Sources of preanalytical error in primary health care

-Implications for patient safety

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ABSTRACT

Background Venous blood tests constitute an important part in the diagnosis and treatment of patients. However, test results are often viewed as objective values rather than the end result of a complex process. This has clinical importance since most errors arise before the sample reaches the laboratory. Such preanalytical errors affect patient safety and are often due to human mistakes in the collection and handling of the sample. The preanalytical performance of venous blood testing in primary health care, where the majority of the patients contact with care occurs, has not previously been reported.

Aims To investigate venous blood sampling practices and the prevalence of haemolysed blood samples in primary health care.

Methods A questionnaire investigated the collection and handling of venous blood samples in primary health care centres in two county councils and in two hospital clinical laboratories. Haemolysis index was used to evaluate the prevalence of haemolysed blood samples sent from primary health care centres, nursing homes and a hospital emergency department.

Results and discussion The results indicate that recommended preanalytical procedures were not always followed in the surveyed primary health care centres. For example, only 54% reported to always use name and Swedish identification number, and 5% to use photo-ID, the two recommended means for patient identification. Only 12% reported to always label the test tubes prior to blood collection. This increases the possibility of sample mix-up. As few as 6% reported to always allow the patient to rest at least 15 minutes before blood collection, desirable for a correct test result. Only 31% reported to have filed an incident report regarding venous blood sampling, indicating underreporting of incidents in the preanalytical phase. Major differences in the prevalence of haemolysed blood samples were found. For example, samples collected in the primary health care centre with the highest prevalence of haemolysed samples were six times (95% CI 4.0 to 9.2) more often haemolysed compared to the centre with the lowest prevalence. The significant variation in haemolysed samples is likely to reflect varying preanalytical conditions.

Conclusions This thesis indicates that the preanalytical procedure in primary health care is associated with an increased risk of errors with consequences for patient safety and care. Monitoring of haemolysis index could be a valuable tool for estimating preanalytical sample quality. Further studies and interventions aimed at the preanalytical phase in primary health care are clearly needed.
ORIGINAL ARTICLES


III. Söderberg J, Grankvist K, Brulin C, Wallin O. Incident reporting practices in the preanalytical phase: Low reported frequencies in the primary health care setting. Submitted.


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<th>Abbreviation</th>
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<tr>
<td>CI</td>
<td>Confidence interval</td>
</tr>
<tr>
<td>COES</td>
<td>Computerised order entry system</td>
</tr>
<tr>
<td>ED</td>
<td>Emergency Department</td>
</tr>
<tr>
<td>HI</td>
<td>Haemolysis index</td>
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<tr>
<td>LID</td>
<td>Laboratory identification number</td>
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<tr>
<td>OR</td>
<td>Odds ratio</td>
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<tr>
<td>PHC</td>
<td>Primary health care centre</td>
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<td>POCT</td>
<td>Point-of-care testing</td>
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<td>TTP</td>
<td>Total testing process</td>
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DEFINITIONS

Enrolled nurses  Upper secondary school. Perform VBS and basic health care duties in the PHCs.

Registered nurses  3 years of university studies. Have their own reception in the PHCs, make house calls to patients and perform VBS.

Biomedical technicians  3 years of biomedical university studies. Manage analytical equipment and perform VBS in hospital clinical laboratories and sometimes in PHC laboratories.
INTRODUCTION

Patient safety

Patient safety is defined as “freedom from accidental injury” by The Institute of Medicine [1] and “protection from health care related injury” by the Swedish National Board of Health and Welfare [2]. The latter further defines health related injury as “suffering, discomfort, physical or mental injury, disease or death caused by the health care system that is not an unavoidable consequence of the patients condition”. The Institute of Medicine report “To Err is Human” [1] suggested that between 44 000 and 98 000 patients died in the United States each year because of medical errors. This report estimated that as many as one million patients were injured each year, with an annual cost for society of between 17 an 29 billion dollars.

In 2007, the Swedish National Board of Health and Welfare conducted a survey of health care injuries [3] and concluded that more than 100 000 patients treated at Swedish hospitals suffered from medical errors each year. Of these patients, almost 10% received lasting injuries and 3% died. In fact, health care related injuries are estimated to lead to 600 000 days of unnecessary hospital treatment annually in Sweden [3]. Patient safety seems like an important area for improvement in the health care systems worldwide.

A medical error is defined by the Institute of Medicine as “The failure of a planned action to be completed as intended or the use of a wrong plan to achieve an aim” [1]. The definition of medical errors, however, vary substantially and a commonly agreed definition can be interpreted differently by different individuals [4]. Adverse event is another frequently used term which can be defined as “injuries that result from medical management rather than the underlying disease” [5]. This is closely related to the Swedish National Board of Health and Welfares definition of health related injury [2], but a universally accepted definition is still lacking [4]. This lack of definitions could lead to difficulties in comparing medical error rates and the effect of patient safety interventions. This could in turn obstruct appropriate action towards improved patient safety.

Taken together, medical errors and patient safety are areas that require urgent attention in order to reduce patient suffering and death. Further, the modern health care systems are challenged by increased access to more advanced and expensive treatments leading to increased health care spending [6]. Considering the growing elderly population in several
European countries, including Sweden [7], health care costs will probably increase in the near future. A reduction of medical errors could, except for the reduction of injuries and human suffering, lead to increased availability of resources which would be most welcome elsewhere in the health care system. The possibility for patients to compare and choose caregivers will put demands on improving patient safety. Thus, important challenges in patient safety persist.

When reducing medical errors, all attention in modern health care should not focus on extensive examinations of rare events. Often, such events are the unfortunate combination of events that are unlikely to be repeated [8]. It is therefore important to survey frequently occurring, error prone everyday tasks since repeated errors will lead to consequences for a large number of patients. One current example of the importance of such an approach is the increased focus on health related infections, a common problem affecting patient safety, where one of the most important preventive actions is improved basic hygiene routines [9].

**Systems perspective**

Recent years, new insights and theories on the causes of medical errors have emerged, by which the systems perspective is commonly used. A system is made up of mutually dependent components working together with a common goal [10]. Researchers managing quality in health care have conveyed the view that a system often fails due to its organization and structure rather than its unique constituents [10]. A 85/15 rule has even been suggested, implying that 85% of all mistakes are due to the system, and only 15% are due to the individual [11]. Hence, the mistakes are made by human individuals, but system shortcomings are the cause of most of them. Many errors in the health care systems are predictable and made by staff capable of performing the task safely [12]. This stresses the importance of viewing health care services as a system, which not always is the case these days [13].

One of the main conclusions in the national investigation of patient safety in Sweden [14], appointed by the government and presented 2008, was that modern health care must be viewed as a system in order to improve patient safety. One main conclusion in the Institute of Medicine report, previously mentioned, is that effort should be put into designing safe systems rather than blaming individuals [1]. One example of system improvements leading to enhanced patient safety is the introduction of the ATLS-concept in the emergency departments.
**Primary health care**

In Sweden, primary health care is defined as the first level of health care, covering basic diagnostics, treatment and care, as well as preventive work and rehabilitation, without restrictions regarding disease, age or patient characteristics [15]. Primary health care is the most utilized health care resource is Sweden as well as internationally [16, 17]. In fact, hospitals are the least frequently used component of the health care system [17]. In 2006, 16.8 million physician appointments were made in primary health care centres (PHCs) in Sweden compared to 14.3 millions in hospitalized care [16]. PHCs form the base of Swedish health care and deals with a wide spectrum of diagnosis and treatments.

Most previous studies on patient safety have had an inpatient perspective [18] even though medical errors also occur in PHCs [18-21]. Such errors are costly for the health care provider [22] and can result in serious consequences, including patient death [19, 23]. Research regarding medical errors in hospitals have found several threats to patient safety such as medication [24] and laboratory errors [25], but experience from the inpatient setting can not always be transferred into PHCs [18, 20]. Most studies on patient safety in PHCs have focused on the physicians practice [20] despite the fact that PHCs include several other staff categories, such as registered nurses specialized in general practice, registered nurses, enrolled nurses, physiotherapists, occupational therapists, midwives, biomedical technicians, psychologists and counsellors [15]. Therefore, patient safety in PHCs seems like an important area for future research.

**Laboratory testing**

Laboratory services play an important part in modern health care [26]. Laboratory tests performed on blood samples are commonly used and contribute to a substantial part of the health care budget [27]. These samples can be collected from capillaries, arteries, central or peripheral veins, were samples collected from veins and capillaries occur most frequently. It has been stated that 60-70% of all decisions regarding critical patient care are impacted by laboratory test results [28]. Clinical guidelines used by physicians and other health care staff, rely on tests performed on blood samples as criteria for medical decisions [29]. Tests performed on venous blood samples influence the certainty of diagnosis in primary health care [30].

The majority of the blood samples are analysed by clinical chemistry testing. Common examples include quantification of levels of glucose, electrolytes, C-
reactive protein, haemoglobin and cardiac and coagulation markers. Blood samples can also be used for microbiological, pre-transfusion and genetic testing and analysis of oxygen tension levels. Other samples used for laboratory testing include tissues, urine and faces.

The vast majority of all laboratory testing is performed in clinical laboratories located in hospitals. These conduct analyses on specimens sent from hospitals and PHCs. To a varying degree they also perform in- and outpatient sample collection. Laboratory testing can also be performed by the local laboratories in the PHCs, so called point of care testing (POCT). Common examples include haemoglobin count and C-reactive protein levels, mainly from capillary samples.

Clinical laboratories have a long history of improving quality of daily work which have considerably lowered analytical error frequencies [31]. Most hospital clinical laboratories in Europe are accredited [32], often according to the ISO/IEC 17025 standard [33]. This implies that the competence of the organisation is assessed by an external evaluator. Sample collection by an accredited laboratory is performed according to documented routines, aimed at reducing errors. Certification is an evaluation of competence on the individual level. One example is a competence certificate, mandatory for performing sample collection in some clinical laboratories.

**Venous blood sample collection**

Venous blood sampling (VBS), the subject of this thesis, refers to blood samples collected from peripheral veins by a needle and a vacuumised test tube. VBS is the most common way of obtaining blood samples for clinical chemistry testing. VBS can reveal infections and ongoing cardiac ischemia, point out tumour markers in the blood and lead the way to diagnosis and treatment of a large number of diseases and conditions. In the clinical chemistry laboratory of Umeå University Hospital, 3 million analyses are performed on venous blood samples annually. Venous blood samples are unquestionably an important part of modern health care.

**Context for blood sample collection**

Staff performing blood sample collection varies, both among different settings and internationally. In PHCs in Sweden, most blood samples are collected by enrolled nurses and to a lesser extent by registered nurses. In a few PHCs, biomedical technicians are employed to perform sample collection. Blood collection staff in PHCs varies internationally. For example, in the Unites States most blood samples in PHCs are collected by registered
nurses [34], while trained laboratory technologists perform most of the VBS in PHCs in Finland [35]. In clinical laboratories, biomedical technicians perform sample collection along with managing the analytical equipment. Sometimes enrolled nurses are employed to perform sample collection in the laboratory phlebotomy room. In Swedish hospitals most blood collection is performed by enrolled nurses and to a lesser extent by registered nurses. Internationally, hospital blood collection staff include specially trained nurses [34], registered nurses, physicians, or laboratory staff (most often biomedical technicians).

