an increased risk of PAE in small children (CLSI, 2017; Simundic et al., 2018; World Health Organization, 2010). From a child's perspective, VBS appears to be less painful than CBS for neonates and well babies (Jewell et al., 2007; Shah & Ohlsson, 2011).

This study generated some novel findings by showing that PAE risk increases when the number of tubes in a blood sample increases from one to two or more. When stratified for both CBS and VBS, a tube number greater than one still remains a high risk; this has not been described before, to our knowledge. Healthcare professionals working in a pediatric context report that needle procedures are challenging (Kennedy et al., 2008) therefore, while sampling blood from children, extra arms are needed to change tubes and maintain a good procedure all the way through. A study from Canada demonstrated that nurses viewed the VBS process less time consuming, less painful for the infant, and an easier method for blood collection than CBS (Jewell et al., 2007). Even though VBS is considered a more advanced procedure than CBS, it is the gold standard. We, therefore, recommend that CBS be used sparingly in children visiting the hospital as this will allow obtaining of a good blood sample while considering sample quality, patient safety, and the wellbeing of the pediatric patient.

Our results also indicate the need of improving the CBS method in children. CBS in children, whether administered as a finger prick or a heel prick, requires that nurses have sufficient clinical skills, (World Health Organization, 2010). CBS should be approached with caution in pediatric hospital care; only small blood volumes can be recommended and CBS should not be used as first choice when the analyses require added anticoagulant. Immediately mixing of the blood with anticoagulant can prevent clotting (Krleza et al., 2015). A reason to ensure CBS is present is when repeated sampling is needed and to preserve iv-sight in sick neonates and infants (Coffin et al., 2002).

5 | LIMITATIONS

This study used a relatively large number of observations and was based on information from a laboratory register from two study sites. The results can be generalized in relation to other hospital-based pediatric contexts where both VBS and CBS are utilized. Based on our results, we plan to revise and implement local hospital guidelines focusing on staff education for avoiding clotting. Future research needs to assess the effect and feasibility of such intervention, and stratify the blood collection data for CBS and VBS, as well as stratify pediatric health care separately, as this may have a major influence on different rejection errors. The limitation of this study is that the size of the sample tube was not recorded, we cannot distinguish if Microtainers or venous sample tubes were used. The size of the sample tubes may influence the PAE.

6 | CONCLUSION

In this study, the risk of PAE was significantly higher with CBS compared with VBS. Associated risk factors were blood collection using multiple sample tubes and low body weight in children. This study indicates that PAE, such as clot can be avoided in pediatric healthcare by introducing more VBS.

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CONFLICT OF INTERESTS

The authors declare that there are no conflict of interests.

HOW MIGHT THIS INFORMATION AFFECT NURSING PRACTICE?

This study indicates that implementing more venous blood sampling instead of capillary sampling could reduce the number of preanalytical errors in pediatric hospitals.

DATA AVAILABILITY STATEMENT

Data sharing including nonpersonal data will be possible if Ethical Authority approves the sharing prior do delivery.

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SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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III

Title

Cost analysis of failed blood sample collections in tertiary paediatric hospital care

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Abstract

Background: Blood sampling is a common hospital procedure involving both laboratory and clinical disciplines, is important for the diagnosis and management of illnesses in children. Blood samples with pre-analytical errors (PAE) have been associated with high costs for hospital organisations providing adult health care. The overall costs of blood sampling following PAE have not been fully described for paediatric hospital care.

Aim: The aim of this study was to estimate the average cost of PAE, both annually and by 10,000 blood samplings in tertiary paediatric care.

Method: Combined information from the hospital's laboratory register year 2013-2014, and clinical observations at a tertiary children referral hospital, Astrid Lindgren Children's Hospital in Sweden, were used in a bottom-up cost analysis. The analysis hypothesised recollection of all failed blood samples, included costs of sampling materials, salary of health care personnel, laboratory analyses and inward hospital expenses.

Results: The annual cost of PAE was estimated to 84,000 € per 54,040 blood samples, which corresponded to 15,500 € per 10,000 samples or 1.5 € per each PAE. The personnel cost represented 65% of the cost due to PAE at 55,000 € per year followed by the hospitalization 19,000 € (22%), laboratory 6,000 € (7%) and material 4,300€ (5%).

Conclusion: This study address that the costs of failed blood samples is 84,000 € which represents about 5% of the annual blood sampling costs in tertiary paediatric hospitals.

Keywords: Cost analysis, pre-analytical errors, paediatric hospital care

1. Introduction

Blood sampling is important for the diagnosis and management of illnesses in children. It involves many stakeholders in both laboratory and clinical settings [1]. Therefore, blood sampling errors cause many problems for both patients and different health care workers, resulting in the need for repeated blood samples [2, 3]. From a laboratory perspective, the total testing process can be divided into three phases: the pre-analytical, analytical and post-analytical. About 70% of errors occur in the pre-analytical phase [4]. The pre-analytical phase errors (PAE) are defined by samples clotted or haemolyzed, incorrectly filled samples, incorrect sample types, test transcription errors, unsuitable samples for transportation, storage problems and misidentification errors [5]. PAE can lead to severe health issues, such as inappropriate treatment or even misdiagnosis, and delayed care [6-8]. There are evidence that improvements in blood sampling procedures would support quality and safety in healthcare services [9].

We have previously reported a considerable high prevalence of rejected laboratory blood analyses due to PAE, especially due to clotted and unfilled analyses, in a paediatric tertiary hospital [10]. For hospital organisations, all laboratory costs represent approximately 5% of the total budget, but the diagnostic importance is nevertheless extensive, as tests may influence about 60–70% of all medical decisions [11]. There are few studies describing the bottom-up cost of blood sample collections. Several studies have shown increased health care costs related to PAE using different data sources reflecting on personnel, material and analytical outcomes [12-14]. Furthermore, other variables, such as PAE cost in relation to a specific blood analysis [15], have been studied, but few have evaluated the costs of PAE in paediatric care.

Therefore, the aim of this study was to estimate the average cost of PAE, both annually and by 10,000 blood samplings in tertiary paediatric care.

2. Methods

2.1 Design and setting

This pragmatic bottom-up approach cost analysis study of annual blood test affected by PAE, combined information from the hospital's laboratory information system (FlexLab™), hospital economical information system (Tableau software©), hospital supply system (Medicarrier AB) and clinical observations. The study was performed at a tertiary paediatric hospital, Astrid Lindgren Children's Hospital in Stockholm, Sweden, with an available number of 129 beds in year 2019.-The hospital provides regional and national health care for children 0–18 years of age. Care provided includes various specialities of surgery, medicine, oncology, neonatology and intensive care, treating approximately 13,000 children yearly.

