Original Article

Improving Quality at the Preanalytical Phase of Blood Sampling: Literature Review

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Aim. This paper describes a literature review of studies on the effect of the preanalytical phase on the quality of laboratory results, and consequently on the quality of nursing. The aim was to describe quality errors in the preanalytical phase of blood sampling, in order to increase nurses' awareness of preanalytical errors and to facilitate improvements in nursing practice associated with blood sampling.

Background. The quality of the preanalytical phase plays a vital role in obtaining reliable test results, thus promoting patients' health, diagnostics and facilitating analysis of the effectiveness of the treatment. Data sources. Medline and CINAHL.

Review methods. A narrative literature research was carried out (1990-2010). The inclusion criteria were: 1) an original study or review; and 2) studies involving blood sampling. The selected papers were screened and irrelevant studies were excluded. By examining the references cited in the selected papers an additional five relevant studies were identified.

Results. Twenty four papers met the inclusion criteria and fell into three categories. The preanalytical errors associated with blood sampling were related to: 1) preparing patients for the tests; 2) collecting samples; and 3) the effects of handling, storage and transportation of blood samples. All these three factors can influence the quality of laboratory results.

Conclusion. The information provided by this study review may be used to improve and evaluate the quality of blood sampling praxis. Nurses should be aware of the preanalytical errors on blood sampling and their influence on laboratory results on account of patient safety. Also multi-professional co-operation with laboratory personnel in sampling could decrease failures in preanalytical phase.

Key words: blood sampling, laboratory results, preanalytical quality, literature review

Introduction

Laboratory results play a key role in patient care. It is estimated that around two thirds of important clinical decisions about admissions, discharge and medication are based on laboratory test results (1). Consequently, laboratory testing is also an important source of medical errors that can affect patient safety (2-4). Laboratory testing is a highly complex process, which is usually divided into three phases: preanalytical, analytical and postanalytical (Figure 1). The preanalytical phase occurs outside the laboratory (beyond its control), consisting of the selection of appropriate tests on the basis of the clinical question, ordering, collection and handling, transportation and preparation of samples to make them suitable for analysis (2). The process always starts and ends with the patient. The preanalytical phase can be classified on the basis of patient-associated, specimen-associated and sample-associated factors (5), or divided into periods (6) before, during and after collection.

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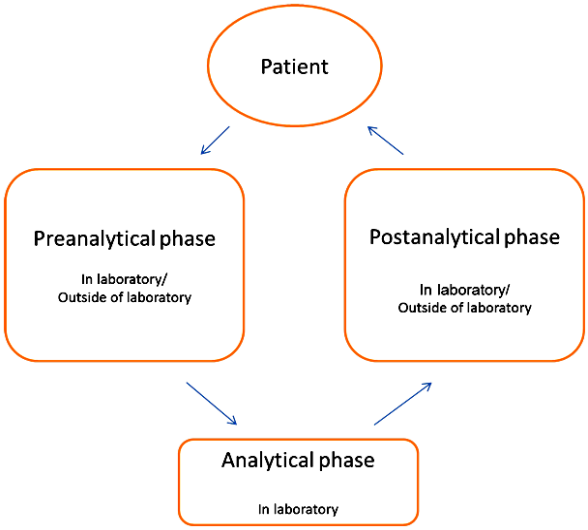

Fig.1 Laboratory testing process in relation to patient

Traditionally the focus has been on evaluating the reliability of laboratory results based on the analytical phase. Less attention has been paid to the preanalytical phase and its potential influence has been underestimated. However most of the mistakes are human errors occurring before the samples reach the laboratory**,** i.e. in the preanalytical phase (7-14). These errors are related to manual activities during this phase. From the patient's perspective, the point in the testing process at which the errors occur or who is responsible for them is irrelevant. Patients have a right to receive reliable results. Tests involving spurious information must be repeated, producing unnecessary costs to the healthcare system. This may cause delays in the patients' treatment and may also affect therapeutic decisions (12,14, 15-17).

Previous authors have reported that the preanalytical phase of the testing process has an important effect on the reliability of patients' laboratory results and consequently, on the quality of patient care and on patient safety (1,11,18-21). Thus, recognition of these factors is a challenge to nurses and to the quality of nursing care. Nurses play an important role in taking and handling blood samples and in providing patients with accurate information prior to the tests. Healthcare professionals should**,** therefore, be fully aware of the effects on test results of individual preanalytical factors and their combinations.

