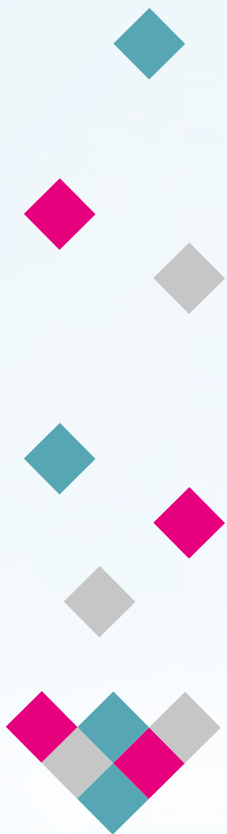


# BLOOD SAMPLING GUIDELINES



**EUSEM EUSEN EFLM**

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The sponsors played no role in the development of these guidelines. Sponsoring organizations cannot recommend panellists or topics, nor are they allowed prepublication access to the manuscripts and recommendations. Guideline panel members, including the chair, and members of the Health & Science Policy Committee are blinded to the funding sources. Further details on the Conflict-of-Interest Policy form are available online at the annex

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### **Endorsements:**

This guideline is endorsed by the European Society for Emergency Medicine (EUSEM), European Society for Emergency Nursing (EUSEN), and European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Working Group for the Preanalytical Phase.

### **Limitations:**

This guideline is based on data from Jan 1 2017 to December 31 2022. We encourage professionals to propose revisions to the actual version of this guideline, based on quality research. This guideline is not intended to establish medicolegal standards of care or has the pretension to cover all the clinical situations.

# 1. Abstract

## Executive summary

Blood sampling prior to performing laboratory measurements is one of the most frequent interventions performed in managed care. In the emergency department (ED), obtaining rapid, high-quality test results to inform patient management is a mainstay. However, it is noteworthy that the majority of errors associated with laboratory testing are not analytical in nature, but occur in the preanalytical phase, particularly during blood sample collections (herein referred as “phlebotomy” or “venipuncture”). Three European scientific societies - EUSEM, EUSEN and EFLM - have jointly collaborated to produce these recommendations for the preanalytical phase.

The GRADE methodology was used for the identification of important questions, as well as for literature searches, appraisals of the literature and elaboration of the recommendations. Sixteen questions were elaborated, with corresponding recommendations produced. These constitute the core of this document. The results have been organised into four sections: pre-sampling, sampling, post-sampling and quality assurance. The final recommendations for each question, along with the level of evidence and the strength of the elaborated recommendation, are provided below.

### Pre-sampling phase

**Question 1.** Do patients who are transported to hospital ED by ambulance and in whom prehospital phlebotomy is performed have shorter blood sample transport times to the laboratory, shorter time to diagnosis and shorter ED Length of Stay (LOS), and do these effects decrease ED crowding compared with patients in whom phlebotomy was performed after arrival at the ED (typical care).

#### Recommendation

There is limited evidence to prove that pre-hospital blood sampling reduces the time taken for specimens to reach the laboratory, the turnaround time, or the patient’s LOS.

However, the group does not recommend against prehospital blood sampling, since this can benefit the flow of samples to the hospital laboratory, provided that sampling time and storage conditions are standardised and fulfil minimum quality criteria.

Quality of the evidence	
Overall quality of evidence for the endpoint “turnaround time”	VERY LOW
Overall quality of evidence for the endpoint “blood sample arrival time”	VERY LOW
Overall quality of evidence for the endpoint “ED LOS”	VERY LOW
Strength of the recommendation	
For turnaround time, weak strength of the recommendation	2D GRADE
For blood sample arrival time, weak strength of the recommendation	2D GRADE

For ED LOS weak strength of the recommendation	2D GRADE
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**Question 2.** Is there a difference in the rate of identification errors when blood tubes are labelled either before or after sampling in patients visiting the ED?

**Recommendation**

The guidelines group suggests that blood sampling tubes should be labelled in the presence of the patient prior to phlebotomy to reduce the rate of identification errors.

Quality of the evidence	
Overall quality of evidence for the endpoint "identification errors"	VERY LOW
Strength of the recommendation	
A weak recommendation, with very low-quality evidence	2D GRADE

**Question 3.** In adult patients at the ED with indication for a blood test, does patient's preparation (fasting status, or posture) affect the test results?

**Recommendation**

**Posture:**

The guidelines group recommends that the sampling posture should not be changed. If the patient has been lying for some time, blood should be collected again in a lying position.

Level of recommendation: Good practice

**Fasting status:**

The guidelines group suggests always verifying and registering the patient's fasting status, along with previous alcohol consumption.

Level of recommendation: Good practice

**Previous exercise:**

The guidelines group suggests that previous exceptional exercise should always be verified and registered.

Level of recommendation: Good practice

The recommendations for this question are based on the group's experience, due to the lack of quality information to support the recommendation. In consequence these recommendations have been graded as good practice.

## Sampling phase

**Question 4.** Effect of the profession who draws blood samples in the quality of the process

### Recommendation

In the ED we suggest that blood sampling in the adult patients should be performed by specifically trained healthcare professionals. Considering the patient workflow.

Quality of the evidence	
Overall quality of evidence for all the outcomes	VERY LOW
Strength of the recommendation	
A weak recommendation, with very low quality evidence	2D GRADE

**Question 5.** In adult ED patients, does the disinfectant choice (chlorhexidine-alcohol versus povidone iodine) affect rate of blood culture contamination? Or laboratory results?

Note: Only blood culture contamination as outcome has been considered, as there was not enough evidence in the literature for an assessment on the impact of different skin antiseptics on test results .

### Recommendation

When sampling for blood culture in the ED, chlorhexidine-alcohol should be used to disinfect needle insertion sites to prevent contamination.

Quality of the evidence	
Overall quality of evidence for all the outcomes	VERY LOW
Strength of the recommendation	
A weak recommendation, with very low-quality evidence	2D GRADE

**Question 6.** Effect of using non-sterile gloves in blood sampling for analytical tests

### Recommendation

The working group does not recommend the use of sterile gloves for venous blood collection. For standard phlebotomy, the use of non-sterile single-use gloves as a protective measure can be considered to be good practice.

The use of non-sterile gloves is recommended as one of the protective measures that health care professionals may take. Sampling for blood cultures has to be considered as a separate topic- details are described in question 14.

The recommendations for this question are based on the group experience due to the lack of quality information to support the recommendation. Hence , these recommendations have been graded as good practice.



**Question 7.** In adult ED patients, does the tourniquet site (cm localisation from the venipuncture) affect the rate of complications: test results, haemolysis, haematomas, patient satisfaction, or professional acceptance?

**Recommendation**

No literature specifically covering this PICO question was found in the search period; the working group has no new recommendations to add about the tourniquet position.

**Question 8.** In adult patients undergoing a new phlebotomy for laboratory testing at the ED, does venipuncture using butterfly or straight needles, as opposed to short peripheral IV catheters, decrease the rate of haemolysis or the frequency of phlebotomy-related complications, such as haematomas and what is the effect on patient satisfaction?

**Recommendation**

The use of straight needle venipuncture or butterfly needles rather than sampling from IV catheters is recommended.

Quality of the evidence	
Overall quality of evidence for the endpoint haemolysis	LOW
Strength of the recommendation	
A weak recommendation	2C GRADE

**Question 9.** In adult ED patients with a new placed the peripheral intravenous catheter (PIVC), including catheters with infusions in place, are blood samples drawn from PIVC admissible, compared to a new venipuncture.

Note: Haemolysis rate was the only measured outcome due to limited studies suitable for appraisal regarding the other selected outcomes, based on the validity of the results.

**Recommendation**

Blood samples should be drawn through new venipuncture in adult ED patients.

In the process of placing a new peripheral venous catheter with a needle gauge ≤ 18, we suggest that blood samples could be drawn through the PIVC, after carrying out a risk/benefit analysis, and given the proper standard operating procedure (SOP) is followed to reduce risks. In any case, precautions to reduce haemolysis rates, such as the use of low-vacuum tubes or manual aspiration, is recommended in these cases.

The risk analysis should include the contraindications of a new venipuncture and an estimate of the risk of haemolysis using the newly placed PIVC.

Quality of the evidence	
Overall quality of evidence for the endpoint haemolysis	VERY LOW
Strength of the recommendation	
A weak recommendation, with very low quality of evidence	2D GRADE

**Question 10.** Effect of the sampling devices used through PIVC, vacuum versus manual aspiration.

Haemolysis rate has been used as an undesirable outcome. Other endpoints such as turnaround time (TAT), local haematomas or phlebotomist acceptance were not analysed due to the lack of information.

### Recommendation

To reduce the haemolysis rate, we recommend, for patients with already established peripheral intravenous catheters, in whom blood sampling is necessary for laboratory tests, not to sample through the PIVC.

If after a risk analysis blood is drawn from a PIVC, the professional should use a closed manual aspiration or low vacuum system, to reduce the risk of haemolysis.

Quality of the evidence	
Overall quality of evidence for the endpoint haemolysis	VERY LOW
Strength of the recommendation	
A weak recommendation, with very low quality of evidence	2D GRADE

**Question 11.** In the “Difficult venous access” what is the role of facilitators; ultrasonography-guided peripheral venous access?

### Recommendation

We recommend, in patients with difficult vascular peripheral venous access, the use of ultrasound guided access.

Quality of the evidence	
Overall quality of evidence for the selected outcomes	HIGH
Strength of the recommendation	
A strong recommendation with a high level of evidence	2A GRADE

## Post-sampling phase

**Question 12.** In adult ED patients, does transporting the blood samples via pneumatic tube systems affect haemolysis rate, compared to manual transportation?

### Recommendation

If available, the group is in favour of using a PTS for sample transportation from the ED to the laboratory to reduce TAT and LOS, especially when EDs are dependent on a central laboratory that is not located near the ED.

Quality of the evidence	
Overall quality of evidence for the endpoint haemolysis	VERY LOW
Strength of the recommendation	
A weak recommendation in favour of the use of a PTS for sample transportation	2D GRADE

**Question 13.** Is it reasonable to collect a standard set of samples in all adult ER patients for future analysis (Rainbow sampling).

Is the collection of a standard set of samples for eventual future analysis (rainbow draw) in all adult ER patients more effective compared to collecting distinct samples for the selected tests.

### Recommendation

The group does not recommend the collection of a standard set of samples in all adult ER patients for future analysis.

**Question 14.** Blood sampling for BC, using existing peripheral intravenous catheters versus new venipuncture

### Recommendation

We suggest that in case of BC collections in EDs in adult patients, a new phlebotomy should be preferred over collection from available catheter lines to minimise the risk of sample contamination. In any case, we suggest discarding the first few ml of blood either by using a discard tube or initial specimen diversion devices when sampling is done through a PIVC.

Quality of the evidence	
Overall quality of evidence for the endpoint false positive blood cultures	VERY LOW
Strength of the recommendation	
A weak recommendation in favour of the use of a new venipuncture	2D GRADE

## Quality assurance

**Question 15.** What is the effect of POCT for the working process in the ED, using TAT as the main outcome?

### Recommendation

We recommend POCT as one possibility to reduce the total TAT after interdisciplinary risk/benefit analysis under consideration of the below-mentioned circumstances.

Quality of the evidence	
Overall quality of evidence for the endpoint TAT	VERY LOW
Strength of the recommendation	
A weak recommendation in favour of implementing POCT, when using TAT as the outcome	2D GRADE

**Question 16.** Impact of monitoring preanalytical blood sampling quality indicators in management for ED blood samples.

### Recommendation

We recommend the selection and implementation of quality indicators (QI) /key performance indicators (KPI), to support ED and laboratory teams to maintain / improve the preanalytical, analytical and postanalytical process quality of ED blood sampling.

Suitable quality indicators include: contamination rate of blood cultures, the incidence of duplicate chemistry tests and other reasons for samples being rejected such as haemolysis, underfilling, and clotting.

We recommend including TAT as a key performance indicator (KPI) for ED laboratory processes

Quality of the evidence	
Level of evidence	VERY LOW
Strength of the recommendation	
The recommendations for this question are based on the group's experience, due to the lack of evidence to support them. In consequence these recommendations have been graded as good practice.	

# 2. Introduction

## a. Introduction

Blood sampling for in vitro diagnostic tests (IVDTs) is a key element of patient care in emergency medical systems. Between 60% and 70% of patients attending European emergency departments have at least one laboratory test during their hospital episode.

<sup>1</sup> In clinical settings, over 50% of medical decisions in emergency settings are based on one or more IVDTs.<sup>2</sup>

Emergency medicine is a primary specialty established using the knowledge and skills required for the prevention, diagnosis and management of urgent and emergency aspects of illness and injury, affecting patients of all age groups with a full spectrum of undifferentiated physical and behavioural disorders,<sup>3,4</sup> and as such is dedicated to the assessment, diagnosis and first treatment of acute illness or injury. Emergency nursing is the care of individuals of all ages with perceived or actual physical or emotional alterations of health that are undiagnosed or require further interventions and as such are episodic, primary and usually acute.<sup>4</sup> In Europe, the majority of out-of-hospital emergency medical services (EMS) personnel in the first response to an emergency situation are paramedics or emergency medical technicians (EMTs).<sup>5</sup> Emergency care by these professionals encompasses in-hospital as well as out-of-hospital care, triage, resuscitation, initial assessment, telemedicine and the management of undifferentiated urgent and emergency patients until discharge or transfer to the care of another healthcare professional.<sup>3</sup> In hospitals, timely diagnosis and treatment is reliant on many medical and paramedical professionals, including phlebotomists and laboratory medical professionals (laboratory technicians, biochemical analysts, laboratory physicians, pathologists) who are responsible for quickly processing patient samples and accurately measuring the quantitative or qualitative presence or absence of different parameters. By definition, laboratory medicine is at the heart of modern healthcare, and plays a vital role in screening for disease, diagnosis, risk assessment, treatment selection, monitoring of therapy, prognosis and other aspects of clinical decision-making. It is thus central to effective patient care.

The development of out-of-hospital emergency services (EMS) preceded some aspects of critical care, thus expanding and providing higher levels of acute clinical care, while remaining closely integrated with hospital emergency departments (EDs).<sup>5</sup> Clinical management in the EMS setting, as well as in hospitals, requires reliable information obtained from the patient and their clinical history, as well as complementary information from clinical signs, imaging studies, and laboratory test results.

When considering laboratory testing, it is useful to think of all aspects of the total testing process (TTP). An important part of the TTP – the preanalytical phase process (PPP) – covers all typically manually-intensive activities prior to laboratory analysis (e.g. blood collection, sample transportation, sample preparation). The relevance of the PPP is supported by evidence that close to 70% of all erroneous laboratory values are caused by mistakes within the PPP, potentially resulting in misdiagnosis or inappropriate clinical treatment.<sup>6</sup> When test results cannot be reported by the laboratory due to inadequate samples or other errors in the PPP, there may be a need for repeat phlebotomy, causing diagnostic delays. On the other hand, the interaction between the clinical process of care and the subprocess of blood sampling requires analysis and recommendations, based on evidence, focusing on quality, timely results and patient preferences.<sup>7</sup>

The practice of emergency care focuses on rapid identification of serious conditions, stabilisation of patients, and an accurate diagnosis. Patient stratification according to the severity of the condition reduces the risk of an undesirable outcome, and leads to appropriate clinical care. In this complex environment the time spent prior to a clinical decision being made is crucial, and significantly associated with patient outcomes across an array of time-sensitive clinical conditions.<sup>8-10</sup> IVDTs, along with other diagnostic information, form the basis of clinical decision-making.<sup>11</sup> In order to integrate this information effectively into clinical pathways and to allow for rapid clinical decision-making, IVDTs should yield reliable and timely results, based on predefined turnaround time (TATs) that are as short as possible.<sup>7</sup> One strategy for reducing TATs has been the development of point of care testing (POCT) within the ED, which avoids the time-consuming transportation of blood samples to the laboratory. However, as with testing within the laboratory, POCT requires strict quality control, either managed by the laboratory personnel or the ED team.

While many medical emergencies require fast and reliable clinical information of which laboratory values are particularly crucial, the working environment within emergency care is characterised by high stress, caused by the multitude of tasks to be completed and the need for timely decisions leading to appropriate action. The impact of diagnostic errors on clinical management is particularly significant in critical care areas such as the ED.<sup>12</sup> To avoid mistakes and maintain the highest possible standards in the emergency care process, standardisation and active quality management are key elements.<sup>13</sup> <sup>14</sup> Numerous key performance indicators (KPIs) have been established to quality-control the testing phase in the laboratory, and these are strictly supervised by the laboratory team to guarantee valid laboratory values.<sup>15</sup> Regarding the PPP, standard operating procedures (SOPs) and KPIs can also help to reduce the number of erroneous laboratory test results, though this process is less well supervised compared to the laboratory testing itself. In addition, SOPs can help to reduce the risk of accidental contamination with biological materials<sup>16</sup> which is more likely to occur with ED personnel, compared to other hospital staff. This risk has been recognised as one of the peculiarities of the ED and is another argument for a specific approach to the PPP in the emergency setting.

Safety in the clinical process is based on the use of standardised evidence-based processes. Clinical guidelines provide systematically developed statements and tools for making patient care more consistent and efficient across the healthcare delivery system. Although clinical guidelines are not the only tool to improve the quality of patient care, they are particularly useful where practitioners are unclear about appropriate best practice and when scientific evidence can provide an answer.<sup>17</sup>

A recent survey, issued by this working group and focusing on the ED PPP across European countries, demonstrated variability in practice and quality control measures regarding these process steps, emphasising the importance of an interdisciplinary approach whereby clinicians and laboratory professionals jointly describe and evaluate the process for safety and quality.<sup>1</sup>

## b. Guideline purpose

The general purpose of this document is to provide recommendations about the PPP in the ED in the European context.

### i Target audience

1. The document is specifically targeted at emergency medicine-related professionals involved in the blood sampling process (e.g. physicians, nurses, phlebotomists working in the ED), as well as laboratory physicians and other related professionals.
2. The recommendations are also targeted at the professionals in charge of the patient care process in the ED.
3. The document is also relevant to professionals responsible for managing the organisation, and for designing optimised care processes and managing their quality control.

### ii Target population

1. Recommendations have been limited to adult patients in which a venous blood test is requested in the process of clinical care during ED management.
2. Venous blood sampling is the objective of the guideline. As a result, the sampling of other specimens has been excluded.
3. Venous blood sampling for microbiological studies (blood cultures) has been included.
4. Venous samples drawn from central venous catheters or other central intravenous permanent devices (e.g. PICC, Hickman catheters, or portcaths) are not discussed in this document.

### iii Added value of the document

International recommendations and guidelines focusing on the PPP have been produced by various organisations. In 2010, the World Health Organization (WHO)<sup>18</sup> published an evidence-based document focusing on blood sampling covering all aspects of the pre-analytical phase with three main focuses: patient security, provider security and quality of the process. The European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) has dedicated substantial resources to the topic through its Preanalytical Working Group, which has contributed a number of publications, including several surveys<sup>19</sup> covering the status of the PPP at the European level, as well as a consensus guideline on venous blood collection.<sup>20</sup>

European national societies have provided local guidelines relating to the blood sampling process<sup>21</sup> highlighting the need for quality control, standardisation training and adaptation to local factors.

This document, which takes a multidisciplinary and multiprofessional approach that is based on previously reported recommendations, aims to enhance the quality and efficiency of the PPP in a specific setting: the ED.

## c. Healthcare burden

Emergency medical systems are a crucial part of healthcare systems. Despite the existence of organisational and/or structural differences across European countries, they share a common process of care. Patients receiving care via these services have a wide spectrum of medical or surgical conditions with different levels of severity, in which the general approach is to triage, carry out rapid identification of the vital risks and establish the needs of care, including management to obtain the stabilisation of the most severe patients. In this context, the evaluation of patients using diagnostic tests is fundamental. Obtaining fast and accurate laboratory test results is of paramount importance.<sup>7</sup>

The number of patients receiving care in these systems varies substantially across European countries. The median figure is 500 annual ED visits per 1,000 inhabitants. Most are discharged after evaluation and treatment, with 10–20% admitted to hospital wards after appropriate vital stabilisation. The estimated number of patients who will undergo blood sampling for one or more laboratory tests is close to 60%<sup>11</sup> highlighting the relevance of this diagnostic procedure.

The preanalytical phase is a critical stage of the IVDT, in which the majority of errors within the TTP takes place.<sup>6</sup>

Harmonising both the procedures and the quality evaluation of the preanalytical phase has been a constant preoccupation of the EFLM through its working group and multiple publications<sup>15 22 23</sup>. The benefits of this approach in terms of quality of medical care and patient safety are accepted by EuSEN and EUSEM as clinical associates of this process of care.

## d. Methodology

The development of these blood sampling guidelines for the ED setting is based on the collaboration of three European scientific societies that have a role to play in the PPP: EuSEN, EFLM, and EUSEM. The guideline aims to summarise the current literature on the PPP in order to provide evidence-based recommendations and set out the highest quality standards based on a clear, transparent and exhaustive procedure. The Grading of Recommendations, Assessment, Development and Evaluations (GRADE) methodology encompasses all these objectives, and the grading of the recommendations provides an adequate system for the emergency medicine environment.<sup>24</sup>

### i Methodology

The panel working group (PWG) involved in the development of the current guidelines was composed of members of three societies: EuSEN, EFLM and EUSEM. A parallel external review group (ERG), based on the same multiprofessional criteria, was created to carry out an external review of the first draft of the guidelines. Patient representatives from two international patients organisations were also included in the external review process in order to improve the patients' values incorporated in the recommendation strength.<sup>25</sup> None of the contributors to the PWG or ERG declared any conflicts of interest. (See Appendix (COI)).



## ii General methodology

GRADE methodology<sup>26</sup> was selected for the development of the guidelines based in the following steps:

1. Objectives of the guidelines and their anticipated setting
2. Constitution of the working groups
3. Selection of questions to include in the guidelines, based on PICO methodology
4. Structured search of the literature
5. Appraisal of the literature
6. Elaboration of the recommendations
7. External review of the guidelines
8. Development of final guidelines document
9. Dissemination

## iii Guideline questions

The selection of the questions of interest was elaborated by the PWG based on the PICO (Population, Intervention, Comparison, Outcome) methodology,<sup>27</sup> following an online session to review the methodology. The list of questions that were initially proposed is included in section B of the annex. Following group discussion, an aggregation of this initial list of 44 questions was carried out and the most relevant questions were selected. Questions were then graded based on the relevance of their outcomes following the PWG agreement. The final list of 18 questions is detailed in section C. Following a literature search, question 11 was excluded and questions 10 and 15 were merged, leaving a final list of 16 questions which are reported and discussed in this document.

## iv Structured search of the literature

A structured literature search was carried out using the following databases: Cochrane Library, Embase (Excerpta Medica database) and Medline, using PubMed as the search engine. The keywords and mesh for each PICO are listed as additional online information. The search period was from 2017 to 2022.

## v Appraisal of the literature

The selection of the studies in the systematic reviews was made using the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) flow diagram, per PICO question, and the results included in the appendix.<sup>28</sup>

The four levels from the GRADE methodology were used for the evaluation of the evidence quality: high, moderate, low, and very low.<sup>29</sup> The basic methodology is shown in the annex, section D.

The quality of the evidence for each question's critical outcomes (across studies) is shown in the summary of findings (SoF) tables, collected as additional online information for each PICO question. The selected studies were evaluated in parallel using the Newcastle Ottawa Scale (NOS) for non-randomised cohort studies,<sup>30</sup> and the Cochrane checklist for randomised clinical trials.<sup>31</sup>

## vi Recommendations

The recommendations were elaborated by the PWG following the GRADE methodology<sup>29,32</sup> with the final decision to agree or reject the proposed alternative, and rank the strength of this decision as a strong or weak recommendation, based on the following

domains: quality of the evidence; balance between benefits and harms; patient values; resource use (feasibility), and impact on the health system, equity, and acceptability. Detailed concepts collected in section E.<sup>33</sup>

This process was carried out independently by all the PWG members, divided into four working groups, based on the previously elaborated summary of findings tables (SoFTs) and the evidence to recommendation (EtR) tables (framework included in the annex, section F). The final recommendation was established after consensus was reached among the group members. Any conflict in the level of recommendations was solved following debate first at the group level, and thereafter among the PWG. If no consensus was reached, this was reported in the final document.

In summary, the elements used to determine the strength of the recommendations are sustained using the following aspects.<sup>24</sup>

- Quality of the evidence
- Benefits and harms of the intervention
- Patient or user values
- System estimation of the intervention
  - Equity
  - Feasibility
  - Resources needed
  - Cost
  - Stakeholder acceptance

To facilitate and standardise the process, standardised EtR tables were used by the PWG members for each question and outcome.

The recommendations are based on studies included in these summary tables, which are available in the online data supplement. Additional studies may have been referenced in the narrative part, but the recommendations were based entirely on studies in the SoFTs.

In cases without sufficient evidence but high relevance for the PPP, the WG developed recommendations based on the existing literature and clinical experience after consensus discussion.

In circumstances in which not enough quality evidence existed, but a reasonable benefit was deduced from selected references, recommendations were classified as good clinical practice (GCP) by the PWG.

The PWG worked in four independent groups, each of which reviewed 4–5 questions. The groups individually elaborated the first draft of the recommendations, which was then reviewed by the PWG to produce the draft which was finally sent to the ERG for revision.