2.2 Use of resources related to blood sampling

To calculate an estimation of annual costs and by 10,000 samplings, due to PAE in paediatric blood sampling, a bottom-up approach was used. In the bottom-up approach the total cost generates by two steps. First step is to measure and quantify the health care inputs and the second step is to multiplicate the identified unit costs by the quantified resource use [16, 17]. This cost analysis included direct health care costs related to healthcare personnel, materials, laboratory analyses and hospitalisation. The direct costs are defined as the cost for medical care related to diagnosis, treatment [16]. The resource use included in the cost analysis are shown in Figure 1. In the analysis, it was assumed that PAE lead to a need for a recollected

sample and affect the costs in the total testing process derived in three phases (pre-analytical, analytical and post-analytical).

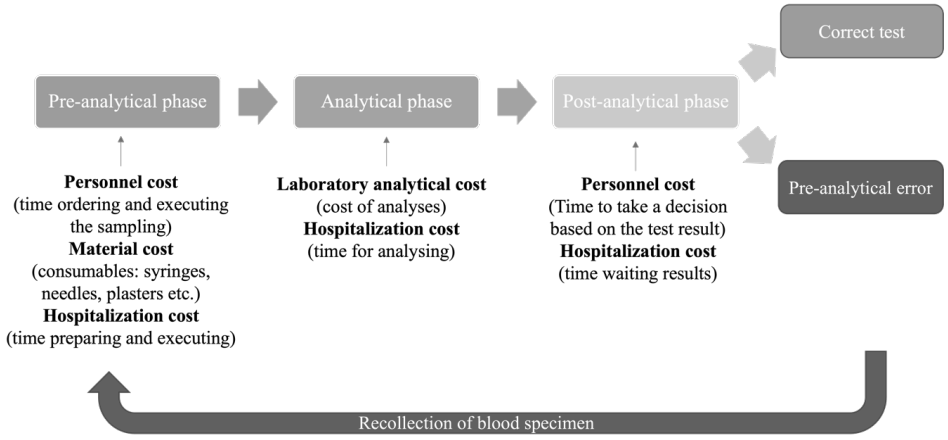

Figure 1: Outline of resources and costs related to blood specimen collection.

2.2.1 Personnel cost

The time health care personnel (medical doctors, nurses and nurse assistants) spend on blood sample collection was estimated by clinical observations in May 2021. The observations included timing the following procedures: ordering blood tests in the electronic health record; preparing the materials and the patient; collecting the blood samples, both capillary or venous; arranging the transport of the sample to the laboratory and making a new decision for repeated sampling when analysis results arrived. The allocated time for each procedure was documented in relation to each health care profession and multiplied by the average hourly salary. Data on average salary per hour for medical doctors, nurses and nurse assistants were gathered from the hospital's economic information system, Tableau software© (Table 1).

2.2.2 Material cost

Material use was estimated by clinical observations of one paediatric nurse with pre-specified knowledge concerning blood sample collection, and the materials used are described in Table 1. Unit costs for consumables were collected from the hospital supply system and price lists for the year 2020 (Medicarrier AB, Stockholm Sweden; Supplementary Table 1). An estimate of the average costs of different consumables related to blood sampling methods (venous and capillary) is stated in Table 1. The average material costs for capillary and venous sampling were calculated by using the observations of the proportions of the different sampling methods based on data from 951 blood collections [18].

2.2.3 Laboratory cost

At Karolinska University laboratory approximately 54 040 blood samples are received from Astrid Lindgren Children's Hospital and analysed at the laboratory sections of coagulation, haematology and chemistry analysing including around 570 000 blood analyses per year [10]. In the analytical phase, the study covered laboratory costs for the most common blood sample analyses in the biochemistry laboratory at Karolinska University Hospital, Sweden. The chargeable price of the analyses were collected from the hospital laboratory price list for 2019 (Supplementary Table 2). Rare and unusually expensive blood analyses were excluded from the cost analysis by only including blood analyses requested at least 1000 times per year in the cost analysis. The average analytical cost of blood samples was estimated by dividing the total cost for all blood analyses by the total number of blood analyses.

2.2.4 Hospitalisation cost

The resources used in relation to hospitalisation time for blood sampling were estimated by the time from start to end of all phases (Figure 1). A summary of the observational timesheet is presented in Supplementary Table 3. Costs for hospitalisation during blood sampling were

based on the hospitalisation costs of 112.7€ per patient and day (only including facilitating costs with a 2% overhead) from the general and neonatal wards and analysed from the hospital's economic information system (Tableau software©).

Table 1. The direct costs of personnel, material, laboratory analysis and hospitalisation for blood sample collection (venous and capillary)

Resource	Allocation per blood sampling*	Unit cost (Euro)	Total cost per blood sample (Euro)
Personnel costs			
Doctor	5 min	39.22/h	3.27
Registered nurse	30 min	22.77/h	11.39
Nurse assistant	15 min	16.63/h	4.16
Summary of personnel cost per sampling			**18.81**
Material costs			
Venous sampling by open needle	2.6%	4.17	0.11
Venous sampling by periphery vein catheter (PVC) draw when new insertion	11.3%	4.58	0.52
Venous sampling by PVC draw	23.7%	0.87	0.21
Venous sampling by butterfly needle	3.1%	4.07	0.13
Venous sampling by straight needle Vacutainer	1.6%	3.55	0.06
Venous sampling by drawing from central lines	20.6%	1.41	0.29
Capillary sampling by finger prick	35.3%	0.38	0.14
Capillary sampling by side of heel	1.89%	1.42	0.03
Summary of material cost per sampling			**1.46**

Laboratory average cost			
Analysis	1	2.06	**2.06**
Hospitalisation cost			
Paediatric wards	82.7 min	112.7	**6.42**
Total resources cost			**28.75€**

*refers to the frequency of different blood sampling methods and based on clinical surveys and observations[18].

2.3 Data analysis

Descriptive statistics were used to illustrate the different costs of the total testing process and in relation to PAE for the mentioned variables and outcomes. Information about the frequency of PAE was retrieved from the Karolinska University Hospital laboratory information system, FlexLab™ between 2013 and 2014 [10]. The PAE was defined as blood test being rejected by the laboratory due to such errors as haemolysis, clotting, unfilled or wrong tubes, missing samples and transportation errors [8]. The direct costs of personnel, material, laboratory analyses and hospitalisations were summarised and separately calculated (Table 1). The prevalence of PAE was set to 5.4% (5.6% in 2013 and 5.2% in 2014) [10]. A one-way sensitivity analysis was made to illustrate costs per 10,000 blood samples related to one percentage change in the frequency of PAE. The currency Swedish kronor was converted to the Euro at 1 SEK = 0.0945 EURO (€), 2019.