A wide range of medical and biomedical scientific research has identified and illustrated the effects of preanalytical errors on patients' laboratory results and patient safety (8- 12, 14, 17, 21) but there has been hardly any research conducted from the nursing perspective. The language and concepts used in medical and biomedical research may not be suitable for the nursing context. In this literature review we try to translate such "laboratory" knowledge into the clinical setting and we focus on the meaning of the preanalytical phase of the laboratory process in blood sampling. This is a fundamental aspect of practical care, the improvement of which would increase the reliability of laboratory results and thus enhance patient care. In this research we chose to focus on blood samples because they are the most common type of specimen sampled in clinical practice.

The aim of this review was to describe preanalytical quality errors that occur during blood sampling; we focus on venous blood sampling. We hope that, as a result of this study**,** nurses will be able to apply the knowledge gained to the preanalytical phase and improve the quality of blood samples collected. The updated information provided in this review could be used to improve and evaluate the quality of blood sampling practices.

Methods

A narrative literature review was chosen as a means of using existing data to investigate the topic of interest. An integrative design was used to be broad enough to include, simultaneously, primary sources utilising different methodologies, existing review information and theoretical commentaries. This allowed us to extract evidence-based knowledge about the effects of preanalytical factors on the laboratory results obtained from blood samples.

Search methods A narrative research review was carried out in order to summarize, explain and interpret evidence, both qualitative and quantitative (22). Exploratory engagement with existing literature enabled the reviewers to identify subjects to exclude, allowing us to focus on examining the relevant literature.

Search strategy and selection criteria A literature search was carried out using the Medline and CINAHL databases. The Medline database was searched to find articles written from the medical perspective in order to gain a biomedical view of preanalytical factors. The Cinahl database was used to find papers written from the nursing perspective. This approach was intended to provide a diverse view of the subject. Papers included were published in the period 1990 to 2010, written in English and examined preanalytical errors. The earliest studies concerning preanalytical factors were published in the 1990s.

'Pre-analytical', 'preanalytical' and 'laboratory test' or 'laboratory investigation' were used as key search

phrases. This initial search yielded 43 studies. The inclusion criteria were: 1) an original study or review; and 2) studies involving blood sampling. Abstracts were examined and papers relating to sample material other than blood were excluded. The selected papers were screened and irrelevant studies were excluded. Full-text copies of the remaining studies were obtained. This process allowed us to identify nine relevant papers. By examining the references cited in the selected papers an additional five relevant studies were identified.

Literature search outcome In total, 24 studies were identified and examined (Table 1). Two researchers carried out the initial research and the initial assessments of the papers. This allowed us to confirm the reliability of assessment and discuss the papers until a consensus was reached.

Table 1. The studies included in review (n=24)

References and their titles	Type of study	Preanalytical quality failures
Gräsbeck R (36) The evolution of the reference value concept	Review	Prolonged tourniquet use
Gama R, Teale J, Marks V (37) Clinical and laboratory investigation of adult spontaneous hypoglycaemia	Theoretical	Wrong specimen type
Suryaatmadja M (29) Specimen collection and handling	Review	Collection from infused arm Wrong cleaning solution Puncture site not dry Prolonged tourniquet use Wrong anticoagulant in collecting tube Haemolysis Tube underfilled Wrong sequence in sampling
Capel P, Chatelain B, Leclerq R, Lust A, Masure R, Arnout J (28) Quality control in haemostasis	Theoretical	Wrong sequence during sampling Prolonged tourniquet use Size of needle Sampling through catheters in haemostasis tests Wrong collecting tube Wrong anticoagulant in collecting tube
Chaigneau C, Cabioch T, Beaumont K, Betsou F (5) Serum biobank certification and the establishment of quality controls for biological fluids: examples of serum biomarker stability after temperature variation	Experimental	Site of collection Rate of collection Prolonged tourniquet use Type of collection Tube additive Transport Haemolysis Blood cells
Wagar EA, Tamashiro L, Yasin B, Hilborne L, Bruckner DA (30) Patient Safety in the Clinical Laboratory: A Longitudinal Analysis of Specimen Identification Errors	Experimental	Mislabelled specimens Unlabelled specimens Clotted samples Container leaking Contaminated samples Haemolysis Improper collection Improper handling Specimen not suitable for test Quantity not sufficient Tube overfilled Tube underfilled