The total testing process

The total testing process (TTP) is the chain of events starting with the ordering of a test and ending with the interpretation of the test result (Figure 1). The TTP starts and ends with the patient. The patient has a problem and contacts a health care provider, in Sweden most often a physician in a PHC. If judged as necessary, the physician translates the patient’s history, signs and symptoms into the ordering of one or several analyses. The responsible staff performs patient preparation, sample collection and sample handling. The sample is thereafter most often transported to a hospital laboratory for analysis. The analytical part of the process ends with the delivery of a test result. This test result, when correctly interpreted, will ultimately contribute to helping the patient with her/his problem.

Figure 1. A summary of the total testing process with error frequencies for each stage [36].
As shown in Figure 1, the TTP includes many steps, and errors can arise in all parts of the process. Error rates in the TTP range from 0.01% to 0.5% [36], but no studies have been performed in Sweden. These error rates may seem rather low, but when considering the amount of tests analysed, the total number of errors becomes very high. The marked difference in error frequencies can partly be explained by the heterogeneity in study designs and differences in error definitions [26].

It has been estimated that about 75% of all errors will generate results within the reference interval [37], increasing the possibility of passing unnoticed for the interpreter. Since many studies investigating errors in laboratory medicine have focused on investigating abnormal test results [25, 38, 39], errors leading to normal test results are probably often not recognised. Thus, the “true” error frequencies in the TTP are probably higher than what is found in most studies. Many incidents are also recognised before the sample is analysed [26] which can lead to renewed sample collection and/or a delayed test results, even if the correctness of the test result itself is not affected.

Approximately 25% of the TTP errors have consequences for the patient, both in hospitals [25, 38] and in primary health care [40]. This can result in erroneous medication and radiographic examinations [41], delayed diagnosis of HIV [40], false positive tests, including false positive pregnancy tests and repeated testing [40]. This is accompanied by increased costs for the health care provider. Of errors reported by PHC staff, as much as one fourth [42] of all errors have been found to originate in the TTP. Thus, it is apparent that the TTP in primary health care has its share of errors negatively effecting patient safety.

It is important to view laboratory testing as a process. From the patient’s point of view, it is the end result, a reliable and correct test result that is important. It is of less importance if one part of the process is safe and reliable, if another is error prone and unstable. A theoretical approach to such problems is the widely used Pareto principle (Figure 2). According to this principle, a small number of causes will most likely contribute to a large part of the problem. The clinical implication of the Pareto principle for laboratory testing is that available resources should be aimed to the part of the TTP with the largest contribution to the total number of errors.

The TTP is usually subdivided into three phases (Figure 1): The preanalytical phase, before the sample is analysed in the laboratory, the analytical phase, when the sample is analysed in the laboratory and the postanalytical phase,
when the test result is transferred and interpreted [36]. Each phase is given a presentation below.

![Graph showing different categories of errors]

**Figure 2.** The Pareto principle indicates that a few categories of errors will contribute to the vast majority of the total errors.

**The preanalytical phase**

The preanalytical phase of the TTP includes all events from the ordering of the test until the analysis is initiated in the laboratory. A large body of evidence has emerged in recent years, indicating that the majority of errors in the TTP arise in the preanalytical phase [25, 31, 36, 38-40]. There is also evidence that most of these errors are caused by human mistakes in the sampling process [39]. Knowledge of preanalytical errors is important when interpreting test results [34].

**Patient preparation**

Depending on the analysis, the patient may have to be prepared before the blood sample is collected to assure a correct test result. One important example is patient rest. Shifts in body position may cause loss of plasma volume from the vessels into the interstitial space [43, 44]. Thereby, concentrations of remaining components in the blood, mainly proteins and protein-bound molecules, will increase. The body position of the patient can
therefore affect the test result [45, 46]. For some analytes, changes of as much as 70% can be seen [47]. It is therefore difficult to compare test results separated in time, if the body position of the patient before sampling is not standardised. The sample should preferably be collected after 15 minutes of rest [48] with the patient in a supine position [49] to avoid influence on the test result [47]. To assure that test results are reliable and comparable, and that reference intervals can be applicable, most laboratory manuals recommend 15 minutes of patient rest before the sample is collected.

Other patient preparation factors affecting the accuracy of the test result include smoking, fasting status, alcohol intake, exercise and the menstrual cycle [47]. Circadian variation is another factor that can affect certain analyses [46]. Knowledge of preanalytical factors affecting test results is essential when preparing the patient for VBS, as well as when interpreting the test result.

Patient identification

Patient identification is the most important step in VBS - it is unimportant if all other parts of the TTP are performed correctly if the sample is collected from the wrong patient. A patient identification error may also affect two patients. Misidentification of patients occurs in both hospitals [25, 38, 50] and PHCs [51]. Depending on the definition, identification errors can constitute as much as 27% of all preanalytical errors [39].

Patient identification errors in PHCs can lead to serious consequences [52] including diagnosing a healthy patient with HIV-infection [51]. The Swedish National Board of Health and Welfare has mandatory instructions for patient identification for VBS for pre transfusion testing [53]. These instructions apply for all VBS [54]. Hence, the patient’s identity should be checked by asking the patient for full name and Swedish identification number, and the identity should be confirmed with photo-ID.

Test request management

Paper based test requests are an important source of error in the preanalytical phase [55, 56]. A large part of rejected samples can be due to erroneous test requests [57]. Test request errors have been found to range between 4% and 8% of all errors in the TTP [55, 56, 58]. Error frequencies as high as 39% has been reported for transcription of information from requests [59]. As for all errors, the error rates depend on study design and the definition of error, but it is apparent that test request errors can lead to clinically significant errors, such as wrong test ordered, delivering wrong test
result to the patient and ineffective use of resources [59]. Test requests
should be completed with the patient’s full name and identification number
and this information should be rechecked during the identification
procedure. The information on the test request should be compared with the
 corresponding information on the test tube labels. The test request should
finally be signed to assure that the patient is correctly identified.

**Test tube labelling**

Mislabelling of test tubes is a frequently occurring preanalytical problem [57,
60]. Frequencies as high as 50% of all identification errors in the TTP have
been reported [50]. Test tubes should always be labelled prior to blood
collection [49, 53] in order to avoid mislabelling. Mislabelling of test tubes
will potentially have equally serious consequences as patient identification
errors. In one study, 4% of all test tubes from PHCs, and as many as 20% of
all test tubes from a single PHC, were labelled with the wrong patient
identity [61]. Test tubes with minor labelling errors are 40 times more likely
to contain the wrong patient’s blood [62]. The labelling procedure is
therefore of great importance for patient safety in the TTP.

**Sample collection and handling**

The collection of the blood sample can be a clinically important source of
preanalytical errors. In fact, a large part of uncertainties in the TTP may
arise from errors in sample collection [63]. One important example is
prolonged venous stasis, which causes extravasations of fluid, leading to
increased relative concentrations of remaining components. In addition,
prolonged venous stasis causes leakage of potassium from cells [64].
Prolonged venous stasis can therefore significantly affect certain analyses
[65], including increased potassium levels [66] and the diagnosis of
hypercholesterolemia [67]. In addition, prolonged venous stasis can cause
haemolysis in the specimen [68, 69]. If venous stasis is necessary, it should
preferably be applied for as short time as possible and removed before the
first test tube is filled.

If several test tubes are to be used, a particular sequence should be used as
stated by the local laboratory to avoid contamination of additives. Test tubes
should be properly filled to achieve an appropriate concentration of
anticoagulants [49]. Sample collection from intravenous catheters,
commonly used in emergency rooms, is known to cause haemolysis [70, 71].
Haemolysis rates are inversely correlated to catheter size [70]. Blood
sampling from intravenous catheters should preferably be avoided.
After phlebotomy, test tubes with additives should be inverted to allow for proper mixing of additives with the blood [49]. Inappropriate inversion of test tubes and non-vertical test tube storage may cause clotting of the blood, reported to constitute an important part of all preanalytical errors [72]. However, conflicting findings are reported, indicating that absence of test tube inversion is of less importance [73, 74]. Certain test tubes need to be centrifuged before storage and transport. Prolonged time to centrifugation [75], high centrifugation speed [76] and storage temperatures [77] can all cause preanalytical errors. All in all, the practical performance of sample collection and handling has importance for a correct test result.

Information search

The laboratory manual contains information on a correct procedure for handling, collecting and ordering of samples. Reference intervals and decision limits, commonly used by physicians for interpretation of test results [78], require that sample collection should be performed under similar conditions as used for the samples collected to define the reference data [79]. However, as previously described, not all steps in commonly used laboratory manuals are fully supported by the literature. The practical performance of the VBS procedure is also described in the general instruction manual for all health care staff (in Sweden known as “Handboken”) [80].

Correct laboratory information is important for an efficient workflow in health care [81]. The laboratory manual contains important information of specimen collection and handling [82]. Adherence to the laboratory manual helps to maintain accurate and reliable test results [83]. Online manuals have replaced many of the older, paper-based manuals, and this allows for frequent updates and better access and thus increased possibility of correct information. Online manuals are necessary because of the dynamic nature of laboratory information (test methods change) and online manuals are needed to keep the users up to date [84]. Information in a paper based manual will become obsolete and can contradict other laboratory information [82]. Further, paper based manuals are expensive, difficult to update and can lead to an increased workload for the laboratory staff [85]. Thus, utilization of laboratory information by an online manual is important when performing VBS.
Table 1. Instructions for preanalytical procedures according to the investigated laboratory manuals, recommendations by authorities and scientific evidence. Included is the authors overall rating of the validity of the laboratory instructions.