3. Ethical considerations

This study did not need any ethical approval, DNR 2021-00846 since no personal data were included, but the original study plan was approved by the Regional Ethical Review Board in Stockholm (original registration number, 2015/206-31/4).

4. Results

The analysis demonstrated that the annual estimated cost for a 5.4 % prevalence of PAE was 83,891€ or 1.55€ per each instance of PAE (Table 2). The personnel cost represented the highest cost at 54,891€ per year, hospitalisation was 18,735€, laboratory analysis was 6,011€ and materials was 4,261€ (Table 2).

The average cost per blood sample was 28.75€, divided by costs for personnel (18.8€), materials (1.5€), laboratory analysis (2.1€) and hospitalisation of the patient (6.4€; Table 2). Thus, annual average cost was approximately 1,500,000 € for 54,040 blood samplings, representing approximately 0.8% of our children's hospital budget of approximately 195,100,000€ for 2019 (Tableau software©).

Table 2. Average annual health care costs of blood specimen collection and obtaining test results in a tertiary paediatric hospital

Resources	**Cost per blood sampling**	**Annual cost per 54040 samplings**	**Cost due to PAE (frequency 5.4%*)**	**Cost proportion (%)**
Personnel cost	18.8€	1,016,492€	54,891€	65.4
Material cost	1.5€	78,898€	4,261€	5.1
Laboratory analytical cost	2.1€	111,322€	6,011€	7.2
Hospitalisation cost during blood sampling	6.4€	346,937€	18,735€	22.3
Total cost	**28.8**€	**1,553,650**€	**83,897**€	**100**

.*refers to the frequency of PAE based on Flexlab Data (2013-2014)

The PAE cost due to repeated samplings per 10 000 samples was estimated to be 15,541€, whereas the total cost was 287,787€ (Table 3).

Table 3. Average costs of 10,000 blood sample collections

Resources	**The cost per 10,000 samplings without PAE**	**Cost due to PAE (frequency 5,4%*) of 10,000 samplings**
Personnel cost	188,150€	10,160€
Material cost	14,648€	791€
Laboratory analytical cost	20,790€	1,123€
Hospitalisation cost during blood sampling	64,200€	3,467€
Total cost:	**287,787**€	**15,541**€

*refers to the frequency of PAE based on Flexlab Data (2013-2014)

Table 4 demonstrates the sensitivity analysis of costs related to each percentage change in the frequency of PAE. For each percentage change from the PAE frequency of 5.4% increases or decreases the cost with 2,878.9 € per 10,000 blood samples.

Table 4. Costs of one percentage change in the frequency of PAE per 10,000 blood samples.

Rate difference	**PAE frequency**	**Cost of PAE (10,000 samplings)**	**Cost difference**
- 1 %	4.4 %	12,662.6€	- 2,878.9 (↓ 18.5 %)
± 0	5.4%	15,541.5€	-
+ 1 %	6.4%	18,418.4€	+ 2,876.9€ (↑ 18.5 %)

5. Discussion

The aim of this study was to estimate the specific costs in relation to the recollection of blood samples due to PAE in a tertiary paediatric hospital. The direct costs for PAE at Astrid Lindgren Children's Hospital in Stockholm were annually 84,000€ per 54,040 blood samples at one year, or 15,500 € per 10,000 blood samples.

At Astrid Lindgren Children's Hospital the cost per blood sampling was 28.75€, with the highest cost being personnel costs (65% of the total costs) whereas the annual cost for blood sampling were approximately 1,500 000€. The annual average cost for PAE was substantial in relation to the total annual blood sampling cost. For instance, the average annual salary for two registered nurses in 2019 at Astrid Lindgren Children's Hospital may be calculated to 80,000€ (Tableau software). This study elucidated the importance of the awareness of PAE and the need for the right competence to avoid PAE among blood samples in paediatric tertiary care.

To our knowledge, the cost of PAE in a paediatric hospital has seldom been analysed separately from adult hospital laboratory analysis reports. We believe this is important, as the blood sampling procedure differs significantly between paediatric and from adult care in terms of locating veins, lower blood sampling volume, longer preparations and sometimes stressful situation for both the child and staff create unique circumstances [19-21].

Our estimated PAE costs, which were approximately 15,500€ per 10,000 samplings, were higher than those of an adult emergency department based in Italy [13] and a tertiary care hospital in Canada [15], which had a cost of around 1,174€ (2014) and 3,275€ (2013) per

10,000 samplings, respectively. However, it was lower than a German study from 2015 that estimated costs ranging from 34,000 to 61,000€ [12]. The study from Canada only investigated Coagulation INR-blood analysis, which could explain the low cost [15]. Interestingly, in Italy and Germany, the mean time for the nurses to execute an adult venepuncture was 2.5 and 10 min, respectively, which is very short in relation to paediatric samplings in our study, which was 30min for a nurse. Furthermore, the studies from Italy, Canada and Germany did not include the cost of doctors and nurse assistants which could result in higher cost in our paediatric sampling. Even though the above-mentioned studies excluded hospitalisation costs, we argue that hospitalisation costs are an important estimate that needs to be considered as PAE can affect delayed care and hospital stay. Overall, paediatric hospital care could also be more expensive than general hospital care due to more complex type healthcare [22].

In our cost analysis, we assumed that all PAE led to 100% recollection. Future research on how often recollection occur due to PAE in paediatric care is needed; the adult context has shown that 86.6% of PAE potentially leads to a repeated sample [2], meaning if this is similar in paediatric care, the associated PAE cost could be less than stated in our results. Sometimes in paediatric wards, recollections are not always executed to spare the children any additional punctures [23]. Contrary to some cases, it is necessary to repeat samplings more than once. Future research will have to evaluate the best practices and interventions for paediatric care and reduce the PAE and the number of recollections, thereby saving costs. The one-way sensitive analysis of this study illustrated that only 1 percent change on the frequency of PAE may affected the PAE cost per 10,000 blood samples by almost 19%. This indicates that small measures bringing down the frequency of PAE may have large impact on the overall costs.