Lippi G, Blanckaert N, Bonini P, Green S, Kitchen S, Palicka V et al. (12) Causes, consequences, detection, and prevention of identification errors in laboratory diagnostics	Review	Misidentification in laboratory diagnostics: Physician ordering laboratory tests on the wrong patient, incorrect or incomplete entry of patient's data in the information system, collection of specimens from the wrong patient, inappropriate labelling of the specimens
Lippi G, Montagnama M, Giovanni D (20) National survey on the pre-analytical variability in a representative cohort of Italian laboratories	Survey	Specimen not suitable for tests Lack of reference guidelines Conditions for specimen storage Sample transportation
Lippi G (17) Governance of pre-analytical variability: Travelling the right path to the bright side of the moon	Review	Inaccurate procedures Collection of specimens from wrong patient Inappropriate labelling of the specimens Variation in tube filling
Rattan A, Lippi G (38) Frequency and type of preanalytical error in a laboratory medicine department in India	Review	Incorrect specimen received Haemolysed samples Specimens not received Inappropriate storage conditions Discrepancy between test code and test request Clinical history not received Identification errors Insufficient sample Test prescription net received Specimen lipemic Whole blood specimen clotted
Roberts G (24) Pre-analytical Variables Affecting laboratory test Results	Theoretical	Describes the meaning of Uncontrollable and manageable variables Patient and sample identification Transportation and processing
Stroobants A, Goldschmidt H, Plebani M (25) Error budget calculations in laboratory medicine: linking the concepts of biological variation and allowable medical errors	Theoretical	Error frequencies specified in pre-pre-analytical and pre-analytical phase were 12.0% and 5.0% in the laboratory process

Bowen R, Hortin G, Csako G, Otanez O, Remaley O (31) Impact of blood collection devices on clinical chemistry assays	Review	Discuss how blood collection devices such as needel, syringes, and catheters, collection tube components can alter laboratory results
Da Rin G (2) Pre-analytical workstations: A tool for reducing laboratory errors	Review	Inappropriate test request Misidentification of patient Inappropriate container Mislabelled specimens Specimen not suitable for test Variation in tube filling Improper storage period and conditions
Wiwanitkit V, Lekngarm P (39) Requisition Errors for Blood Glucose Tests: A Hospital-Based Study	Review	Overlapping tests
Plebani M (4) Exploring the iceberg of errors in laboratory medicine	Review	Describes testing process errors in primary care and in an emergency department
Shahangian S, Krola J, Gaunt E, Cohn R (26) A System to Monitor a Portion of the Total Testing Process in Medical Clinics and Laboratories. Feasibility of Split-Specimen Design	Experimental	Assesses the feasibility of using split-specimen design to assess integrity of a portion of the total testing process in medical clinics and laboratories
Piva E, Plebani M (3) Interpretative reports and critical values	Review	Describes how to prevent interpretation errors and improve patient safety
O' Kane M (40) The reporting, classification and grading of quality failures in the medical laboratory	Theoretical	Reports, classifies and grade quality failures in laboratory polices and procedures
Nauck M, Nauck M, Koetting J (32) A Recapping System for Automatic, Semiautomatic, and Manual Use	Review	Samples are covered insufficiently when storing
Steindel S, Jones B (33) Routine Outpatient Laboratory Test Turnaround Times and Practice Patterns	Review	Delays in collection and transport stages
Favaloro E, Soltani S, McDonald J, Grezchnik E, Easton L (27) Laboratory Identification of Familial Thrombophilia: Do the Pitfalls Exceed the Benefits? A Reassessment of ABO-Blood Group, Gender, Age, and other Laboratory Parameters on the Potential Influence on a Diagnosis of Protein C, Protein S, and Antithrombin Deficiency and the Potential High Risk of a False Positive Diagnosisn	Review	Describes some pre-analytical variables effect on thrombofilian testing. Request wrong time Wrong person
Tripodi A, Breukink-Engbers W, Besselaar A and M (41) Oral Anticoagulant Monitoring by Laboratory or Near-Patient Testing: What a Clinician Should Be Aware Of	Review	Describes preanalytical conditions and analytical variability in relation to INR Blood collection tubes Temperature and storage time
Roshan T, Rosline H, Rapiaah M, Zaidah A, KhattakM (42) Hematological reference values of healthy Malaysian population	Theoretical	Patient preparation Blood sampling and processing