<table>
<thead>
<tr>
<th>Preanalytical procedure</th>
<th>Recommended by authorities</th>
<th>Evidence</th>
<th>Rating*</th>
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<tbody>
<tr>
<td>Information of sample collection and handling should be obtained from the online manual issued by the laboratory</td>
<td></td>
<td>[34, 81, 82, 85]</td>
<td>Strong</td>
</tr>
<tr>
<td>Test tube labelling before sample collection</td>
<td>Swedish National Board of Health and Welfare</td>
<td>[49]</td>
<td>Strong</td>
</tr>
<tr>
<td>15 minutes of patient rest prior to blood collection</td>
<td>General instruction manual (“Handboken”)</td>
<td>[43, 45-47]</td>
<td>Strong</td>
</tr>
<tr>
<td>If stasis is necessary it should be used as short as possible</td>
<td>General instruction manual (“Handboken”)</td>
<td>[66, 68, 86]</td>
<td>Strong</td>
</tr>
<tr>
<td>Test request information is compared to ordering information. Patient identification information is compared to corresponding information on test request. The test request is signed</td>
<td>Swedish National Board of Health and Welfare. Clinical and Laboratory Standards Institute. General instruction manual (“Handboken”)</td>
<td>[58]</td>
<td>Strong</td>
</tr>
<tr>
<td>Test tubes with additives should be inverted and then stored vertically</td>
<td>Clinical and Laboratory Standards Institute. General instruction manual (“Handboken”)</td>
<td>[72]</td>
<td>Weak</td>
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*A combination of recommendations, evidence and the author’s judgement.
Preanalytical incident reporting

Learning from mistakes is a key factor for improving the quality and safety in health care [1]. Errors in VBS affecting patient safety must be carefully recognised before they can be analyzed and adjusted for [87]. To avoid preventable adverse events, it is important to gather reliable information on incidents occurring in the preanalytical phase. Incident reports can be used to gain such information, both in hospitals and in PHCs [87, 88]. Reported errors include identification and labelling errors [89] with potential to cause patient inconvenience [50]. Thus, reporting incidents related to VBS is important to identify preanalytical risks with potential to cause patient harm. Previous research indicates that self-reporting is likely to underreport incidents in health care [90, 91]. However, no previous studies have reported results regarding frequencies of preanalytical incident reporting in PHCs. This has importance for patient safety since underreporting of preanalytical incidents in PHCs would decrease the possibility to discover preventable system vulnerabilities in the TTP.

Haemolysis

Haemolysis is the release of haemoglobin and other intracellular components to the surrounding plasma following damage to the erythrocyte cell membrane [76]. Haemolysis is most often caused by inappropriate collection and preanalytical handling of the specimen [76]. Examples include prolonged stasis [68], blood collection from intravenous catheters [71] and the site of venipuncture [68]. The amount of haemolysis can be estimated by a subjective visual assessment, based on the colour of the sample. At the laboratory, haemolysis can be measured as free haemoglobin with a spectrophotometer with detection limits below 0.020 g/L. Haemolysis levels above 0.2 g/L may be visible in the centrifuged blood sample [92]. Most automated clinical chemistry analysers can now identify and grade haemolysis as a haemolysis index (HI). HI is an automated measurement, based on a spectrophotometric technique.

The prevalence of haemolysed specimens has been suggested as a suitable marker for preanalytical quality [56]. Most previous studies evaluating prevalence of haemolysis, have used subjective visual assessment [68, 70, 71, 93-95] or analysis of free haemoglobin with laborious manual spectrophotometric techniques [94, 96-98]. To use HI in automated analysers is a more efficient method in detecting haemolysis. However, the possible use of HI as a marker of preanalytical quality in PHCs has not previously been reported.
Haemolysed specimens frequently occur in laboratory practice with reported prevalence’s as high as 3.3% of all routine samples [96]. Haemolysis is the leading source of unsuitable specimens in the laboratory [99]. Haemolysis can falsely increase or decrease levels of several analysed substances [97, 98]. This may be mediated by release of intracellular enzymes and changed concentrations [76]. Even mild or almost undetectable haemolysis by visual inspection can lead to clinically significant alterations of, for example, potassium and lactate dehydrogenase [98]. Troponin T levels can be falsely decreased due to haemolysis [76] which can result in giving a clean bill of health to a patient with ongoing cardiac ischemia. Analytical specimen rejection and the following renewed sampling may cause a delay in treatment and will also impede patient flow. Causes of haemolysis and examples of potentially affected analytes are listed in Table 2.

**Table 2.** Causes of haemolysis and examples of potentially affected analytes

<table>
<thead>
<tr>
<th>Affected analyte</th>
<th>Bias*</th>
<th>Factors causing haemolysis</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Troponin T</td>
<td>Negative</td>
<td>Intravenous catheters</td>
<td>[70, 71]</td>
</tr>
<tr>
<td>Troponin I</td>
<td>Positive</td>
<td>Prolonged venous stasis</td>
<td>[68, 69]</td>
</tr>
<tr>
<td>Potassium</td>
<td>Positive</td>
<td>Excessive shaking of test tube</td>
<td>[76]</td>
</tr>
<tr>
<td>Glucose</td>
<td>Negative</td>
<td>Under filling of test tube</td>
<td>[68]</td>
</tr>
<tr>
<td>Haptoglobin</td>
<td>Negative</td>
<td>Needle size</td>
<td>[68]</td>
</tr>
<tr>
<td>Creatinine</td>
<td>Positive</td>
<td>Blood drawing from distal arm</td>
<td>[68, 93]</td>
</tr>
<tr>
<td>D-dimer</td>
<td>Positive</td>
<td>Delayed separation of specimens</td>
<td>[76]</td>
</tr>
<tr>
<td>Albumin</td>
<td>Negative</td>
<td>Centrifuging at to high speed</td>
<td>[76]</td>
</tr>
<tr>
<td>Sodium</td>
<td>Negative</td>
<td>Exposure to hot or cold temperature</td>
<td>[76]</td>
</tr>
</tbody>
</table>

*Modified from [76].

Comprehensive knowledge on the type of interference exerted by haemolysis on laboratory testing, along with appropriate training of VBS staff are essential to minimise errors in laboratory activity [76, 93]. This has importance in primary health care since haemolysis will not be known until the test result is delivered. If the test result is rejected, the patient will have to visit the practice again for renewed sampling. The prevalence of haemolysed samples in PHCs has implications both as a potential indicator of preanalytical quality and also as a source of rejected specimens, impeding patient flow.
The analytical phase

The analytical phase includes analysis of the sample in the laboratory. Previously, quality improvement in laboratory testing has mainly focused on reducing errors in the analytical phase [25]. This has significantly decreased analytical errors rates, by automation, improved technology, standardization and informatics [100]. The analytical phase now contributes to the lowest frequencies of errors in the TTP, in both hospitals and PHCs [36, 40].

It has been suggested that it is time for the laboratories to broaden their perspective and focus on the pre- and postanalytical parts of the TTP in order to achieve maximal reduction of errors from the patients point of view [101]. Analytical quality, however, still has potential for quality improvement. One example is immunoassays [101] where analytical errors can have clinically significant consequences [41]. The analytical variation can be reduced but can never be zero [29]. Further, biological variation, the variation of an analyte in an individual, can also affect the test result [102].

POCT brings other sources of analytical errors than analyses performed in clinical laboratories. POCT, unlike laboratory analysis, is performed by a variety of clinical staff on multiple devices at various locations [103]. Sources of errors include inappropriate storage of reagents, use of outdated reagents, deviations from manufacturers instructions and absence of required quality control [103]. Since different analytical methods often are used, a test result from POCT could not always be compared to a test result obtained from a clinical laboratory. Since the laboratory part of the TTP errors are now below 15% of all errors in the TTP [36] the greatest reduction of errors in the TTP is likely to result from improvements of the specimen collection in the preanalytical phase [104].

The postanalytical phase

The postanalytical phase concerns delivery and interpretation of the test result. Errors in this phase may account for 18.5% to 47% of all errors in the TTP [36]. These errors include delayed or not reported results, results reported to the wrong provider and wrong results reported because of transcription errors [31]. Thus, improved information technology is of great importance for improvements in the postanalytical phase [31]. Use of inappropriate reference interval is another postanalytical error affecting the clinical interpretation of the test result and leading to errors in clinical decision making [105]. Timely and correct interpretation of test results is also of importance in the postanalytical phase [106]. This is most definitely an important area for future studies.
RATIONALE

Patients are entitled to health care with a high degree of quality and safety. This is not always the case in the health care systems of today. One important example is errors occurring in the total testing process in primary health care, where most of the patient’s contacts with care occur. These errors have consequences: for patient safety due to care based on erroneous or incomparable test results and for the health care systems due to increased costs.

Previous research and clinical insights indicate that most errors in the total testing process are preanalytical: they occur before the sample reaches the laboratory for analysis. Such errors are often the result of human mistakes during sample collection or handling. Thus, the preanalytical process has importance for patient safety in primary health care.

Previous studies of preanalytical errors have mainly focused on quantifying error rates rather than investigating the practices leading to the errors. Available reports from hospitals indicate that preanalytical practices are associated with an increased risk of errors, but no such studies are presented from the primary health care setting.

Haemolysis in vitro, the release of haemoglobin following damage to red blood cells, is mainly caused by mistakes in the preanalytical process. Haemolysis is a common preanalytical problem, and the prevalence of haemolysed blood samples is suggested as a suitable marker for preanalytical quality. Haemolysis index is a modern automated and sensitive method for measuring haemolysis, but the possible use as a marker of preanalytical quality in primary health care has not previously been reported.

In summary, it is important for patient safety and care to survey the practical performance of venous blood sampling in primary health care. By identifying error prone steps and suitable indicators for sample quality, the total testing process could be improved in a patient-centred way.
AIMS

General aim:

To investigate sources of preanalytical error in primary health care by surveying the preanalytical procedure in primary health care centres.

Specific aims:

• To survey reported preanalytical practices (patient identification, test request management, test tube labelling, patient rest, stasis removal, test tube handling and information search) among staff responsible for venous blood sampling in primary health care (Papers I and II).

• To compare reported preanalytical practices between primary health care and hospital clinical laboratory staff (Papers I and II).

• To survey if staff characteristics (re-education and access to documented routines regarding venous blood sampling, professional category, employment time, years since basic education, age and sex) are associated with reported preanalytical practices among staff responsible for venous blood sampling in primary health care (Papers I and II).

• To investigate incident reporting frequencies and barriers against reporting incidents related to venous blood sampling among staff responsible for venous blood sampling in primary health care, in comparison to hospital clinical laboratory staff (Paper III).

• To investigate differences in the prevalence of haemolysed blood samples between individual primary health care centres and between primary health care centres, nursing homes and an emergency department (Paper IV).
MATERIAL AND METHODS

The first part of this thesis was a questionnaire survey of preanalytical practices and incident reporting practices related to VBS in PHCs (Papers I-III). The second part of the thesis was an investigation of haemolysis in samples collected in PHCs, nursing homes and an emergency department (Paper IV).

The questionnaire survey

Setting

The investigated county councils contained a total of 70 PHCs, all included in the survey. The majority of the VBS in the investigated PHCs was performed by enrolled nurses. The other staff categories collecting blood samples were biomedical technicians and registered nurses (Table 3). The clinical laboratory in one of the investigated PHCs was accredited according to ISO 17025 [33]. In the investigated county councils, there were several PHCs, but only a few clinical laboratories located in the nearest hospital. The PHC staff performed VBS on request from the PHC physicians and to a lesser extent from hospital physicians. The test results were sent to the referring specialist.

In one of the investigated county councils, the neighbouring hospital clinical laboratory had conducted educational efforts aimed at PHC staff. The VBS staff was invited once a year to the hospital clinical laboratory to receive re-education on different aspects of VBS. However, not all PHCs had been offered this re-education and different PHCs had received the re-education during a varying number of years. Thus, some PHCs (n=18) had received re-education in VBS four times a year during the past 10 years while other PHCs (n=18) had received similar re-education in VBS four times during the year prior to the survey. In the other investigated county council no equivalent re-education had occurred (n=34) (Table 3).