5.1 Methodical discussion

This cost analysis study divided the expenses by personnel, materials and analytical direct costs, but adapted changes for the context of a paediatric hospital setting in a similar design as previous studies [12, 15, 24]. The effect of PAE on hospitalization costs could be questioned as a fixed expense with limited association to the frequency of PAE. In this study we argued that delayed blood test results due to PAE have substantial effects on the timing of children's hospitalization and that makes it relevant to consider as a part of the direct cost of the blood sampling. Furthermore, we could not estimate the unpredicted indirect cost of possible consequences of PAE such as treatments, blood transfusion, antibiotics, x-rays or rehabilitation. Green (2013) estimated that, annually, approximately 16,000 patient hours are lost due to PAE, leading to the redraw of samples and additional patient treatment with a ranged cost of 178–245€ per PAE [25], which is much higher compared to this study result of 1.5€ per PAE. In a Swedish paediatric hospital context, there is also sometimes a need for consulting anaesthesia nurses due to the difficulties of needle-related procedures, which could also lead to increased personnel costs. The long-term effects of children developing needle phobia due to excessive blood sampling also have potential costs on the societal level, as well as costs for when play therapists are needed for distraction and rehabilitation for post-traumatic experiences [26].

The included costs in the study were also only specified when specimens were sent to the biochemistry section of the laboratory. Other blood test analyses, such as microbiology, pathology, immunology and patient-near analysis, were not included which means PAE-related cost could be even higher if all laboratory sections receiving blood from paediatric patients were included.

Awareness' of the cost consequences, the management of the blood sampling process and related failed samples in pediatric care could lead to cost savings and increased quality care. The costs of PAE may be reduced by targeted interventions such as educational and technical solutions [24, 27, 28], which potentially could reduce costs and PAE in paediatric healthcare.The next step of future research should focus on evaluate the interventions involving multiple educational activities for reducing the costs of PAE and also increasing patient safety in paediatric hospital care.

7. Conclusion

This cost analysis study estimated blood sample recollection costs due to PAE, address substantial annual costs of 84,000€ or 15,500 € per 10,000 blood samples for tertiary paediatric hospital. Personnel costs represented the highest cost in relation to blood sampling procedures and PAE. Reducing PAE could yield significant cost reductions, not only in children's suffering and patient safety, but also in organisational costs.

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IV

Title

Nurses' experiences of blood sample collection from children: A qualitative study from Swedish paediatric hospital care

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Abstract

Background: Blood sampling collections are necessary and important for diagnosis and treatment in paediatric hospital care. Nurses play an active role in helping the children with the blood sampling experience. Unfortunately, the blood sampling collection procedure is often affected by pre-analytical errors, leading to consequences such as delayed diagnosis, treatment and hospital stay, as well as repeated sampling. Moreover, children state that needle procedures are the worst experience of their hospital stay. Nurses working in children's hospitals are responsible for conducting most of the needle related procedures but their experience of errors occurring during blood sample collection is unknown. The aim of this study therefore was to describe paediatric nurses' experiences of blood sampling collections from children.

Method: We used a qualitative study design with a (reflexive) thematic analysis (TA) method. Three focus group interviews were conducted, with 19 nurses from Sweden working at two different paediatric hospitals, focusing on their experiences of the blood sample collection procedure.

Results: From the three focus group interviews we analysed patterns and meanings of the following themes: *Paediatric blood sampling is a challenge for the nurses*, *Nurses' feelings of frustration with unsuccessful samplings*, *Nurses believe in team work*, *Venous blood sampling was experienced as the best option*, and *Nurses' thoughts and needs regarding skills development in paediatric blood sampling*.

Conclusion: The narrative results of this study illustrate that nurses working in paediatric hospital care face a big challenge in blood sampling collection from children.
The nurses felt frustrated due to unsuccessful blood samplings and frequently could not understand why pre-analytical errors occurred. Nevertheless, they felt strengthened by colleagues in their team and shared feelings of responsibility to help each other with this complex procedure.

The implications of this study are that paediatric hospital care needs to focus on improving guidelines for and increasing competence in blood sampling children and helping nurses to understand why samplings may be unsuccessful and how this can be avoided.

Key words: Nurses' experiences/ perspective, thematic analysis, focus group, blood sampling procedure, children

Background

Blood sampling collection is crucial to determining the correct diagnosis and providing children with treatment. Nurses on children's wards play an active role in helping the children with the experience and also in reducing potential adverse effects of sampling collection (1). The blood sample process can be divided into three phases: pre-analytical, analytical and post-analytical phases, where errors in pre-analytical phases represent up to 70% (2). The pre-analytical phase includes prescription of a blood sample test, preparation and execution of blood sample collection, as well as safe transportation of the blood sample to the laboratory where the analytical phase starts (3). Unfortunately, the pre-analytical phase in blood sampling collection from children has been found to be commonly affected by pre-analytical errors, which could risk patient safety and comfort (4). Possible consequences of pre-analytical errors are many: delayed treatment, wrong diagnosis, repeated sampling and increased costs (5-7). The literature states that the most common pre-analytical errors are haemolysed sample, unfilled or inappropriate sample, clotted sample, wrong container, patient identification or transport problems (8). Inside Swedish paediatric hospitals, blood sampling is mainly performed by nurses without support from laboratory personnel (9). Blood sampling collection from children is a difficult and complex procedure, meaning that the procedure requires the hospital staff to receive special training and pay extra attention in order to achieve good patient care and good quality blood sampling (10, 11).

Hospitalized children list blood sampling and needle procedures as one of the worst experiences of their hospital stay (12, 13). They have difficulties complying with blood sampling collection because it often leads to pain and stressful situations (11, 14).

The interaction in the hospital between the child and the paediatric nurse is also complex. By listening to the child's and the parents' proposals, pain and discomfort can be limited during invasive procedures (15). Anaesthetic nurses have described that knowledge about children's fears and their stages of development are necessary for an optimal caring situation (16).

Recently, on 1st January 2020, children's rights became law (2018:1197) in Sweden, meaning that the rights of the child shall be taken into account in all deliberations and assessments made in decision-making processes in cases and matters concerning children. This is pertinent to the role of nurses working in Swedish paediatric hospitals, who must have knowledge, skills and specific competence concerning blood sampling procedures, which include preparations and support adapted to each individual child's development (17). In paediatric hospitals in Sweden, nurses perform both venous- and capillary blood sampling methods on hospitalized children. In general, the existing national and international guidelines for blood sampling procedures specific to paediatric hospital care are thinly designed. The Swedish Handbook of Health Care (18) is mostly focused on adult care, as are the European Federation of Clinical Chemistry and Laboratory Medicine(EFLM) venous guidelines (19) and the American Clinical and Laboratory Standards Institute(CLSI) guidelines(20, 21). CLSI are not open access but they include venous and capillary guidelines focusing on adult care with some extra information for children. The World Health Organization(WHO) phlebotomy guidelines (22) provide some structured information but omit a number of children-specific topics, for example, how to approach children's different developmental stages, ages and anatomical challenges, and how to avoid pre-analytical errors.