## **vii External review of the guidelines**

An ERG including representatives from the three scientific societies involved reviewed the draft of the elaborated document. Before the review process, an online meeting was arranged with the ERG to facilitate the review process and agree the methodology used in the elaboration of the guideline. All members of the ERG signed a conflict of interest document. After the review process, the PWG used the ERG's suggestions and corrections to improve and finalise the document.

# 3. Key questions

The recommendations elaborated by the PWG are organised based on the different preanalytical phases.

## 1. Pre-sampling/test request/patient identification

- 1 Effect of prehospital blood sampling on the emergency care process.
- 2 Effect of tube labelling time.
- 3 Status of patient preparation (fasting, position).

## 2. Sampling

- 4 Effect of the profession who draws blood samples
- 5 Effect of disinfectant choice (chlorhexidine-alcohol versus povidone iodine) on rate of infection and laboratory results
- 6 Effect of using non-sterile gloves in blood withdrawal
- 7 Effect of the tourniquet site (cm localisation from the venipuncture) on the rate of haematomas
- 8 Differences in laboratory results in sampling done using needles or short catheters
- 9 In adult ED patients with established peripheral venous access, are blood samples drawn from the peripheral intravenous catheter acceptable, comparable to those collected by venipuncture
- 10 Effect of the sampling devices, aspiration models, through peripheral intravenous catheters
- 11 "Difficult venous access": the use of facilitators; ultrasonography-guided peripheral venous access

## 3. Post-sampling/transport

- 12 Effect of transporting blood samples via pneumatic tube systems on haemolysis rate, compared to manual transportation
- 13 Use of collected samples for future analysis
- 14 Blood sampling for blood cultures

## 4. Quality assurance

- 15 Effect of point of care testing (POCT)
- 16 Impact of monitoring preanalytical blood sampling quality indicators in management for ED blood samples.

# 1. Pre-sampling/test request/patient identification

## 1. Effect of prehospital blood sampling on the emergency care process

### Background

The goal of every ED is to assess, triage and treat patients promptly. Increased patient LOS at the ED and increased crowding are associated with poorer outcomes, lower patient satisfaction, and increased staff stress.<sup>34</sup> ED staff state that waiting for laboratory results increases patients' ED LOS and ED crowding<sup>34-36</sup> although research shows that crowding is a multifactorial problem, mainly caused by issues that block effective patient discharge.<sup>37-39</sup> Non-laboratory factors that may prolong ED LOS include inadequate number of hospital beds; poor patient flow through these beds; abnormal access to healthcare as a result of emergencies (epidemics, natural disasters etc.); and staff shortages. Multiple system interventions are often required to decrease patients' ED LOS and mitigate against overcrowding.<sup>40</sup> One intervention that may increase the efficiency of emergency medical care is prehospital blood sampling in patients arriving at the ED by ambulance, in whom venous access is frequently established pre-arrival at hospital, and could be used to sample blood.

Approximately 16% of all patients seen in typical hospital EDs arrive by ambulance.<sup>41</sup> Sixty per cent of patients brought to EDs meet emergency medical services (EMS) protocols for intravenous access<sup>34</sup>. Whenever a patient is taken care of by EMS before admission to the ED and venous access has been established, there is an opportunity to secure blood specimens.

For certain patient groups, prehospital blood sampling may accelerate the availability of laboratory results, saving time in the TTP and allowing more rapid identification of those patients who require admission to hospital<sup>42</sup>. Other advantages of prehospital phlebotomy include decreased time to disposition and reduced ED LOS, which may help reduce crowding in the ED.

### Key question

Do patients who are transported to hospital ED by ambulance and in whom prehospital phlebotomy is performed have shorter blood sample transport times to the laboratory, shorter time to diagnosis and shorter ED LOS, and do these effects decrease ED crowding compared with patients in whom phlebotomy was performed after arrival at the ED (typical care).

<b>Population</b>	Patients who were transported to the hospital ED by ambulance. Analysed with different patterns (chest pain, sepsis, trauma).
<b>Intervention</b>	Pre-hospital blood draw was performed
<b>Comparison</b>	Patients in whom phlebotomy was performed upon arrival at the ED (usual care)
<b>Outcomes</b>	blood sample transit times to the laboratory, troponin turnaround times, time to diagnosis, ED LOS, and ED patient crowding.

## Recommendation

There is limited evidence to prove that pre-hospital blood sampling reduces the time taken for specimens to reach the laboratory, the turnaround time, or the patient's LOS.

However, the group does not recommend against prehospital blood sampling, since this can benefit the flow of samples to the hospital laboratory, provided that sampling time and storage conditions are standardised and fulfil minimum quality criteria.

Quality of the evidence	
Overall quality of evidence for the endpoint "blood sample arrival time"	VERY LOW
Overall quality of evidence for the endpoint "turnaround time"	VERY LOW
Overall quality of evidence for the endpoint "ED LOS"	VERY LOW
Strength of the recommendation	
For turnaround time, weak strength of the recommendation	2D GRADE
For ED LOS, weak strength of the recommendation	2D GRADE
For Blood sample arrival time, weak strength of the recommendation	2D GRADE

## Justification

The group is in favour of prehospital blood sampling rather than blood sampling at the ED. Although the overall quality of evidence is very low for all outcomes assessed according to GRADE,<sup>24</sup> the guidelines group considers that prehospital phlebotomy in patients arriving at a hospital ED by ambulance has the potential to shorten the time from hospital arrival to the availability of laboratory results, when arranged using a suitable protocol with the laboratory, ED and ambulance services. Effects are more significant for critical tests such as cardiac troponin and coagulation.

Robust evidence on the benefits of prehospital phlebotomy in this patient group is currently either unavailable or inconclusive. Mattila et al.<sup>43</sup> found significant time savings in terms of availability of results among patients with stroke when prehospital blood sampling was carried out. Another benefit of prehospital blood sampling in the stroke patient group is that large prehospital sample sets could enable the development of novel ambulance biomarkers to improve early differential diagnosis and treatment of thrombolysis candidates<sup>43</sup>. Curtis et al.<sup>44</sup> and Stopyra et al.<sup>45</sup> found that the introduction of prehospital phlebotomy reduced the time to blood results availability by 38%, decreased blood sample arrival time, and decreased time from patient ED arrival to laboratory arrival, with no differences in haemolysis rates compared to samples collected in the hospital for those who had arrived by ambulance. Gyldenholm et al.<sup>46</sup> found that the time from sampling to analysis was longer when sampled prehospital compared with intrahospital sampling, although this is not surprising since, in prehospital sampling, transport time to the ED is included. DuCharme et al.<sup>36</sup> found that time from arrival to disposition decision in chest pain patients was similar between groups. According to Matilla et al.,<sup>43</sup> time from sampling to treatment decision was longer for prehospital sampling in stroke patients. Time from arrival to availability of laboratory results was decreased in patients who underwent prehospital blood sampling for chest pain, and in a general population. There was no evidence in the selected literature of an effect on the endpoint time to diagnosis. For the endpoint 'total LOS', DuCharme et al.<sup>36</sup> found no differences between the chest pain groups, while Stopyra et al.<sup>45</sup> found a significant decrease in predicted LOS of 72.5 + SD 35.7 minutes, also in chest pain patients. The

latter study calculated the predicted LOS using the time difference between the EMS blood draw and the first clinical ED draw.

Many factors affect the time of a specimen's arrival in the laboratory, the endpoint TAT and patients' LOS, other ED process bottlenecks may nullify the effect of prehospital blood sampling, such as delays in the sample transport system, waiting time for a medical specialist and waiting time for ancillary diagnostics such as contrast tomography scanning or ultrasound.<sup>47 48</sup> In some studies, it appears that the specimen transit route is different for specimens taken prehospital and those taken in the ED. These potential confounding effects were not well considered or described in the literature reviewed. Individual hospitals should carefully consider their preanalytical processes and whether prehospital blood sampling would reduce transit time to the laboratory, TAT, ED LOS, or ED overcrowding at their institutions. These considerations should also be borne in mind for specific subgroups of patients. To properly judge these effects, high-quality research that considers all of the confounding factors in the total testing process is needed.

In a testing process where other preanalytical processes, including specimen transport, laboratory accessioning and specimen preparation, are the same for these pre-drawn samples as for specimens taken from patients following arrival at the ED, it would seem logical that prehospital blood specimens should arrive at the laboratory sooner after patient presentation and lead to results being generated earlier.

## Patient values

A lengthy stay in an overcrowded ED waiting either for a consultant or diagnostic test results can be a source of great anxiety for patients and their families, some of whom will already be acutely ill. Any process or change that can reduce this waiting time may lead to better patient care and an improved patient experience.

## Differences of opinion among the WG

The question was extensively debated based on the difficulties on the selection of the tests to be requested, the different team level across the European prehospital systems limits the generalisation of the recommendation. This recommendation is supported by the cumulative experience and opinion of subject experts in the guidelines group. In the opinion of the group, having pre-drawn blood for a patient arriving in ED by ambulance eliminates the time for phlebotomy in the ED

## Subgroup considerations that may be relevant

Some low-quality evidence in chest pain patients and stroke patients supported pre-hospital blood sampling.<sup>36 43-45</sup>

A prehospital blood drawing procedure could be expanded to other patient groups. Approximately 60% of patients who arrive by ambulance meet EMS protocols for intravenous access.<sup>41</sup>

## Implementation considerations

According to Mattila et al., a structured implementation strategy is needed, including training for paramedics,<sup>43</sup> Healthcare professionals with expertise in process mapping should also be involved in designing specimen pathways that ensure the full benefits of prehospital phlebotomy can be realised. The logistics for specimens taken prehospital and specimens taken inside the hospital can differ and need to be part of the implementation strategy.

## Suggestions for monitoring and evaluation

When deciding to implement a prehospital blood draw procedure, monitoring is recommended based on the KPIs mentioned here, since there is only limited evidence available.

## Research priorities or future research needs

Prospective and randomised controlled studies are needed to expand the evidence on the effects of prehospital blood draws on critical time points for patients and ED crowding.

### 2 Effect of tube labelling time

#### Background

ED staff are at risk of suboptimal patient identification behaviours, and may have difficulties following critical steps to correctly label pathology specimens. While ED care pathways assume patient identification and specimens' integrity, in practice there are differences<sup>49</sup> between centres. One study reported that most rejected samples were from the ED<sup>50</sup>, and 0,32% of all rejected specimens were due to mislabelling.

Poor patient identification in the ED setting is a recognised safety risk<sup>51</sup>. It is plausible that errors in identification are more likely to occur in a busy ED environment where the sample collector is managing multiple tasks and patients.<sup>44</sup> Care is negatively impacted by poor patient identification during blood collection.<sup>52</sup>

Diagnostic blood specimens collected by phlebotomy are the most common type of specimen sent to the medical laboratory. Since phlebotomy contributes to the diagnosis, management, and treatment of patients, it must be viewed as a critical procedure for patient safety.<sup>53</sup> The rejection of phlebotomy specimens by the laboratory on the grounds of poor sample quality has a wide range of direct negative impacts on patient care,<sup>50</sup> reflecting the importance of the PPP and the role of professionals intervening in this phase. Patients may be diagnosed or managed inappropriately if a mislabelled sample goes unnoticed. When the identification error is not detected in a reasonable time, inappropriate action may be taken based on results derived from the wrong patient, with potentially adverse effects on patient care<sup>54</sup>. Rejected specimens also lead to the inconvenience and discomfort of repeated specimen collection for the patient, with an accompanying delay in reporting test results. Specimen rejection leads to a median lag of 65 minutes in the availability of test results,<sup>55</sup> potentially delaying the availability of critical values, the ability to make diagnoses, and the initiation or cessation of treatment. One of the reasons for the rejection of phlebotomy specimens is incorrect labelling.<sup>56,57</sup>

An analysis of specimen rejection in an academic medical centre in Baltimore showed that clotted and haemolysed specimens together comprised 94.6% of rejected specimens.<sup>50</sup> This suggested that rejection rates for other types of preanalytical errors, including mislabelling and insufficient volume, were low. The authors concluded that their barcode labelling and test requesting systems provided a reliable system for high-volume labelling of patient specimens. However, Valenstein et al.<sup>58</sup> categorised errors involving clinical laboratories from 120 institutions and showed that 55.5% of identification errors arose from inappropriate labelling of primary blood tubes. Wallin et al.<sup>59</sup> and Soderberg et al.<sup>60</sup> examined how most non-laboratory staff labelled specimens after collection. They classified this practice as a substantial risk for the generation of labelling errors. In both studies, the suggested procedure was the labelling of primary tubes alongside the patient, prior to the phlebotomy. The EFLM also recognises patient identification

as a critical aspect of the PPP, urging the preanalytical phase working group (PP-WG) to promote harmonisation of this aspect.<sup>61</sup>

Several studies<sup>62</sup> failed to support the recommendation to prelabel blood sample tubes. Historically, labelling post-sampling has been the standard, and three international organisations support this procedure<sup>18 63 64</sup>.

In an editorial in 2014, Lima-Oliveira et al.<sup>65</sup> refer to the Croatian national guidelines, which state that there is no robust evidence to support labelling primary tubes either before or after venipuncture.<sup>53</sup>

## Key question

Is there a difference in the rate of identification errors when blood tubes are labelled either before or after sampling in patients visiting the ED?

<b>Population</b>	In patients visiting the ED
<b>Intervention</b>	Labelling of the blood tubes pre-sampling the blood
<b>Comparison</b>	Labelling of the blood tubes post sampling the blood
<b>Outcomes</b>	Effect on the rate of identification errors

## Recommendation

The guidelines group suggests that blood tubes should be labelled in the presence of the patient prior to phlebotomy to reduce the rate of identification errors.

Quality of the evidence	
Overall quality of evidence for the endpoint "identification errors"	VERY LOW
Strength of the recommendation	
A weak recommendation, with very low-quality evidence	2D GRADE

## Justification

In the literature search performed for this PICO question, no evidence was found relating to the impact of labelling samples pre- or post-phlebotomy and its effect on identification errors. The European guideline on venous blood collection<sup>66</sup> states that whether tubes should be labelled before or after collection depends on the local setting, but that labelling should always be done in the presence of the patient.

The most important findings from both appraised studies are as follows.

In their retrospective controlled cohort study evaluating the impact of prehospital blood collection on time to pathology results and error rates, Curtis et al<sup>44</sup> found no labelling errors in the prehospital blood collection group. The paper's conclusions and implications for practice support the introduction of prehospital phlebotomy, noting that this resulted in fewer labelling errors. Among non-prehospital blood collection patients, the overall error rate was 5.1% (1,592/31,002), of which 0.2% (55/ 31,002) of the samples were mislabelled and 0.1% (41/31,002) were unlabelled.



Rooper et al<sup>50</sup> did an assessment of specimen rejection rates and concluded that they are an important quality measure for laboratories because of their potential negative impact on patient care. They examined the reasons for specimen rejection at a single, tertiary care healthcare institution and proposed a framework for designing an efficient intervention. During a one-year period, they identified all specimens that were rejected at the hospital and analysed a wide range of associated variables: reason for rejection; patient location; type of phlebotomist; tests ordered; priority status; collection container used; transport time. Their results revealed that clotted and haemolysed specimens accounted for the majority of rejected specimens, but that there were significant differences in reasons for specimen rejection between patient care areas. Eighty-five percent of rejected specimens came from the ED and eight other inpatient care areas. Registered nurses drew approximately 85% of rejected specimens, while phlebotomy staff drew only 4%. The authors concluded that while haemolysis and clotting are primary causes for specimen rejection, collection of all available data regarding the rejection of specimens is essential to enable laboratories to determine which factors are the most significant causes of rejection. In this case, labelling errors were lower than at other reported centres,<sup>67</sup> perhaps due to the use of a barcode labelling system.

Because it is plausible that errors in identification are more likely to occur in a busy ED environment where the sample collector has multiple patients, the group recommends labelling the blood tubes pre-sampling, as suggested by Curtis et al<sup>44</sup>. Patient safety should be the primary aim in improving the identification process with the use of arm badges and scanners.<sup>68</sup>

## **Patient values**

Labelling blood specimens with the correct demographics is a fundamental issue for patients and the quality of the care they receive. Patient safety is compromised when samples are labelled incorrectly. Patients may be misdiagnosed or managed inappropriately if a mislabelled sample goes unnoticed. Where samples are unlabelled, patients may have to undergo blood sampling a second or third time, with accompanying delays in reporting laboratory test results.

## **Differences of opinion among the WG**

There were no conflicting opinions among members of the working group.

## **Subgroup considerations that may be relevant**

Accurate sample labelling is especially important for patients who are unconscious or unable to communicate, as they constitute a high-risk group for labelling errors.

## **Implementation considerations**

Education of ED staff was a relevant factor in all the quality improvement implementations proposed by Rooper et al.<sup>50</sup>

## **Suggestions for monitoring and evaluation**

Monitoring PPP errors constitute relevant tools for the implementation of quality improvement programmes

## Research priorities or future research needs

High-quality studies are required to answer this PICO question, as part of the of the needed research, cost analysis of IT support for the labelling process and the implication on the process of care.

### 3 Status of Patient preparation

#### Background

Several aspects can affect blood test results, leading to a potential impact on the emergency care blood sampling process. Factors including fasting and position during sampling have been extensively analysed.<sup>69</sup> Consumption of a variety of substances can affect test results, including alcohol, over-the-counter (OTC)<sup>70</sup> drugs and dietary supplements. Fasting status, and food or medications that the patient has consumed previously cannot be modified in the emergency setting, and position recommendations are sometimes difficult to follow, so a practical approach must focus on recognising and interpreting these factors.

#### Posture

Changing body position from supine to upright and vice versa may affect the concentration of some laboratory parameters.<sup>66 71-73</sup> According to studies, patients should ideally not change body position for 15 minutes prior to phlebotomy. If the patient was lying down, blood sampling should be performed in the supine position (this is typically the case for hospitalised patients). Outpatients should ideally rest in a seated position for 15 minutes prior to blood sampling. If a change in posture is unavoidable within this period, it should be documented to allow the correct interpretation of the test results.<sup>73</sup> Additional considerations are required when interpreting blood test results in cases where strenuous exercise has been undertaken prior to sampling.

#### Fasting status:

It is known that various controllable factors such as diet, physical activity, smoking and alcohol consumption may affect laboratory test results.<sup>66</sup> Serum concentration of cholesterol and triglycerides are influenced by a range of factors, such as food composition, physical activity, smoking, and consumption of alcohol and coffee.

The type and severity of the impact of food on laboratory values depends on its composition (for example fatty diets containing lipids; high protein diets containing ammonia, urea and uric acid), time since last meal, physical activity, smoking, alcohol, consumption of coffee, and time of day.<sup>74 75</sup>

One reason for preferring fasting lipid profiles is the increase in triglyceride concentration seen during a fat tolerance test in non-fasting patients. However, the increase in plasma triglycerides observed after habitual food intake in most individuals is much smaller than that observed during a fat tolerance test.<sup>76</sup> The acute effects (within 2-4 hours) of ethanol consumption are decreased plasma glucose and increased lactate due to the inhibition of hepatic gluconeogenesis. After one to several days of alcohol ingestion, gamma-glutamyl transferase (GGT) activities are induced. The long-term effects of ethanol ingestion include an increase in the activity of liver enzymes.

Nonfasting lipid profile testing is convenient for patients and has been proved to be reliable – and even superior to – fasting lipid testing in assessing risk of atherosclerotic cardiovascular disease.<sup>77</sup>

Although there are clear guidelines for fasting status<sup>69</sup> during planned blood sampling, for obvious reasons patients visiting the ED cannot follow these recommendations. On the other hand, there is variability in patient preparation for laboratory testing.<sup>73</sup> There is heterogeneity in the definition of fasting, and stipulations such as whether water is allowed during fasting differ between organisations and guidelines.<sup>66</sup> **The EFLM have clear guidance on what constitutes fasting, and laboratory medicine professional bodies in most EU countries endorse this. However, borne out by data from the UK and Republic of Ireland, it is fair to say that the guidelines are often poorly observed.<sup>78</sup> In any case, these guidelines are applicable to non-urgent phlebotomy in most cases. We cannot expect an acutely presenting patient to have observed ideal fasting conditions or always to be aware of their fasting status when requesting or interpreting tests and results.**

## Key question

In adult patients at the ED with indication for a blood test, does patient's preparation (fasting status, or posture) affect the test results?

<b>Population</b>	Adult ED patients with indication for a blood test
<b>Intervention</b>	Patient preparation (fasting status, posture)
<b>Comparison</b>	Non fasting, no resting position
<b>Outcomes</b>	Modifications in the test results

## Recommendation

### Posture:

The guidelines group recommends that the sampling posture should not be changed. If the patient was lying for some time in the ED, the blood should be collected in a lying position.

Level of recommendation: Good practice

### Fasting status:

The guidelines group for blood samples which are drawn at the ED, suggested to always verify and register the patient's fasting status, previous alcohol consumption and OTC drugs.

Level of recommendation: Good practice

### Previous Exercise:

The guidelines group for blood samples, which are drawn at the ED, suggested that previous exceptional exercise should always be verified and registered.

Level of recommendation: Good practice

The recommendations for this question are based on the group experience due to the lack of quality information to support the recommendation; in consequence, these recommendations have been graded as good practice.

## Justification

There is poor patient knowledge and awareness about the need to prepare for laboratory testing and the potential effect of diet, physical exercise, stress, smoking, alcohol, OTC drugs and other modifiable factors on test results.<sup>66</sup> Most of the time, patients arrive at the ED unforeseen, therefore they cannot prepare in advance. However, for some laboratory testing, patients need to be informed about the importance of the proper preanalytical procedure, for example for urine collection. In relation to fasting status, it is important to make patients aware that their fasting status has been registered and that their laboratory results will be interpreted based on this status.

No articles have been selected for quality appraisal for this question. The recommendations provided are based on discussions among the working group and their personal experience. The recommendations from the actual guidelines, focus<sup>18 66 69</sup> on patient conditions like fasting, position or previous exercise, limited to the emergency settings.

Control of the factors that can modify test results and impact proper interpretation of those results form an important part of the patient care process. Errors in the interpretation of tests and the need to repeat tests can affect the quality of care. An overview of the blood test values that can be modified by a non-fasting situation or excessive exercise is included in the annex in tables h.

## Differences of opinion among the WG

There were no conflicting opinions among members of the working group.

## Subgroup considerations that may be relevant

With regard to fasting status, it was observed that fasting linked to religious holidays led to altered presentation patterns in the ED, with, in general, more gastrointestinal complaints, more night-time presentations, and a higher incidence of dehydration.<sup>79</sup> This prolonged fasting (a mean of 12 hours) needs no special consideration.<sup>80</sup> Within countries made up of different ethnic groups, non-fasting policies might need to be further refined. For example, individuals of South Asian or Latin American descent are more likely to have severe triglyceride elevations compared with individuals of non-Hispanic white and black descent.<sup>76</sup>

## Implementation considerations

Laboratories should implement standardised procedures for blood sampling and patient preparation, such as those recommended by EFLM.<sup>66</sup> Laboratories should set out sample acceptance criteria with regard to fasting samples. Laboratory professionals are responsible for disseminating information about fasting requirements to patients as well as to clinicians. For patients at the ED, however, it is important to note that fasting status requirements are often not feasible. Therefore fasting status or dietary restrictions should be registered in the patient's medical record at the ED during the triage process, or as early as possible during the patient's ED journey. Information recorded should include the use of alcohol, along with other factors like recent high levels of exercise, so that these can be taken into account when interpreting the laboratory results.

## 2. Sampling

### 4 Effect of the phlebotomist on the quality of sampling process

#### Background

Phlebotomy is the most common invasive intervention in the hospital and prehospital setting. It is a low-risk procedure for patients, although contamination with infected materials ranks as a serious risk for health professionals. The impact of the PPP on laboratory results is far-reaching. 60–70% of errors in laboratory outcomes are based on the preanalytical phase<sup>6</sup> and to a great extent related to the blood sampling procedure.

In the European context, blood sampling in the ED is performed by different professionals with different training backgrounds. Nurses are the healthcare professionals most commonly responsible for the procedure.<sup>81 82</sup> Other professionals such as junior doctors or dedicated phlebotomists are less universally found in the ED across the continent. Training programmes for different professions show great variability. There are also significant differences between members of the same profession working across different settings.<sup>81</sup>

In the emergency setting the cannulation of a peripheral vein is a common procedure, and a newly placed catheter is consequently often used for blood sampling, as well as for the immediate administration of fluid or drugs. This specific management of ED patients forms part of the routine care provided by healthcare professionals (mainly registered nurses). The ED workflow is impacted by the professional that performs the phlebotomy, as time to treatment can be shortened by drawing the blood sample as soon as possible, i.e. by the first healthcare professional that assesses the patient.<sup>83 84</sup> Continuing education and training to raise awareness of the correct sampling procedure is important to minimise the risk of sample rejection.<sup>83</sup>

Evidence of the impact that particular professions have on blood sampling results in terms of their level of efficiency or inefficiency is limited. Most studies do not provide sufficient information about the scope of training programmes or the presence/absence of protocols for difficult intravenous access (DIVA) patients.

Conversely, a shortage of health professionals has resulted in a tendency to transfer some procedures to appropriately trained allied health professionals.<sup>85</sup> The COVID-19 outbreak accelerated this process. A similar trend can be observed in the ED, although to a lesser extent, with venipuncture still typically being performed by core health professionals.