Quality appraisal This literature review has some limitations. It is impossible to study all possible preanalytical factors and their combinations using such an approach and the database searches yielded a fairly small number of papers. Despite this, applicability in terms of the study design and sample selection addressed the aim of study and fulfilled the aim of providing a broader understanding of preanalytical factors and their effect on the quality of patients' laboratory results. The results can be considered reliable when taking into account the papers accepted for examination in this study**;** all papers included described the samples and methods according to scientific criteria. A critical assessment of the literature was made. Selected studies provided information about the effects of preanalytical factors on the quality of laboratory results (23). The data analysis methods were suitable for describing the preanalytical errors, thereby adding to the reliability of the study. Another limitation concerns classification of the data. The boundaries of categories should not be considered seen as exclusive, because the blood sampling process does not always progress logically.

Data abstraction and synthesis After initial review of the papers, the data were abstracted using a table to summarize the study aims, study design, sample size, methods of assessments and key findings. Table 1 is evidence table detailing the empirical papers reviewed.

To synthesize the data, papers were organized into three major categories, based on content. The contents of the selected studies were grouped into three categories according to the steps within the preanalytical phases (Table 2). Papers in Group 1 relate to preparing patients for the blood tests and the significance for the quality of patients' laboratory results (*before collection*). Papers in Group 2 relate to handling and collecting blood samples and their effect on the quality of patients' laboratory results (*during collection*). Papers in Group 3 relate to the storage and transportation of blood samples and their effect on the quality of patients' laboratory results (*after collection*).

Table 2 Preanalytical errors in blood sampling

Before Collection	Reference
Inappropriate test request	Winwanitkit & Lekngarm (2007), Da Rin (2009),
Improper time of collection	Tripod *et al*. (2003),Lippi *et al.* (2006),
Overlapping tests	Winwanitkit & Lekngarm (2007),
Order entry errors	Da Rin (2009), Lippi *et al.* (2009) , Plebani (2009),
Misidentification of patient	Roberts (1997), Shahangian *et al.* (1998), Da Rin (2009), Plebani (2009), Lippi (2009), Lippi *et al.* (2009), Rattan & Lippi (2008), Stroobants et al. (2003), Falvaloro *et al*. (2005),
Inadequate procedures	Capel *et al.* (1992), Suryaatmadja (1999), Lippi *et al*. (2006), Roshan *et al.* (2009), Piva (2009), Lippi (2009), Lippi *et al.* (2009),
Patient preparation	Roberts (1997), Shahangian *et al.* (1998), Stroobants *et al.* (2003), Tripodi *et al* (2003), Lippi e*t al* (2006), Roshan *et al.* (2009),
Wrong sampling equipment	Capel *et al.* (1992), Roshan *et al.* (2009)
During Collection	
Duration of tourniquet use	Capel *et al.* (1992), Suryaatmadja (1999), Gräsbeck (2004), Chaigneau *et al.* (2007),
Inappropriate container	Capel *et al.* (1992), Suryaatmadja (1999), Stroobants *et al* (2003) Da Rin (2009), Chaigneau *et al.* (2007), Plebani (2009), Lippi (2009) , Lippi *et al.* (2009),
Mislabelled specimens	Wagar *et al.* (2006), Da Rin (2009), Lippi *et al.* (2009), O'Kane (2009),
Specimen not suitable for test	Roberts (1997), Gama *et al.* (2003), Stroobands *et al.* (2003), Lippi *et al* (2006), Wagar *et al*. (2006), Da Rin (2009), Lippi *et al.* (2009), Bowen *et al.* (2010),
Variation in tube filling	Suryaatmadja (1999), Stroobands *et al.* (2003), Wagar (2006), Rattan & Lippi (2008), Da Rin (2009), Plebani (2009), Lippi (2009), Lippi *et al.* (2009), Bowen *et al* (2010),
Clotted sample	Wagar *et al.* (2006), Rattan & Lippi (2008) Lippi *et al.* (2009),
Haemolysis	Shahangian *et al.* (1998), Suryaatmadja (1999) Wagar *et al.* (2006), Chaigneau et al. (2007), Rattan & Lippi (2008),
After Collection	
Improper storage period and conditions	Lippi *et al.* (2006), Rattan & Lippi (2008), Da Rin (2009), Bowen *et al.* (2010),
Delays in processing samples	Roberts (1997), Shahangian *et al*. (1998), Steindal & Jones (2002), Stroobands *et al.* (2003), Lippi *et al.* (2006), Nauck *et al.* (2008), Da Rin (2009),