There is a lack of evidence surrounding paediatric nurses' experiences of the blood sampling procedure with children and of their experiences of the errors occurring in the pre-analytical

phase. Their experiences are important for aligned interventions to be created in the future, with tailored educational activities for reducing pre-analytical errors.

Aim

To describe nurses' experiences of blood sampling procedures with hospitalized children in a paediatric hospital context.

Method

Study Design

We performed a qualitative study design using focus group interviews with nurses from two different academic paediatric hospitals in Stockholm, Sweden.

Data collection

We conducted three focus group interviews with registered nurses that perform blood sampling collections from children. Focus group interviews are particularly good when it comes to describing people's experiences and attitudes. The object of focus group interviews is to receive data which is high-quality and in a social context where the participants can reflect on their own views in relation to others (23). The Consolidated criteria for reporting qualitative research (COREQ) checklist was used in this study to ensure a comprehensive report (24).

Sampling

In this study, purposeful sampling was carried out to find different heterogeneity groups characterised by nurses in different stages of their career. We did this to generate rich informative data and in-depth information about the particular chosen subgroups (23). The

participants were approached by email or face-to-face and given information by the nurse managers.

A flexible interview guide was first conducted by the main author (HH) and then discussed and revised by the co-authors (NA, BMY). Each interview started with open-ended questions and followed by probing questions to elicit more elaborative answers (23). NA conducted the first interview. NA and BMY were present for the second interview, while HH and NA were present for the final one. The interviews lasted between 39-58 minutes and were audio recorded. The interviews were carried out between September-December 2019.

Participants

The focus groups included registered paediatric nurses with different levels of experience and education. Table 1 describes their age and clinical background. A written consent document was handed out and signed at the time of the interviews.

Setting

This study included participants from two paediatric hospitals in Stockholm, Sweden, caring for a wide range of conditions. One hospital is a tertiary hospital with oncology, surgical, medical and intensive care units, while the second hospital is smaller regional hospital, with two medical wards. The nurses came from different wards in the hospitals, as well as from their emergency department. Approximately 220,000 children and adolescents from birth to 18 years of age are living in the area covered by Stockholm County Council. The interviews were conducted in comfortable and nicely spaced conference rooms close to the clinic, which aimed to create a relaxed and peaceful environment for the interviews.

Data analysis

A qualitative (reflexive) thematic analysis (TA) was chosen as a theoretical framework for this study, and the applied method of analysis was used for the transcribed interviews. Research with qualitative design gives access to patient perspectives and offers a wide range of methods to investigate whatever interest, including interaction between health care provider and patient or health organisation politics (25). Due to there being only fragmented previous knowledge of our research question (26, 27), we converged the TA with an "inductive" approach, as described by Clark & Braun (2006) and recently clarified and discussed by the same (2020). The organisation of data went through the six described phases, including transcribing, making notes and coding, and creating themes composed from code patterns and meaning of data (28). The software Microsoft Excel and Microsoft Word were used to organize the data. The authors (HH, NA, BMY) familiarized themselves with the data and then discussed the initial patterns after the coding. The first author is a specialist paediatric nurse with preunderstanding of the blood sampling process and the affected errors. The three other authors were previously clinical active in the tertiary paediatric hospital, but now work with research or educational activities.

The analysing process went back and forth and as themes were discussed, a thematic map was created and revised and refined throughout the process (Figure 1).

Ethical Considerations

All registered nurses who were asked volunteered to participate in this study. Participants were given oral and written information about the study beforehand and told they had the right to withdraw at any time. All participants were assured confidentiality and their identities were coded and concealed from all parties apart from the first author (HH). The study was approved by the Regional Ethical Review Board in Stockholm (2015/206-31/4).

Table 1. Demographics of participants.

Interviews number	Participants (n)	Age (Mean)	Work place	Registered Nurse(RN) /Master degree Nurse(MSN)	Length of work experience (mean)
Nurses Group 1	9	26.3	4 wards	RN	10.6 months
Nurses Group 2	6	33	2 wards	MSN	6.7 years
Nurses Group 3	4	28	2 wards	RN	7 months

Results

From the transcribed data of the three focus group interviews we found patterns and meaning for five themes. The main theme was "Paediatric blood sampling is a challenge for the nurses", with the subthemes: "Nurses' feelings of frustration with unsuccessful samplings", "Nurses believe in team work", "Venous blood sampling was experienced as the best option", and "Nurses' thoughts and needs in regard to developing skills in paediatric blood sampling". These themes are presented as a narrative, with illustrative quotes describing the participants'

experiences of blood sampling procedure with children.

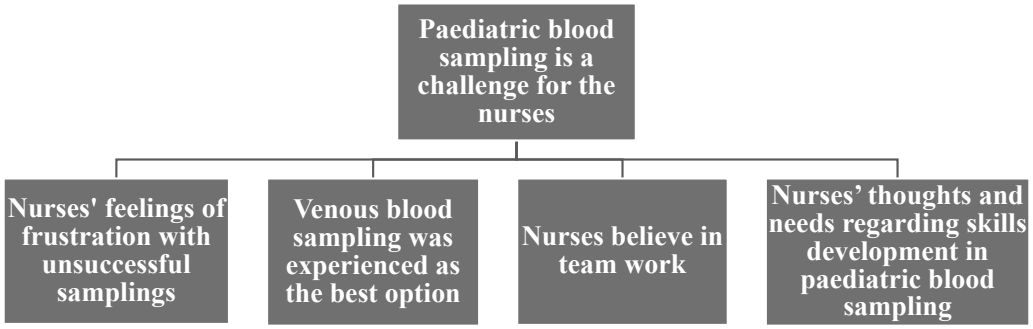

Figure 1). Thematic map

Main theme: Paediatric blood sampling is a challenge for the nurses

The nurses believed it was more of a challenging process to take blood samples from children than from adults. They viewed the sampling process as more complex and complicated. It was not only the puncture itself which was more difficult, but also the whole situation surrounding it.

"Yes, there's a huge difference when you're working on adults but with a child it could be a process that takes a whole morning just to get near them." (Nurses Group 2)

The nurses felt that they first had to build the children's confidence to ensure the blood sampling procedure went smoothly. Building confidence was important because the nurses knew the procedure might be repeated several times during the child's hospital visit. Feeling stressed and wanting to perform high quality care but being unsuccessful was another challenging aspect. The informants were often experienced in adult care, where they felt self-confident, but this changed when they started working in the paediatric hospital.