#### Key question

Effect of the profession who draws blood samples in the quality of the process

<b>Population</b>	In adult ED patients with indication for a blood test
<b>Intervention</b>	Blood withdrawal by RN
<b>Comparison</b>	Any other profession (EMT's, paramedics, phlebotomist, biomedical scientists, clinical nurse specialists, APN, nurse assistants, junior doctors, specialty physicians, consultants)
<b>Outcomes</b>	Process quality (using TAT). Complications (haemolysis rate). Patient satisfaction.

## Recommendation

In the ED we suggest that blood sampling in the adult patients should be performed by specifically trained healthcare professionals. Considering the patient workflow.

Quality of the evidence	
Overall quality of evidence for all the outcomes	VERY LOW
Strength of the recommendation	
A weak recommendation, with very low-quality evidence	2D GRADE

## Justification

The appraised literature included one SR<sup>86</sup> that compared haemolysis rates for samples drawn by dedicated sampling professionals (phlebotomists) versus clinical non-dedicated professionals (nurses, physicians), and produced heterogenous results. Other studies found that the rate of haemolysis was lower in samples taken by phlebotomists (as reported by Saleem<sup>87</sup> and Davidson<sup>88</sup>), while Ong<sup>89</sup> and Dugan<sup>90</sup> found no difference, and Cadamuro<sup>91</sup> reported lower levels of haemolysis in samples taken by nurses. The literature search also included an observational study by Rooper,<sup>50</sup> in which phlebotomists had lower sample rejection rates compared to registered nurses working in the ED. All the studies that were appraised have important limitations with heterogeneity in the results, risk of bias and indirectness. For these reasons the overall quality of the evidence was considered to be low. The heterogeneity in the results would merit further quality research focusing on the efficiency of the different professionals.

Three studies were appraised for the outcome TAT. In DIVA, with the use of ultrasound, Davis<sup>92</sup> found that trained nurses were associated with shorter times to establish IV access, faster laboratory results, and faster time to analgesia compared with physicians. Supporting the efficiency of trained nurses in this specific protocol. The remainder of the studies that were reviewed focused on process changes, and were based on sampling at the triage station by nurses<sup>93</sup> or prior to evaluation by a physician. These process changes reduced the LOS of patients in the ED. The final publication<sup>84</sup> that was appraised was oriented to acute ischemic stroke (AIS) protocol activation with no consideration of the professionals that performed the phlebotomy.

Changes to the process of care within different sampling settings and among different professionals are tackled in other studies. Stowell looks at specimen collection that is performed after triage and a physician test order by a dedicated ED phlebotomist (technician trained),<sup>94</sup> and compares this with sampling carried out by an ED nurse when the patient is in the ED and formal evaluation has taken place. In the study, patients with prolonged door-to-physician time (>20 minutes) were selected. A dedicated phlebotomist was associated with a reduction in the percentage of patients who left the ED before treatment completion (LBTC) to 2.74% (95% CI, 2.09%–3.59%) versus 5.31% (95% CI, 4.97%–5.67%). This study demonstrated the feasibility of using a dedicated ED phlebotomist and the impact on LBTC, although the authors reported a negative impact on the door-to-physician evaluation and in ED LOS. No overall increase in patient satisfaction was reported in this study.

Further research is required to establish the effect of an ED phlebotomist on ED workflow in order to overcome the consequences of discontinuity of patient care and the close connection between intravenous access for blood sampling and treatment administration (drugs, fluids).

Considering how important it is that nurses have very high skill-levels in obtaining IV access across all levels of difficulty in order to be able to tackle DIVA cases, prioritising these professionals in the phlebotomy procedure seems sensible. In the Stowell <sup>94</sup> study there were delays in the patient flow (physician contact and door-to-room) when phlebotomist's is sampling. These results are a relevant negative effect that reflects some work-flow interferences. These factors add weight to the recommendation to focus on nurses as having the preferred professional profile for blood sampling procedures in the ED. However, it is the opinion of the group that training is more important than the original curriculum of the sampling professional.

Patients' values has not been explored with regard to this question; although safety, professionalism and integration of care are the elements of healthcare delivery that are most valued by patients.<sup>95</sup> Focusing on IV access, all of these issues relate to appropriate training of the relevant professionals.

## **Subgroup considerations that may be relevant**

Special consideration should be given to patients requiring IV access, and more specifically those with DIVA (defined as two or more failed attempts at PIV access <sup>96</sup>). In these cases, appropriately trained professionals should carry out the procedure following the previously defined protocol. <sup>97</sup> As reported by Davis, nurses achieve excellent results using ultrasound-guided peripheral intravenous catheters.<sup>92</sup>

## **Implementation considerations**

Training is a fundamental factor that underpins achieving excellence in any procedural task. It was considered the most relevant factor in several surveys carried out to evaluate the efficiency of the professionals across European centres. The results of these surveys indicate that levels of compliance with accepted procedures are low in European countries, <sup>98</sup> while a self-reported survey by emergency nurses revealed some lack of knowledge of best practices relating to blood sampling and prevention of haemolysis<sup>83</sup>. These reports illustrate the need for the standardisation of training and implementation of effective quality improvement actions<sup>99</sup>. Implementing training programmes that lead to the certification of professionals in the curriculum described by the WHO <sup>18</sup> should be considered.

## **Research priorities or future research needs**

More research is required to establish the impact of different professionals on blood sampling in the ED, both to establish the factors that affect the quality of the blood sampling procedure, and the impact on service performance. The scarcity of studies, their limited quality, and the variability seen across European centres elaborating conclusions. A common consensus was the importance of training, continuous training and certification for the professionals responsible for drawing blood. Other blood sampling guidelines do not tackle this point. <sup>18 100</sup>

## 5 Disinfectant choice (chlorhexidine-alcohol versus povidone iodine) for venipuncture.

### Background

The importance of skin preparation prior to phlebotomy has been considered in guidelines produced by various scientific organisations.<sup>18 100</sup> The literature recommends the use of 70% ethyl alcohol for lab-tested blood samples, with the avoidance of povidone-iodine due to its potential impact on potassium results<sup>101</sup>, although no recent reports were found that related to potassium measurement. A clear SOP for the use of disinfectants is described in the published guidelines.

Theoretically, povidone-iodine offers certain benefits over other antiseptics<sup>102</sup> due to its particularly broad spectrum of antimicrobial activity, along with skin tolerance in its aqueous and hydroalcoholic formulations.

Chlorhexidine has a broad spectrum of antimicrobial activity and is not deactivated by organic material. Its use in combination with alcohol – or the use of alcohol as a disinfectant – is important due to its excellent antiseptic characteristics.<sup>103</sup>

Antisepsis of the skin at the location where either phlebotomy will be performed or a peripheral intravenous catheter (PIVC) will be placed is important both to avoid the introduction of septic material that can cause an infection of the vein or surrounding tissues, and to prevent contamination of sampled blood, especially in the case of blood cultures. While the rate of infections following blood sampling is low, the level of contaminated blood cultures and false positive blood cultures (FPBCs) seems to be significant in the adult ED population (this has not been verified by any randomised controlled trials). A recent Australian study reported that 42% of positive blood cultures were FPBC.<sup>104</sup> Contamination is mainly produced by coagulase-negative staphylococci and other skin flora, which are unfortunately sometimes the cause of severe infections. The clinical and economic consequences of contaminated blood cultures were highlighted in a systematic review.<sup>105</sup> The multifactorial aspects of this problem have been addressed in education programmes that when applied have demonstrated substantial benefits in reducing contamination rates.<sup>106</sup>

Careful consideration has been given to the role played by the type of antiseptic used to prepare the skin for phlebotomy for blood cultures. A study comparing aqueous povidone with hydroalcoholic chlorhexidine as antiseptic preparations for blood cultures in an intensive care unit (ICU) setting, with false positive blood cultures as the outcome, demonstrated the superiority of chlorhexidine in terms of a reduction in the false positive rate (odds ratio, 0.40(95% CI, 0.21 to 0.75)).<sup>107</sup> Similar results were obtained among paediatric patients in an ED.<sup>108</sup> This study concluded that chlorhexidine-alcohol was superior to povidone-iodine. The results were questioned because alcohol, which has its own antiseptic properties, was only present in the chlorhexidine group, although the action time is also shorter for this form of antiseptic.<sup>109</sup> The recommendation from expert groups is to use skin antiseptic for blood cultures,<sup>110</sup> with insufficient evidence to indicate which option is more efficient.

A debate persists over which antiseptic is best, and recently researchers have pointed out that the choice of antiseptic is just one element of the procedure, emphasising that attention should be paid to ensuring the method itself is adequate and that the procedure is carried out by a suitably trained professional.<sup>110</sup>



## Key question

In adult ED patients, does the disinfectant choice (chlorhexidine-alcohol versus povidone iodine) affect rate of blood culture contamination? Or laboratory results?

<b>Population</b>	In adult ED patients with blood cultures indication, or blood sampling for laboratory tests.
<b>Intervention</b>	Chlorhexidine-alcohol use as disinfectant for blood cultures
<b>Comparison</b>	With povidone iodine for blood cultures
<b>Outcomes</b>	Rate of contamination of the blood cultures.

Blood culture contamination was the only outcome that was considered, as there was insufficient literature to assess the impact of different skin antiseptics on test results. Analysis of other outcomes of the antiseptic procedure, such as local infection at the venipuncture site, was not possible due to a lack of publications examining this. The limited number of local infections generated by blood sampling may be one of the reasons for the lack of studies.<sup>111</sup>

## Recommendation

In case of sampling in the ED for blood culture, chlorhexidine-alcohol should be used to disinfect sites of needle insertion for blood samples to prevent contamination.

Quality of the evidence	
Overall quality of evidence for all the outcomes	VERY LOW
Strength of the recommendation	
A weak recommendation, with very low-quality evidence	2D GRADE

## Justification

Sufficient studies have been published to recommend the use of chlorhexidine-alcohol during blood sampling for blood cultures. In the literature that was reviewed for these guidelines, the blood culture contamination rate was 9.6% higher (95% CI 5.0 to 14.2) when using aqueous povidone-iodine (PVI), compared with alcohol/chlorhexidine gluconate (ACHX).<sup>112</sup> The same result was observed for chlorhexidine in a previous study published by the same author that looked at contamination rates.<sup>113</sup> The quality of the evidence is very low, with only observational studies to support the results. However, evidence of the superiority of ACHX was also found by Suwanpimolkul<sup>114</sup> in an RCT that showed a 6% reduction in false positive BCs drawn in the ED using ACHX. These results are controversial when viewed alongside a systematic review of RCTs<sup>115</sup> published in 2016, in which no differences were demonstrated in FPBCs between alcoholic and non-alcoholic solutions of antiseptics; ACHX and PVI; chlorhexidine and iodine compounds; and PVI and iodine tincture. However, a reduction of false positive blood cultures was confirmed in an SR<sup>105</sup> that reported 59% of patients with a FPBC received unnecessary antibiotics, with an increase in hospital LOS and an increase in the number of tests required, along with subsequent incremental costs. No secondary effects have been reported with the use of ACHX. In rare cases, some people may get red, itchy or irritated skin.

## Differences of opinion among the WG

There were no conflicting opinions among members of the working group.

## Subgroup considerations that may be relevant

When carrying out blood sampling for haematology or biochemistry tests, skin preparation requirements are described in the sampling guidelines.<sup>18 100</sup> Although the use of isopropyl alcohol following the SOP is the general approach,<sup>103</sup> special consideration should be given to patients in which blood sampling is being performed to establish alcohol levels – although the publication by Lippi demonstrated no interference with the use of ethanol-containing antiseptics in the measured level of alcohol.<sup>118</sup> Alcohol used to clean the venipuncture site does not jeopardise blood and plasma alcohol measurement with head-space gas chromatography and an enzymatic assay.

## Implementation considerations

Development and dissemination of the blood sampling SOP for BCs is the key implementation goal for this question. Appropriate training should form part of the strategy for reducing FPBCs. Including measurement of false positive rates as a QI in the ED also have a positive impact on reducing FPBCs.<sup>104 116</sup>

The SOP for the antiseptic procedure is relevant. As an example, the use of an alcoholic solution requires some time (1 minute) before antiseptic action is achieved, and venipuncture immediately following application can reduce its efficacy. Based on the evidence (albeit weak), the implementation of an SOP per se, including the mandatory use of a specific antiseptic, is good clinical practice.<sup>113</sup> However, not following the SOP and not allowing enough time for the alcohol to dry did not cause alterations to the blood test results in Salvano's study.<sup>117</sup>

## Suggestions for monitoring and evaluation

The number of FPBCs is a good indicator of the effectiveness of the aseptic process being used in blood sampling for BC. It should be included as a panel QI.

## Research priorities or future research needs

The use of an antiseptic technique when simple venipuncture is performed, needs further analysis in light of publications discussing the role of antiseptics in skin wounds.<sup>119</sup>

## 6 Effect of using non-sterile gloves in blood sampling

### Background

Phlebotomy is an interventional procedure with some safety risks for the patient and the health professional.<sup>120</sup> Local injury, contamination of the blood sample or local infection are the most relevant biological complications for the patient. The transmission of infectious disease is the main risk for the health professional. Both can be reduced using an adequate SOP, including the deployment of proper aseptic techniques and appropriate use of personal protective equipment (PPE).

In the ED, three different venipuncture procedures are frequently performed, each of them with different levels of aseptic requirements: phlebotomy for simple blood sampling; intravenous peripheral catheter insertion; and blood sampling for blood culture.

Local infection (phlebitis, cellulitis) is a rare complication in simple phlebotomy.<sup>111</sup> The use of a peripheral catheter placed in the ED, particularly following a longer insertion period if the patient is not discharged, is associated with additional infection risk, especially if it is maintained after the ED evaluation, during the hospital admission. The infectious complications from these PIVCs are estimated as 2.2 cases per 10,000 patient-days,<sup>121</sup> a figure that merits action to lower the risk.

The published guidelines recommend gloves as part of both the aseptic and personal protective measures that should be used by the health professional.<sup>18 100</sup> For simple phlebotomy, non-sterile gloves are recommended, while sterile gloves should be used for collecting blood cultures. The role of gloves to minimise the risk of health professionals being exposed to accidental contact with contaminated blood or needle-stick injuries is generally accepted, although it is not supported by evidence-based studies.

Environmental issues relating to the reduction of plastic waste are also becoming a more important factor, and plastic gloves need to be considered with regards to economic and environmental costs. The increase in plastic waste was exacerbated by the COVID pandemic<sup>122</sup> but not only considering the PPE both with regard to PPE and other disposable materials. The need to dispose of plastic waste appropriately requires consideration of the pros and cons of using all disposable plastic products.

## Key question

Effect of using non-sterile gloves in blood sampling for analytical tests

<b>Population</b>	Patients in ED with blood sampling for analytical tests needs
<b>Intervention</b>	Using sterile gloves as part of the SOP when withdrawing blood
<b>Comparison</b>	Using non sterile gloves as part of the SOP when drawing blood
<b>Outcomes</b>	Risk of phlebitis/infections at needle point, blood culture contamination

The recommendations for this question are based on the group experience due to the lack of quality information to support the recommendation, in consequence these recommendations have been graded as good practice.

## Recommendation

The working group is against recommending the use of sterile gloves, for the professionals performing blood sampling in the ED. The recommendation is to use non sterile single-use gloves for standard phlebotomy as a protective measurement can be considered with the strength of a good practice.

The use of non-sterile gloves as part of the professionals' protective measures is advised. Sampling for blood cultures has a specific consideration, and details are described in question 14.

The recommendations for this question are based on the group experience due to the lack of quality information to support the recommendation. Hence , these recommendations have been graded as good practice.

## Justification

Based on the search-defined keywords, the literature search for this question did not produce valid results. After discussing the two alternatives, the panel recommends current standard practice as good practice, i.e. the use of non-sterile gloves for phlebotomy, and the use of sterile gloves for blood culture sampling. The standard procedure, for simple phlebotomy, is to use non-sterile gloves, and this is supported by daily practice. It is based on the infection paradigm, with the goal of reducing the patient's risk of phlebitis or skin infection at the puncture site, along with preventing cross-contamination between patients. However, wearing gloves is not a substitute for hand-hygiene routines. Since the emergence of HIV in 1984, and the recognition of the potential for its transmission through blood or other human body fluids, health centres have implemented universal preventive measures in which non-sterile gloves are worn for all procedures that involve the manipulation of blood. Preventive measures set out by The Centers for Disease Control and Prevention (CDC) include the use of barrier precautions, such as gloves, for every health professional who performs procedures in which potential contact of blood or fluids with the skin can be anticipated. Venipuncture is specifically mentioned in the CDC's guidance.<sup>123 124</sup> Over the last 40 years the use of gloves has become the norm for both patient and provider safety.

Arguments against the use of gloves refer to the challenge of locating a vein via palpation when wearing gloves. However, safety benefits outweigh the reduction in sensitivity regarding vein location, which can make the procedure more difficult. The recommendation is to train professionals with gloves as set out by OSHA.<sup>125</sup>

## Subgroup considerations that may be relevant

There are special considerations for two groups of patients: those in which the procedure is performed with the cannulation of a peripheral vein, with blood sampling carried out subsequently; and those in whom blood sampling is for a blood culture.

Placement of a PIVC is a practice that is associated with higher levels of infectious complications, especially if the catheter is left in place for more than four hours. Most guidance is based on the CDC and epic3 guidelines,<sup>126</sup> with the use of non-sterile gloves considered appropriate for PIVCs if the access site is not touched after the application of skin antiseptics.<sup>127</sup> With a low level of recommendation Category IC.<sup>128</sup> The guidelines also refer the use of sterile gloves and the need for adequate hand washing.

In the case of blood sampling for blood cultures, the guidelines only stipulate the use of sterile gloves if palpation of the vein is required after antiseptic has been applied to the skin.<sup>129</sup> Both the use of antiseptic and the application of protocols based on appropriate educational programmes are of great importance in reducing FPBCs. Sterile gloves have been shown to have an impact in reducing contamination when used as part of a wider quality programme.<sup>121</sup>

## Implementation considerations

The use of gloves as part of safety protocols must be complemented by other actions, such as hand-washing, the appropriate use of antiseptics, and the selection of low-risk materials. These should form part of appropriate educational programmes for the professionals that will perform the procedures.

Including KPI parameters that can indirectly flag up lapses in the safety SOP, such as FPBCs, will act as red flags and help evaluate the impact of the intervention.

Research using simulation is required into the efficacy of PPE, and should include the training methodology and retention programmes.<sup>130</sup>

In the light of a recent publication that illustrated the low risk of open wound manipulation in the ED using non-sterile gloves, further research is needed into the use of non-sterile gloves for blood sampling through PIVCs.<sup>131</sup>

## 7 In adult ED patients, does the tourniquet site (localisation from the venipuncture) affect the rate of complications; haemolysis, or haematomas?

### Background

As an accessory during blood sampling, the main role of the tourniquet is to facilitate blood return from the punctured vein, rather than to help locate the vein. Its use is optional and is not without complications. A risk of cross-infection, with particular reference to multiresistant bacteria, has been demonstrated when reusable tourniquets are applied.<sup>132</sup> The length of time the tourniquet is left in place is of concern due to its effect on haemolysis, for example decreases in erythrocyte deformability at 90 seconds, 120 seconds, and 180 seconds after removal, and increases in erythrocyte aggregation at 5 seconds and 30 seconds after removal. A significant increase in granulocyte respiratory burst has been observed at 60 seconds, confirming leukocyte activation due to the application of the tourniquet,<sup>133</sup> and clinically relevant changes in white and red cell counts have been observed when the tourniquet is in place for 3 minutes.<sup>134</sup> Two observational studies both found that a tourniquet time of more than 1 minute led to significantly higher rates of haemolysis (20.2% (n=20) versus 1.3% (n=3),  $P < 0.001$ ),<sup>135</sup> and in the Wollowitz et al. study 17.5% (n=214) versus 10.7% (n=352), OR 1.3 [95% CI: 1.0–1.6]<sup>136</sup> respectively, providing good evidence of this effect. In consequence 1 minute is considered the maximum time a tourniquet should be kept in place,<sup>137</sup> a finding that is supported by Saleem et al.'s study.<sup>87</sup>

Stasis is the cause of the findings described above, and as a result a short distance from the tourniquet site to the puncture site can enhance this effect.

Tourniquet site (defined in terms of cm localisation from the venipuncture) is mentioned in various guidelines, with no special consideration given to potentially undesirable effects such as the rate of haematomas, patient satisfaction, or professional acceptance. The recommendation in the WHO guidelines<sup>18</sup> is as follows: "Apply the tourniquet about 4–5 finger widths above the venipuncture site," while the EFLM recommends: "The tourniquet should be applied approximately one hand width (7.5 cm) above the anticipated puncture site".<sup>66</sup> Dutch guidelines state that the tourniquet should be placed 7.5–10cm above the puncture site,<sup>138</sup> although no rationale is given for this.

### Key question

In adult ED patients, does the tourniquet site (cm localisation from the venipuncture) affect the rate of complications: test results, haemolysis, haematomas, patient satisfaction, or professional acceptance?

<b>Population</b>	In adult ED patients with blood test indication
<b>Intervention</b>	Tourniquet site away from the venipuncture (Guideline criteria >7 cm)

<b>Comparison</b>	Tourniquet site close to the venipuncture (< 7 cm)
<b>Outcomes</b>	Rate of haematomas, patient satisfaction, or professional acceptance

## Recommendation

No references covering specifically this PICO question were found in the search period; the working group has no new recommendations to add about the tourniquet position.

## Justification

Two studies met the search criteria for this PICO question and were included in the appraisal process.<sup>86 139</sup> In McCaughey et al.'s review article,<sup>86</sup> no mention was made of complications, haematomas, patient satisfaction, or professional acceptance. In Phelan et al.'s retrospective cohort study<sup>139</sup>, the authors analysed 54,531 potassium results, assessing the incidence of haemolysis. Their findings indicated that shorter tourniquet time (less than 60 seconds) and the use of larger gauge needles for IV draws, were significantly associated with lower haemolysis.

Tourniquet position was not considered to be a factor that could modify rates of haemolysis or impact on laboratory results, and the working panel did not consider the position of the tourniquet to be relevant.

## Research priorities or future research needs

No research priorities were identified.

## 8 Differences in laboratory test results between sampling done using needles and short catheters (in patients with no IV access)

### Background

Laboratory tests from blood samples are a major component in the diagnostic work-up of emergency patients. Haemolysis (the breakdown of red blood cells) is one of the quality limitations of the testing process, and sampling techniques are one of the major contributing factors. Sampling includes several sub-processes and variables such as: vein selection, use of tourniquet, sampling device (needle; butterfly; catheters of different sizes, length and materials), aspiration method, container. All of these can potentially contribute to sample haemolysis, which can lead to inaccurate or delayed blood test results, and additional requirements for new phlebotomy. The American Society of Clinical Pathology defines the acceptable sample rejection rate due to haemolysis as 2% or less.<sup>140</sup> Published studies have reported that haemolysis rates range from less than 1% to 36%, depending on multiple variables<sup>139</sup> including phlebotomy equipment.<sup>86</sup>

Hospital EDs have been identified as the setting with the highest source of haemolysed blood samples<sup>141</sup>. It is important to reduce the rate of haemolysis because of its many consequences. These may include delays to prompt diagnosis and clinical decision-making; an increase in laboratory and phlebotomy staff workload; increased costs; unnecessary pain, inconvenience and anxiety; and an increased risk of iatrogenic injury and infection for patients requiring repeat phlebotomy.<sup>142 143 144</sup>

When comparing the impact of sampling devices on the haemolysis rates between specimens drawn using PIVC and straight needle venipuncture, an RCT<sup>140</sup> and three observational studies all<sup>145-147</sup> reported significantly higher rates of haemolysis for specimens drawn through a PIVC or with a butterfly needle, compared to straight needle venipuncture. A more recent RCT<sup>148</sup> also described a higher rate of haemolysis for PIVC than straight needle venipuncture, although no statistical analyses were included. Reported comparisons of the haemolysis rates using different sampling techniques are not uniform: one observational study with 40 specimens per group<sup>135</sup> and another with 19 specimens per group<sup>149</sup> found no significant differences in haemolysis rates between the two techniques (PIVC and straight needle venipuncture). These studies may have been underpowered due to the small number of observations.

An extensive meta-analysis including 17 studies concluded there was a higher risk of haemolysis using a PIVC compared to a straight needle, with an estimated OR 3.4;(95% CI = 2.9 to 3.9).<sup>150</sup>

Two observational studies compared haemolysis rates for specimens drawn using PIVC with those drawn using butterfly needles. Both studies found significantly higher rates of haemolysis for the specimens collected using PIVC compared to butterfly needles,<sup>136</sup> or when using either butterfly needles or PIVC compared to butterfly needles only.<sup>136 151</sup>

The size of the PIVC is widely recognised as a relevant factor. An observational study by Tanabe et al.<sup>145</sup> found that while increased IV catheter gauge (i.e. narrower diameter) led to a significant increase in haemolysis rates, there was no relationship between steel needle gauge size and haemolysis rates. Ong et al.<sup>146</sup> also found no significant difference in haemolysis rates for gauge sizes <21G compared to their narrower counterparts. Finally, Ibrahim et al.<sup>152</sup> reported higher haemolysis rates when using 29G insulin needles compared to 23G standard needles. However, this study confounded the needle gauge size with different syringes and needle lengths.

Due to these consistent findings, evidence that there is no effect of steel needle gauge size on haemolysis rates was classified as good, while evidence that a higher IV catheter gauge (narrower IV catheter) leads to increased haemolysis was also classified as good.