Results

Before collection

This domain focuses on test requests and patient identification. The studies exploring the procedures available for blood sampling revealed that they were inadequate, even though they constitute the core element of standardised sampling (2,5,17, 24-25). These studies show that this may be serious problem from the point of view of nurses as members of multi-professional teams. Failure to use reliable guidelines is a problem for the standardisation of this critical part of the testing process (20). When advising patients how to prepare for tests it is essential that nurses know when samples should be taken, the timing of the last meal, the time after taking any drugs and how long the patient has to remain seated

before taking the sample (5).

Several reviews (1, 2, 12,17, 24-27) revealed that patient misidentification in the preanalytical phase is a serious error that can be associated with high risk to the real patient. Blood transfusion is a particular area of risk in this case (12). Accuracy of patient identification is the most important goal in improving patient safety (1, 3). Da Rin (2) addressed patient misidentification by the use of either non-technical methods (patient safety guidelines and procedures) or a technical solution (identification wristbands). A non-technical solution means that medical staff must follow procedures to reduce risks and ensure that samples are obtained from the correct patient. Focusing on the sources of errors that could translate into harm and adverse events for the patient would encourage nursing staff to adopt a patient-centred view.

During Collection

In this domain the focus is on drawing blood from the patient**;** this is the source of many possible errors. The use of a tourniquet makes it easier to locate veins, but any prolonged use alters laboratory results. Some studies reported that samples were collected in inappropriate containers (1-2, 5, 12, 17, 25, 28-29)**,** preventing their analysis and causing harm to patients as a result of the need for re-collection. There were also problems associated with filling test tubes, both overfilling and underfilling (2, 4, 12, 17, 25, 29-31)**,** leading to unreliable laboratory results. Haemolysis (destruction of red blood cells) often takes place when blood collection is not conducted correctly (e.g. when the needle is not properly inserted in a vein). Unfortunately, haemolysis, which prevents many laboratory tests, was commonly reported (5, 29-30, 32). In addition, mislabelled and unlabelled samples were common errors in the preanalytical phase (1, 3, 5, 29-30).

After Collection

This domain focuses on sample preparation aimed at rendering a sample suitable for analysis.

The studies showed that handling and storage of samples outside the laboratory both have an impact on the quality of blood samples (24- 25, 20, 31). Clotted samples were reported (12, 30); this is in fact a significant problem in practice. If blood samples are not mixed properly but gently after collection there may be clotting. Clotted samples are not suitable for analysis. Haemolysis can also occur after collection if the samples are handled roughly. After collection the samples should be transported as quickly as possible to the laboratory. The effects of evaporation are routinely underestimated, and can be avoided by sealing the tubes. Nauck *et al.* (32) showed that evaporation can significantly change analyte concentrations; the evaporation effects should be less than 3% after one day at room temperature and less than 5% after one week of storage.

Inappropriate storage conditions can cause errors in laboratory results (3). Delays in processing (4, 20, 24-25, 30, 26, 32) can also adversely affect laboratory results and thereby patients' care. Steindel & Jones (33) noted that transport time for samples collected from outpatients increases during the day and is more variable than that for samples from inpatients. This makes it more difficult to control sample quality for the former group.

Discussion

This literature review represents an attempt to describe the preanalytical quality failures in blood sampling and to present information about blood sample collection. As a result of this research it should be possible to improve and evaluate blood sampling praxis. This study presents a new way to understand the steps associated with blood sampling and the need, during the process, to involve patients and other professionals. Traditionally in laboratory medicine the focus has been on the analysis phase when laboratory results are produced; less attention has been paid to the preanalytical phase (17) and its importance has been underestimated. This literature study revealed that the preanalytical phase has a considerable effect on the reliability of laboratory results and on patients' safety. Focus on patient safety calls for increased attention to this issue and highlights the need to develop a new mode of action to avoid errors in blood sampling.