Of the investigated clinical laboratories, one was located in a district hospital and the other in a university hospital. Both laboratories were accredited according to ISO 17025 [33] which implies that their VBS routines were regulated and documented. The surveyed laboratories had regular, mandatory competence certificate renewal for all VBS staff. In- and outpatient VBS was mainly performed by biomedical technicians, and to a lesser extent, by enrolled nurses in the laboratory phlebotomy room (Table 3).
Since two county councils were involved in the survey, laboratory manuals containing VBS instructions were issued by two different laboratory organisations. However, all laboratories were equally accredited and their laboratory manuals were both based on the Clinical and Laboratory Standards Institute regulations [107]. The content of the manuals were matching. All surveyed units used identical vacuum test tubes (EDTA, citrate, Li-Heparin or without anticoagulant) and similar paper-based test requests with pre-printed adhesive test tube labels on the back. The recommended VBS procedures in the two counties were therefore judged to be comparable. All PHCs (n=34) in one of the investigated county councils used a Computerised Order Entry System (COES) for a minority of their VBS (VBS on request from hospital physicians). The surveyed clinical laboratories used the COES for samples collected on behalf of hospital wards which had introduced the system. Thus, paper based requests were used by all units for the vast majority of their VBS.

Table 3. Basic characteristics of venous blood sampling (VBS) staff in the investigated units. Modified from Papers I-III.

<table>
<thead>
<tr>
<th></th>
<th>Primary health care centres</th>
<th>Hospital laboratories</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td>Response rate</td>
<td>277 (93)</td>
<td>40 (100)</td>
<td>1.000</td>
</tr>
<tr>
<td>Women</td>
<td>265 (96)</td>
<td>39 (98)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VBS at least weekly</td>
<td>264 (97)</td>
<td>15 (39)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Profession</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enrolled nurse</td>
<td>139 (50)</td>
<td>2 (5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Registered nurse</td>
<td>128 (46)</td>
<td>0 (0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Biomedical technician</td>
<td>10 (4)</td>
<td>38 (95)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>VBS re-education</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Previous 10 years</td>
<td>68 (25)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Previous year</td>
<td>58 (21)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>No</td>
<td>151 (55)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Documented routines</td>
<td>118 (43)</td>
<td>40 (100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Accreditation</td>
<td>2 (0.7)</td>
<td>40 (100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Competence certificate</td>
<td>0 (0)</td>
<td>40 (100)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>n Median (25th, 75th)</td>
<td>n Median (25th, 75th)</td>
<td>p</td>
</tr>
<tr>
<td>Years employed at unit</td>
<td>263 8 (3, 18)</td>
<td>40 21 (3, 29)</td>
<td>0.021</td>
</tr>
<tr>
<td>Years since basic education</td>
<td>265 21 (12, 26)</td>
<td>40 23 (5, 32)</td>
<td>0.526</td>
</tr>
<tr>
<td>Age, years</td>
<td>267 50 (43, 57)</td>
<td>40 50 (36, 54)</td>
<td>0.055</td>
</tr>
</tbody>
</table>
Participants

All staff performing VBS and on duty during the study period (November 2006 to January 2007) in the investigated PHCs (n=70) and clinical laboratories (n=2) were included. In total, 298 participants were recruited from the PHCs (response rate 93%) and 40 participants from the clinical laboratories (response rate 100%). Background characteristics of the participants are listed in Table 3.

The vast majority of the participants were women. Of the surveyed PHC staff, 50% were enrolled nurses and 46% registered nurses. In the clinical laboratories, 95% were biomedical technicians. The laboratory staff had been employed a longer period of time, performed VBS less frequently, and had more often access to documented routines in VBS, compared to the PHC staff. The group of PHC staff with no re-education had introduced the online laboratory manual 2 years prior to the survey, whereas the two re-education groups had introduced the online manual 7 years prior to the survey.

The questionnaire

The questionnaire [108] developed in this thesis addressed VBS practices in PHCs as well as background characteristics of the respondents, such as age and education level. The questionnaire was based on a pilot study [109], performed in a highly specialized somatic ward at a university hospital. Before the main survey, the questionnaire was further developed and validated. First, the questionnaire was extensively discussed and assessed with experts in questionnaire design. The structure, construction, content and layout were thoroughly discussed. The questionnaire was also discussed with experts in clinical chemistry and staff with VBS experience including registered nurses, enrolled nurses and biomedical technicians regarding these aspects. Relevant laboratory manuals, literature and international guidelines were also consulted.

In this thesis the term question is used for a group of items, exemplified in Figure 3. The items were constructed to cover the practical performance of the VBS procedure. The procedures mentioned above resulted in several modifications from the pilot study; the answer alternatives were reduced from five to four, several items were modified, some items removed and some new added. The questionnaire was also specifically modified to suit the PHC setting in cooperation with VBS staff in PHCs along with VBS instructors at the hospital clinical laboratory. One patient identification item on hospital wristband was removed and replaced by an item on photo-ID. Further, three items on test tube storage and centrifugation were added.
The modified questionnaire was then distributed to a focus group consisting of staff in the work pool in Umeå University Hospital (n=7). The work pool consisted of enrolled nurses working at different PHCs and hospital wards with temporary staff shortage. Thus, they had considerable experience of VBS in a different range of settings. After discussions and modifications the questionnaire was re-distributed to the focus group for a second discussion session. The focus group meetings resulted in removal of one question (order of test tube collection). A few items were also rephrased and further modified.

During the development process, extensive efforts were made to assure that each item was easy to understand, clearly outlined and could not be misinterpreted. The number of included items was judged to be possible to complete in a reasonable amount of time. The final questionnaire consisted of 38 questions and 120 items. A careful instruction containing an illustration on how to complete the questionnaire was located on the front page of the questionnaire. It was clearly pointed out that the respondents were to state how they usually performed VBS practices and not how they knew they were to be performed.

![Figure 3. Example of dichotomisation of items in a question.](image-url)
Most items had answer alternatives with a four-point scale; Never, Seldom, Often and Always, in order to assess the frequency of a preanalytical practice. The questionnaire also contained open ended items with the possibility to complete opinions and suggestions. For example of a question with included items from the questionnaire see Figure 3. The questionnaire also contained 14 questions concerning a newly implemented COES in one of the county councils. These are not discussed in the present thesis.

**Data management**

In the analysis of the questionnaire data, the responses where dichotomised according to the recommended procedure for VBS. For items were the correct response (according to the laboratory manual, Swedish National Board of Health and Welfare or Clinical and Laboratory Standards Institute) was obvious, the response alternatives were dichotomised into Always versus Often, Seldom, Never or Never versus Seldom, Often, Always (Figure 3). When the correct response was more ambiguous, the response alternatives were dichotomised into Always and Often versus Seldom and Never.

For the items on venous stasis practices (n=3), storage of test tubes after sampling (n=3), centrifugation of citrate test tubes (n=2), centrifugation of serum test tubes (n=2) and test tube labelling practices (two scores, n=4 and n=2), a grouped variable was created for each group of items. The response for each item was given a number from one to four, where four represented the correct response. The numbers for all items of the question were then added and divided with number of included items creating a mean score for the grouped question and its included items. Finally the score was dichotomised into four or below.

Most questions included an open ended answer alternative as the last item. These were excluded since the nature of the responses most often were related to the specific PHC. The questionnaire also contained one open ended question allowing for suggestions for improvement. These responses were grouped into emerging categories. This was also the case for the last open ended item concerning reasons for not reporting incidents. One question regarding centrifugation was excluded since the outline was judged to be unclear. Patient rest was grouped into below 15 minutes or 15 minutes and above. Frequency of VBS was grouped into ‘at least weekly’ or ‘more seldom’. Number of completed incident reports was grouped into ‘No report’ and ‘At least one report’.

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Data collection

Permission to perform the survey, along with a list of all available VBS staff at the units, including their professional status, sex and working hours, were obtained from the head of each PHC and hospital clinical laboratory. Information about documented VBS routines was also collected. Documented routines in VBS were defined as local VBS routines at the PHC, apart from the VBS instructions in the laboratory manual. Examples included local routines for sample storage or if a specific staff member was responsible for sending samples for transport to the hospital clinical laboratory.

Each questionnaire was given a code in order to make it possible to send new questionnaires to non-responders. Only the investigators (JS, OW) had access to the codes and the corresponding names. This information was kept confidential in a locked space and all questionnaires were decoded prior to entry into the data file. The questionnaires and an anonymous answering envelope were distributed in an envelope marked with the name of each participant. The questionnaires were delivered by postal mail to each PHC. An assigned staff member (most often the head of the PHC) assisted in the distribution and collection of the questionnaires. The questionnaire was accompanied by an information letter, describing the purpose of the survey and informing the participants of their voluntary participation, that they could withdraw from the survey at any time without declaring any reason, and that data would only be presented at group level. The participants were asked to put the completed questionnaire in the anonymous answering envelope, seal the envelope and hand it in to the staff member responsible for collecting the questionnaires. The unmarked envelopes were then sent back to the investigators. After two weeks, a reminder was sent to the investigated units. Questionnaires were sent to the non-responders after four weeks.

Statistics

Questionnaire data and background characteristics of the respondents were typed in to an Excel 2003 for Windows data sheet (Microsoft Corp., Redmond, WA) and then transferred to SPSS 14.0 for Windows (SPSS Inc., Chicago, IL). Categorical variables were compared by Chi-Squared or Fischer’s exact test. Due to skewed distributions, Mann-Whitney’s U-test was used to compare continuous variables. Univariate analyses were used to study differences between PHCs and laboratories and associations between reported practices and background characteristics among the PHC staff. The significance level was set to $p<0.05$. This was followed by multivariate
logistic regression analysis, to study how PHC staff characteristics simultaneously affected the likelihood of reported VBS practices. Of the associations in the univariate analyses, only variables with a p-value <0.10 were included in the multivariate model. To measure association, odds ratios (OR) and their corresponding 95% confidence intervals (CI) were used.

**Survey of haemolysis index**

**Subjects and setting**

The investigated test tubes were sent to a university hospital clinical laboratory from the neighbouring PHCs (n=14), nursing homes (n=12), and the emergency department (ED) located in the university hospital. We studied samples sent for analysis on the Vitros 5, 1 multianalyser (Ortho-Clinical Diagnostics, Inc., Rochester, NY). In the PHCs and nursing homes, samples were collected by enrolled nurses and registered nurses. The ED was subdivided into sections; one section staffed by hospital physicians (e.g. internal medicine, orthopaedics and surgery) and one section staffed by PHC physicians, handling patients with less critical conditions. During nights (10 pm to 8 am) the ED was staffed by physicians specialised in emergency medicine. The ED VBS staff (nurses and enrolled nurses) manned both sections on a rotating schedule both day and night. This distribution of VBS staff in the investigated units is typical for Sweden.

The laboratory manual was identical for all investigated units. During day time, samples collected in the ED were registered at the clinic to which responsible physician belonged (e.g. internal medicine, orthopaedics and surgery or PHC physicians section). In the night time, all samples were registered at the ED where the physicians specialised in emergency medicine belonged.