An important aspect that needs to be considered when interpreting the findings of these studies is the negative pressure with which blood was drawn through the collection devices.<sup>153</sup> Phelan<sup>139</sup> found a clear relationship between the concentration of free haemoglobin (i.e. haemolysis) and the level of negative pressure of different vacuum tubes, regardless of the PIVC gauge used for sample collection. The authors concluded that the use of so-called low-vacuum tubes may reduce haemolysis rates in samples collected via PIVC.

The type of materials in contact with the blood has been demonstrated to be another influencing variable. Burns et al.<sup>154</sup> found higher haemolysis rates when using a plastic IV cannula compared to a metal one, while other elements such as aspiration through a hub or an extension tube were not associated with significant differences in haemolysis rates.<sup>155</sup> No differences in haemolysis rates were found when specimens were drawn directly through an IV cannula hub, or a needleless device connected to the IV cannula cap. When samples were<sup>156</sup> collected using a BD Vacutainer One Use Holder compared to a Greiner Holdex, no differences were reported. However, it should be noted that in the last study, the concentrations of cell-free haemoglobin and the frequency of gross haemolysis were higher using the BD Vacutainer One Use Holder than the Greiner Holdex.<sup>157</sup> This study confirms previous findings that the use of straight needles and the antecubital location is significantly associated with reduced haemolysis, supporting the original conclusion of Heyer and colleagues.<sup>158</sup>

Given the large quantity of consistent supporting observations, the evidence for higher haemolysis rates when specimens are drawn using a PIVC compared to venipuncture is reflected in the current guidelines. However, most guidelines<sup>159 160</sup> state that blood samples may be drawn from a PIVC directly after insertion.

It is important to clarify that PIVCs are an approved medical device for IV fluid therapy, but not for blood drawing. The most obvious reason for the higher haemolysis rates in PICV blood collections is the fact that straight needles are designed to provide a laminar flow without any turbulence, while PIVCs have different openings where such turbulence may occur, the intensity of which increases with increasing suction, thereby inducing red blood cell rupture. PIVCs may also contain valves or luers that impede the reverse flow of blood. Consequently, the use of PIVCs for blood collection is off-label, and a local documented risk stratification needs to be performed prior to using them for this.

## Key question

In adult patients undergoing a new phlebotomy for laboratory testing at the ED, does venipuncture using butterfly or straight needles, as opposed to short peripheral IV catheters, decrease the rate of haemolysis or the frequency of phlebotomy-related complications, such as haematomas and what is the effect on patient satisfaction?

<b>Population</b>	In adult ED patients with blood test indication.
<b>Intervention</b>	Venipuncture using short IV catheters
<b>Comparison</b>	Venipuncture using butterfly needles or straight needle
<b>Outcomes</b>	Rate of haemolysis, complications (haematomas), patient satisfaction.

## Recommendation

In favour of recommending the use of straight needle venipuncture, or butterfly needles, rather than sampling from IV catheters.

Quality of the evidence	
Overall quality of evidence for the endpoint haemolysis	LOW
Strength of the recommendation	
A weak recommendation	2C GRADE

In the ED, venipuncture using needles rather than drawing blood from a PIVC is recommended to minimise the frequency of phlebotomy-related haemolysis.

## Justification

Two articles comparing haemolysis rates between specimens drawn using IV catheters and straight needle venipuncture were selected based on the literature search criteria. McCaughey et al.'s<sup>86</sup> systematic review of peer-reviewed articles from 2000–2016, in which the rate of haemolysis is related to at least one factor that can influence haemolysis rates, included 40 articles, 20% of which were RCTs. Focusing on the sampling device – PIVC versus needle venipuncture – the authors found a higher risk of haemolysis when blood samples were drawn from PIVCs, compared to straight needle venipuncture. The



estimated risk ratio of haemolysis, comparing PIVC with needle venipuncture, had an OR of 4.4 (95% CI: 1.5 to 13.0), in the SR reference.

Only two small observational studies were evaluated in this SR (4,025 and 1,932 specimens in each study group) which found no significant difference in haemolysis rates between specimens collected using a PIVC or venipuncture (0% versus 2.5% (n = 1), p = 0.6425 and 23.5% (n = 4) versus 0%, p = 0.0932). However, this may have been due to the small sample sizes in both studies. The overall quality of evidence (systematic review and single studies) for the endpoint haemolysis rate was rated as low. However, due to the large number of consistent supporting findings of higher haemolysis rates when specimens are drawn using an IV catheter compared to venipuncture, the evidence was classified as excellent.

The second study by Phelan et al.<sup>161</sup> confirms previous findings that the use of straight needles, along with the antecubital location, is significantly associated with reduced haemolysis. Straight needle haemolysis was significantly lower than in samples obtained from IV lines (5.4% (33 of 615) versus 10.2% (4,821 of 47,266), P < .001). However, the evidence from this study was graded 'very low', based on the design (observational) and the serious risk of bias.

When an analysis was carried out based on the two observational studies from McCaughey et al.'s systematic review,<sup>86</sup> the risk of a sample taken from a PIVC being haemolysed was again higher compared to the use of butterfly needles, with an OR of 7.7 (95% CI: 4.9 to 12.0). The quality of these results was graded as low.

Due to the consistency of these findings, the group considered there was good evidence of higher haemolysis rates for specimens drawn using IV catheters, compared to straight needles or butterfly needles.

This recommendation is supported by the cumulative experience and opinion of the subject experts in the guidelines group, who also considered the results of the comprehensive and systematic literature review. In the group's opinion, phlebotomy using straight needles or butterfly needles is preferable to drawing blood from IV catheters.

The literature that was appraised provided consistent evidence to show that haemolysis rates are higher in samples taken from catheters, compared with those taken by vein punctures using straight needles or butterfly needles<sup>86</sup>. Use of one of the latter options is therefore associated with a reduced likelihood of the need for a new venipuncture due to the sample being invalid (leading to an associated delay in the process of care).

It is of course inconvenient for staff and patients to be punctured twice, firstly for a blood sample and then for the insertion a catheter. Furthermore, drawing blood from IV catheters with a low gauge may be appropriate in some patient groups, for instance when a patient has limited vascular access; is at increased risk of bleeding; or is receiving intravenous medication. It may also be applicable in patients that need multiple blood tests to monitor their condition, such as those with gastrointestinal bleeding or acute coronary syndrome. In these cases, a documented risk stratification needs to be conducted to justify the off-label use.

### **Advantages of collecting blood from a PIVC include:**

- Convenience of access
- Decreased staff workload (assuming no re-collection is necessary due to haemolysis)
- Decreased costs (assuming no re-collection is necessary due to haemolysis)
- Decreased pain for the patient due to the avoidance of an additional venipuncture

## Disadvantages:

- Off-label use of a medical device
- Risk of haemolysis
- Non-equivalence of the blood test results
- Risk of infection
- Risk to the patency of the cannula

In patients where the sole requirement is blood sampling, venipuncture is the best practice. If peripheral venous access is required (for example if the patient is unstable or at risk of instability, or if IV infusion of drugs is required) or a new venipuncture is contraindicated (fibrinolytic treatment, history of bleeding disorders, or if receiving anti-coagulation therapy) these factors can form part of the risk stratification to support the use of PIVC sampling. Conversely, a new venipuncture is strongly recommended when a real or spurious haemolysis is a diagnostic problem.

## Patient values

Placement of a PIVC allows future blood samples to be taken without another venipuncture. Although phlebotomy is generally considered to be a minimally invasive procedure, it is not without risk. For patients, using an IV catheter for blood sampling means avoiding the need to subject them to additional venipunctures, with the associated risks of procedural complications such as nerve injury, thrombosis, and infection.<sup>112 162</sup> From the health professional's perspective, inserting a short IV catheter may be more time-consuming than inserting a needle. However, when additional blood sampling is required, and a new venipuncture is needed, this is more time-consuming than extraction from the placed IV catheter.

## Differences of opinion among the WG

The recommendation generated lively discussion, due to the difficulty in agreeing on specific subgroups with specific needs.

## Subgroup considerations that may be relevant

The recommendation is based on the subgroup of patients arriving at the ED without venous access, in a stable situation, and with no need of venous access.

## Implementation considerations

Key implementation considerations (in addition to those that are specified in the recommendation), including strategies to address any concerns about the acceptability and feasibility of recommendation can be summarised as follows adaptation or implementation of local:

- Venipuncture SOPs prescribing
- PIVC SOPS prescribing
- Training for handling of wider gauge PIVCs
- Documented risk stratification for the intended off-label use of a PIVC for blood collection

## Suggestions for monitoring and evaluation

Using data from laboratory systems to monitor the incidence of haemolysis over time, combined with a quality programme with pre-established acceptable limits for haemolysis.

## Research priorities or future research needs

Focused research to estimate the benefits of specific protocols for blood sampling in the ED based on patient status.

### **9 In adult ED patients with established peripheral venous access, are blood samples drawn from the peripheral intravenous catheter acceptable, comparable to those collected by venipuncture.**

## Background

As many as 45%<sup>163</sup> of ED visits have been reported to include the insertion of a PIVC, even though the efficiency of this procedure is the subject of discussion and needs further analysis.<sup>164</sup> A third of all established catheters in the ED are not used for any infusion procedure.<sup>163</sup>

The use of PIVCs for blood sampling in daily practice is associated with potential complications, as reported in an Australian survey which also found that PIVCs are more frequently used for blood sampling in the ED than in other hospital departments. More than 50% of the professionals that took part in the survey took blood samples via a PIVC.<sup>165</sup> Potential side effects include infection; breach of patient safety due to possible management errors; and the need for resampling due to haemolysis. Haemolysis was systematically reported as the most relevant issue associated with this blood collection procedure.

Haemolysis is one of the most frequent causes of sample rejection in most clinical laboratories, and may lead to unreliable test results, along with delayed diagnosis and therapy for patients. EDs have the highest sample rejection and haemolysis rates in any hospital setting.<sup>141</sup> The proportion of haemolysed specimens in EDs was significantly higher compared to other hospital departments, with rates ten times higher than other medical wards according to one study.<sup>154 166</sup> Collection of blood through a PIVC is one of the known factors for haemolysis in the ED. This is because PIVCs do not ensure a laminar flow through the collection device, causing the blood to swirl and the red blood cells to rupture, leading to haemolysis. The magnitude of this effect is higher than the greater vacuum force that is applied during phlebotomy.<sup>153</sup>

Haemolysis compromises the quality of care that patients who require blood sampling in the ED receive, impacting on LOS, cost and patient safety.<sup>150 161 167</sup>

The implementation of strategies to reduce haemolysis rates, such as the use of low-vacuum blood collection tubes,<sup>153</sup> is an important step towards developing high-quality practices that improve patient care. Previous studies have shown that samples drawn from a PIVC have higher haemolysis rates compared to samples drawn from new needle phlebotomy.<sup>150 153</sup>

On the other hand, a recent SR demonstrated the validity of laboratory results using blood samples from PIVCs for blood cell counting and biochemistry; besides blood gases.<sup>168</sup><sup>169</sup> With specific reference to saline lock catheters, laboratory results have been demonstrated to be valid for cell counts, biochemistry and coagulation analysis.<sup>148</sup>

Selected haematology, biochemistry, venous blood gases and coagulation parameters have been analysed from blood retrieved from PIVCs used for infusions, including drugs, after discarding an amount of blood aspirated from the catheter line. The results demonstrated the validity of most of the parameters.<sup>170</sup> However, as illustrated in other

studies, different laboratory tests might indeed be influenced by collecting blood from existing catheters, especially after the administration of IV therapy.<sup>171</sup>

Based on the increased risk of haemolysis, blood sampling from IV catheters is not endorsed by the organisations that evaluated the evidence in order to develop recommendations (WHO, EFLM)<sup>18 20</sup>.

As set out in the evidence reviewed for questions 8 and 10, PIVCs are not approved for blood collection. Their use as such is off-label, and a local documented risk stratification needs to be performed prior to this intended use.

## Key question

In adult ED patients with a new placed PIVC, including catheters with infusions in place, are blood samples drawn from the peripheral intravenous catheter (PIVC) admissible, compared to a new venipuncture.

<b>Population</b>	In adult patients with established peripheral venous access in the prehospital or ED, and indication for a blood test.
<b>Intervention</b>	Blood samples drawn from the PIVC.
<b>Comparison</b>	Blood samples drawn from a new venipuncture.
<b>Outcomes</b>	Validity of the test results, haemolysis rate.

Haemolysis rate was the only used outcome due to limited studies suitable for appraisal in the other selected outcomes, based on the validity of the results.

## Recommendation

In adult ED patients blood samples should be drawn through new venipunctures.

In the process of placing a new peripheral venous catheter with a needle gauge  $\leq 18$ , we suggest that blood samples could be drawn through PIVC, after risk/benefit analysis, and following the proper SOP to reduce risks. In any case, precautions such as the use of low-vacuum tubes or manual aspiration is recommended.

The risk analysis should include the contraindications of a new venipuncture and the estimation of the haemolysis risk using the new placed PIVC.

Quality of the evidence	
Overall quality of evidence for the endpoint haemolysis	VERY LOW
Strength of the recommendation	
A weak recommendation, with very low quality of evidence	2D GRADE

## Justification

The appraised papers included an SR<sup>86</sup> featuring seven studies. In four of these the results were consistent: haemolysis rates were higher in samples taken from PIVCs, with a net benefit in haemolysis reduction when sampling via a new venipuncture, leading to a drop in the haemolysis rate from 17.6% to 5.3%. Only two small observational studies in the SR did not demonstrate a significant difference between samples drawn

through the two different sources. Overall, this SR supports the recommendation of a new venipuncture for blood sampling to avoid the higher risk of haemolysis when drawing blood from a PIVC.

## Risk benefit

Haemolysis is one of the main reasons for sample rejection, but haemolysis is a multifactorial undesirable consequence. The three most significant contributing factors to haemolysis are the sampling technique; training of professionals; and transport of the sample. In particular, the use of a PIVC and vacuum techniques for sampling play an important role.<sup>172</sup> In this context, an accurate estimate of the benefits of one specific intervention (vein puncture for blood sampling in patients with a PIVC) has important limitations. The estimated reduction in haemolysis rates when the sample is taken from a new venipuncture, versus from the established PIVC, is 5–15%, without taking into account the grade of haemolysis and the clinical impact of the laboratory results.<sup>148</sup> This reduction also does not take into account the second and third contributing factors set out above. On the other hand, recent publications have not been able to demonstrate differences in haemolysis rates when controlling these other factors.<sup>173 174</sup>

Venipuncture is the most common invasive procedure performed in healthcare settings. It is a safe procedure, although not exempt from minor risks. Furthermore, some serious complications, such as cellulitis, phlebitis, reactive hypotension, near syncope, syncope, and seizure activity have been reported, accounting for 3.4% of all phlebotomies.<sup>111</sup> In addition, it is important to consider the fear of the procedure (trypanophobia); the inherent pain associated with it; and the vasovagal complications of the anxiety generated by the procedure. Venipuncture with a metallic needle can also cause haemolysis, affecting up to 5% of blood samples taken in the ED (depending on the grade of adherence to blood collection recommendations).<sup>161</sup> Therefore this percentage should also be taken into consideration during comparisons. Finally, the manipulation of an established catheter for blood sampling risks potential catheter displacement and infection.

## Patient values

Safety is usually the main concern of patients. From the overall perspective of ED performance, a new venipuncture is more time-consuming and more of a procedural threat than extraction from a placed IV catheter, and no substantial changes in the needed materials are anticipated.

## Subgroup considerations that may be relevant

Patients with difficult vein access, including<sup>96</sup> burns patients and patients undergoing thrombolysis, should not undergo further venipunctures.

A new venipuncture is recommended in the following cases: patients with a small-diameter PIVC in place ( $\leq 20G$ ), due to the direct correlation between reduced catheter diameter and haemolysis rates;<sup>175</sup> patients with a PIVC placed in a vein with limited flow; patients with a PIVC placed on a dorsal hand vein; patients with difficult access.<sup>158</sup> The antecubital fossa is the optimal site for PIVC insertion.

There is consensus that the length of time between the PIVC being placed and blood being drawn from it affects haemolysis rates. Grant et al.<sup>176</sup> found significantly higher rates of haemolysis leading to sample rejection when a new PIVC was used compared to venipuncture, and no significant difference when an existing PIVC was used compared to venipuncture. Dietrich et al.<sup>177</sup> also reported higher haemolysis rates when using newly inserted PIVCs than for existing catheters. However, there were confounding factors in this study, including multiple professional groups performing phlebotomy. Additionally,

no statistical analyses were performed. Therefore, evidence of higher haemolysis rates when using new PIVCs, compared to existing ones, was classified as poor.

The group of patients that requires clarification of the possibility of in vivo haemolysis, or in which a precise determination of the tests more influenced by in vitro haemolysis (LDH, potassium and magnesium, D-dimer, troponins<sup>178</sup> or if a bacteriological tests are needed; a new venipuncture is always recommended.

## Differences of opinion among the WG

This controversial question led to extensive debate within the working group. However, members of the group unanimously agreed on the recommendation for a new venipuncture, and agreed that aspiration from a PIVC should only be carried out following an extended risk analysis.

## Implementation considerations

The use of a PIVC for blood sampling requires consideration of the local SOP for obtaining samples, including the procedure for saline lock catheters. In prior or concurrent use of the cannula for administration of fluid or drugs, the infusion should be stopped for 2–3 minutes, and the first 3–5ml discarded<sup>179 180</sup>. It is extremely important that laboratory professionals develop SOPs for blood collection in collaboration with clinical professionals from the ED.

As an additional precaution, the use of a tourniquet should be avoided if possible. Alternatively, the tourniquet should be applied for <1 minute and released immediately when blood begins to flow.<sup>173</sup>

Any special equipment required for the blood collection should be taken into consideration,<sup>181</sup> along with the need for training to manage the range of materials required to connect to the catheter, as well as the implementation of closed systems with aspiration.

The preparation of a documented risk stratification for the intended off-label use of PIVCs for blood collection is good practice.

## Suggestions for monitoring and evaluation

The ED should use the rate of haemolysis per sampling place as a process quality indicator.

## Research priorities or future research needs

Research needs to be carried out to evaluate the different SOPs describing sampling processes in established catheters – with or without fluids – in order to provide an evidence-base for recommendations,<sup>165</sup> including evidence for safe practice that supports hospital policies.<sup>173</sup>

## 10 Effect of the sampling devices, aspiration models, through peripheral intravenous catheters

### Background

Compared to open systems (i.e. a syringe), the use of a closed system for blood sampling increases the quality of the sample procedure and safety levels for the patient and professionals involved. Based on these benefits, closed systems are recommended by

several guidelines.<sup>18 100</sup> They reduce the risk of direct exposure to blood and can prevent contamination. They also ensure that an adequate amount of blood is sampled, avoiding the problem of insufficient sample volume. However, prefill vacuum systems are not free of undesirable effects compared to manual aspiration. The most common issue encountered is haemolysis, the rate of which is higher with vacuum extraction systems compared to manual aspiration.<sup>90 146 157 176</sup>

Mrazek et al.<sup>153</sup> found that the force (negative pressure) with which blood was drawn through the collection device was the major factor contributing to haemolysis rates, regardless of the type of collection container. Additionally, the authors found that the use of low-vacuum tubes reduces haemolysis rates by lowering negative pressure (suction) during phlebotomy.

Factors that affect haemolysis rates in blood samples drawn from newly placed IVs in the ED include catheter size, the position of the PIVC, the medical staff involved and difficulties in placement.<sup>90</sup> Fernandez et al.<sup>182</sup> found significantly higher haemolysis rates when syringes were used to aspirate specimens compared to evacuated tube systems.

Haemolysis is the most frequent cause of sample rejection<sup>142 143</sup> in most clinical laboratories, and may lead to unreliable test results, delayed diagnosis or treatment, or the initiation of inappropriate medical actions.<sup>183</sup> Haemolysis rates in samples drawn in the ED have been reported to be higher than in other hospital departments, with a range of 10.7–12.4% versus 1.6–2.9%.<sup>154 166</sup> The higher levels were seen in the more critical areas. Haemolysis that causes sample rejection affect quality of care and also increases LOS in the ED and cost, as well as impacting patient safety.<sup>141</sup>

The blood sampling process, and specifically the use of vacuum extraction systems when compared to manual aspiration systems, is one of the factors associated with increased haemolysis rates in blood samples collected from intravenous catheters.<sup>89 153 184</sup>

Implementation of strategies to reduce haemolysis rates when sampling via PIVCs is important for developing practices that improve the quality and safety of patient care.

As set out in the previous question (n° 9), it is important to note that PIVCs are not approved for blood collection. As such, the use of PIVCs for blood collection is off-label and a local documented risk stratification needs to be performed prior to this intended use.

## Key question

Effect of the sampling devices used through PIVC, vacuum versus manual aspiration.

<b>Population</b>	In adult ED patients with indication for a blood test and PIVC in place.
<b>Intervention</b>	Blood sampling devices, close vacuum systems.
<b>Comparison</b>	Manual aspiration systems.
<b>Outcomes</b>	Effect on TAT, haemolysis, haematomas. Users' acceptance

## Recommendation

To reduce the haemolysis rate as undesirable outcome, we recommend, for patients with already established peripheral intravenous catheters, in whom blood sampling is necessary for laboratory tests, not to sample through the PIVC.

If after a risk analysis blood is drawn from a PIVC, the professional should use a closed manual aspiration or low vacuum system, to reduce the risk of haemolysis.

The risk analysis should include the contraindications of a new venipuncture and the estimation of haemolysis risk using freshly placed PIVCs.

Quality of the evidence	
Overall quality of evidence for the endpoint haemolysis	VERY LOW
Strength of the recommendation	
A weak recommendation, with very low quality of evidence	2D GRADE

Other outcomes like TAT, local haematomas or users' acceptance have not been analysed due to the lack of publications.

## Justification

The papers reviewed for this question looked at haemolysis as the outcome. Six papers were evaluated: one SR and five observational studies. The results of the SR<sup>86</sup> provided no consensus on how different aspiration methods affect haemolysis rates. The RCT included in the SR reported that the risk of haemolysis when comparing vacuum systems with manual aspiration using a syringe was higher in blood samples collected with vacuum systems from a PIVC, with an OR of 6.0 (95% CI: 2.3 to 15.2).<sup>146</sup> Fernandez et al. report the same higher rate of haemolysis for sampling through a PIVC using vacuum tubes, with an OR of 2.2 (95% CI: 1.5 to 3.3).<sup>182</sup> A reduced risk of haemolysis when manual aspiration is used is also supported by Grant.<sup>176</sup>

The other observational studies did not support these findings, reflecting inconsistency in the findings of the SR. However, other observational studies from Cakir Mo, et al, Karezoglu C, and Millius L, et al,<sup>185-187</sup> demonstrated the superiority of the manual aspiration technique, with lower haemolysis rates compared to vacuum systems, including closed manual aspiration systems. Only one study failed to statistically demonstrate the superiority of manual aspiration,<sup>161</sup> although the blood in this study was drawn with a syringe and then transferred to blood tubes (i.e. an open system, which should be avoided under all circumstances). This study had important limitations due the large amount of missing information regarding the technique used for blood drawing (>50%). All the observational studies<sup>185-187</sup> were graded very low quality, although the existence of consistencies in all of them, and the size of the effect in the results in favour of manual aspiration, with no negative effects, formed the basis for supporting this intervention.

## Risk benefit

A manual, open aspiration system is associated with negative outcomes, as it leads to an increased risk of biological contamination. In open systems, the use of the syringe to transfer blood from the PIVC to the tube container is listed as one of the causes of accidents as additive carryover between tubes and the start of coagulation in the non-anticoagulated syringe, leading to inaccurate coagulation results.<sup>188-190</sup> A closed system with manual aspiration minimises this risk, and its efficacy and safety were documented in the studies appraised.<sup>185-187</sup> Manual closed system are associated with the greatest drop in haemolysis rates.

## Patient values

From the patient's perspective, this intervention reduces the number of rejected samples and test interpretation errors, with a consequent reduction in the total time spent in the ED. This benefit for the patient is associated with a wider benefit for the ED workflow, with a reduction in ED crowding.<sup>142 183</sup>



For the professional involved, an open system increases the risk of biological accident (needle-stick, blood contact) so a closed manual aspiration system should be considered in conjunction with strict application of the SOP. In one paper, nurses reported that they were more comfortable using closed manual aspiration systems, although the quality of the paper was considered to be very low. The overall benefit was assessed as being additional comfort for the patient, and a gain of time that could be dedicated to patient care by reducing unnecessary tasks and stress.<sup>187</sup>

## Differences of opinion among the WG

There was an extensive debate among WG members based on a reluctance to make a recommendation for a procedure (blood aspiration through a PIVC) that had recognised negative effects on the quality of the blood sampling.

## Implementation considerations

The implementation of a new aspiration procedure through a PIVC requires appropriate training, along with SOP design and implementation, including taking safety aspects into account. Training programmes for blood sampling professionals have been shown to be effective in reducing rejection rates and increasing safety for patients and professionals.<sup>141 191</sup> Considerations for implementing the proposed changes in the blood sampling process, including the use of new materials, requires a suitable training programme combined with a thorough understanding of the causes of collection refusal. Short interventions have proved effective in this context.<sup>146</sup> Documented risk stratification for the intended off-label use of a PIVC for blood collection is mandatory.

## Suggestions for monitoring and evaluation

To ensure proper management of the PPP, QIs should include continuous monitoring of rejection rates and haemolysis rates, both in the laboratory and the clinical setting, reflecting the role of clinicians in the PPP and the interrelationship between the ED workflow and the laboratory.