According to previous studies (5,18,19,34,35) it was already known that patient-related factors, such as posture, heavy physical exercise, physical stress, psychological stress, fasting and timing of sampling can have an effect on subsequent laboratory tests. In general this issue has been considered from the medical point of view (17), but unfortunately there has been hardly any discussion from the nursing perspective. Any discussion of quality failures associated with blood sampling should be conducted in the context of multiprofessional and multidisciplinary practice. Healthcare professionals play an essential role in blood sample collection and in advising

the patients on how to prepare for this. Awareness of quality failures in the blood sampling process and cooperation with personnel outside the laboratory are key factors for improving the quality of clinical laboratory procedures and producing reliable results, thus enhancing patient safety.

In this literature review the most common preanalytical quality errors were identified: they were associated with blood sampling outside laboratories. The errors occurred during three phases: *before, during and after blood sample collection*. The results indicate that the most serious errors *before blood sample collection* were patient misidentification and inappropriate advice to patients. It is essential to ensure that blood samples are collected from the right patients. Blood samples should never be taken before the identity of the patient is confirmed. It is important to follow established guidelines for sample collection in all circumstances, including on the wards. Following these guidelines ensures the standardisation of blood collection. *During collection* the main errors were technical in nature**,** for example using a tourniquet for too long. It is essential that nurses know and understand how to use different equipment and materials and appreciate why standardised handling will ensure the quality of the blood sample. Finally, *after blood sample collection* transportation and storage of samples are critical in the preanalytical phase. It is essential that samples are stored at the correct temperature and treated gently in order to eliminate the possibility of haemolysis**.** Our findings about the sources of error during the preanalytical phase are confirmed by several studies, e.g. Szecsi & Ødum (13) and Carraro & Plebani (15). Standardised blood collection is a prerequisite for being able to compare the patients' results both with reference values and with their own earlier and subsequent results.

This study provides information based on clinical studies that can be used at the most fundamental level of practical care work. By applying this knowledge, preanalytical variation in blood collection could be reduced and patient safety increased. The application of updated knowledge of preanalytical factors when taking blood samples is recommended when professionals are advising patients to prepare for laboratory tests or when they are going to take blood samples themselves. To prevent errors it is necessary to see blood sampling as a competence to be attained not just a technical trick. The process begins and ends with the patient, so patients are also part of that team. If the team fails it is the patients who suffer most.

The value of this study is that it combines results and, thus, draws attention to the blood sampling undertaken by nurses and the possible consequences of their specific actions. The results of many studies have been integrated to provide a broader understanding of the phenomenon. This literature review brings together the combined knowledge and skills of a number of researchers.

The results of this literature review should not be extrapolated, but it can serve as a contribution to improving blood sampling as a part of patient safety in nursing care, an area that is not widely acknowledged in nursing. The different approaches and methods described in the articles provided a broad picture of factors affecting blood sampling. It, thus, enhances our understanding of the preanalytical factors operating during blood sampling and the results should be used to improve the quality of sampling and to increase patient safety. In this study, we used text from the selected articles as the research material. The authors have attempted to be as honest and careful as possible when describing the texts so as to interpret them correctly.

This study should prove useful in practice. Patient safety and blood sampling quality improvement in practice only begins if professionals are aware of the various factors that have effect on blood collection and how these relate to good nursing care. Further research is required to investigate whether healthcare professionals follow the standardised sampling procedure and how they understand its importance with respect to the quality of the samples and patient safety.

Conclusion

This evidence-based study describes the preanalytical errors that can have a crucial effect on reliable laboratory results and thus on patient safety. All those who collect blood samples should be informed of these factors, so that they can avoid them. If patient safety is to be improved, integration between laboratory services and healthcare is needed. New fields of research are required, such as monitoring regular staff training and the attitudes of nurses' attitudes; in addition nurses should discuss quality errors in blood sampling and take responsibility for them. Nurse education provides a basic knowledge of blood sampling; this should be extended in the curriculum and in-service training, and certification of blood sampling should be considered. Multi-professional co-operation with respect to sampling, involving laboratory personnel, could reduce the number of errors in the preanalytical phase. Research is also needed into how

nurses follow standardised procedures for taking samples and how well they understand their importance for the quality of samples and patient safety.

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