**Sample collection and measurements**

The investigated test tubes contained routine venous blood samples collected by needle, and to a varying degree by intravenous catheter in the ED, in plastic 3.5 mL evacuated serum separator test tubes with an inert polymer gel barrier and a clot activator (Becton Dickinson, Franklin Lakes, NJ, cat-no 367957). After allowing for clotting for 30 minutes, the samples were centrifuged in the PHCs, nursing homes or in the hospital laboratory and then analysed for routine chemistry testing on a Vitros 5.1 automated analyser. Like many of today’s analysers, the Vitros 5.1 automatically analysed haemolysis index (HI) with a spectrophotometric technique [110].
In order to establish the relationship between HI and the amount of free haemoglobin, HI from the Vitros 5,1 was evaluated by serial dilution of a purified haemolysate to two serum samples with a low degree of haemolysis. The amount of free haemoglobin in these samples was measured using a spectrophotometric assay [111]. The relationship between HI and the amount of free haemoglobin was linear ($R^2=0.9865$) and 1 g/L of haemoglobin corresponded to a HI of 99. The samples were considered haemolysed at HI $\geq 15$ (equivalent to 0.15 g/L of free haemoglobin) which was the detection limit for the analyser.

Data collection

Data on HI for 9504 unique test tubes was collected retrospectively from May to September 2008. Of the ED samples, those collected from the section staffed by PHC physicians and those collected during the night shift, and thereby registered at the ED, was obtained. HI values and the Laboratory Identification number (LID) for analyses conducted during the study period were obtained from the Vitros 5.1 analyser. Three identical analysers were used on a rotating schedule.

To obtain information on the unit sending the request as well as information on age and sex of the patients, data was collected from the laboratory information system Flexlab 2.2 (TietoEnator, Kista, Sweden), including a corresponding LID. The PHCs were divided in two groups; group one which included 8 PHCs with distances to the laboratory ranging from 1–8 km; and group two with the other 6 PHCs (distances to laboratory ranging from 17–86 km). Test tubes from the PHCs were transported to the laboratory in cooled insulated transport boxes ($5–12^\circ$C). Test tubes were collected twice a day from PHCs close to the hospital and once a day from the more remote PHCs.

Statistical analysis

Data from the Vitros 5,1 instrument and the laboratory information system was fused using the corresponding LID for each analysis. This created a complete file containing the analysis, HI value, ordering unit and information about patient age and sex for each test tube. Excel 2003 for Windows was used to obtain this file. As many requests included several different analyses for the same test tube, duplicates were excluded by using the aggregate routine in SPSS. This resulted in a file with only one HI value and LID for each test tube. Cases with missing HI due to machine error (n=191) and cases where invalid patient identification data did not allow for determination of patient age and sex (n=5) were excluded from the analysis.
Categorical variables were compared by Chi-Squared test. Multivariate logistic regression analysis was used to study how different units, sex and age simultaneously affected the likelihood of samples having a HI ≥ 15. To measure association, odds ratios (OR) and their corresponding 95% confidence intervals (CI) were used. The significance level was set at p < 0.05. SPSS 14.0 for Windows was used for all statistical analyses.
CONSIDERATIONS

The questionnaire survey

Study design

A cross-sectional study design was used for the questionnaire survey in this thesis. This study design collects data at one point in time and the investigated phenomenon is captured as it manifests itself during the period of data collection [112]. Practical advantages with the cross-sectional study design include that it is economical and easy to manage. This design is also suitable when several variables are to be measured at the same time. Since this thesis investigated a large number of VBS staff in different county councils and settings and also several different practices, these features made the cross-sectional design suitable.

One important limitation with the cross-sectional design is that causality cannot be established since the exposure and the outcome is measured at the same time. However, cross-sectional studies are appropriate when there is evidence or logical reasoning indicating that one variable exceeds the other, or when there is a strong theoretical framework guiding the analysis [112]. Both evidence [36, 39, 40, 45, 76, 98] and logical reasoning indicate that an error in VBS is followed by an erroneous test result why the cross-sectional design seemed appropriate for the survey of preanalytical practices.

Data collection

In this thesis, data was collected by means of a questionnaire. Alternative methods for data collection could have been a direct observational study. However, the probability of bias due to change of practice during observation was judged to be too great for this method to be used. Structured interviews would have been a possible alternative. However, the questionnaire has several benefits over interviews; possibility for a greater number of respondents and no interview bias [112]. The questionnaire also allows for confidentiality which is an advantage since this will increase the chance of an honest response.

Questionnaires are suitable when using large sample sizes and for measuring practices [112]. However, a questionnaire provides a measure of the reported practice, which not necessarily will correspond to the performed practice. This must be considered when interpreting the results. The actual frequency of preanalytical errors in the investigated units could also have been
quantified. However, as far as I have found, studies of preanalytical error frequencies are common in the literature but there is a considerable lack of studies investigating practical aspects of VBS in PHCs.

A questionnaire survey can be subject to response bias. During the development process, extensive efforts were made to assure that each item was easy to understand, clearly outlined and could not be misinterpreted. Response bias due to interference of memory is also possible [112]. This can affect the result of a questionnaire survey since the respondents simply can forget how a task was performed or only report how they performed the task the last time. However, the absolute majority of respondents in this survey performed VBS very frequently. VBS is also a limited and defined task, usually performed several times during a normal workday. VBS is also to be identically performed at all times. Further, the response rate was high, a fact that decreases the risk of response bias [112]. Response bias can also be due to respondents under- or over reporting the investigated phenomena. We specifically asked the respondents to honestly state how a task was usually performed and not how they knew it was to be performed. The survey was also confidential, which should increase the possibility of an honest answer. In this survey, bias in responses would probably tend to make the respondents “look good” which often is the most common type of response bias [112]. Thus, the reported results seem likely to underestimate VBS procedures in need of improvement.

Validity and reliability

Validity is a term for how well an instrument measures what it is supposed to measure [112, 113]. Content validity refers to the degree of which the instrument samples all the relevant or important content or domains [114]. Face validity refers to if the instrument looks as if its assessing the desired qualities [112, 113]. These measures are closely related and can be summarised as how the instrument is judged by an expert [114]. The questionnaire was developed after a pilot study and in cooperation with professionals in clinical chemistry and VBS. Relevant literature was consulted [112, 115]. The questionnaire was discussed at two occasions by a focus group consisting of members with experience of VBS from various settings. Thus, the content and face validity is judged to be reasonable.

Criterion validity is established when the instrument is compared to a gold standard [113]. To the author’s knowledge, no gold standard for measuring VBS practices existed, why criterion validity could not be tested. Direct observation was judged to be too prone to “good behaviour” bias to be used for assessing validity. Direct observation would also be too time consuming.
However, the results indicated better reported practices from laboratory staff, known to make fewer errors in VBS than other staff categories [99, 116, 117]. The laboratories have also since long time introduced quality improvement initiatives such as accreditation and competence certification. This indicates a degree of validity. Construct validity is applied when measuring “hypothetical constructs” like anxiety rather than something that can be readily observed, why this type of validity not is applicable to this thesis.

External validity refers to if the results can be generalised to settings other than the studied [112]. One example of possible bias is selection bias due to distortion of the results by a skewed selection of participants. This is probably not an issue in this thesis since a total survey of all staff responsible for VBS in PHCs in the investigated county councils was performed. Loss of respondents [113] can also affect the ability to generalise the results. This is not likely to be a problem in this thesis since the response rate was very high and the survey included all VBS staff in PHCs in two county councils.

In this thesis, results from a local situation are compared with studies in an international context. However, VBS is a task that is to be performed similarly all around the world. Error frequencies in the TTP are also reported to be fairly constant world wide [31, 39, 40]. Further, the laboratory manual in this thesis is based on international recommendations of the Clinical and Laboratory Standards Institute [107]. All professional categories involved in the absolute majority of VBS in Sweden were included and they are most comparable to other VBS staff internationally.

Reliability concerns whether the results are reproducible, (measured by test-retest) and/or homogeneous (measured by testing for internal consistency) [114]. Internal consistency is used when a large number of items measure the same underlying dimension, for example when measuring depression or psychosocial work environment. In this case, all items are related to the others. For the questionnaire survey in this thesis, test-retest reliability is most applicable. However, test-retest has several disadvantages. Many measures have a tendency to changes regardless of the stability of the instrument [112]. Test-retest is therefore most applicable for measures of, for example height, blood pressure and analytical instruments [112], and less suitable when measuring practices which easy can be altered. The subject’s responses could also be affected by the memory interference from the first administration of the instrument [112]. There is also a risk of low motivation among participants during the second administration, why responses could be haphazard [112]. Because of the above mentioned reasons, test-retest where not calculated by the project group. The findings of this thesis were
largely in line with the pilot study [109] as well as with a study performed in hospitals [118] with another version of the instrument. This indicates that the findings could be reproducible

Ethical considerations

Respondents in this thesis were asked to state how they performed VBS practices. The aim was to identify error prone steps in order to be able to correctly target quality interventions. Pointing out and presenting reported VBS deficiencies involves a certain risk of feelings of guilt and self-criticism among the respondents. This risk will always be present, but in order to minimise it, the procedure for data collection was confidential. Further, the results are only presented at group level, ruling out the possibility to identify certain individuals or units. The results of this thesis will hopefully result in improvements of daily work with VBS and thereby benefit the surveyed VBS staff. This thesis will lead to an increased focus on the important task of VBS, giving credit to the enrolled nurses, registered nurses and biomedical technicians performing the important task of VBS in the investigated units.

The questionnaires were most often distributed and collected by the head of each PHC. This could have made some of the respondents feel obliged to participate. However, the respondents had the possibility to put an uncompleted questionnaire in the answering envelope, without possibility for the head to know whether it was completed or not. The questionnaires were collected in sealed unmarked envelopes and only the investigators had access to the identity of the participants to further assure confidentiality. The questionnaires could have been totally anonymous. This would however have made it more difficult to achieve a high response frequency. A low response frequency was judged to be a bigger ethical problem since the value of the results would have been lower. The respondent's contributions would then not have been as useful.

The study protocol conformed to the principles outlined in declaration of Helsinki [119]. The returning of the questionnaires was accepted as informed consent. The research plan was approved by the Regional Ethical Review Board in Umeå (D-No 06-104M).

Statistical analysis

The level of significance was set to p<0.05. It is therefore a 5% risk that significant findings could have been due to chance. In this thesis a lot of correlations have been tested, increasing the risk that some of the significant correlations are due to mass significance. However, the risk for this was
reduced by using logistic multivariate regression analysis in addition to the univariate testing. Analysis of missing values was not performed because of the high response frequency. General scores (indices) were calculated and dichotomised for some of the items. This gives the risk of misclassifications of responses when a response lies close to the dichotomisation point. In this thesis, scores were consequently dichotomised at the number corresponding to a correct answer according to the laboratory manual or valid recommendations, minimising the risk of misclassification.