The participants experienced ethical and moral conflicts related to blood sampling which were challenging, especially when they had to do something against the child's will. The nurses felt it was inhumane to repeat the blood sampling procedure multiple times. However, the nurses sometimes felt they had no other choice because the sample was key to the diagnosis and proper management of the child.

"How many times is it humane to needle a child? That's always the ethical question that's difficult". (Nurses Group 1)

Working with the whole family was another challenging aspect of the blood sampling procedure. The children's parents could often interfere and make the nurse's relationship with the child difficult. For example, the parents could say things that made the nurses feel angry or frustrated.

"No, it's not really ideal when a parent says: "here comes the stupid nurse to jab you (laughing) and it'll hurt". (Nurses Group 2)

Other times the parents wanted to be optimistic for the child, telling them the blood sampling procedure would "go fine with no pain" and that it would be just "one jab", when the nurses knew this was not true. This made the nurses feel insecure and could lead to lack of confidence and trust between the nurse and child. The nurses often had to deal with the anxiety and fears of both the child and their parents.

The nurses also expressed awareness that children of certain ages or with special needs could present an extra challenge to the procedure. For example, hospitalized children with severe acute or chronic conditions were a category that made the process even harder. The nurses reflected on the fact that the sampling process was time consuming and planning their work

could be a challenge. Additionally, the participants felt that moments such as preparations could be challenging but were very important.

"Sometimes when you go in to take samples it all goes really smoothly and that's good but quite often you have to give yourself time to ensure it goes well, the next time and the time after that". (Nurses Group 2)

The participants occasionally had poor self-confidence, which could be challenging to cope with. It was easier to help a colleague with a difficult patient than to succeed with their own patients.

Sub theme 1. Nurses' feelings of frustration with unsuccessful samplings

The nurses experienced frustration around several aspects of unsuccessful blood sampling. Although they might have thought a sampling went well, the hospital lab results recorded in the medical journal reported otherwise, due to pre-analytical errors, such as a clot or haemolysis. The nurses were frustrated that the laboratory never explained what went wrong, merely stating that the sample could not be analysed. Many times the nurses had put all their effort and fighting spirit into the procedure and when the results came back reporting errors, this caused sadness, frustration and anger.

"You get very angry and I called the lab and asked why it was like this and then they had no real answer so then you get really angry." (Nurses Group 1)

Sometimes the nurses felt that the "machines", especially the bedside analyses, were working against them. They also perceived that certain blood analyses like the blood gas test, INR coagulation test and amniotic fluid analysis test were difficult to fulfil, which illustrated a lack of knowledge around these aspects. Often the nurses felt they had problems getting too

little or too much blood in the collecting micro tubes. The participants thought they had the correct amount and were then perplexed when the laboratory responded by reporting the result to be an "unfilled sample".

"And then on occasion, when I've taken the same sample from a child three times and all three have coagulated each time, and when I really know I turned everything and warmed it up and did everything, that from here on, now there's something strange – something spooky about it". (Nurses Group 3)

When the nurses could not believe it was their own mistake, they tried to give other explanations for why sampling was unsuccessful . If not the machines, could it be the quality of materials or even sloppy laboratory staff? The nurses' ambiguity and uncertainty seemed to nudge them into a blaming culture.

"Sometimes I've got the feeling that they just drop the samples and then they (the lab) have the cheek not to report it. Everything went perfectly, and then the haemolysis, you just go what?! Oh no!" (Nurses Group 2)

The nurses thought it was better to send the collected blood samples to the laboratory, even though they were uncertain they had been successful. Often they defended this by expressing concerns for the children in that they did not want them to have too many punctures or suffer from hospital-acquired anaemia. The nurses felt the doctors were unaware of how many blood samples they prescribed or the risks of anaemia, which led the nurses to difficult prioritisations.

"What priorities so we can try to take them if you've jabbed (the child) once or twice to get the first samples then you want to chance it and send them, sometimes you can write 'very

difficult patient to needle' so sometimes I do that…it's kind of the best we can get". (Nurses Group 1)

There were occasionally situations when help was needed but not given from elsewhere and communication was poor. The nurses felt frustrated, bringing their concerns for the child in focus.

"Yes, but it feels disappointing. I'm not asking help for my sake – I can push the needle in ten times but it's for the child's sake, isn't it – so you don't damage the vessels." (Nurses Group 1)

During the interviews the nurses frequently expressed uncertainty about how to handle the samples or about what and why pre-analytical errors occurred for their specific sampling.

Subtheme 2: Nurses believe in team work

As demanding and complex as the blood sampling can be, the nurses said they felt the presence of facilitators could ease the procedure. They believed a supportive team and good communication would contribute to successful sampling and that having at least two to three colleagues on hand during the procedure was a good idea, helping them to make use of distraction methods and manage the samples effectively.

"…better if there's more of you, not just for distraction but also so you have someone who can hand you things, stand and turn tubes". (Nurses Group 3)

The nurses felt that both physical and psychological support from each other were essential for a qualitative sampling procedure. They mentioned that they were able to ask for help and, if necessary, they could spontaneously change blood sampling method or even who was in charge of the needling.

"…but it's also thanks to having such great back-up and support from our colleagues that no-one ever sighs when you ask for help, they're very positive and cheerful". (Nurses Group 1)

During the interviews, the nurses described experiences which showed that they had a deeper understanding of the child's needs and comfort. They viewed good communication in the team with parents as important and often of benefit in the situation.

"But they (the parents) are really important in it going well. Because if they start getting stressed about things or say stuff that has nothing to do with it or whatever, it can go belly up because of it". (Nurses Group 2)

The experienced nurses often investigated the child's condition first and could feel when sampling was unnecessary, prompting them to ask the clinicians to rethink the ordering of blood samples in order to reduce the number of punctures.

Subtheme 3: Venous blood sampling was experienced as the best option

Another subtheme was "Venous blood sampling was experienced as the best option". The different sampling methods discussed were capillary- and venous blood sampling. During these discussions, the participants interacted and asked each other questions about which method they preferred. Pros and cons were discussed and venous sampling was mainly viewed as the best option by all focus groups. The nurses said venous sampling could benefit the blood flow and increased the chances of capturing good quality blood specimens.

"If you've learnt venous it's easier than capillary, better flow and it increases the chances of getting good samples". (Nurses Group 1)

One of the participants was positively surprised when she performed a venous puncture on an infant, which led to her suddenly having collected six micro tubes without problem, the tricky part instead being that she had too much blood to handle.