## Research priorities or future research needs

Further research is recommended to clarify the clinical and professional impact of new materials or process modifications, with a focus on professional acceptance of the process and its influence on the clinical decision or outcome. Cost analyses of closed manual aspiration system are required as part of the evaluation of new devices.

No mention of this recommendation that requires attention, due to the frequent use and the quality implications, is made in other blood sampling guidelines.<sup>18 100</sup>

## 11 “Difficult venous access” The use of facilitators; ultrasonography-guided peripheral venous access

### Background

Ultrasound (US) is an imaging technique that is becoming increasingly widely used in the ED.<sup>192</sup> US has several advantages over other imaging modalities, including its use of non-ionising radiation, portability, accessibility, non-invasive nature and relatively simple learning curve. US is used for clinical as well as diagnostic purposes. It is of great importance in treating patients (mostly critically ill patients) where diagnosis and appropriate management are time-sensitive.<sup>193</sup>

in patients with difficult venous access (DIVA), US can expedite diagnosis by enabling blood samples to be drawn more quickly and easily, and is also associated with fewer side effects.<sup>196 197</sup> Patients with DIVA include obese patients with a range of comorbidities; hypotensive patients;<sup>194 195</sup> and patients with anticoagulation where blind cannulation could generate further complications.

US guidance can increase the safety and efficiency of venous access procedures and offer improved outcomes. The potential for these improvements is compelling, especially among patients with DIVA, who are defined as meeting at least one of the following criteria:

- More than two failed attempts or previous history of failed attempts, using traditional techniques
- No visible or palpable veins during the physical examination
- Anticoagulated patients<sup>96</sup>

One of the greatest advantages of US is its increase in the success rate of drawing blood on the first attempt, without increasing the risk of complications.<sup>198</sup>

## Key question

In the “Difficult venous access” what is the role of facilitators; ultrasonography-guided peripheral venous access?

<b>Population</b>	In ED patients (adults) with “difficult venous access”, without indication for central venous access.
<b>Intervention</b>	Ultrasound-guided venipuncture performed by any professional (nurse, technician, physician).
<b>Comparison</b>	1. Other interventions (e.g., application of warm tissues, arm bath). 2. Puncture of other locations than the forearm (cervical veins, lower extremities). 3. Typical care.
<b>Outcomes</b>	Pain, infection, number of attempts, time to blood sampling, patient experience, feasibility.

## Recommendation

We recommend, in patients with difficult vascular peripheral venous access, the use of ultrasound guided access.

Quality of the evidence	
Overall quality of evidence for the selected outcomes	HIGH
Strength of the recommendation	
A strong recommendation with a high level of evidence	2A GRADE

## Justification

When reviewing the use of US-guided vascular access, four papers were appraised: one RCT<sup>197</sup> and three SRs<sup>195 198 199</sup> focusing on five different end-points. These were: first venous access attempt; number of attempts; length of the procedure; patient satisfaction; and adverse events.

All four manuscripts were evaluated for the outcome 'first venous access attempt using US', with a relatively high level of associated evidence, ranging from moderate to high. All the papers concluded that US-guided vascular access increases the likelihood of successful first cannulation.

In a recent publication, Yalcinli et al.<sup>197</sup> report that the success of the first attempt was higher (56 of 90 (62.2%) vs. 71 of 90 (78.9%),  $p = 0.014$ ) – in patients who underwent US-guided vascular access, compared with the standard or infrared-guided groups. Since the study is an RCT, the quality of the evidence was initially graded as high for all outcomes. However, it was downgraded due to imprecision since the event rates were fewer than 300. For this endpoint the evidence was finally rated as moderate.

In an SR published in 2021, Tran QK et al.<sup>199</sup> found higher success rates using US, with an OR of 2.1, (95% CI 1.65 to 2.7),  $p < 0.001$ . The quality of the evidence was consider high.

In the next SR, Tran QK et al.<sup>198</sup> found that US-guided cannulation was associated with double the likelihood of a successful first attempt, (OR 2.08; (95% CI, 1.43 to 3.0),  $p < 0.001$ ). Since all the studies selected were randomised controlled trials, the level of evidence was rated as high.

Egan et al.<sup>195</sup> confirmed these findings in their SR, which also demonstrated superior success using US (OR 2.42 (95% CI 1.26 to 4.68),  $p < 0.001$ ). However, in this study the quality of evidence was downgraded to moderate due to minor risk of bias.

Four manuscripts were included in the outcome 'number of attempts', with a level of evidence rated between low and high. The purpose of this endpoint was to analyse whether US-guided vascular access could reduce the number of attempts; three of the four studies demonstrated that it did.

In their SR, Egan G et al.<sup>195</sup> showed that the use of US for peripheral Intravenous access had a weighted mean difference of -0.64 ((95% CI -0.76 to -0.53),  $p < 0.0001$ ) regarding the number of attempts. The study was ranked with a low level of evidence due to serious risks of bias.

In an SR including eight studies, Tran QK et al.<sup>199</sup> reported a standard mean difference (SMD) in the number of attempts between US and standard procedure of -0.272 ((95% CI -0.539 to -0.004),  $p = 0.047$ ), with a high level of evidence.

In an SR including six studies, Tran QK et al.<sup>198</sup> reported a mean difference (MD) in the number of attempts between US and standard procedure of -0.151 (95% CI -0.311 to 0.010), with a moderate level of evidence due to imprecision issues.

Yalçınlı S, et al.<sup>197</sup>, compare in DIVA phlebotomies, three different methods to facilitate cannulation; Ultrasound-guided (USG), standard procedure, and Near-Infrared Light (NIR) transillumination, the authors found differences in terms of the e first attempt success rates; 78.9%, 62.2%, and 58.9%, respectively. Sawing the USG group statistically higher rate of success compared with the two other methods. ( $p < 0.014$ ). Although the total procedure median (IQR) procedure time was longer in patients undergoing USG compared with standard and INR procedures 107 (69-228), 72 (47-134), and 82 (61-163) seconds, respectively, with the statistical difference between USG and the standard procedure, ( $p < .001$ ).

Four manuscripts were included for the outcome 'length of the procedure', with a level of evidence rated as low to moderate. This endpoint analysed the procedure time to vascular access. Only Yalcinli et al.<sup>197</sup> found that US-guided vascular access was more time-consuming than the standard procedure. The total median IQR procedure time for US and standard methods was 107 (69-228) and 72 (47-134) seconds respectively

( $p < 0.001$ ). The evidence was ranked as moderate due to imprecisions. The other three studies found no difference in the procedure time.

Data regarding the time needed to obtain vascular access are contradictory. An earlier publication by Costantino<sup>200</sup> found that the use of US-guided vascular access is less time-consuming than the standard procedure, reflecting some controversy in this outcome

Focusing on patient satisfaction, two papers – SRs by Tran – reported on patient satisfaction. The review published in 2021<sup>199</sup> describes significantly higher levels of patient satisfaction in the US group (SMD: 1.467 (95% CI 0.92 to 2.012)  $p < 0.001$ ), with the level of evidence considered to be high, although this finding was not confirmed in their 2022 study<sup>198</sup> (moderate level of evidence).

Only one manuscript was included in the appraisal for the outcome 'adverse effects'. This was assessed as providing a moderate level of evidence. In this review, Tran QK et al.<sup>198</sup> analysed potential adverse events as catheter extravasations, and found no significant differences when compared to standard care.

The findings in the appraised literature support the recommendation for US-guided venous access, based on higher rates of first attempt success; lower numbers of attempts; no demonstrated longer procedure time; and no demonstrated significant increase in adverse events or patient dissatisfaction with the procedure.

## **Differences of opinion among the WG**

There were no conflicting opinions among members of the working group.

## **Implementation considerations**

Training is required before the implementation of US-guided vascular access,<sup>201</sup> so a suitable training programme for ED professionals is of paramount importance. Also, availability of equipment is mandatory, and this is linked to associated costs and investment, both in terms of training and materials, compared to the standard method of vascular access.

Training programmes<sup>202</sup> are fundamental to the success of US-guided vascular access, and care needs to be taken to develop appropriate programme content in order to deliver a comprehensive, structured educational programme that includes didactic elements, hands-on training and the application of practical skills.<sup>203</sup>

Establishing a group trained in US requires workflow modifications in the ED.

## **Suggestions for monitoring and evaluation**

Recordings of DIVA rates and the impact of the US programme can be used to monitor and evaluate its success.

## **Research priorities or future research needs**

Evaluation of a protocol for DIVA based on US.

### 3. Post-sampling/transport

#### 12 In adult ED patients, does transporting the blood samples via pneumatic tube system affect haemolysis rate, compared to manual transportation?

##### Background

Sample transport is one of the preanalytical processes and is often a significant contributing factor to total turnaround time (TAT). If the laboratory is close by samples may be delivered by hand, while for longer distances vehicle transport (car, train, plane or drone) may be necessary. As demands for faster TATs increased over time, sample transportation via pneumatic tube systems (PTSs) became widespread in healthcare facilities. This method is claimed to be not only faster but also less of a drain on personnel resources.

A recent survey involving 376 European EDs<sup>1</sup> found that laboratory testing was performed in a centralised hospital laboratory in 62.6% of facilities, while 27.1% used a combination of centralised and point-of-care-testing (POCT); and the remaining 9.92% of the centres had a dedicated laboratory within the ED. In the group processing blood specimens in a central lab, with information about (n=184), the samples were transported via a PTS in 65.2% of cases and manually in 30.4% cases.

Although studies looking at the role of PTSs commenced as early as 1964, and there have been many subsequent observational studies, no general recommendations for or against the use of PTSs for blood sample transportation are currently available, due to the high degree of heterogeneity of these studies.<sup>204 205</sup> In theory, the mechanical impact on the transported blood sample may cause red blood cells to rupture, leading to haemolysed serum/plasma. Analytical measurements from such samples may result in biased test results and lead to potentially inappropriate medical interventions.<sup>23</sup> However, some authors report that PTS transportation has no impact of on sample haemolysis.<sup>206 207</sup>

The impact on samples that have been transported via PTS may depend on several factors, including the length, speed and g-forces of the PTS; the number of turns and drops; as well as on the potential formation of air bubbles or the type of container inserts; and of course on the type of tests requested.<sup>208 209</sup>

Data loggers have been developed to monitor and document time, temperature and g-forces during sample transportation and proposals for using sample haemolysis as a quality indicator for PTS transportation have been issued.<sup>210</sup>

##### Key question

In adult ED patients, does transporting the blood samples via pneumatic tube systems affect haemolysis rate, compared to manual transportation?

<b>Population</b>	In adult ED patients with indication for a blood test.
<b>Intervention</b>	Use of the pneumatic tube transportation.
<b>Comparison</b>	Pneumatic tube transportation versus manual transportation.
<b>Outcomes</b>	Effect on TAT, and haemolysis.

## Recommendation

If available, the group is in favour of using PTS for sample transportation from the ED to the laboratory to reduce TAT and LOS, especially when EDs are dependent on a central laboratory that is not located near the ED.

Quality of the evidence	
Overall quality of evidence for the endpoint haemolysis	VERY LOW
Strength of the recommendation	
A weak recommendation in favour of the use of a PTS for sample transportation	2D GRADE

## Justification

The literature that was appraised included four studies: one SR and three cohort studies. In his SR, McCaughey, E.<sup>86</sup> identifies one RCT and two observational studies. The SR reports homogeneous results from Kara et al.<sup>211</sup>, Pasqualetti et al.<sup>212</sup> and Ellis et al.<sup>213</sup>, showing higher rates of haemolysis in PTSs compared with manual delivery (MaD): 100% (n = 53) versus 16.3% (n = 8),  $p < 0.0001$ ; 10.9% versus 3.3%,  $p < 0.0001$ ; and 9.4% (n = 908) versus 6.6% (n = 655),  $p < 0.001$ . Böckel-Frohnhofer et al.<sup>214</sup> found a higher haemolysis rate when specimens were collected in lithium heparin tubes.

In an extensive cohort study, Casati et al.<sup>215</sup> found that the percentage of haemolysed samples delivered on ice using a pneumatic tube system was double that of the number delivered on ice via MAD (10% (n=21), vs. 5% (n=34), ( $p < .01$ )).

Wei et al.<sup>216</sup>, found a significantly higher haemolysis rate for specimens transported by pneumatic tube compared to MaD. 56.67% of PTS samples were haemolysed, while no haemolysis occurred in MaD. Compared with the MaD samples, levels of free plasma Hb in the PTS samples was significantly higher (MaD:  $4.46 \pm 3.59$  mg/dl; PTS:  $59.68 \pm 46.89$  mg/dl,  $P < .001$ ).

Another observational study by Saleem et al.<sup>87</sup> found a borderline significant increase in haemolysis rates for specimens transported by these two methods.

These homogeneous results support the conclusion that PTS transport is associated with higher haemolysis rates than manual transport. The strength of the evidence was classified as low.

Only one study was appraised that focused on TAT. In a study with small number of subjects, Raimann, F.J.<sup>217</sup> reports that transportation time for samples transported via PTS was significantly shorter than for MaD systems: 8 versus 18.5 minutes;  $p < 0.001$ . The quality of evidence was classified as very low.

Reduction of TAT depends heavily on local settings, e.g. the distance between the ED and the lab, PTS speed, the location of distribution centres etc.

## Risk benefit

### Benefit

Blood samples may be transferred faster by pneumatic tubes than by manual transportation.

## Risk

The transfer of blood samples via pneumatic tubes seems to be associated with higher haemolysis rates compared to manual transportation.

## Patient values

Timely test results lead to a shorter length of stay at the ED, and hence to increased patient satisfaction.

## Differences of opinion among the WG

The working group discussed whether samples being tested for haemolysis-sensitive parameters such as lactate dehydrogenase (LD) should always be transported manually. However, the benefit fast transport outweighed the risk of haemolysis.

## Subgroup considerations that may be relevant

Patients with a high risk of preanalytical alterations to samples due to PTS transportation (e.g. those with severe leucocytosis) should be identified. The mode of sample transport should be considered in the case of patients whose test results for haemolysis-sensitive parameters (e.g. LD, CK-MB, AST, potassium) show inexplicable deviations.

## Implementation considerations

Before installing a new PTS, a cost-benefit analysis should be performed, taking into account the distance between the ED and the laboratory, as well as the possibility of installing POCT testing. Streichert et al.<sup>210</sup> have published practical recommendations on how to determine the haemolysis threshold in samples transported via PTS. In cases where blood is being collected via IV-catheter, an a priori estimation of possible haemolysis rates, based on the blood collection tubes in use, can be carried out by applying the formula published by Mrazek et al.<sup>153</sup> Additionally, the tube inserts should be carefully evaluated before the system is selected, as their design may be a significant factor in reducing mechanical sample stress.<sup>209</sup>

## Suggestions for monitoring and evaluation

When choosing to implement PTS transportation, continuous quality assurance measurements, including assessment of haemolysis rates, possibly in conjunction with a tracking device, must be planned. As haemolysis rates have been demonstrated to be higher in samples transported via a PTS, the number of such haemolysed samples should be documented and evaluated on a regular basis. Where an initial sample is rejected due to haemolysis, the replacement should be transferred to the laboratory manually.

Haemolysis levels need to be reported and acknowledged as part of the evaluation of test results. Ideally, the laboratory should provide this information, including flagging clinically relevant test result biases according to EFLM WG-PRE recommendations.<sup>218</sup>

## Research priorities or future research needs

Additional research is required to evaluate ways of reducing the occurrence of haemolysis during PTS transportation, such as through the use of innovative tube inserts.<sup>209</sup>

## 13 Collection of a standard set of samples in all adult ER patients for future analysis

### Background

In some EDs a standard set of samples is collected, despite not all these samples being needed for the required tests. This practice sometimes involves drawing predefined tubes, to allow for add-on testing later if requested. The cost-effectiveness of drawing the extra tubes has not been widely analysed. One study from a single centre<sup>219</sup> concluded that the extra tubes were only used in 2.8% of cases, a low figure that does not support the cost-effectiveness of the process and the authors observed reduction in the use of the extra samples, along the seven years of study.

Optimising blood-testing resources is part of professional patient management. Usually, a test is requested if it is considered essential for patient management and if it adheres to clinical guidance. In consequence, the sampling of blood for tests that are not needed in the evaluation process is difficult to justify.

The studies which have examined the usefulness of this strategy are limited in scope, and the literature search performed for these guidelines only identified one suitable paper.<sup>220</sup> This found a reduction in the need for additional blood drawings using the “rainbow draw”, and also noted that the cost was not negligible (more than \$60,000 a year for 28,000 annual ED visits). The question is whether the results of this study could be extrapolated to other hospitals. The hospital where the study was performed used a rapid serum tube for some routine chemistry analyses and collected an additional standard serum separator tube for possible add-on testing. However, other hospitals either perform routine chemistry analyses for the ED in plasma separator tubes or standard serum tubes.

A well-established practice is to request additional tests from blood samples already in the lab, but this process is not within the scope of this PICO question.

### Key question

Reasonability of collecting a standard set of samples in all adult ER patients for future analysis (Rainbow sampling).

<b>Population</b>	In adult ED patients with indication for a blood test.
<b>Intervention</b>	Collection of standard set of blood samples in all adult ED patients for future analysis.
<b>Comparison</b>	No extra sampling.
<b>Outcomes</b>	Need for additional blood drawings, feasibility.

### Recommendation

The group does not recommend the collection of a standard set of samples in all adult ER patients for future analysis.



## Justification

The literature search performed for this project only identified one study.<sup>220</sup> This found a reduction in the need for additional blood drawings using the “rainbow draw”, and also noted that the cost was not negligible (more than \$60,000 a year).

## Risk benefit

### Benefit

No need for additional phlebotomy.

A shorter TAT to obtaining results of add-on tests can result in the patient being discharged faster.

### Risk

Iatrogenic anaemia due to collection of unnecessary blood samples has been described in paediatric and adult trauma patients.<sup>221</sup>

Decreasing quality of samples when stored as whole blood for a longer period of time.

The unused blood samples is also a concern for the generalisation of this practice.

### Cost

Substantial cost of additional blood tubes in the study by Snozek et al.<sup>220</sup> (more than \$60,000 a year)

### Balance

No consensus recommendation. Only one study was identified during the literature search, the results of which cannot straightforwardly be extrapolated to other hospitals. The risk/benefit ratio will depend on local factors.

## Patient values

A shorter TAT can result in a shorter time to discharge for the patient.

## Differences of opinion among the WG

There were no conflicting opinions among members of the working group.

## Subgroup considerations that may be relevant

In patients with (iatrogenic) anaemia and paediatric patients, only samples that are necessary should be collected.

When a patient is severely ill but without an evident diagnosis, and the anatomy for blood sampling is difficult, clinicians might consider taking extra samples for possible future analysis.

## Implementation considerations

If the collection of additional, primarily unnecessary, samples is being considered, a number of factors should be taken into account. These include the preanalytical conditions;

the tests that it is assumed will be ordered from these tubes; and the maximum desired storage times. These factors need to be discussed with the local laboratory, with storage times based on current stability study results.<sup>222</sup>

## Suggestions for monitoring and evaluation

As there is no consensus recommendation, no suggestions for monitoring and evaluation were put forward.

## Research priorities or future research needs

The WG considers that the topic do not merit extra research with the actual information.

### 14 Blood sampling for blood cultures

#### Background

Blood cultures (BCs) collected in the ED form the basis of targeted antibiotic therapy in suspected cases of sepsis. As BCs are incubated for a certain amount of time in order to multiply bacteria or fungi, special care needs to be taken to avoid any form of contamination. Skin bacteria from non-clean, non-sterile puncture sites are a common source of such contaminations, with reported contamination rates ranging from 0.8% to 23% of all BCs.<sup>223</sup> The Clinical and Laboratory Standards Institute (CLSI) Guideline on BC collection and handling recommends keeping contamination rates below 3%.<sup>224</sup> False positive BCs (FPBCs) are not only a severe patient risk due to inadequate treatment, but are also associated with significantly increased hospital and laboratory charges.<sup>225</sup> In conjunction with adherence to according guidelines and appropriate skin disinfection prior to phlebotomy, a sterile collection procedure might additionally reduce contamination rates, compared to the traditional clean process.<sup>226 227</sup>

Sources of blood culture contamination are numerous<sup>228</sup> and one of the major contributing factors is the collection of blood through existing IV catheters following inadequate antisepsis in the access area of the intravenous device (e.g. Luer connector). By comparison, collection of blood via peripheral venipuncture have been reported to be associated with lower contamination rates.<sup>229 230</sup> However, in order to avoid additional phlebotomy for blood culture collection, especially in patients with difficult venous access, collection from intravenous catheters may be appropriate in certain circumstances.

#### Key question

Blood sampling for BC, using existing peripheral intravenous catheters versus new venipuncture

<b>Population</b>	In adult ED patients with BC indication.
<b>Intervention</b>	BC from PIV catheter lines
<b>Comparison</b>	BC from new venipunctures
<b>Outcomes</b>	Rate of contaminated specimens.

#### Recommendation

We suggest that in case of BC collections in EDs in adult patients, a new phlebotomy should be preferred over collection from available catheter lines to minimise the risk

of sample contamination. In any case, we suggest discarding the first few ml of blood either by using a discard tube or initial specimen diversion devices when sampling is done through a PIVC.

Quality of the evidence	
Overall quality of evidence for the endpoint false positive BC	VERY LOW
Strength of the recommendation	
A weak recommendation in favour of the use of a new venipuncture	2D GRADE

## Justification

The two studies that were appraised (Arenas et al.<sup>231</sup> and Rupp et al.<sup>232</sup>) pointed towards a reduction in BC contamination rates and lower false positive rates when a novel specimen collection/diversion system was used.<sup>233</sup>

Studies comparing contamination rates in BCs collected from peripheral veins versus intravenous catheters all conclude that contamination rates are higher with the latter collection method.<sup>229 230</sup> In the absence of further evidence, specifically for the ED setting, it must be assumed the same facts apply here. The results suggest that more evidence is needed to establish the appropriateness of using diversion devices.

The effect of sterile gloves in blood sampling is addressed in question 6.

## Risk benefit

Collecting BCs from existing intravenous catheters may result in a higher rate of sample contamination, compared to separate venipuncture. Subsequent medical choices might be misinformed by false positive blood culture testing.

Conversely collection of blood cultures from catheter lines means the phlebotomist does not need to take an additional sample, and the patient does not need to undergo an additional puncture.

## Patient values

We believe that following procedures that are most likely to ensure accurate test results should always be preferable to time-saving actions. Therefore performing a separate venipuncture, and thereby minimising blood culture contamination rates, contributes far more to patient safety than collecting blood using existing intravenous catheters.

## Differences of opinion among the WG

There were no conflicting opinions among members of the working group.

## Implementation considerations

When introducing new medical processes and materials, such the use of an initial specimen diversion device, appropriate training of the medical staff performing phlebotomy is required.

In cases of high (>3%) or increasing contamination rates, re-education of the entire blood culture collection team should be carried out.

## **Suggestions for monitoring and evaluation**

Blood culture contamination rates should be documented and evaluated on a regular basis as a quality process indicator.

## **Research priorities or future research needs**

Prospective, randomised and controlled studies are needed to specifically compare the contamination risk of BC samples drawn from a PIVC versus a new venipuncture in an ED setting.

## 4. Quality assurance

Quality indicators (QIs) can be thought of as key performance indicators (KPIs) for maintaining and improving quality in patient care.<sup>234</sup> The use of KPIs is well established and they are widely used in most medical laboratories and clinical settings.<sup>235</sup> Such indicators can be any measure (frequency, time, occurrence etc.) that is important to assess quality, but for the most part they represent the number of errors within a process. After retrieval, QIs need to be documented and monitored over time, and ideally benchmarked against other healthcare institutions.<sup>236 237</sup> Additionally, written standard operating procedures (SOPs)<sup>234-236</sup> need to be available, indicating what to do when QI numbers deviate above or below a certain threshold, with the goal being continuous quality improvement.

Most errors in laboratory processes occur during the preanalytical phase, and the rate of preanalytical mistakes is higher in the ED compared to other departments.<sup>238</sup> There are several well-established indicators reflecting preanalytical phase process quality which are directly correlated with the reliability of laboratory values. Monitoring and quality management of these indicators significantly influences patient safety, as well as the patient's LOS in the ED. Among the most common preanalytical errors are the rate of sample haemolysis; sample underfilling; and misidentification errors. Monitoring these can help to identify preanalytical quality failures.<sup>6 153</sup> Based on the frequency of their occurrence, additional QIs may be introduced, depending on the local setting.

It is important for EDs that laboratory values are both reliable and available swiftly. This is particularly true for laboratory markers that are of immediate relevance for therapy, such as blood glucose, electrolytes or blood gas, but is also relevant for diagnostic biomarkers like troponin which indicate cellular injury of specific organ systems. Therefore, in addition to the aforementioned QIs, total turnaround time (TAT) is a QI that is particularly relevant to the ED process. It can be defined as the period from physician test selection to result retrieval. TAT comprises a large number of elements and its deterioration can be due to a wide range of factors in the preanalytical, analytical, and/or postanalytical phase. It includes transportation time as well as the core laboratory process, plus the time the physician takes to retrieve the results. It is affected by all the above-mentioned QIs because non-adherence to the quality standards for these indicators, such as underfilling, could trigger the need for a repetition of the whole process. As a result, quality indicators for the preanalytical phase within EDs cannot be neglected, as they also affect TAT.