**Survey of haemolysis index**

*Study design and data collection*

We used a retrospective design including all consecutive blood samples taken during a defined time period from the studied units. A strength of this study is that all samples sent for analysis on the Vitros 5, 1 analyser from the investigated PHCs and nursing homes during the study period were investigated. This provides a good estimate of the prevalence of haemolysed samples in the investigated units. From the ED however, only samples collected from the section staffed by PHC physicians and samples collected during the night shift could be analysed due to the registration of the requesting physician. This could affect the ability to draw general conclusions from this material and apply them to samples collected during the day. However, the same VBS staff manned both the night shift and the day shift why the preanalytical practices would be equally performed. Further, the high frequency of haemolysed samples in the ED is in line with previous findings [68, 120]. This indicates that the results could be generally applicable. The low frequency of blood collection in the investigated nursing homes made the sample size rather low in this setting. A longer study period would have made it possible to perform sub group analysis on the nursing homes.

*HI determination*

In this thesis, HI was used as a haemolysis determinant. This sensitive and automated measurement provides the possibility of continuous monitoring of a large amount of samples. Visual inspection has been used for determining haemolysis, but is less accurate [121] and not automated, making it less suitable for large sample sizes. Manual spectrophotometric techniques are time consuming and would not be possible to perform in a large study. Categories of VBS staff in this study are representative for Sweden and most comparable to VBS staff internationally. To the author’s knowledge, no previous study on haemolysis frequencies in samples
collected in primary health care exists, why confirmation of these findings from other settings would be valuable.

**Statistical analysis**

The level of significance was set to $p<0.05$. Therefore there is a 5% risk that a significant finding could have been due to chance. As we evaluated many different units in the multivariate analyses, there was a risk of mass significance. However, our associations had a $p=0.001$ or below. Therefore, mass significance would be less of a problem when interpreting the results.

**Ethical considerations**

The research plan was approved by the Regional Ethical Review Board in Umeå (D-No 07-13M). The study protocol conformed to the principles outlined in declaration of Helsinki [119]. Informed consent was not possible to obtain considering the vast amount of samples. The final file did not contain the patient’s Swedish identification numbers and only researchers (JS, JH) had access to the files. A possible benefit for included patients is a safer testing process as a result of the study. The results may make individual VBS staff feel pointed out as less skilled. However, the results are only presented at group level. Other major ethical issues are not likely to be present.
RESULTS AND DISCUSSION

Patient identification in PHCs

The results for patient identification in PHCs are presented in Paper I, Tables 2 and 3. According to the Swedish National Board of Health and Welfare, the patient should always be identified by asking for name and Swedish identification number [53]. Only 54% of the respondents in the PHCs reported to always identify the patient in this manner. Serious consequences have been reported when patients with similar names have been mixed up [51]. This further stresses the importance of a correct patient identification procedure.

According to the Swedish National Board of Health and Welfare, the patient’s identity should always be confirmed by checking the photo-ID [53]. In this thesis, only one in twenty (5%) reported to always identify the patient with photo-ID. The use of photo-ID decreases the risk of sample collection from patients deliberately stating the wrong identity, which have been reported to occur [51]. In this thesis, no more than 41% reported to never use previous knowledge as a means for patient identification. This patient identification method certainly involves a risk of patient misidentification.

Only 10% reported to never use the health care card as a means for patient identification. The health care card, issued for all Swedish citizens, contains no photograph and should never be used for identification purposes. Although undesirable, some of the low reported frequencies of correct methods for patient identification could be due to that elderly and children may not be able to participate in the patient identification procedure. In those cases, a relative or parent should be asked for name and Swedish identification number. To never/seldom use this identification practice was reported by 86% of the respondents. Altogether, the results of this thesis indicate that patient identification during VBS is in need of improvement in the surveyed PHCs.

Test request management in PHCs

The results regarding test request management in PHCs are presented in Paper II, Tables 2-4. According to the laboratory manual and the Clinical and Laboratory Standards Institute, the patient’s name and identification number should always be compared with the corresponding information on the test request. Of the PHC staff, 80% stated to perform this practice. Not performing this practice increases the risk of using test requests with
erroneous information, reported as an important source of preanalytical errors and rejected samples [57]. To always compare barcodes between test tube and test request was reported by 68% of the PHC staff. Not checking test requests is reported to be associated with higher test request error frequencies [58].

Of the participants, only 11% reported to never use test requests completed by someone else. This practice most definitely increases the risk of an erroneous test request. Further, 56% reported the correct practice of always adjusting the time of sampling on the test request when necessary (more or less than 30 minutes from the VBS time). Time of sampling is important for analytes with a circadian variation, such as cortisol, or when an analyte is followed over time, such as cardiac enzymes. Time of sampling can also have importance when prioritising which analyses to be performed in the laboratory. Test requests can be associated with clinical important error frequencies with possible consequences for patients [55, 56]. Altogether, the results of this thesis are in line with previous findings and indicate that test request management in the investigated PHCs needs consideration.

A COES will eliminate several error prone steps associated with the manual handling of paper based test requests. A COES is under introduction in all PHCs in one of the investigated county councils, initially for VBS on request from hospital physicians. When fully implemented, this system will cover all VBS in these PHCs. However, the implementation of a COES and other computerised information systems could lead to unwanted consequences, including increased mortality [122]. The implementation should therefore proceed under continuous survey.

**Test tube labelling in PHCs**

The results for test tube labelling in PHCs are presented in Paper II, Tables 2-4. International preanalytical recommendations states that test tubes should be labelled prior to blood collection to avoid mislabelling [49]. This is in line with recommendations from the Swedish National Board of Health and Welfare [53]. Of the respondents in this thesis, only 12% reported to always label the test tube before collecting the blood sample. This practice is most definitely associated with an increased risk of the wrong patient blood in the test tube, reported to occur in clinically important frequencies even in the highly controlled pre-transfusion testing [60]. The majority of the respondents (86%) reported to always label the test tube themselves, in line with recommended practices. However, this suggests that among 14% of the respondents, someone else will at times label the test tubes, a practice which increases the risk of mislabelling. High frequencies of mislabelled test tubes
have been found in PHCs [61], supporting the results of this thesis. Mislabeled test tubes can result in adverse events [50]. Altogether, the test tube labeling practices reported in this thesis are associated with an important risk of mislabeling of test tubes. Therefore, test tube labeling practices represent an important area for improved safety and care in the investigated PHCs.

**Patient rest and venous stasis practices in PHCs**

The results regarding patient rest and venous stasis practices in PHCs are presented in Paper I, Tables 2 and 3. According to the laboratory manual, the patient should always rest for 15 minutes prior to blood collection. Only 6% of the PHC staff reported to always allow the patient to rest for at least 15 minutes. Insufficient patient rest increases the risk of postanalytical errors since this complicates the use of reference intervals and decision limits. This has importance in PHCs where the effect of medications and interventions are monitored over time. One common and important example is blood fats, which can vary substantially depending on body position [123, 124].

Only 12% of the respondents reported to always release venous stasis as soon as possible. Prolonged venous stasis can cause haemolysis [68], a common reason for specimen rejection [99]. Prolonged venous stasis can also cause clinically significantly alterations of several analytes [65, 66] of which potassium is the most sensitive in clinical practice. In fact, prolonged venous stasis can introduce as much as a 7% variation in the prevalence of hypercholesterolemia [67]. This could lead to errors when making diagnosis and also cause problems when following the effect of a treatment. The results of this thesis indicate that patient rest and venous stasis practices in the surveyed PHCs are associated with an increased risk of preanalytical errors. The results also further stress that; in order to correctly interpret test results according to the reference interval, the clinician must assure that VBS is performed in line with recommended procedures.

**Sample handling in PHCs**

The results regarding sample handling in PHCs are presented in Paper I, Tables 2 and 3. According to the laboratory manual, which is in line with international recommendations [49, 125], test tubes with additives should be gently inverted after sampling to mix anticoagulants with the blood. To always perform this practice was reported by 66% of the respondents. Further, 74% reported to always use an automatic test tube inverter, used to assure proper test tube inversion. It has been stated that the absence of test tube mixing can cause clotting in the test tube, reported to constitute a large
part of rejected samples in the laboratory [72, 126]. However, conflicting studies have been published [73, 74] indicating that different or absent test tube inverting procedures do not affect the test result. Other factors, such as correct test tubes filling and phlebotomist experience, are suggested as being of greater importance. Therefore, studies of specific sample handling practices are recommended to assure an evidence based laboratory manual.

Of the respondents, 71% reported to always store the test tubes vertically after VBS, in line with the laboratory manual. It has been stated that horizontal test tube storage can cause clotting. However, to the author’s knowledge, no studies of this relationship exist. Almost all (96%) of the investigated PHC staff reported the correct practice to always centrifuge the sample before storing the blood sample over night. However, only 28% reported to always use the centrifugation speed recommended in the laboratory manual. Centrifugation at too high speed is reported to cause haemolysis in the sample [76] which could lead to specimen rejection. The results of this thesis indicate that sample handling practices needs further investigation in the surveyed PHCs.

**Information search in PHCs**

The results for information search procedures in PHCs are presented in Paper II, Tables 2-4. Information of an accurate VBS procedure is needed to ensure a correct test result. Examples include the time of patient rest, the use of venous stasis and the time and speed for centrifugation of samples. Such information is these days found in the online laboratory manual. Of the staff in PHCs, 60% reported to always use the updated online laboratory manual when unsure about a preanalytical practice. Creating an online manual does not automatically lead to easily accessible and correct information [81]. One possible explanation for the low reported use of the online manual includes complicated access to the manual via the internal network, since several headings had to be passed to reach the manual. In order to achieve a high grade of use, the online manual has to be user friendly, easy accessible and the users must be aware of its existence.

As few as 53% of the respondents reported the correct practice of never using the paper-based laboratory manual. Since paper-based laboratory manuals are difficult to update, the information may be inaccurate [82]. Thus, utilisation of these manuals can lead to unreliable test results, thereby affecting patient safety. Only 45% of the PHC staff stated to never/seldom ask a colleague for VBS information, a habit entailing a risk of distributing incorrect information, particularly if the colleague has used unreliable sources of VBS information. The results of this thesis indicate that the
information search procedures in the surveyed settings are in need of improvement. Therefore, continuous improvement of the laboratory manual, such as surveying the users and their queries [81], is recommended.

**Comparisons between PHCs and clinical laboratories**

The results of the comparisons between PHC staff and hospital clinical laboratory staff are presented in Paper I, Table 2 and Paper II, Table 2. Responses to five out of ten items regarding patient identification, test tube handling, venous stasis and patient rest differed significantly between the two groups. For all significant differences, a higher proportion of the laboratory staff reported recommended practices. For three of the thirteen items that concerned information search procedures, test request management and test tube labelling, there were significant differences in responses between the groups. Two out of the three significant differences were in favour of the hospital clinical laboratory staff.

Several studies have reported that VBS by laboratory staff is associated with fewer errors than VBS by other types of staff [99, 116, 117]. This is in line with the findings of this thesis. Therefore, the quality improvement strategies used by the surveyed laboratories, and similar measures used by other laboratories, are likely to have contributed to improved preanalytical practices, and thus improved patient safety – even if the results of the present thesis also indicate room for further quality improvement in the laboratories.