Choosing a method according to the individual child in front of them was described as important. The nurses felt that they had many factors to think about, such as the child's age and developmental stage. One nurse stated that the choice of sampling method could minimize pain for child.

"It depends on the child. I often think it hurts more if you sample the finger." (Nurses Group 2).

In regard to capillary sampling, one participant explained it as a minor procedure, while another stated it was seldom used. However, capillary sampling was possibly a better choice if a child had special needs, for example, spasticity. Getting the right amount of blood for the ordered analyses was another aspect discussed in regard to choosing the right method. For the nurses, the fewer punctures they made, the better.

"And then maybe it only takes one needle in the vein instead of three capillary, yes, to get enough blood". (Nurses Group 3)

Blood sampling is a multifaceted task and the nurses described their skills in planning for the best interests of the child. If the child needed a periphery cannula, the nurses tried to collect blood specimens at the same time from the same cannula. The nurses said that when patients had a new existing cannula, it made things more pleasant for both them and the child, as they could continuously withdraw samples without punctures and pain for the child. It was necessary to plan your procedure accordingly, due to the few available chances nurses have

for collecting blood. Another factor the nurses discussed was the limited number of visible and small vessels a small child has.

" ...Not just to have fewer needlings but also because you might not have that many chances to take, in the first instance, venous samples – they've kind of got a certain number of vessels that are even possible to try on". (Nurses Group 2)

Subtheme 4: Nurses' thoughts and needs regarding skills development in paediatric blood sampling

The last subtheme was "Nurses' thoughts and needs regarding skills development in paediatric blood sampling". The nurses described how it felt to lack knowledge of paediatric care and mentioned what they had missed out on during their introduction programs or even university nursing education. Some participants also felt important information had been omitted about the differences between paediatric and adult blood sampling procedures and that university nursing programs had failed to mention this in their training. The nurses felt that learning by doing and by observing colleagues was the main way nurses embraced knowledge. They reflected on their own competence related to blood sampling children, stating that they often tried to "join in" with more experienced colleagues conducting blood sampling procedures to discover "tips and tricks" for their own use. The first focus group stated that, in future, they would like an annual CPD(continuous professional development) course in sampling techniques.

"Everyone should get trained...just like getting CPR once a year, you can have needle training once a year." (Nurses Group 1)

Another aspect was that some nurses lacked education concerning preparations and choosing the right blood sampling method, as well as knowledge about the amount of blood that could be taken from the children.

"The thinking around sampling and perhaps a bit more on which ones I can actually take from capillaries and which ones have to be venous, so that's what I wish I had in my training." (Nurses Group 3)

Some nurses said that simulation training was a bonus during their paediatric nurse introduction, but that it did not feel like reality and could not simulate real clinical situations they experienced. The nurses were eager to learn more and wanted to improve their skills but did not know how and when it could done.

"*It's hard to practise all situations on a simulation doll or things like that, also that there are things that have to be done in order to improve".* (Nurses Group 2)

Discussion

This study sought to describe the nurses' experiences of the blood sampling procedure with children. From the study data, we described five themes which relate to successful or unsuccessful blood sampling procedures. The overall theme *Paediatric blood sampling is a challenge for the nurses* illustrates that nurses working in paediatric hospital care face a big challenge with the blood sampling collection procedure for children. The four subthemes: *Nurses' feelings of frustration with unsuccessful samplings*, *Nurses believe in team work*, *Venous blood sampling was experienced as the best option and Nurses' thoughts and needs regarding skills development in paediatric blood sampling* describe the nurses' diverse experiences concerning blood sampling in children. To the best of our knowledge these are new findings and not published elsewhere.

In this study, *Nurses' feelings of frustration with unsuccessful samplings* was one of the most interesting subthemes we analysed. Unsuccessful samplings with pre-analytical errors, such as clots, unfilled sample and haemolysis were something the nurses often experienced. They could not believe it when the blood sample came back from the laboratory as a failed analysis, which created stress, anger and frustration. This dilemma illuminates the knowledge gap and the grey zone between nursing care and laboratory medicine in paediatric hospital care. In the aforementioned blood sampling guidelines, there is seldom any detailed instruction on how to avoid possible pre-analytical errors, something which could have helped the paediatric nurses. None of the participants in the focus groups mentioned reporting unsuccessful samplings as incidents. This was recently demonstrated in another study, where nurses described that they lacked time, routines and guidance for incident reporting unsuccessful sampling (29). Unsuccessful samplings also meant the nurses needed to take time from other important care. Nurses in other contexts have been found to lack knowledge about pre-analytical errors but are eager to learn (30), which was also the case with the nurses in our study. The participants mentioned several aspects regarding pre-analytical problems, for example, technical issues, communication with the laboratory, as well as not knowing why a clot or other errors had occurred.

The nurses in our study were at liberty to choose the appropriate sampling method. Our analysis revealed they felt that *Venous blood sampling was experienced as the best option,* and this was another theme in this study. There was a difference between inexperienced and experienced nurses in the way they discussed sampling method. The more experienced nurses expressed deeper concerns about the child's needs and comfort. This shows how important it is to motivate the younger nurses to take part in CPD (continuous professional development)

to increase their knowledge(31). Overall, venous sampling was more often considered the first and best choice because blood flow would be better and more blood could be collected. This has been demonstrated to be more successful in Hjelmgren et al 2021(32). The nurses could have been helped further if the guidelines had been more specific about when to use which sampling method for age and developmental stages and analyses. Interestingly, the safety of both personnel and child were seldom discussed, even though the different sampling methods incur different risks for both patient and staff and are described in WHO phlebotomy guidelines (22). The methods were more often discussed in terms of whether the procedure was complicated or not. Capillary blood sampling was seen as an option when the child had few visible veins or had special needs. However, there are medical devices that visualise the veins, which could benefit venous withdrawal of blood in children(33).

The overall main theme of our study was *Paediatric blood sampling is a challenge for the nurses*. The nurses felt that the whole procedure was very different from sampling adults, and this highlights their holistic approach and concerns for the hospitalized child. Our results also highlighted challenges in coping with parents, children with special needs and the nurses' own self-confidence during the procedure. An American study investigating phlebotomist experiences (34) described anxious patients and parents as a primary problem in relation to several aspects of blood sampling in children. Parents can often unwittingly transfer their own fears and anxiety to their children, something nurses must often be well-prepared to manage. In our study, the nurses also faced ethical dilemmas, for example, the number of punctures required and sometimes, restraining the child against its will. This highlights the wide range of issues a paediatric nurse must cope with when executing blood sampling. Nurses in other clinical contexts have also described conflicting emotions when they deviate from instructions, have to hold patients still or when parents interfere during their children's blood

sampling (35). To assure the safety of the child and protect its rights, nurses must use their clinical judgement in each situation and for each individual child so that they can appropriately tailor the best preparations and interventions, before, during and after the procedure (36). The United Nations children's convention from 1989 confirmed the rights of children to be supported, protected and respected, and for them to participate with their dignity recognised. Although these obligations are clearly stated, an Italian study of paediatric nurses' responses found that hospitalized children's rights are still not implemented fully (37). Another study has also pointed out that the organization must recognise that extra time and a high level of clinical competence and resources are needed for advanced paediatric care (16).