Point of care testing (POCT) could be an effective method for reducing TATs. However, the same quality standards apply to POCT as they do to routine laboratory tests, even though POCT is mostly performed by ED personnel, rather than trained laboratory staff. This means there is a need for written SOPs on the use and quality control of the instruments, including QIs used for the quality control of preanalytical errors such as haemolysis, sample underfilling and misidentification errors.<sup>239 240</sup>

Several free-to-use platforms are available for the documentation, monitoring and benchmarking of laboratory-specific QIs. The most prominent one is the Model of QIs, developed by the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) working group on laboratory errors and patient safety (WGLEPS)<sup>241</sup> Additionally, there are some national initiatives such as the US College of American Pathologists' Q-Tracks programme<sup>242</sup> and the Australian Key Incident Monitoring and Management System (KIMMS),<sup>243</sup> as well as a German speaking database solely for haemolysis data<sup>244</sup>

## 15 Effect of Point of Care Testing (POCT) on the quality of the laboratory process

### Background

Time is essential in an emergency setting. Obtaining specific laboratory results as quickly as possible is mandatory in a range of clinical situations and has the potential to improve patient flow and reduce overcrowding in the ED. As a result, TAT is an important KPI for the ED-laboratory process chain. POCT eliminates the time taken to transport the blood sample to the laboratory, and thus has the potential to reduce TAT when compared to central laboratory testing, depending on the local conditions. POCT can also help physicians make decisions regarding diagnoses and treatment within minutes at the point of care.

However, there are many aspects to consider prior to introducing POCT to the ED. POCT devices are usually more costly and often provide lower analytical quality than the high-throughput devices that are used in dedicated laboratories. POCT instruments are often operated by staff who have not been trained in laboratory medicine, and are hence prone to errors in the analytical phase. Additionally, preanalytical errors such as haemolysis rates are not routinely checked in POCT settings.<sup>245</sup>

The use of POCT reduces or avoids transportation time and paves the way for faster clinical action. This is particularly important for determining levels of metabolites such as glucose and lactate, as well as blood gas and electrolytes.<sup>246</sup> In the majority of hospitals POCT is used for specific parameters within the ED and ICU. High-quality patient care requires early diagnosis, which is achieved by eliminating pre- and postanalytical errors and delays. Blood testing is associated with prolonged length of stay.<sup>247</sup> Intralaboratory TATs for Standard Analyses usually range from 30–45 minutes, or 10–15 minutes for haematological analyses (no centrifugation required). When transportation times are added, the total TAT<sup>247</sup> from test request to result retrieval may exceed 60 minutes, compared to 10–25 minutes for POCT, depending on the parameter being tested for and the local setting.

Many studies on POCT report a reduced length of stay within the ED (although the majority focus on selected tests and limited patient populations).<sup>248–250</sup> Based on this outcome, POCT increases the satisfaction of emergency medicine physicians with the laboratory process. However<sup>251</sup>, others have also reported that a POCT strategy alone has not necessarily reduced LOS, or that it has only had an effect on certain groups of patients.<sup>252</sup> Some monocentric studies on POCT have demonstrated its diagnostic accuracy<sup>253 254</sup> in addition to process improvement.

The full benefit of POCT is obtained when it is implemented together with process redesign, as reported by Larsson.<sup>255–257</sup> When used properly, POCT can lead to a range of improvements in the quality and efficiency of care. (Larsson A, et al.).<sup>257</sup> With regard to turnaround times, it is important to acknowledge that POCT is only one of several options to reduce TATs. The choice of which action could reduce TAT most effectively depends on the specific local conditions of each hospital.

If the decision is made to implement POCT in the ED, it is important to bear in mind that many mandatory regulations apply with respect to quality control. As well as national regulations, there are international standards such as the ISO 15189:2022 guideline on POCT<sup>258</sup> which requires multidisciplinary consensus decisions on implementation, analytical quality and comparability, user education, clear responsibilities, documented traceback of all measurements, and adherence to commonly accepted quality standards, including daily internal and regular external quality control. Adhering to these

regulations is critical to ensure the quality of the analyses performed, which is even more important than reducing the TAT for patient diagnosis.

## Key question

What is the effect of POCT for the working process in the ED, using TAT as the main outcome?

<b>Population</b>	In adult ED patients with indication for a blood test.
<b>Intervention</b>	Implementation of POCT in the ED for blood sampling analysis, including biomarkers, and blood gasses.
<b>Comparison</b>	Blood analysis done in the central laboratory.
<b>Outcomes</b>	Effect on Turnaround time (TAT), rejected samples rate, professionals' satisfaction.

## Recommendation

We recommend POCT as one possibility to reduce the total TAT after interdisciplinary risk/benefit analysis under consideration of the below-mentioned circumstances.

Quality of the evidence	
Overall quality of evidence for the endpoint TAT	VERY LOW
Strength of the recommendation	
A weak recommendation in favour of the POC implementation, using TAT as outcome	2D GRADE

## Justification

Seven papers were appraised looking at two different outcomes: treatment time (TT, or total time from doctor contact to final disposition), and patient satisfaction.

Six papers were reviewed for TT. Goldstein's RCT<sup>259</sup> featured two branches; the control branch followed the standard workflow, with tests carried out at the onsite hospital laboratory following evaluation of the patient by medical staff. The enhanced workflow branch followed a pathway using POCT. The study concluded that there was a clear reduction in TT in the enhanced workflow for any combination of the tests performed. One substantial limitation was the inclusion of a change in the patient workflow in the enhanced branch, namely that any tests that were required prior to contact with the doctor. This can limit the application in many ED settings. Furthermore, the study only looked at a range of selected complaints (abdominal pain, dyspnoea, mental status alteration) limiting its application.

The other papers that were appraised were cohort design studies, including the following which focused on specific conditions, such as stroke, chest pain and trauma.

Bagnoux et al.<sup>260</sup> analysed the inclusion of creatinine in the POC panel (tests available), of stroke patients, using the time to CT as the outcome. Including creatinine in POCTs reduced the time to CT from 2.57 hours (95%CI 1.53 to 3.48) to 1.73 hours (95%CI 0.75 to 3.01). Han et al.<sup>261</sup> found that including the INR time in the POCT panel for non-haemorrhagic stroke patients was quick and reliable and played a pivotal role in expediting

thrombolysis. The door-to-IPA time was decreased from 46 minutes (IQR, 36.0 to 57.0) based on results from the central laboratory, to 23 minutes (IQR, 16.0 to 29.8) with the use of POCT for the INR calculation.

In patients with chest pain, Hight et al.<sup>262</sup> compared the measurement of troponin I using POCT, with troponin T tested via a central laboratory. The median time to results for the POC troponin and conventional assays were 11 minutes (IQR 10:00 to 15:30) and 40 minutes (IQR 31 to 30 & 52 to 30) respectively ( $p < 0.001$ ). As most POCT devices only measure non-hsTn,<sup>263</sup> the detection of biomarker dynamics takes longer, meaning that patients with intermediate troponin concentrations spend at least three hours in the ED. This can be shortened substantially when using high-sensitive (hsTn) testing carried out via a central laboratory.<sup>264</sup> In this specific circumstance, it should be noted that the preferred recommended method for the diagnosis of non-ST elevated myocardial infarction (NSTEMI) is the use of high-sensitive troponin (hsTn) assays.<sup>265</sup>

Spagnolello<sup>266</sup> compared laboratory (viscoelastic) coagulation testing and POCT coagulation testing (CCT) in trauma patients, study that includes a reduce group of patients. CCT was performed at admission as part of standard care, in addition to thromboelastometry viscoelastic coagulation testing using the ROTEM Sigma instrument. The median time from admission to CCT results. via POCT was 83 minutes (IQR 60–93), compared to 51 minutes(IQR 32–93);  $p = 0.0006$  for ROTEM A5 results. However It should be noted that the methods are not comparable in terms of diagnostic usefulness. While it is difficult to detect some coagulation disorders with the ROTEM test, other symptoms such as hyperfibrinolysis are not detectable by CCT. Therefore, viscoelastic methods have a clinical role in perioperative coagulation, as well as in trauma patients, but not preoperatively or as the sole method for coagulation disorder detection.<sup>267</sup> A combination of CCT and viscoelastic methods would seem to be optimal.

Finally, in undifferentiated patients visiting the ED in Helsinki, Kankaanpaa et al.<sup>256</sup> found that those in the POCT track had shorter TATs compared with standard care. The POCT track was faster both for patients that were discharged home and those who were admitted. In discharged patients blood test results were available 1:01 minutes faster (POCT results 00:06 (95% CI 0:05 to 0:07) versus lab-based results 1:07 (95% CI 1:01 to 1:13),  $p < 0.001$ ), while in admitted patients time to results was 1:39 min faster (0:06 (95% CI 0:04 to 0:07) versus 1:45(95% CI 1:33 to 1:57),  $p < 0.001$ ). However, ED LOS for the POCT track was only shorter in the group of patients who were discharged home (55 minutes faster in patients who didn't require imaging (4:57 (95% CI 3:59 to 6:17) vs. 5:52(95% CI 5:21 to 6:35),  $p = 0.012$ ) and 1 hour 22 minutes faster with imaging (5:48 (95% CI 5:26 to 6:18) vs. 7:10 (95% CI 6:47 to 8:26),  $p = 0.010$ ). A reduction in LOS was not seen among those patients who were admitted to hospital.

Although all the studies found a significantly shorter treatment time, reduced time to results, and reduced patient waiting time for POCTs in comparison to standard care (laboratory analysis), the quality of the evidence was classified as very low (D) due to risk of bias, limiting the strength of this recommendation.

Looking at the outcome 'users satisfaction', Goldstein's<sup>251</sup> study, which was a CT, compared the standard workflow with a workflow based on POCT using user opinion (doctors') as the determinant. In the POCT workflow model, the tests, including ECG and low radiation tests, were carried out before contact with the doctor. In this case the user's (i.e. the doctor's) opinion was clearly in favour of the POCT-based workflow. However, replicating the findings of the study would require a substantial change in ED workflow, as requesting tests before contact with a doctor can be a substantial limitation in many ED settings. This study was graded as moderate, and was limited by imprecision due to the small number of participants.



As a key message, POCT should be considered if process improvement is needed, but the implementation decision has to be based on patient benefits.

## Risk benefit

The drawbacks of POCT are lower analytical quality, less quality control and operation by inexperienced and less well-trained personnel.<sup>245</sup> The overall costs are higher, including the working time of ED physicians and nurses, which compounds the higher costs of a single test. The benefits of POCT have only been demonstrated in monocentric studies. The findings are not generalisable and are only applicable in settings where analytical process times cannot be reduced by other organisational actions (i.e. faster lab transport, specific laboratory SOPs for ED samples etc.).

Additionally, it is crucial to note that haemolysis, a major cause of biased laboratory test results, is not regularly examined in whole blood samples when performing POCTs, potentially increasing the risk of misinterpretation and incorrect medical action (e.g. potassium levels being overestimated). In a study evaluating 550 POCT potassium readings, the authors found that 22% of patients who were considered normokalemic were actually hypokalemic and 14% of patients who were hyperkalemic were actually normokalemic.<sup>268</sup> These results were supported by Duhalde et al., Nigro et al. and O'Hara et al.<sup>269-271</sup>, who found that 7.9%, 12% and 40% of POCT samples respectively had undetected haemolysis. The latter study also stated that 5 out of every 100 admissions had their patient care altered as a result of the biased potassium values.

Depending on local needs, POCT can improve the analytical process in the ED, and thus improve satisfaction levels among emergency physicians.

## Patient values

Patients whose condition and treatment depend on timely blood analysis (e.g. chest pain (troponin), SOB, stroke, massive transfusion need) are the group in which the benefit is more substantial.

## Differences of opinion among the WG

The decision to introduce POCT within the ED is a compromise between the need for short TATs, and the fact that POCT often offers less well-advanced and less well-controlled testing methods, performed by ED personnel who are not well trained to avoid common preanalytical errors. Finding practical yet high-quality solutions requires interdisciplinary collaboration between emergency physicians and laboratory specialists.

## Subgroup considerations that may be relevant

Patients admitted to the ED with chest pain, SOB, stroke or the need for massive transfusion have the most to gain from a reduction in TAT.

## Implementation considerations

Prior to the implementation of POCT, quality control for the total analytical process has to be considered to ensure that it follows the same rules as laboratory analysis in the central laboratory. POCT needs to be incorporated into a standardised quality-controlled analytical process which is comprehensive and involves all professions, particularly laboratory professionals, who must share responsibility for the analytical process, to ensure adherence to mandatory guidelines (e.g. ISO 15189:2022<sup>258</sup> guideline). Guidance on which factors should be considered prior to the implementation of POCT in the ED have been published elsewhere.<sup>272</sup>

An interdisciplinary and interprofessional committee should define the scope of the POCT, and be responsible for overseeing all aspects of a high-quality POCT programme.<sup>272</sup> This committee should also assess the workflow process and its implications on the workload of the various professions involved. A staff member from the ED who is responsible for continuous education, device maintenance, ordering the consumables and error handling, must be appointed.

The POCT programme has to meet mandatory quality standards such as ISO 15189:2022,<sup>243</sup> plus internal and external quality assurance standards. It must also include documentation of test results in the hospital information system, including all relevant information, such as date, time, user, patient, valid calibration and QC controls, and room temperature (if applicable). SOPs must be developed for the entire testing process, including reporting, with defined and documented processes for scenarios including failed QCs.

Continuous education of all personnel handling POCT devices is mandatory and needs to be properly documented.

Workflow processes in the ED must be reviewed with a focus on the workload of professionals.

The availability of appliances and consumables must be guaranteed.

A cost-benefit analysis needs to be carried out in order to establish the financial impact of POCT.

## **Research priorities or future research needs**

In most hospitals POCT is solely an adjunct to routine laboratory processes, and its effect on test duplication needs to be formally evaluated.

Making the choice between POCT and standard laboratory processing needs to be based on defined scientific criteria. The effect of POCT on the diagnostic and therapeutic strategy needs to be evaluated.

Finally, there is a lack of randomised multicentric studies that compare POCT with central laboratory testing with regard to clinical impact (LOS, mortality) and other outcome parameters.

## 16. Impact of monitoring preanalytical blood sampling quality indicators in management for ED blood samples.

### Background

EDs provide complex medical services, which aim to deliver timely and appropriate care to every patient seeking medical treatment, based on reliable clinical information.

The complexity of the current healthcare environment, combined with an increase in patient expectations, has increased the potential for medical errors, which contribute to more than a million injuries and between 44,000 and 98,000 deaths in hospitals annually.<sup>273 274</sup> These numbers make hospital-based errors the eighth leading cause of death in the United States, ahead of breast cancer, AIDS and motor vehicle accidents.<sup>275</sup> In addition, these errors have been shown to result in 2.4 million extra days of hospitalisation and a possible increase in hospital costs of \$17 billion.<sup>276 277</sup> Reducing these errors requires the concerted effort of a range of stakeholders, including healthcare organisations, product manufacturers, policy makers, physicians, and nurses.<sup>278 279</sup>

Laboratory testing provides essential information that is used by physicians in the majority of medical decision-making.<sup>280</sup> However, this critical component of healthcare is also a key source of errors which may affect patient safety.<sup>281</sup> Errors may occur in each phase of the testing process: preanalytical, analytical and postanalytical. The preanalytical phase is a complex process, encompassing steps that occur outside as well as inside the laboratory. Attempts to reduce errors should begin with a review of the sources of these errors. The most frequently encountered causes of preanalytical errors are haemolysis, incorrect patient identification, insufficient sample volume, and clotted specimens.<sup>282</sup> Each of these variables has the potential to adversely affect the quality of laboratory test results. Studies have estimated that 26% of these variables may result in unnecessary investigations or inappropriate treatment.<sup>281</sup>

Specimen rejection because of preanalytical errors also causes delays, ultimately leading to prolonged LOS at the ED. A prolonged diagnostic stage also delays therapeutic interventions, and leads to discomfort for the patient if additional venipunctures are required. There is also the potential for a missed or incorrect diagnosis to occur. This could be associated with considerable liabilities, placing an economic burden on the hospital, on the physician in charge as well as on laboratory budgets.<sup>283 284</sup>

The reliability of laboratory values obtained from testing depends on the quality of the TTP. The generation of any laboratory test result in this TTP involves nine consecutive steps: ordering, collection, identification, transportation, separation or preparation, analysis, reporting and action.<sup>285 286</sup> Emergency medicine is mainly responsible for the preanalytical phase and critically depends on the fastest possible return of the results, and thus on a short TAT. The TTP for emergency values involves several medical professions, and at least two different hospital departments (the ED and the laboratory) and is facilitated by appropriate hospital information technology.

Given the importance of a robust and comprehensive TTP for laboratory values, ED and laboratory staff need to be aware of the critical importance of quality assurance in the preanalytical and analytical phases of blood sample processing for patients in the ED. The preanalytical phase is particularly prone to quality deficits.<sup>6</sup>

Quality assurance systems must be established in order to detect and correct such deficits. A recent survey demonstrated that only 32% of clinical departments and 80% of laboratory departments staff in hospitals in Austria, Germany and Switzerland were aware of TAT as one of the most relevant quality parameters for emergency situations.<sup>287</sup>

Quality management depends on identification of quality indicators, and a subsequent quality improvement process (e.g. the PDCA cycle).<sup>19 288</sup> To deliver this, key performance indicators (KPIs) must be defined. Several quality parameters have been identified for the TTP.<sup>19</sup> Data linked to these parameters should be automatically generated and retrievable from an IT system in order to measure the effects of a quality improvement programme.<sup>289</sup>

The present guideline evaluated the literature relating to quality management during the preanalytical phase. Specifically, it evaluated whether the monitoring of KPIs can help to improve the quality of the preanalytical process, and which KPIs have proved valuable in the detection of sampling problems.

## Key question

Impact of monitoring preanalytical blood sampling quality indicators in management for ED blood samples.

<b>Population</b>	In adult ED patients with indication for a blood test.
<b>Intervention</b>	Systematic implementation of quality indicators such as sampling problems detection and TAT as part of a quality assurance program.
<b>Comparison</b>	No quality assurance program.
<b>Outcomes</b>	Reduction of rejected number of samples due to haemolysis, underfilling and other causes for sample rejection as well as effect on TAT

## Recommendation

We recommend the selection and implementation of quality indicators/key performance indicators to support the ED and laboratory teams in improving the preanalytical, analytical and postanalytical process of ED blood samples.

Suitable quality indicators are the contamination rate of blood cultures, duplicate chemistry tests, misidentification errors and various other rejection reasons such as haemolysis, underfilling, clotting and others. We recommend including TAT as a KPI for ED laboratory processes

Quality of the evidence	
Level of evidence	VERY LOW
Strength of the recommendation	
Based on a very low quality of the evidence the group considers this recommendation as a Good Practice.	

## Justification

Four papers reported the results of studies on the effects of quality improvement programmes which were explicitly focused on laboratory tests ordered by an ED. The studies were monocentric and observational and differed in the selection of quality indicators.

The studies were appraised for the following quality indicators:

- Duplicate chemistry tests<sup>290</sup>
- Contamination rate of blood cultures<sup>289</sup>
- Various reasons for sample rejection (haemolysis, underfilling, clotting)<sup>50 291</sup>

Venkatesh<sup>290</sup> and Al-Hamad<sup>292</sup> reported that quality improvement programmes succeeded in reducing the contamination rate of blood cultures and the number of duplicates in chemistry tests. Rooper et al.<sup>50</sup> defined possible quality indicators with relevance to ED blood samples, while Gupta et al.<sup>291</sup> reported on the positive effect of a quality improvement initiative. In this study, however, several steps were introduced to improve quality, but it was not possible to identify which step was the most effective.

Every study reported a positive effect based on the introduction of the quality improvement programme, although there was a risk of bias because no confounding factor adjustment was performed. Additionally, some changes which were implemented in the quality improvement programmes described could not easily be introduced in all settings. For example, in the study by Gupta et al.,<sup>291</sup> blood sampling was performed by specialised phlebotomists. This specific quality measure could probably not be implemented routinely in every ED.

Although laboratory value TAT is of critical importance within the ED – and it is known that the preanalytical phase, which includes transport to the laboratory, is particularly prone to negatively affecting the TAT – no specific report on quality improvement initiatives to improve the TAT was found in the literature.

## Risk benefit

### Benefit

Implementing ED-laboratory process quality indicators and integrating these into a quality improvement programme has been shown to improve the preanalytical and analytical process, thereby significantly improving the validity of laboratory results and reducing rejection rates, overall TAT and LOS within the ED.

### Risk

The definition of KPIs and the establishment of a quality improvement programme requires the commitment of all stakeholders (ED nurses and physicians, laboratory assistants and physicians, as well as the ICT team. Quality management requires investment in time, money and education.<sup>243</sup> Without professional guidance and specifically allocated financial resources, active quality management is likely to fail.

## Implementation considerations

Implementing ED-laboratory process quality indicators can improve the preanalytical and analytical process, with significant benefits and only minor undesirable effects. A multiprofessional group from the ED and the laboratory should be constituted to select appropriate quality indicators, including their format,<sup>293 294</sup> as well as to review the quality management process. This should include initiating steps to improve the quality of samples and reduce the number of rejected samples. Regular educational sessions are important, and systematic interventions based on root cause analysis could be useful in order to solve issues relating to high specimen rejection rates. An electronic system should be put in place to ensure adequate KPI documentation.

## Differences of opinion among the WG

There were no conflicting opinions among members of the working group.

## **Suggestions for monitoring and evaluation**

The inclusion of QIs orientated to the PPP on the ED dashboard shared with the laboratory must include the following as a minimum: TAT, sample rejection rates, haemolysis rates, and false positive blood culture rates.

## **Research priorities or future research needs**

Identification of robust KPIs based on solid endpoints of the ED process.

Identification of the interventions that are most effective in reducing the rejection rate of blood specimens.

An evaluation of the effect of implementing QI programmes on the TTP in EDs, with a particular focus on TAT with regard to relevant KPIs and defined clinical outcome parameters.