**Differences between subgroups of respondents in PHCs**

**VBS re-education and documented routines**

Comparisons between PHC staff with different re-education and access to documented routines are presented in Paper I, Table 3 and Paper II, Tables 3 and 4 and in Table 4. In the univariate analyses, no clear relationship could be found between re-education in VBS and reported practices. The exception was information search, where a higher proportion of re-educated participants reported recommended practices. However, the two re-education groups had introduced the online manual seven years ago. The group that had not received similar VBS re-education had introduced the online manual two years ago. This could be part of the explanation for the differences. Re-education and years of access to the online manual were highly correlated ($r_s=0.956$). The multivariate analyses showed the same patterns as the univariate analyses. Due to the strong correlation between re-
education and access to the online manual, both variables could not be included in the multivariate model.

Documented routines were not clearly associated with reported practices. The results regarding re-education and documented routines indicate that quality improvement efforts should be subject to continuous evaluation to ensure that practices are improved. With a systems perspective, the results also suggest that initiatives on the individual level, such as education and routines, may not be enough to improve VBS practices.

**Participant characteristics**

Results of comparisons between PHC staff with different basic characteristics are presented in Paper II, Tables 3 and 4 and in Table 4. For most significant differences in responses between professional categories, the enrolled nurses and biomedical technicians reported better practices than the registered nurses. This was largely confirmed by the multivariate analyses. In the PHCs, the vast majority of VBS is performed by enrolled nurses and in certain PHCs by biomedical technicians. Their main focus on VBS could be one explanation for this finding. Registered nurses have several other specific tasks at the PHC, such as having their own reception. Registered nurses also perform visits in patient’s homes which can include VBS. These conditions for VBS may be somewhat different to VBS in the PHC. However, the questionnaire only addressed VBS at the PHC. Employment time, years since basic education, years employed at unit, age or sex were not associated with reported practices.

**PHCs and hospital wards**

The findings in this thesis differed somewhat from previous findings in hospital wards in the investigated county councils [127, 128]. For example, the PHC staff reported lower frequencies for correct patient identification practices than hospital VBS ward staff. To always identify the patient with name and identification number, never identify by health care card and never identify by previous knowledge were more seldom reported in PHCs than in the hospital wards. One possible reason for the less correct reported identification practices in the PHCs could be due to that patients could be frequent visitors, and thus known by the VBS staff. However, the patient identification procedure should always be performed correctly to assure patient safety. This further emphasises the importance of the patient identification procedure in the investigated PHCs.
Patient rest was also more seldom reported as recommended in the PHCs compared to the hospital wards. This is notable since proper patient rest will probably be more important in PHCs since hospitalised patients often are in a horizontal position all day. Correct use of the online laboratory manual was more often reported by the PHC staff than by the hospital ward staff. One possible explanation for this could be the main focus on VBS among the enrolled nurses in the PHCs.

**Reporting of preanalytical incidents**

The results for preanalytical incident reporting practices are presented in Paper III, Tables 2 and 3. Of the respondents in the investigated PHCs, 69% stated to have never filed an incident report regarding VBS. This is in line with previous findings of underreporting of incidents in health care [90, 91]. Health care staff is more willing to report witnessed incidents with immediate outcomes [129]. One probable reason for the low incident reporting frequencies could be that the consequence of an error in the VBS process may not be obvious at the time of sample collection. However, considering the employment time (Table 3) and the distribution of errors in the TTP [36], most respondents are likely to be familiar with an incident in VBS that would require a report. It is therefore notable that 24 of the respondents stated that no incidents had ever occurred that would require a report. The Swedish National Board of Health and Welfare states that it is mandatory for all health care staff to report all incidents with potential effects on patient safety [130]. The Institute of Medicine purposes incident reporting as a means to achieve increased patient safety [1]. Information from incident reports have been used to improve preanalytical practices with importance for patient safety [87]. Considering these aspects, increased reporting of preanalytical incidents in the PHCs should be considered a priority.

The most common barrier for not filing an incident report regarding VBS was lack of time. This has previously been reported [129]. Other barriers included a complicated reporting procedure and that no one else filed incident reports, also in line with previous studies [129, 131, 132]. Gladly, a majority (90%) reported to never worry about possible consequences as reason for not reporting incidents, a reason that previously have been found to be more common [129]. Therefore, when designing strategies for increased incident reporting, it is important to consider the barriers and opinions reported by the involved staff.

No major differences in incident reporting frequencies or reported barriers for not reporting incidents could be found between the PHC and hospital
clinical laboratory staff. However, as previously discussed, the clinical laboratory staff are likely to perform a more accurate VBS procedure. The relatively low incident reporting frequencies among the laboratory staff could thus be a reflection of more correct VBS practices rather than an underreporting of incidents. Employment time was associated with higher incident reporting frequencies. An explanation for this finding could be that longer employment time probably will lead to increased potential for exposure to VBS incidents.

It was more common among PHC staff with re-education in VBS to have completed at least one incident report. Incident reporting frequencies can decrease with time [133]. This indicates that continues education may be important to maintain and improve incident reporting practices. A higher proportion of enrolled nurses had filed at least one incident report compared to registered nurses and biomedical technicians. The enrolled nurse’s main focus on VBS could be one explanation for this finding, since this will probably increase the possibility for more witnessed incidents in VBS. In summary, the ability of the surveyed incident reporting system to discover preventable system vulnerabilities needs consideration.

**Staff opinions and suggestions**

The results regarding staff opinions and suggestions are presented in Table 5. Half of the respondents fully agreed to have enough knowledge in VBS and specimen handling while 29% wished to receive re-education in VBS. Further, just over half of the respondents fully agreed to the statement that VBS was seen as an important task at the PHCs. The staffs desire to increase and develop their competence should be considered a valuable recourse when attempting to improve the VBS procedure. Educational efforts in VBS, evaluated during and after implementation, would probably contribute to increased focus on the importance of VBS for a correct TTP.
Table 4. Multiple logistic regression analysis of correlations between background characteristics (independent variables) of respondents in primary health care centres (PHCs) and responses to questionnaire items (dependent variables) presented as odds ratios (ORs) and their 95% confidence intervals (CIs).

<table>
<thead>
<tr>
<th>VBS re-education</th>
<th></th>
<th>Occupation</th>
<th>Documented routines</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>During 1 year</td>
<td>OR (95% CI)</td>
</tr>
<tr>
<td>Always identify with name/ID-number</td>
<td>1.0</td>
<td>0.79 (0.40 to 1.55)</td>
<td>1.78 (0.92 to 3.45)</td>
<td>1.0</td>
</tr>
<tr>
<td>Never/seldom identify by relatives</td>
<td>1.0</td>
<td>0.85 (0.33 to 2.19)</td>
<td>2.36 (0.78 to 7.18)</td>
<td>1.0</td>
</tr>
<tr>
<td>Always identify with photo-ID</td>
<td>1.0</td>
<td>19.51 (1.70 to 224.45)</td>
<td>46.30 (4.9 to 438.1)</td>
<td>1.0</td>
</tr>
<tr>
<td>Never identify by health care card</td>
<td>1.0</td>
<td>0.10 (0.01 to 0.86)</td>
<td>0.31 (0.08 to 1.27)</td>
<td>1.0</td>
</tr>
<tr>
<td>Never identify by previous knowledge</td>
<td>1.0</td>
<td>0.74 (0.36 to 1.54)</td>
<td>0.89 (0.45 to 1.75)</td>
<td>1.0</td>
</tr>
<tr>
<td>Always use test tube inverter</td>
<td>1.0</td>
<td>0.57 (0.26 to 1.23)</td>
<td>1.70 (0.74 to 3.92)</td>
<td>1.0</td>
</tr>
<tr>
<td>Always store test tubes vertically</td>
<td>1.0</td>
<td>1.17 (0.55 to 2.47)</td>
<td>4.45 (1.85 to 10.73)</td>
<td>1.0</td>
</tr>
<tr>
<td>Always let patient rest &gt; 15 minutes</td>
<td>1.0</td>
<td>1.50 (0.40 to 5.58)</td>
<td>0.79 (0.18 to 3.43)</td>
<td>1.0</td>
</tr>
</tbody>
</table>

VBS= Venous blood sampling. RN=Registered nurse, BMT=Biomedical technician, EN=Enrolled nurse.
Of the respondents, 31% filed suggestions for improvements of the VBS process in the last, open ended, item. The most common suggestions concerned a desire for education. For example, several respondents asked for education in VBS performed by the hospital clinical laboratory. The second most common suggestions concerned laboratory equipment and technical solutions regarding VBS where most suggestions proposed implementation of a COES for all tests performed. Altogether, this indicates that the VBS staff in the surveyed PHCs are interested in actively developing their daily work with VBS.

Table 5. Opinions and suggestions regarding VBS and VBS education in the surveyed PHCs.

<table>
<thead>
<tr>
<th></th>
<th>n(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wants to receive VBS education</td>
<td>75 (29)</td>
</tr>
<tr>
<td>Do not agree</td>
<td></td>
</tr>
<tr>
<td>Slightly agree</td>
<td></td>
</tr>
<tr>
<td>Fully agree</td>
<td></td>
</tr>
<tr>
<td>n (%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>“I have enough knowledge to work with VBS”</td>
<td>11 (4)</td>
</tr>
<tr>
<td>“VBS is considered a priority at my PHC”</td>
<td>23 (9)</td>
</tr>
</tbody>
</table>

Examples of suggestions for improvements filed by the VBS staff:

“ I want education in blood sampling, preferably by staff from the hospital laboratory”

“ Education in blood sampling for all staff, by staff from an external organisation”

“ I want to get rid of the paper based test requests”

“ Introduce the COES for all samples taken”
Haemolysis

Results for the survey of haemolysed blood samples are presented in Paper IV, Tables 1 - 3. Of the 8849 test tubes that were analysed from the PHCs, 10.4% had HI ≥ 15 (equivalent to 0.15 g/L of free haemoglobin). Of the blood samples from PHCs, those collected from men were 1.3 times (95% CI 1.1 to 1.5) as often haemolysed (HI≥15) compared to samples collected from women. Blood samples from patients above the median age (63 years) were 1.2 times (95% CI 1.1 to 1.4) more often haemolysed compared to blood samples collected from patients below the median age. This is different from a previous hospital report which found no differences in haemolysis with respect to age and gender [134]. Elderly can have veins which are more difficult to access, why several attempts may be necessary. Several attempts to get venous access can cause haemolysis [95] and also lead to blood collection from veins other than the preferred antecubital, also contributing to more haemolysis prone samples [68, 93]. There are no obvious explanation for the differences in haemolysed samples between men and women.

The investigated PHCs had less frequently haemolysed (10.4%) samples compared to the emergency department (31.1%, p<0.001). No differences between men and women, or with respect to median age, were found for samples collected in the nursing homes or in the ED. However, the shortage in statistical power due to the lower numbers of samples from these units has to be considered.