The subtheme *Nurses believe in team work* illustrates that the nurses searched for ways to cope with the complex blood sampling procedure and did so by communicating with parents and gathering colleagues in the team. Other studies have described the importance of promoting the safety of hospitalized children as a challenge shared by both parents and the health personnel team (38). In our study, having an assistant on hand to stabilize the arm or distract the patient was viewed as important, which is consistent with the recommendations in CLSI venepuncture guidelines (20). The nurses in our study viewed it as important for both capillary and venous sampling.

The nurses sometimes felt doctors ordered a lot of unnecessary sampling, creating unwanted suffering for the children. They were also worried that all this sampling could lead to risk of hospital-acquired anaemia. If the child's condition changed for the better, the nurses often questioned whether sampling was necessary. Literature has described an overutilization of laboratory testing in hospital settings and that resting is often of no clinical importance (39). The frequent overdraw is a documented potential risk of hospital-acquired anaemia (40),

which confirms the nurses' concerns and should lead to doctors and health organisations improving care and communication concerning this aspect.

Nurses' thoughts and needs regarding skills development in paediatric blood sampling evolved into our last subtheme. The participants had many thoughts and ideas on educational aspects, such as being given a good introduction to paediatric blood sampling, practical tips and repeated training in order for them to feel comfortable with the procedure. Previous research has shown that simulation learning could be a strategy which could create competency-based education, with holistic and context-dependent content for nurse educators to use(41). The nurses in this study had mainly acquired knowledge from college or learning by doing. These findings indicate that nurses lack knowledge and deeper understanding of handling specimens and avoiding pre-analytical errors, such as clots and haemolysis. Another study has described that by providing standardized training and education pre-analytical errors could be reduced (42). The role of experts in laboratory medicine also has a part to play. This includes improved communication and provision of support and education to nurses and doctors, as well as the patients. The blood sampling process is a multilevel process that includes nursing care, laboratory medicine and medicine science, and this makes cooperation and communication for the patient's best especially important (43).

Strength & Limitations

The COREQ guidelines were used as a help for reporting in this study and increased trustworthiness. COREQ contains a 32-item checklist including three domains: 1) research team and reflexivity, 2) study design and theoretical framework and, 3) analysis and findings (24). We chose not to return the transcript (item 23) to the participants after the interviews, as we had not taken notes on who said what in the group.

To achieve credibility, it is crucial to find participants who are likely to have experiences of the phenomenon under study and are able to talk about it (44). Our purposive sampling approach had this intention. This study used focus groups, which is a method that could give the researcher a certain depth of data and context . A strength of the study is that the method could also generate group effects and participant interaction, leading to a learning moment which is not possible during individual interviews (45, 46). To attain trustworthiness, one of the authors (NA) was present at all focus group interviews. We also illustrated our findings and interpretations with quotes that give another aspect of transparency and trustworthiness in qualitative studies (24). We believe we reached information power, as described in Malterud et al, 2016, after the three interviews including 19 participants. The more information the data holds, the lower number of participants needed (47).

In TA analysis, researcher subjectivity is seen as a resource which strengthens the reflexive engagement with the interpretation of data and theory (27). The first author (HH) has deep knowledge and understanding of the given subject, which was a resource for the interpretation of the data. The first author was not present at the first two group interviews, as he knew some of the participants well. Self-awareness of the researcher is important to sustain credibility (48). Even though we used a more inductive approach, it is meaningful to say that as researchers, we are not in a theoretical vacuum with no previous knowledge. The analysis process was therefore more like a continuum going back and forth (27).

These findings could be transferable to other similar contexts where paediatric nurses are in charge of the procedure, although we believe nurse assistants, phlebotomists or even doctors performing blood sampling on children could have similar experiences and gain knowledge by reading this paper. As stated in previous research, paediatric care nurses are already aware of comfort methods, such as distraction techniques and pain-reducing treatments (49).

Consequently, as a nurse you could execute a perfect distracted and comfort measured blood sampling procedure but still fail to get a satisfactory blood test result from the laboratory.

Further research needs to focus on improving the support and education of nurses performing blood sampling on children and in so doing, reducing the pre-analytical errors in paediatric hospital care. This may be done by implementing the latest evidence-based research in this field, along with a children's rights approach. Increasing the knowledge, competence and skills of paediatric nurses is key to reducing the number of unsuccessful samplings in the future.

Conclusion

The narrative results of this study illustrate that nurses working in paediatric hospital care face a big challenge in blood sampling children. The nurses felt frustrated due to unsuccessful blood samplings and could often not understand why pre-analytical errors occurred. They felt strengthened by colleagues in their team and shared feelings of responsibility to help each other with this complex procedure.

Relevance to clinical practice

The implications of this study are that paediatric hospital care needs to focus on improving guidelines for and increasing competence in blood sampling children and helping nurses to understand why samplings may be unsuccessful and how this can be avoided.

Abbreviations

CLSI: Clinical and Laboratory Standards Institute

COREQ: The Consolidated criteria for reporting qualitative research (COREQ)

CPD: Continuous professional development

CPR: Cardiopulmonary resuscitation

EFLM: European Federation of Clinical Chemistry and Laboratory Medicine

TA: Thematic analysis

WHO: World Health Organization

Declarations

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Ethics approval and consent to participate
The study was approved by the Regional Ethical Review Board in Stockholm (2015/206-31/4). Written consent was obtained from all participants before the interviews were recorded. Ethical approval and consent to participate is presented in the manuscript.

Consent for publication
The article does not contain any individual's details, and consent for publication is not applicable.

Competing interests
The authors declares that we does not have any competing interests.

Authors' contributions
All authors confirm that they have contributed to and approved to the final version of the article. HH, BMY and NA led study conception and design; data collection, analysis and interpretation; and writing and review of the manuscript. BN contributed to study conception and design; data interpretation; and writing and review of the manuscript.

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The authors have no conflict of interest to report.

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Availability of data and materials
The data used and analysed during the current study are available from the corresponding author on reasonable request.

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