# 4. References

1. Garcia-Castrillo Riesgo L, Lauwaert D, Cadamuro J, et al. The preanalytical process in the emergency department, a European survey. *Clin Chem Lab Med* 2023;61(1):93-103. doi: 10.1515/cclm-2022-0581 [published Online First: 2022/10/28]
2. Rohr UP, Binder C, Dieterle T, et al. The Value of In Vitro Diagnostic Testing in Medical Practice: A Status Report. *PLoS One* 2016;11(3):e0149856. doi: 10.1371/journal.pone.0149856 [published Online First: 2016/03/05]
3. What is Emergency Medicine: Eusem; 2022 [Available from: <https://eusem.org/about-us/emergency-medicine/what-is-em> accessed September 2022.
4. Emergency nursing scope of practice. Emergency Nurses Association (ENA). *J Emerg Nurs* 1989;15(4):361-4. [published Online First: 1989/07/01]
5. Tjelmeland IBM, Masterson S, Herlitz J, et al. Description of Emergency Medical Services, treatment of cardiac arrest patients and cardiac arrest registries in Europe. *Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine* 2020;28(1):103. doi: 10.1186/s13049-020-00798-7
6. Carraro P, Plebani M. Errors in a stat laboratory: types and frequencies 10 years later. *Clinical chemistry* 2007;53(7):1338-42. doi: 10.1373/clinchem.2007.088344 [published Online First: 2007/05/26]
7. Howanitz JH, Howanitz PJ. Laboratory results. Timeliness as a quality attribute and strategy. *Am J Clin Pathol* 2001;116(3):311-5. doi: 10.1309/h0dy-6vtw-nb36-u3l6 [published Online First: 2001/09/14]
8. Herlitz J, Wireklintsundström B, Bång A, et al. Early identification and delay to treatment in myocardial infarction and stroke: differences and similarities. *Scand J Trauma Resusc Emerg Med* 2010;18:48. doi: 10.1186/1757-7241-18-48 [published Online First: 2010/09/08]
9. Mitra B, Bade-Boon J, Fitzgerald MC, et al. Timely completion of multiple life-saving interventions for traumatic haemorrhagic shock: a retrospective cohort study. *Burns & trauma* 2019;7:22. doi: 10.1186/s41038-019-0160-5 [published Online First: 2019/07/31]
10. Bisarya R, Song X, Salle J, et al. Antibiotic Timing and Progression to Septic Shock Among Patients in the ED With Suspected Infection. *Chest* 2022;161(1):112-20. doi: 10.1016/j.chest.2021.06.029 [published Online First: 2021/06/30]
11. Ngo A, Gandhi P, Miller WG. Frequency that Laboratory Tests Influence Medical Decisions. *J Appl Lab Med* 2017;1(4):410-14. doi: 10.1373/jalm.2016.021634 [published Online First: 2017/01/01]
12. Hussain F, Cooper A, Carson-Stevens A, et al. Diagnostic error in the emergency department: learning from national patient safety incident report analysis. *BMC Emerg Med* 2019;19(1):77. doi: 10.1186/s12873-019-0289-3 [published Online First: 2019/12/06]
13. Baker WE, Solano JJ. Quality Assurance in the Emergency Department. *Emergency medicine clinics of North America* 2020;38(3):663-80. doi: 10.1016/j.emc.2020.05.002 [published Online First: 2020/07/04]
14. Levy R, Goldstein B, Trott A. Approach to quality assurance in an emergency department: A one-year review. *Annals of Emergency Medicine* 1984;13(3):166-69. doi: [https://doi.org/10.1016/S0196-0644\(84\)80606-X](https://doi.org/10.1016/S0196-0644(84)80606-X)
15. Cadamuro J, Baird G, Baumann G, et al. Preanalytical quality improvement - an interdisciplinary journey, on behalf of the European Federation for Clinical Chemistry and Laboratory Medicine (EFLM) Working Group for Preanalytical Phase (WG-PRE). *Clin Chem Lab Med* 2022 doi: 10.1515/cclm-2022-0117 [published Online First: 2022/03/09]
16. Johnston JE, Oconor O. Needlestick injuries and infectious diseases in emergency medicine. *Critical Care* 2008;12(2):P348. doi: 10.1186/cc6569
17. Woolf SH, Grol R, Hutchinson A, et al. Clinical guidelines: potential benefits, limitations, and harms of clinical guidelines. *BMJ (Clinical research ed)* 1999;318(7182):527-30. doi: 10.1136/bmj.318.7182.527 [published Online First: 1999/02/19]
18. WHO. WHO guidelines on drawing blood: best practices in phlebotomy. [https://www.euro.who.int/\\_data/assets/pdf\\_file/0005/268790/WHO-guidelines-on-drawing-blood-best-practices-in-phlebotomy-Eng.pdf2010](https://www.euro.who.int/_data/assets/pdf_file/0005/268790/WHO-guidelines-on-drawing-blood-best-practices-in-phlebotomy-Eng.pdf2010) [accessed 10/07/2022 2022.
19. Cadamuro J, Lippi G, von Meyer A, et al. European survey on preanalytical sample handling - Part 2: Practices of European laboratories on monitoring and processing haemolytic, icteric and lipemic samples. On behalf of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Working Group for the Preanalytical Phase (WG-PRE). *Biochem Med (Zagreb)* 2019;29(2):020705. doi: 10.11613/bm.2019.020705 [published Online First: 2019/06/22]
20. Simundic A-M, Bölenius K, Cadamuro J, et al. Joint EFLM-COLABIOCLI Recommendation for venous blood sampling: v 1.1, June 2018 %J Clinical Chemistry and Laboratory Medicine (CCLM). 2018;56(12):2015-38. doi: doi:10.1515/cclm-2018-0602
21. Simundic AM, Cornes M, Grankvist K, et al. Survey of national guidelines, education and training on phlebotomy in 28 European countries: an original report by the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) working group for the preanalytical phase (WG-PA). *Clin Chem Lab Med* 2013;51(8):1585-93. doi: 10.1515/cclm-2013-0283 [published Online First: 2013/06/05]
22. Lippi G, Banfi G, Church S, et al. Preanalytical quality improvement. In pursuit of harmony, on behalf of European Federation for Clinical Chemistry and Laboratory Medicine (EFLM) Working group for Preanalytical Phase (WG-PRE). *Clin Chem Lab Med* 2015;53(3):357-70. doi: 10.1515/cclm-2014-1051 [published Online First: 2014/12/10]
23. Simundic AM, Baird G, Cadamuro J, et al. Managing hemolyzed samples in clinical laboratories. *Crit Rev Clin Lab Sci* 2020;57(1):1-21. doi: 10.1080/10408363.2019.1664391 [published Online First: 2019/10/12]
24. Guyatt GH, Oxman AD, Kunz R, et al. Going from evidence to recommendations. *BMJ (Clinical research ed)* 2008;336(7652):1049-51. doi: 10.1136/bmj.39493.646875.AE [published Online First: 2008/05/10]
25. Schünemann HJ, Fretheim A, Oxman AD. Improving the use of research evidence in guideline development: 10. Integrating values and consumer involvement. *Health research policy and systems* 2006;4:22. doi: 10.1186/1478-4505-4-22 [published Online First: 2006/12/07]

26. Guyatt GH, Oxman AD, Vist GE, et al. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. *BMJ (Clinical research ed)* 2008;336(7650):924-6. doi: 10.1136/bmj.39489.470347.AD [published Online First: 2008/04/26]
27. Schardt C, Adams MB, Owens T, et al. Utilization of the PICO framework to improve searching PubMed for clinical questions. *BMC Medical Informatics and Decision Making* 2007;7(1):16. doi: 10.1186/1472-6947-7-16
28. Page MJ, Moher D, Bossuyt PM, et al. PRISMA 2020 explanation and elaboration: updated guidance and exemplars for reporting systematic reviews. *BMJ (Clinical research ed)* 2021;372:n160. doi: 10.1136/bmj.n160 [published Online First: 2021/03/31]
29. Guyatt G, Oxman AD, Akl EA, et al. GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. *Journal of clinical epidemiology* 2011;64(4):383-94. doi: 10.1016/j.jclinepi.2010.04.026 [published Online First: 2011/01/05]
30. GA Wells BS, D O'Connell, J Peterson, V Welch, M Losos, P Tugwell,. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses: Ottawa Hospital Research Institute; 2021 [Available from: [https://www.ohri.ca/programs/clinical\\_epidemiology/oxford.asp](https://www.ohri.ca/programs/clinical_epidemiology/oxford.asp) accessed may/2022 2022.
31. Higgins JPT, Altman DG, Gøtzsche PC, et al. The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. 2011;343:d5928. doi: 10.1136/bmj.d5928 %J BMJ
32. Guyatt G, Akl EA, Oxman A, et al. Synthesis, grading, and presentation of evidence in guidelines: article 7 in Integrating and coordinating efforts in COPD guideline development. An official ATS/ERS workshop report. *Proceedings of the American Thoracic Society* 2012;9(5):256-61. doi: 10.1513/pats.201208-060ST [published Online First: 2012/12/21]
33. Moberg J, Oxman AD, Rosenbaum S, et al. The GRADE Evidence to Decision (EtD) framework for health system and public health decisions. *Health research policy and systems* 2018;16(1):45. doi: 10.1186/s12961-018-0320-2 [published Online First: 2018/05/31]
34. Lindner HS, Wayne. Martin, Marian; Heidt, Mickey; McMahon, Carrie; Romans, Jennifer The impact of prehospital blood collection on time to laboratory test results and emergency department length of stay. *Advanced Emergency Nursing Journal* 2010;32,(4):5.
35. Lee-Lewandrowski E, Corboy D, Lewandrowski K, et al. Implementation of a point-of-care satellite laboratory in the emergency department of an academic medical center. Impact on test turnaround time and patient emergency department length of stay. *Archives of pathology & laboratory medicine* 2003;127(4):456-60. doi: 10.5858/2003-127-0456-ioapsl [published Online First: 2003/04/10]
36. DuCharme B, Macci Bires A, Montanye E, et al. Effect of Prehospital Blood Draws on Length of Stay for Chest Pain Patients in the Emergency Department: A Pilot Study. *Crit Care Nurs Q* 2019;42(2):208-14. doi: 10.1097/cnq.0000000000000257
37. Javidan AP, Hansen K, Higginson I, et al. The International Federation for Emergency Medicine report on emergency department crowding and access block: A brief summary. *Emergency medicine journal; EMJ* 2021;38(3):245-46. doi: 10.1136/emered-2020-210716 [published Online First: 2021/01/15]
38. McKenna P, Heslin SM, Viccellio P, et al. Emergency department and hospital crowding: causes, consequences, and cures. *Clinical and experimental emergency medicine* 2019;6(3):189-95. doi: 10.15441/ceem.18.022 [published Online First: 2019/07/13]
39. Morley C, Unwin M, Peterson GM, et al. Emergency department crowding: A systematic review of causes, consequences and solutions. *PLoS One* 2018;13(8):e0203316. doi: 10.1371/journal.pone.0203316 [published Online First: 2018/08/31]
40. Higginson I, Boyle A. What should we do about crowding in emergency departments? *British journal of hospital medicine (London, England; 2005)* 2018;79(9):500-03. doi: 10.12968/hmed.2018.79.9.500 [published Online First: 2018/09/07]
41. Harrison G, Speroni KG, Dugan L, et al. A comparison of the quality of blood specimens drawn in the field by EMS versus specimens obtained in the emergency department. *J Emerg Nurs* 2010;36(1):16-20. doi: 10.1016/j.jen.2008.11.001 [published Online First: 2010/01/30]
42. Prottengeier J, Jess N, Harig F, et al. Can we rely on out-of-hospital blood samples? A prospective interventional study on the pre-analytical stability of blood samples under prehospital emergency medicine conditions. *Scand J Trauma Resusc Emerg Med* 2017;25(1):24. doi: 10.1186/s13049-017-0371-3 [published Online First: 2017/03/06]
43. Mattila OS, Harve H, Pihlasviita S, et al. Ultra-acute diagnostics for stroke: Large-scale implementation of prehospital biomarker sampling. *Acta neurologica Scandinavica* 2017;136(1):17-23. doi: 10.1111/ane.12687 [published Online First: 2016/09/20]
44. Curtis K, Ellwood J, Walker A, et al. Implementation evaluation of prehospital blood collection in regional Australia: a mixed methods study. *Australasian emergency care* 2021;24(4):255-63. doi: 10.1016/j.aucc.2020.08.007 [published Online First: 2020/09/29]
45. Stopyra JP, Snavelly AC, Ashburn NP, et al. EMS blood collection from patients with acute chest pain reduces emergency department length of stay. *Am J Emerg Med* 2021;47:248-52. doi: 10.1016/j.ajem.2021.04.073 [published Online First: 2021/05/09]
46. Gyldenholm T, Stengaard C, Sørensen JT, et al. Haemolysis in prehospital blood samples. *Scand J Clin Lab Invest* 2021;81(6):508-10. doi: 10.1080/00365513.2021.1941234 [published Online First: 2021/06/30]
47. Hwang U, Baumlin K, Berman J, et al. Emergency department patient volume and troponin laboratory turnaround time. *Acad Emerg Med* 2010;17(5):501-7. doi: 10.1111/j.1553-2712.2010.00738.x [published Online First: 2010/06/12]
48. van der Linden MCC, van Ufford H, van der Linden NN. The impact of a multimodal intervention on emergency department crowding and patient flow. *Int J Emerg Med* 2019;12(1):21. doi: 10.1186/s12245-019-0238-7 [published Online First: 2019/08/29]
49. O'Neill E, Richardson-Weber L, McCormack G, et al. Strict Adherence to a Blood Bank Specimen Labeling Policy by All Clinical Laboratories Significantly Reduces the Incidence of "Wrong Blood in Tube". *American journal of clinical pathology* 2009;132:164-8; quiz 306. doi: 10.1309/AJCPOJA2JRVX0IWC
50. Rooper L, Carter J, Hargrove J, et al. Targeting Rejection: Analysis of Specimen Acceptability and Rejection, and Framework for Identifying Interventions in a Single Tertiary Healthcare Facility. *Journal of clinical laboratory analysis* 2017;31(3) doi: 10.1002/jcla.22060 [published Online First: 2016/09/16]
51. O'Neill KA, Shinn D, Starr KT, et al. Patient misidentification in a pediatric emergency department: patient safety and legal perspectives. *Pediatr Emerg Care* 2004;20(7):487-92. doi: 10.1097/01.pec.0000136895.99271.86 [published Online First: 2004/07/03]
52. Green SF. The cost of poor blood specimen quality and errors in preanalytical processes. *Clin Biochem* 2013;46(13-14):1175-9. doi: 10.1016/j.clinbiochem.2013.06.001 [published Online First: 2013/06/19]



53. Nikolac N, Supak-Smolčić V, Simundić AM, et al. Croatian Society of Medical Biochemistry and Laboratory Medicine: national recommendations for venous blood sampling. *Biochem Med (Zagreb)* 2013;23(3):242-54. doi: 10.11613/bm.2013.031 [published Online First: 2013/11/26]
54. Bolton-Maggs PH, Wood EM, Wiersum-Osselton JC. Wrong blood in tube - potential for serious outcomes: can it be prevented? *British journal of haematology* 2015;168(1):3-13. doi: 10.1111/bjh.13137 [published Online First: 2014/10/07]
55. Karcher DS, Lehman CM. Clinical consequences of specimen rejection: a College of American Pathologists Q-Probes analysis of 78 clinical laboratories. *Archives of pathology & laboratory medicine* 2014;138(8):1003-8. doi: 10.5858/arpa.2013-0331-CP [published Online First: 2014/07/31]
56. Brown JE, Smith N, Sherfy BR. Decreasing mislabeled laboratory specimens using barcode technology and bedside printers. *Journal of nursing care quality* 2011;26(1):13-21. doi: 10.1097/NCQ.0b013e3181e4e6dd [published Online First: 2010/06/01]
57. Morrison AP, Tanasijevic MJ, Goonan EM, et al. Reduction in specimen labeling errors after implementation of a positive patient identification system in phlebotomy. *Am J Clin Pathol* 2010;133(6):870-7. doi: 10.1309/ajcpc95yymsslrcx [published Online First: 2010/05/18]
58. Valenstein PN, Sirota RL. Identification errors in pathology and laboratory medicine. *Clinics in laboratory medicine* 2004;24(4):979-96, vii. doi: 10.1016/j.cll.2004.05.013 [published Online First: 2004/11/24]
59. Wallin O, Söderberg J, Van Guelpen B, et al. Preanalytical venous blood sampling practices demand improvement--a survey of test-request management, test-tube labelling and information search procedures. *Clinica chimica acta; international journal of clinical chemistry* 2008;391(1-2):91-97. doi: 10.1016/j.cca.2008.02.016
60. Söderberg J, Brulin C, Grankvist K, et al. Preanalytical errors in primary healthcare: a questionnaire study of information search procedures, test request management and test tube labelling. *Clin Chem Lab Med* 2009;47(2):195-201. doi: 10.1515/cclm.2009.048 [published Online First: 2009/02/05]
61. Cornes MP, Church S, van Dongen-Lases E, et al. The role of European Federation of Clinical Chemistry and Laboratory Medicine Working Group for Preanalytical Phase in standardization and harmonization of the preanalytical phase in Europe. *Annals of clinical biochemistry* 2016;53(Pt 5):539-47. doi: 10.1177/0004563216643969 [published Online First: 2016/05/04]
62. Ernst DJ, Fritsma GA, McGlasson DLJAOB. Labeling tubes before collection threatens patient safety. *2018* 2018;3(2)
63. S M. Woodcock. Accuracy in Patient and Sample Identification---Approved Guideline (GP33A). Wayne: Clinical and Laboratory Standards Institute, 2010. 2010.
64. Primary sample collection facilities and medical laboratories—patient safety and quality of care—requirements for collecting, transporting, and storing samples. Z316.7-12. Mississauga:: CSA Group, 2012.
65. Lima-Oliveira G, Lippi G, Salvagno GL, et al. Phlebotomist Labelling Primary Blood Tubes for Clinical Laboratory Tests: An Important Step to Medical Diagnostics. *2014*;3:1-2.
66. Simundic AM, Bölenius K, Cadamuro J, et al. Joint EFLM-COLABIOCLI Recommendation for venous blood sampling. *Clin Chem Lab Med* 2018;56(12):2015-38. doi: 10.1515/cclm-2018-0602 [published Online First: 2018/07/14]
67. Snyderman LK, Harubin B, Kumar S, et al. Voluntary Electronic Reporting of Laboratory Errors: An Analysis of 37 532 Laboratory Event Reports From 30 Health Care Organizations. *2012*;27(2):147-53. doi: 10.1177/1062860611413567
68. M. BLHGM. Reducing specimen and medication error with handheld technology.: Healthcare information and Management society; 2001 [Available from: [https://learn.barcoding.com/hs-fs/hub/73917/file-259079263-pdf/Benefiting\\_From\\_Bedside\\_Specimen\\_Labeling.pdf](https://learn.barcoding.com/hs-fs/hub/73917/file-259079263-pdf/Benefiting_From_Bedside_Specimen_Labeling.pdf) accessed May 2022.
69. Simundic AM, Cornes M, Grankvist K, et al. Standardization of collection requirements for fasting samples: for the Working Group on Preanalytical Phase (WG-PA) of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM). *Clinica chimica acta; international journal of clinical chemistry* 2014;432:33-7. doi: 10.1016/j.cca.2013.11.008 [published Online First: 2013/11/26]
70. Simundic AM, Filipi P, Vrtaric A, et al. Patient's knowledge and awareness about the effect of the over-the-counter (OTC) drugs and dietary supplements on laboratory test results: a survey in 18 European countries. *Clin Chem Lab Med* 2018;57(2):183-94. doi: 10.1515/cclm-2018-0579 [published Online First: 2018/07/29]
71. Lippi G, Salvagno GL, Lima-Oliveira G, et al. Postural change during venous blood collection is a major source of bias in clinical chemistry testing. *Clinica chimica acta; international journal of clinical chemistry* 2015;440:164-8. doi: 10.1016/j.cca.2014.11.024 [published Online First: 2014/12/02]
72. Lippi G, Salvagno GL, Lima-Oliveira G, et al. Influence of posture on routine hemostasis testing. *Blood coagulation & fibrinolysis; an international journal in haemostasis and thrombosis* 2015;26(6):716-9. doi: 10.1097/mbc.0000000000000326 [published Online First: 2015/06/18]
73. Lima-Oliveira G, Guidi GC, Salvagno GL, et al. Patient posture for blood collection by venipuncture: recall for standardization after 28 years. *Revista brasileira de hematologia e hemoterapia* 2017;39(2):127-32. doi: 10.1016/j.bjhh.2017.01.004 [published Online First: 2017/06/05]
74. Plumelle D, Lombard E, Nicolay A, et al. Influence of diet and sample collection time on 77 laboratory tests on healthy adults. *Clin Biochem* 2014;47(1-2):31-7. doi: 10.1016/j.clinbiochem.2013.11.002 [published Online First: 2013/11/19]
75. Lis K. Influence of diet on the results of laboratory tests. *2013*;29(4):349-54. doi: 10.5114/ms.2013.39987
76. Nordestgaard BG, Langsted A, Mora S, et al. Fasting is not routinely required for determination of a lipid profile: clinical and laboratory implications including flagging at desirable concentration cut-points—a joint consensus statement from the European Atherosclerosis Society and European Federation of Clinical Chemistry and Laboratory Medicine. *European heart journal* 2016;37(25):1944-58. doi: 10.1093/eurheartj/ehw152 [published Online First: 2016/04/29]
77. Devaraj S, Cao J, Roper SM. To Fast or Not to Fast?: Comments on the Consensus Statement From the European Atherosclerosis Society/ European Federation of Clinical Chemistry and Laboratory Medicine. *Archives of pathology & laboratory medicine* 2017;141(4):487-89. doi: 10.5858/arpa.2016-0309-ED [published Online First: 2017/03/30]

78. Hepburn S, Jankute M, Cornes MP, et al. Survey of patient perception of pre-analytical requirements for blood testing in the UK and Rol. *Annals of clinical biochemistry* 2021;58(2):132-40. doi: 10.1177/0004563220982325 [published Online First: 2020/12/05]
79. Mansi KMS. Study the Effects of Ramadan Fasting on the Serum Glucose and Lipid Profile among Healthy Jordanian Students. *American Journal of Applied Sciences* 2007;4(8) doi: 10.3844/ajassp.2007.565.569
80. Ramadan J. Does fasting during Ramadan alter body composition, blood constituents and physical performance? *Medical principles and practice; international journal of the Kuwait University, Health Science Centre* 2002;11 Suppl 2:41-6. doi: 10.1159/000066413 [published Online First: 2002/11/22]
81. Simundic A-M, Cornes M, Grankvist K, et al. Survey of national guidelines, education and training on phlebotomy in 28 European countries: An original report by the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) working group for the preanalytical phase (WG-PA). *Clinical chemistry and laboratory medicine; CCLM/FESCC* 2013;51:1-9. doi: 10.1515/cclm-2013-0283
82. Simundic A-M. Who is Doing Phlebotomy in Europe? In: Walter GG, Sheshadri N, eds. *Pre-Examination Procedures in Laboratory Diagnostics: Preanalytical Aspects and their Impact on the Quality of Medical Laboratory Results: De Gruyter* 2015:90-94.
83. Burchill CN, Seballos SS, Reineks EZ, et al. Emergency Nurses' Knowledge, Attitudes, and Practices Related to Blood Sample Hemolysis Prevention: An Exploratory Descriptive Study. *J Emerg Nurs* 2021;47(4):590-98.e3. doi: 10.1016/j.jen.2020.12.015 [published Online First: 2021/03/02]
84. Liang X, Gao W, Xu J, et al. Triage Nurse-Activated Emergency Evaluation Reduced Door-to-Needle Time in Acute Ischemic Stroke Patients Treated with Intravenous Thrombolysis. *Evidence-based Complementary and Alternative Medicine* 2022;2022:9199856. doi: <https://dx.doi.org/10.1155/2022/9199856>
85. De Maeseneer J. TASK SHIFTING AND HEALTH SYSTEM DESIGN, Report of the Expert Panel on effective ways of investing in Health (EXPH). In: Directorate B: Health Systems mpai, ed. Luxembourg: Publications Office of the European Union, 2019: European Commission, 2019.
86. McCaughey EJ, Vecellio E, Lake R, et al. Key factors influencing the incidence of hemolysis: A critical appraisal of current evidence. *Critical Reviews in Clinical Laboratory Sciences* 2017;54(1):59-72. doi: <http://dx.doi.org/10.1080/10408363.2016.1250247>
87. Saleem S, Mani V, Chadwick MA, et al. A prospective study of causes of haemolysis during venepuncture: tourniquet time should be kept to a minimum. *Annals of clinical biochemistry* 2009;46(Pt 3):244-6. doi: 10.1258/acb.2009.008228 [published Online First: 2009/04/25]
88. Davidson DF. A survey of some pre-analytical errors identified from the Biochemistry Department of a Scottish hospital. *Scottish medical journal* 2014;59(2):91-4. doi: 10.1177/0036933014529056 [published Online First: 2014/03/20]
89. Ong ME, Chan YH, Lim CS. Observational study to determine factors associated with blood sample haemolysis in the emergency department. *Annals of the Academy of Medicine, Singapore* 2008;37(9):745-8. [published Online First: 2008/11/08]
90. Dugan L, Leech L, Speroni KG, et al. Factors affecting hemolysis rates in blood samples drawn from newly placed IV sites in the emergency department. *J Emerg Nurs* 2005;31(4):338-45. doi: 10.1016/j.jen.2005.05.004 [published Online First: 2005/08/30]
91. Cadamuro J, von Meyer A, Wiedemann H, et al. Hemolysis rates in blood samples: differences between blood collected by clinicians and nurses and the effect of phlebotomy training. *Clin Chem Lab Med* 2016;54(12):1987-92. doi: 10.1515/cclm-2016-0175 [published Online First: 2016/11/02]
92. Davis EM, Feinsmith S, Amick AE, et al. Difficult intravenous access in the emergency department: Performance and impact of ultrasound-guided IV insertion performed by nurses. *Am J Emerg Med* 2021;46:539-44. doi: 10.1016/j.ajem.2020.11.013 [published Online First: 2020/11/17]
93. Zaboli A, Pfeifer N, Solazzo P, et al. Blood sampling during nurse triage reduces patient length of stay in the emergency department: A propensity score-weighted, population-based study. *International emergency nursing* 2020;49:100826. doi: 10.1016/j.ienj.2019.100826 [published Online First: 2020/02/13]
94. Stowell JR, Pugsley P, Jordan H, et al. Impact of Emergency Department Phlebotomists on Left-Before-Treatment-Completion Rates. *The western journal of emergency medicine* 2019;20(4):681-87. doi: 10.5811/westjem.2019.5.41736 [published Online First: 2019/07/19]
95. Bastemeijer CM, Voogt L, van Ewijk JP, et al. What do patient values and preferences mean? A taxonomy based on a systematic review of qualitative papers. *Patient Education and Counseling* 2017;100(5):871-81. doi: <https://doi.org/10.1016/j.pec.2016.12.019>
96. Bahl A, Johnson S, Alsbrooks K, et al. Defining difficult intravenous access (DIVA): A systematic review. *The journal of vascular access* 2021;11297298211059648. doi: 10.1177/11297298211059648 [published Online First: 2021/11/19]
97. Whalen M, Maliszewski B, Baptiste DL. Establishing a Dedicated Difficult Vascular Access Team in the Emergency Department: A Needs Assessment. *Journal of infusion nursing; the official publication of the Infusion Nurses Society* 2017;40(3):149-54. doi: 10.1097/nan.0000000000000218 [published Online First: 2017/04/19]
98. Simundic A-M, Church S, Cornes M, et al. Compliance of blood sampling procedures with the CLSI H3-A6 guidelines: An observational study by the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) working group for the preanalytical phase (WG-PRE). *Clinical Chemistry and Laboratory Medicine* 2014;53 doi: 10.1515/cclm-2014-1053
99. Gupta P, Thomas M, Sbetan N, et al. A Quality Improvement Initiative to Reduce Rejected Laboratory Samples and Enhance Specimen Acceptability. *The Joint Commission Journal on Quality and Patient Safety* 2021;47(8):519-25. doi: <https://doi.org/10.1016/j.jcjq.2021.04.005>
100. Simundic A-M, Bölenius K, Cadamuro J, et al. EFLM Paper Joint EFLM-COLABIOCLI Recommendation for venous blood sampling. *Clinical Chemistry and Laboratory Medicine* 2018;56 doi: 10.1515/cclm-2018-0602
101. Van Steirteghem AC, Young DS. Povidone-iodine ("Betadine") disinfectant as a source of error. *Clinical chemistry* 1977;23(8):1512. [published Online First: 1977/08/01]
102. Lachapelle J-M, Castel O, Casado A, et al. Antiseptics in the era of bacterial resistance: A focus on povidone iodine. *Clinical Practice* 2013;10:579-92. doi: 10.2217/cpr.13.50
103. Maiwald M, Chan ES. The forgotten role of alcohol: a systematic review and meta-analysis of the clinical efficacy and perceived role of chlorhexidine in skin antiseptics. *PLoS One* 2012;7(9):e44277. doi: 10.1371/journal.pone.0044277 [published Online First: 2012/09/18]