The prevalence of haemolysed samples varied considerably between the individual PHCs. It was six times more common (95% CI 4.0 to 9.2) for a sample collected in the PHC with the highest prevalence of haemolysed samples to be haemolysed, as compared to the PHC with lowest prevalence. The differences between the PHCs were adjusted for gender and age. This indicates that the differences were not due to these patient characteristics. Haemolysis is most often caused by mistakes in sample collection and handling [76]. Therefore, the differences are more likely to reflect a variance in the practical performance of sample collection and handling in the investigated PHCs. Samples from the PHCs outside the urban area were more often haemolysed compared to samples from the PHCs located close to the laboratory. This difference could also reflect differences in preanalytical practices between these PHCs.

The emergency department had the highest frequencies of haemolysed samples, in line with previous findings [68, 120]. Interestingly, haemolysis
frequencies were considerably lower in the section handling PHC patients, even when adjusted for age and sex. A possible explanation is less frequent blood collection from intravenous catheters in the PHC section, a practice known to cause haemolysis [70, 71].

Comprehensive knowledge on the type of analytical interferences caused by haemolysis combined with appropriate training of VBS staff are essential to minimise errors in the TTP [76]. Since specimen rejection will be followed by increased costs, increased workload and patient inconvenience, it is important to reduce the prevalence of haemolysed specimens. Specimen rejection of PHC samples could cause additional inconvenience, since haemolysis most likely will pass unnoticed until the analysis in the clinical laboratory. By then, the patient has probably left the PHC. A renewed sampling will therefore demand a new appointment. Continuous monitoring of HI could be a valuable tool to estimate and monitor preanalytical quality in PHCs.
CONCLUSIONS

• In the surveyed primary health care centres, important venous blood sampling practices (patient identification, test request management, test tube labelling, patient rest, stasis removal, test tube handling and information search) were not always reported as recommended.

• Fewer primary health care staff than hospital clinical laboratory staff reported recommended preanalytical practices.

• Re-education and documented routines regarding venous blood sampling were not clearly associated with reported practices in the investigated primary health care centres.

• Enrolled nurses and biomedical technicians reported higher frequencies of recommended preanalytical practices than registered nurses. Employment time, years since basic education, age and sex were not associated with reported practices.

• Very few of the respondents in the surveyed primary health care centres reported to have completed an incident report regarding venous blood sampling. Barriers to incident reporting included lack of time and a complicated reporting procedure.

• There were no differences in incident reporting frequencies between primary health care and hospital clinical laboratory staff. Re-education, employment time over five years and being an enrolled nurse was associated with higher incident reporting frequencies.

• There were significant variations in the prevalence of haemolysed blood samples between the investigated primary health care centres and between the investigated care units. Blood samples collected in primary health care centres were less frequently haemolysed compared to samples collected in the emergency department.
**IMPLICATIONS FOR PATIENT SAFETY**

The results of this thesis indicate that venous blood sample collection and handling in the surveyed PHCs is not always performed as recommended. This increases the risk for preanalytical errors with consequences for patient safety and care. Considering the amount of venous blood samples collected in PHCs annually, the number of affected test results, and thus patients, becomes high. Altogether, the major implication of this thesis is an increased awareness of the importance of the preanalytical procedure for the overall quality and patient safety in the TTP in primary health care.

Modern health care is faced by several challenges that all put demands on increased quality and safety. Therefore, health care providers should apply effectiveness; doing the right things rather than just doing things the right way [135]. The results of this thesis pinpoint the implication for the TTP: an increased focus on the preanalytical part - an accurate analytical process has less importance if an erroneous blood sample is provided.

Interventions aimed at improving preanalytical practices can be successful in clinical practice [136, 137]. The results of this thesis indicate that hospital clinical laboratory staff performs more accurate preanalytical practices than PHC staff, in line with previous studies in hospitals [99, 116, 117]. Given the history of quality improvement in the laboratories [100], including accreditation and individual competence certification for VBS staff, the quality improvement initiatives implemented in the laboratories seems to have been successful. Cooperation with laboratories can improve preanalytical practices [137]. The hospital clinical laboratory staff should therefore be considered a valuable resource when attempting to improve the preanalytical phase.

Knowledge of preanalytical factors is crucial for all staff involved in the TTP [34]. This includes sample collection staff as well as physicians, since a correct interpretation of test results will depend on the conditions under which the sample was collected, e.g. if patient rest was utilised or not. Increased knowledge and awareness of the importance of these factors are relevant for motivating a change in practice [138]. Increased understanding is also an important part of the system approach [12].

A high prevalence of certified staff is related to increased patient safety [139]. Significant differences in test results have been shown between untrained and trained VBS staff [73]. Since the surveyed PHC staff reported a desire for education, the competence certificate utilised by the surveyed
laboratories, combined with re-education, could be one way to assure a desired level of competence among VBS staff. As discussed above, active involvement by laboratory staff is highly recommended when implementing such changes, which should include education of physicians about the preanalytical procedure.

With a COES, the manual handling of test requests is avoided, thereby eliminating a major source of preanalytical error [57]. It is in line with the systems perspective to design safe systems to prevent errors [12]. Other possible benefits of a COES include the possibility to print analysis-specific sampling instructions on the test tube label. However, the implementation of a COES should proceed with caution, since implementation of computerised systems in health care can lead to unwanted effects, including increased mortality [122].

This thesis found no clear correlation between re-education or documented routines and reported preanalytical practices. This indicates that continuous monitoring of implemented efforts is necessary [12]. It is also important to view the TTP as a system: erroneous preanalytical practices are the result of a suboptimal system – not a sign of failure among the individual VBS staff. Health care providers should therefore design a stable system for sample collection and handling that facilitates recommended practices.

The results of this thesis indicate that the investigated incident reporting system is likely to underreport incidents in the preanalytical phase. Incident reporting systems can discover clinically important errors in VBS [87], and information from such systems has been successfully used to improve the VBS process [87]. Further development of the incident reporting system in the investigated units, with focus on the users and their suggestions, is recommended. Re-education in VBS was associated with a higher number of completed incident reports. Since the tendency to report incidents can decrease with time [133], education on incident reporting could therefore be included in the previously mentioned regularly renewed competence certificate.

Quality indicators can be used to monitor and evaluate the quality of patient care [140]. Quality indicators are not necessarily a direct measure of quality, but can indicate important areas in need of improvement. Quality indicators should be reliable, stable and patient focused. Data collection should be simple, and as much as possible of the process should be covered. Quality indicators for the TTP should preferable be relative measures, expressed as percentages of the total activity assessed [56], but certain absolute measures of serious outcomes are also needed [140]. Quality indicators can aim and
facilitate quality improvement in the laboratory [56, 141]. Monitoring of laboratory quality indicators can reduce important preanalytical errors [136]. Frequent practices with a high level of risk are particularly suited for quality indicators [140]. Altogether, quality indicators seem useful for monitoring the preanalytical phase in primary health care.

The results of this thesis and previous research indicate that haemolysis index is suitable as an indicator for overall sample quality in the preanalytical phase. Haemolysis index could be used for monitoring routine samples as well as for evaluating quality improvement initiatives. As previously discussed, the questionnaire developed in this thesis is suggested as a valuable tool to evaluate the preanalytical procedure. Other suitable indicators of preanalytical quality include the number of registered patient identification or test tube labelling errors, rejected or clotted specimens, specimens not received and the total turn around time.

As a result of this thesis, a project aimed at improving the preanalytical process has been initiated in one of the investigated county councils. VBS staff from PHCs will participate in a two-hour education held by laboratory instructors. The participants will also study instructions for specimen collection and handling. Following their education, the participants will complete a test and thereafter receive a competence certificate to be renewed after four years. The ambition is that all VBS staff in all PHCs in the county council should have a valid competence certificate within 3 years.
FUTURE RESEARCH

The questionnaire used in this thesis could be a valuable tool to investigate the practical performance of the preanalytical phase. A suitable continuation of this thesis would be to assess preanalytical practices before and after an intervention aimed at improving the preanalytical procedure in primary health care centres. The results from such an investigation could be compared with a quantification of preanalytical errors, for example among received samples in the laboratory. Another suitable continuation would be to measure reported practices during and after basic education, for example among enrolled and registered nurses, to assess how professional experience alters preanalytical practices.

Qualitative studies could be valuable to provide a deeper understanding of important aspects of the preanalytical phase that could not be gained by a quantitative approach. Insights in perceptions of the venous blood sampling procedure among staff and patients could be useful when developing strategies for improving preanalytical quality.

In order to improve the laboratory manual, practical experiments of specific instructions with low scientific support could be performed. Examples include studies of the effect of horizontal test tube storage and test tube inversion. Investigations of practices that could lead to in vitro haemolysis would also be valuable.

Suitable indicators of preanalytical quality is another area for future studies. Haemolysis index is one important example. This indicator could be used in combination with the questionnaire to assess the effect of an intervention aimed at improving preanalytical practices. Other suitable indicators for future studies include registration of identification and test tube labelling errors, or percentage of rejected and clotted specimens. A national and international consensus on important indicators could be valuable to enable comparison of practices and improvement strategies in the total testing process.

In a wider perspective, investigations of other parts of the total testing process are also needed. Important examples are the pre-preanalytical and post-postanalytical phases. This includes the correctness of ordering of tests and interpretation of test results. In conclusion, further studies of the preanalytical process in primary health care are clearly needed.
**POPULÄRVETENSKAPLIG SAMMANFATTNING**


**Syfte.** Att undersöka utförandet av provtagnings och provhantering av venösa blodprover i primärvård samt att undersöka kvaliteten på venösa blodprov skickade från primärvård.

**Metod.** Enkätundersökning bland provtagna personal på vårdcentraler i två län samt bland provtagna personal på två sjukhuslaboratorier. Undersökning av venösa blodprover skickade från primärvård, vårdhem och en akutmottagning med avseende på skadade röda blodkroppar (hemolys).

**Resultat.** Resultaten från enkätundersöknings tyder på att provtagna personal i primärvård inte alltid utför viktiga moment i enlighet med gällande rekommendationer. Brister rapporterades bland annat för patientidentifiering, provtagnings, prov- och remisshantering samt provrörsförklaring. Det var också ovanligt med avvikelse rapportering av fel rörande blodprovstagnings. Resultaten från studien av kvaliteten på blodproven visade en statistiskt säkerställd skillnad i nivån av skadade blodkroppar i blodprov från olika vårdcentraler. Det fanns också skillnader mellan vårdcentraler och akutmottagningen, där de högsta nivåerna kunde mätas i prover skickade från akutmottagningen.

**Slutsatser.** Avhandlingen tyder på att provtagnings och provhantering ibland utförs på ett sätt som kan påverka patientsäkerheten. Åtgärder för att förbättra blodprovstagnings kan innefatta regelbunden utbildning av provtagna personal med medföljande kompetensbevis. Hemolys är en lämplig markör för den generella kvaliteten på provtagningsprocessen. Sammanfattningsvis rekommenderas fortsatta undersökningar och därefter förbättringsarbete rörande provtagnings och provhantering i primärvård.
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