104. Bool M, Barton MJ, Zimmerman PA. Blood culture contamination in the emergency department: An integrative review of strategies to prevent blood culture contamination. *Australasian emergency care* 2020;23(3):157-65. doi: 10.1016/j.auec.2020.02.004 [published Online First: 2020/04/08]
105. Dempsey C, Skoglund E, Muldrew KL, et al. Economic health care costs of blood culture contamination: A systematic review. *American Journal of Infection Control* 2019;47(8):963-67. doi: <https://doi.org/10.1016/j.ajic.2018.12.020>
106. Moeller D. Eliminating Blood Culture False Positives: Harnessing the Power of Nursing Shared Governance. *J Emerg Nurs* 2017;43(2):126-32. doi: 10.1016/j.jen.2016.07.001 [published Online First: 2017/03/10]
107. Mimoz O, Karim A, Mercat A, et al. Chlorhexidine compared with povidone-iodine as skin preparation before blood culture. A randomized, controlled trial. *Annals of internal medicine* 1999;131(11):834-7. doi: 10.7326/0003-4819-131-11-199912070-00006 [published Online First: 1999/12/28]
108. Marlowe L, Mistry RD, Coffin S, et al. Blood culture contamination rates after skin antisepsis with chlorhexidine gluconate versus povidone-iodine in a pediatric emergency department. *Infect Control Hosp Epidemiol* 2010;31(2):171-6. doi: 10.1086/650201 [published Online First: 2009/12/23]
109. Maiwald M, Widmer AF, Rotter ML. Chlorhexidine is not the main active ingredient in skin antiseptics that reduce blood culture contamination rates. *Infect Control Hosp Epidemiol* 2010;31(10):1095-6; author reply 96-7. doi: 10.1086/656561 [published Online First: 2010/09/04]
110. Ramirez Galleymore P, Gordón Sahuquillo M. Antisepsis for blood culture extraction. Blood culture contamination rate. *Medicina intensiva* 2019;43 Suppl 1:31-34. doi: 10.1016/j.medin.2018.08.007 [published Online First: 2018/12/12]
111. Galena HJ. Complications occurring from diagnostic venipuncture. *The Journal of family practice* 1992;34(5):582-4. [published Online First: 1992/05/01]
112. Ota K, Nishioka D, Ito Y, et al. Regression discontinuity of blood culture contamination rate after changing of disinfectants: retrospective observational study. *Sci Rep* 2021;11(1):21235. doi: 10.1038/s41598-021-00498-x [published Online First: 2021/10/29]
113. Ota K, Oba K, Fukui K, et al. Sites of blood collection and topical antiseptics associated with contaminated cultures: prospective observational study. *Sci Rep* 2021;11(1):6211. doi: 10.1038/s41598-021-85614-7 [published Online First: 2021/03/20]
114. Suwanpimolkul G, Pongkumpai M, Suankratay C. A randomized trial of 2% chlorhexidine tincture compared with 10% aqueous povidone-iodine for venipuncture site disinfection: Effects on blood culture contamination rates. *The Journal of infection* 2008;56(5):354-9. doi: 10.1016/j.jinf.2008.03.001 [published Online First: 2008/04/15]
115. Liu W, Duan Y, Cui W, et al. Skin antiseptics in venous puncture site disinfection for preventing blood culture contamination: A Bayesian network meta-analysis of randomized controlled trials. *International journal of nursing studies* 2016;59:156-62. doi: 10.1016/j.ijnurstu.2016.04.004 [published Online First: 2016/05/26]
116. Shaheen N, Zeeshan M, Fasih N, et al. Efforts to improve diagnosis of bacteraemia by reducing blood culture contamination in an emergency department: strategies and outcome. *J Pak Med Assoc* 2020;70(5):835-39. doi: 10.5455/jpma.12462 [published Online First: 2020/05/14]
117. Salvagno GL, Danese E, Fau - Lima-Oliveira G, Lima-Oliveira G, Guidi GC, et al. Avoidance to wipe alcohol before venipuncture is not a source of spurious hemolysis. 2013(1330-0962 (Print))
118. Lippi G, Simundic AM, Musile G, et al. The alcohol used for cleansing the venipuncture site does not jeopardize blood and plasma alcohol measurement with head-space gas chromatography and an enzymatic assay. *Biochem Med (Zagreb)* 2017;27(2):398-403. doi: 10.11613/bm.2017.041 [published Online First: 2017/07/12]
119. Wynn M. The Benefits and Harms of Cleansing for Acute Traumatic Wounds: A Narrative Review. *Advances in skin & wound care* 2021;34(9):488-92. doi: 10.1097/01.ASW.0000767348.38107.ac [published Online First: 2021/08/21]
120. Buowari O. Complications of venepuncture. *Advances in Bioscience and Biotechnology* 2013;04:126-28. doi: 10.4236/abb.2013.41A018
121. Fakhri MG, Jones K, Rey JE, et al. Sustained Improvements in Peripheral Venous Catheter Care in Non-Intensive Care Units: A Quasi-Experimental Controlled Study of Education and Feedback. *Infection Control & Hospital Epidemiology* 2012;33(5):449-55. doi: 10.1086/665322 [published Online First: 2015/01/02]
122. Jędruchiewicz K, Ok YS, Oleszczuk P. COVID-19 discarded disposable gloves as a source and a vector of pollutants in the environment. *Journal of Hazardous Materials* 2021;417:125938. doi: <https://doi.org/10.1016/j.jhazmat.2021.125938>
123. Hughes JM. Recommendations for Prevention of HIV Transmission in Health-Care Settings. *MMWR* 1987;36
124. Shrinivas, Srivastava L, Sengupta D, et al. HIV infection control in health care settings. *Journal of the Indian Medical Association* 1994;92(1):33-6. [published Online First: 1994/01/01]
125. Berrien H. Occupational Exposure to Bloodborne Pathogens: Directorate of Compliance Programs 1994 [Available from: <https://www.osha.gov/laws-regs/standardinterpretations/1994-04-01> accessed May/2022 2022.
126. Loveday HP, Wilson JA, Pratt RJ, et al. epic3: national evidence-based guidelines for preventing healthcare-associated infections in NHS hospitals in England. *The Journal of hospital infection* 2014;86 Suppl 1:S1-70. doi: 10.1016/s0195-6701(13)60012-2 [published Online First: 2013/12/18]
127. Chaudhary MK, Dhakaita SK, Ray R, et al. Local complications of intravenous access - an often underestimated entity. *J Family Med Prim Care* 2020;9(12):6073-77. doi: 10.4103/jfmpc.jfmpc\_1649\_20 [published Online First: 2021/03/09]
128. Guidelines for the Prevention of Intravascular Catheter-Related Infections 2011 [updated 2017. Available from: <https://www.cdc.gov/infectioncontrol/guidelines/bsi/recommendations.html>.
129. Blood Culture Sampling Policy for Adult and Paediatric Patients: NHS; 2018 [updated 2021. 7<sup>th</sup>:[Available from: <https://www.uhs.nhs.uk/Media/UHS-website-2019/Docs/Policies/Blood-culture-sampling-policy-April-2022-v8.pdf> accessed 22 May 2022.
130. Verbeek JH, Ijaz S, Mischke C, et al. Personal protective equipment for preventing highly infectious diseases due to exposure to contaminated body fluids in healthcare staff. *Cochrane Database of Systematic Reviews* 2016(4) doi: 10.1002/14651858.CD011621.pub2

131. Zwaans JJM, Raven W, Rosendaal AV, et al. Non-sterile gloves and dressing versus sterile gloves, dressings and drapes for suturing of traumatic wounds in the emergency department: a non-inferiority multicentre randomised controlled trial. 2022;39(9):650-54. doi: 10.1136/emmermed-2021-211540 %J Emergency Medicine Journal
132. Culjak M, Gveric Grginic A, Simundic AM. Bacterial contamination of reusable venipuncture tourniquets in tertiary-care hospital. *Clin Chem Lab Med* 2018;56(8):e201-e03. doi: 10.1515/cclm-2017-0994 [published Online First: 2018/02/13]
133. Cengiz M, Ulker P, Meiselman HJ, et al. Influence of tourniquet application on venous blood sampling for serum chemistry, hematological parameters, leukocyte activation and erythrocyte mechanical properties. *Clin Chem Lab Med* 2009;47(6):769-76. doi: 10.1515/cclm.2009.157 [published Online First: 2009/05/12]
134. LIPPI G, SALVAGNO GL, MONTAGNANA M, et al. Venous stasis and routine hematologic testing. 2006;28(5):332-37. doi: <https://doi.org/10.1111/j.1365-2257.2006.00818.x>
135. Berger-Achituv S, Budde-Schwartzman B, Ellis MH, et al. Blood sampling through peripheral venous catheters is reliable for selected basic analytes in children. *Pediatrics* 2010;126(1):e179-86. doi: 10.1542/peds.2009-2920 [published Online First: 2010/06/23]
136. Wollowitz A BP, Esses D, John Gallagher E. . Use of butterfly needles to draw blood is independently associated with marked reduction in hemolysis compared to intravenous catheter. . *Acad Emerg Med* 2013;20:1151-5
137. Serdar M, Kenar L, haşimi A, et al. Tourniquet Application Time During Phlebotomy and The Influence on Clinical Chemistry Testing; Is It Negligible? *Türk Biyokimya Dergisi/Turkish Journal of Biochemistry* 2008;33:85-88.
138. Van Dongen-Lases E, Eppens E DJN, M. R-T. Richtlijn Veneuze bloedafname. *Ned Tijdschr Klin Chem Labgeneesk* 2014;39:18.
139. Phelan MP, Reineks EZ, Berriochoa JP, et al. Impact of use of smaller volume, smaller vacuum blood collection tubes on hemolysis in emergency department blood samples. *American Journal of Clinical Pathology* 2017;148(4):330-35. doi: <http://dx.doi.org/10.1093/AJCP/AQX082>
140. Lowe G, Stike R, Pollack M, et al. Nursing blood specimen collection techniques and hemolysis rates in an emergency department: analysis of venipuncture versus intravenous catheter collection techniques. *J Emerg Nurs* 2008;34(1):26-32. doi: 10.1016/j.jen.2007.02.006 [published Online First: 2008/02/02]
141. Dikmen ZG, Pinar A, Akbiyik F. Specimen rejection in laboratory medicine: Necessary for patient safety? *Biochem Med (Zagreb)* 2015;25(3):377-85. doi: 10.11613/bm.2015.037 [published Online First: 2015/11/04]
142. Bodansky DMS, Lumley SE, Chakraborty R, et al. Potential cost savings by minimisation of blood sample delays on care decision making in urgent care services. *Annals of Medicine and Surgery* 2017;20:37-40. doi: <http://dx.doi.org/10.1016/j.amsu.2017.06.016>
143. Lippi G, Blanckaert N, Bonini P, et al. Haemolysis: an overview of the leading cause of unsuitable specimens in clinical laboratories. *Clin Chem Lab Med* 2008;46(6):764-72. doi: 10.1515/cclm.2008.170 [published Online First: 2008/07/08]
144. Kim JY, Kamis IK, Singh B, et al. Implementation of computerized add-on testing for hospitalized patients in a large academic medical center. *Clin Chem Lab Med* 2011;49(5):845-50. doi: 10.1515/cclm.2011.140 [published Online First: 2011/02/10]
145. Tanabe P, Kyriacou DN, Garland F. Factors affecting the risk of blood bank specimen hemolysis. *Acad Emerg Med* 2003;10(8):897-900. doi: 10.1111/j.1553-2712.2003.tb00637.x [published Online First: 2003/08/05]
146. Ong ME, Chan YH, Lim CS. Reducing blood sample hemolysis at a tertiary hospital emergency department. *The American journal of medicine* 2009;122(11):1054.e1-6. doi: 10.1016/j.amjmed.2009.04.024 [published Online First: 2009/10/27]
147. Fang L, Fang SH, Chung YH, et al. Collecting factors related to the haemolysis of blood specimens. *Journal of clinical nursing* 2008;17(17):2343-51. doi: 10.1111/j.1365-2702.2006.02057.x [published Online First: 2007/12/01]
148. Ortells-Abuye N, Busquets-Puigdevall T, Díaz-Bergara M, et al. A cross-sectional study to compare two blood collection methods: direct venous puncture and peripheral venous catheter. *BMJ Open* 2014;4(2):e004250. doi: 10.1136/bmjopen-2013-004250 [published Online First: 2014/03/01]
149. Seemann S, Reinhardt A. Blood sample collection from a peripheral catheter system compared with phlebotomy. *Journal of intravenous nursing; the official publication of the Intravenous Nurses Society* 2000;23(5):290-7. [published Online First: 2002/02/19]
150. Lippi G, Cervellin G, Mattiuzzi C. Critical review and meta-analysis of spurious hemolysis in blood samples collected from intravenous catheters. *Biochem Med (Zagreb)* 2013;23(2):193-200. doi: 10.11613/bm.2013.022 [published Online First: 2013/07/31]
151. Straszewski SM SL, McGillicuddy D, et al. , 98). Use of separate venipunctures for IV access and laboratory studies decreases hemolysis rates. . *Intern Emerg Med* 2011;6:357-9 (PMID: 214686:357-9
152. Ibrahim I, Yau YW, Ong L, et al. Arterial puncture using insulin needle is less painful than with standard needle: a randomized crossover study. *Acad Emerg Med* 2015;22(3):315-20. doi: 10.1111/acem.12601 [published Online First: 2015/03/04]
153. Mrazek C, Simundic AM, Wiedemann H, et al. The relationship between vacuum and hemolysis during catheter blood collection: a retrospective analysis of six large cohorts. *Clin Chem Lab Med* 2017;55(8):1129-34. doi: 10.1515/cclm-2016-0940 [published Online First: 2017/01/21]
154. Burns ER, Yoshikawa N. Hemolysis in Serum Samples Drawn by Emergency Department Personnel versus Laboratory Phlebotomists. *Laboratory Medicine* 2002;33(5):378-80. doi: 10.1309/PGM4-4F8L-2P1M-LKPB %J Laboratory Medicine
155. Stauss M, Sherman B, Pugh L, et al. Hemolysis of coagulation specimens: a comparative study of intravenous draw methods. *J Emerg Nurs* 2012;38(1):15-21. doi: 10.1016/j.jen.2010.08.011 [published Online First: 2012/01/10]
156. Dwyer DG, Fry M, Somerville A, et al. Randomized, single blinded control trial comparing haemolysis rate between two cannula aspiration techniques. *Emerg Med Australas* 2006;18(5-6):484-8. doi: 10.1111/j.1742-6723.2006.00895.x [published Online First: 2006/11/07]
157. Lippi G, Avanzini P, Musa R, et al. Evaluation of sample hemolysis in blood collected by S-Monovette using vacuum or aspiration mode. *Biochem Med (Zagreb)* 2013;23(1):64-9. doi: 10.11613/bm.2013.008 [published Online First: 2013/03/06]

158. Heyer NJ, Derzon JH, Wings L, et al. Effectiveness of practices to reduce blood sample hemolysis in EDs: a laboratory medicine best practices systematic review and meta-analysis. *Clin Biochem* 2012;45(13-14):1012-32. doi: 10.1016/j.clinbiochem.2012.08.002 [published Online First: 2012/09/13]
159. Standards for Infusion Therapy: Royal Collegue of Emergency Nursing; 2016 [updated 31/07/2021. Available from: <https://www.rcn.org.uk/Professional-Development/publications/pub-005704>. accessed 11/07/2023.
160. Davies H, Coventry, L. L., Jacob, A., Stoneman, L., & Jacob, E. Blood sampling through peripheral intravenous cannulas: A look at current practice in Australia Elseiver: Elseiver; 2020 [Available from: <https://doi.org/10.1016/j.colegn.2019.07.010>.
161. Phelan MP, Reineks EZ, Schold JD, et al. Preanalytic Factors Associated With Hemolysis in Emergency Department Blood Samples. *Archives of pathology & laboratory medicine* 2018;142(2):229-35. doi: 10.5858/arpa.2016-0400-OA [published Online First: 2017/11/07]
162. Dennis J. Ernst LOB, Roger R. Calam, Ruth McCall, Susan S. Smith, Diane I. Szamosi, David J. Warunek,. Applied Phlebotomy: Jones & Bartlett Learning, LLC 2005:286.
163. Hawkins T, Greenslade JH, Suna J, et al. Peripheral Intravenous Cannula Insertion and Use in the Emergency Department: An Intervention Study. *Acad Emerg Med* 2018;25(1):26-32. doi: 10.1111/acem.13335 [published Online First: 2017/10/19]
164. Limm El, Fang X, Dendle C, et al. Half of all peripheral intravenous lines in an Australian tertiary emergency department are unused: pain with no gain? *Ann Emerg Med* 2013;62(5):521-25. doi: 10.1016/j.annemergmed.2013.02.022 [published Online First: 2013/04/30]
165. Davies H, Coventry LL, Jacob A, et al. Blood sampling through peripheral intravenous cannulas: A look at current practice in Australia. *Collegian* 2020;27(2):219-25. doi: <https://doi.org/10.1016/j.colegn.2019.07.010>
166. Berg JE, Ahee P, Berg JD. Variation in phlebotomy techniques in emergency medicine and the incidence of haemolysed samples. *Annals of clinical biochemistry* 2011;48(Pt 6):562-5. doi: 10.1258/acb.2011.011099 [published Online First: 2011/09/29]
167. Cao L, Chen M, Phipps RA, et al. Causes and impact of specimen rejection in a clinical chemistry laboratory. *Clinica chimica acta; international journal of clinical chemistry* 2016;458:154-8. doi: 10.1016/j.cca.2016.05.003 [published Online First: 2016/05/12]
168. Lesser FD, Lanham DA, Davis D. Blood sampled from existing peripheral IV cannulae yields results equivalent to venepuncture: a systematic review. *JRSM open* 2020;11(5):2054270419894817. doi: 10.1177/2054270419894817 [published Online First: 2020/06/12]
169. Jeong Y, Park H, Jung MJ, et al. Comparisons of laboratory results between two blood samplings: Venipuncture versus peripheral venous catheter—A systematic review with meta-analysis. 2019;28(19-20):3416-29. doi: <https://doi.org/10.1111/jocn.14918>
170. Hambleton VL, Gómez IA, Andreu FA. Venipuncture versus peripheral catheter: do infusions alter laboratory results? *J Emerg Nurs* 2014;40(1):20-6. doi: 10.1016/j.jen.2012.03.014 [published Online First: 2012/07/07]
171. Hacker C, Verbeek M, Schneider H, et al. Falsely elevated cyclosporin and tacrolimus concentrations over prolonged periods of time due to reversible adsorption to central venous catheters. *Clinica chimica acta; international journal of clinical chemistry* 2014;433:62-8. doi: 10.1016/j.cca.2014.02.031 [published Online First: 2014/03/19]
172. Heireman L, Van Geel P, Musger L, et al. Causes, consequences and management of sample hemolysis in the clinical laboratory. *Clinical Biochemistry* 2017;50(18):1317-22. doi: <http://dx.doi.org/10.1016/j.clinbiochem.2017.09.013>
173. Jacob E, Jacob A, Davies H, et al. The impact of blood sampling technique, including the use of peripheral intravenous cannula, on haemolysis rates: A cohort study. 2021;30(13-14):1916-26. doi: <https://doi.org/10.1111/jocn.15744>
174. Coventry LL, Jacob AM, Davies HT, et al. Drawing blood from peripheral intravenous cannula compared with venepuncture: A systematic review and meta-analysis. 2019;75(11):2313-39. doi: <https://doi.org/10.1111/jan.14078>
175. Kennedy C, Angermuller S, King R, et al. A comparison of hemolysis rates using intravenous catheters versus venipuncture tubes for obtaining blood samples. *J Emerg Nurs* 1996;22(6):566-9. doi: 10.1016/s0099-1767(96)80213-3 [published Online First: 1996/12/01]
176. Grant MS. The effect of blood drawing techniques and equipment on the hemolysis of ED laboratory blood samples. *J Emerg Nurs* 2003;29(2):116-21. doi: 10.1067/men.2003.66 [published Online First: 2003/03/28]
177. Dietrich H. One poke or two: can intravenous catheters provide an acceptable blood sample? A data set presentation, review of previous data sets, and discussion. *J Emerg Nurs* 2014;40(6):575-8. doi: 10.1016/j.jen.2012.11.002 [published Online First: 2013/01/22]
178. Yanagisawa Y, Isobe K, Naito A, et al. Influence of In Vitro Hemolysis on 80 Different Laboratory Tests. *Clin Lab* 2017;63(2):219-26. doi: 10.7754/Clin.Lab.2016.160305 [published Online First: 2017/02/10]
179. Baker RB, Summer SS, Lawrence M, et al. Determining optimal waste volume from an intravenous catheter. *Journal of infusion nursing; the official publication of the Infusion Nurses Society* 2013;36(2):92-6. doi: 10.1097/NAN.0b013e318282a4c2 [published Online First: 2013/03/05]
180. Taghizadeganzadeh M, Yazdankhahfard M, Farzaneh M, et al. Blood Samples of Peripheral Venous Catheter or The Usual Way: Do Infusion Fluid Alters the Biochemical Test Results? *Global journal of health science* 2015;8(7):93-9. doi: 10.5539/gjhs.v8n7p93 [published Online First: 2015/01/01]
181. Coventry LL, Jacob AM, Davies HT, Stoneman L, Keogh S, Jacob ER. Drawing blood from peripheral intravenous cannula compared with venepuncture: A systematic review and meta-analysis. *J Adv Nurs*. 2019;75(11):2313-2339. doi:10.1111/jan.14078
182. Fernandez P, Llopis MA, Perich C, et al. Harmonization in hemolysis detection and prevention. A working group of the Catalonian Health Institute (ICS) experience. *Clin Chem Lab Med* 2014;52(11):1557-68. doi: 10.1515/cclm-2013-0935 [published Online First: 2014/06/05]
183. Phelan MP, Hustey FM, Good DM, et al. Seeing Red: Blood Sample Hemolysis Is Associated with Prolonged Emergency Department Throughput. *The Journal of Applied Laboratory Medicine* 2020;5(4):732-37. doi: 10.1093/jalm/jfaa073 %J The Journal of Applied Laboratory Medicine
184. Lippi G, Avanzini P, Cervellini G. Prevention of hemolysis in blood samples collected from intravenous catheters. *Clin Biochem* 2013;46(7-8):561-4. doi: 10.1016/j.clinbiochem.2013.01.021 [published Online First: 2013/02/09]
185. Cakir MO, Yildiz Z, Orcun A, et al. Is prevention of hemolysis possible in blood samples collected from IV catheters in the emergency department? *Clinical Laboratory* 2021;67(7):1591-97. doi: <http://dx.doi.org/10.7754/Clin.Lab.2020.201028>

186. Kazezoglu C, Serin E. The Effect of Different Blood Drawing Methods on Hemolysis and Test Results from Intravenous Catheters Used in Emergency Departments. *Clin Lab* 2019;65(1) doi: 10.7754/Clin.Lab.2018.180614 [published Online First: 2019/02/19]
187. Millius L, Riedo E, Caron T, et al. The EPiQ<sup>®</sup>-Study (Evaluation of preanalytical quality): S-Monovette in manual aspiration mode drastically reduces hemolytic samples in head-to-head study. *Practical Laboratory Medicine* 2021;27:e00252. doi: <http://dx.doi.org/10.1016/j.plabm.2021.e00252>
188. King KC, Strony R. Needlestick. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2022, StatPearls Publishing LLC. 2022.
189. Cadamuro J, Felder TK, Oberkofler H, et al. Relevance of EDTA carryover during blood collection. *Clin Chem Lab Med* 2015;53(8):1271-8. doi: 10.1515/cclm-2014-0944 [published Online First: 2015/02/27]
190. Keppel MH, Auer S, Lippi G, et al. Heparin and citrate additive carryover during blood collection. 2019;57(12):1888-96. doi: 10.1515/cclm-2019-0433
191. Giavarina D, Lippi G. Blood venous sample collection: Recommendations overview and a checklist to improve quality. *Clin Biochem* 2017;50(10-11):568-73. doi: 10.1016/j.clinbiochem.2017.02.021 [published Online First: 2017/03/01]
192. Whitson MR, Mayo PH. Ultrasonography in the emergency department. *Critical Care* 2016;20(1):227. doi: 10.1186/s13054-016-1399-x
193. Laura Ann G. The Evolving Role of Ultrasound in Emergency Medicine. In: Ahmed Subhy A, ed. *Essentials of Accident and Emergency Medicine*. Rijeka: IntechOpen 2018:Ch. 7.
194. Liu YT, Alsaawi A, Bjornsson HM. Ultrasound-guided peripheral venous access: a systematic review of randomized-controlled trials. *Eur J Emerg Med* 2014;21(1):18-23. doi: 10.1097/MEJ.0b013e328363bebc [published Online First: 2013/07/25]
195. Egan G, Healy D, O'Neill H, et al. Ultrasound guidance for difficult peripheral venous access: systematic review and meta-analysis. *Emergency medicine journal; EMJ* 2013;30(7):521-6. doi: 10.1136/emmermed-2012-201652 [published Online First: 2012/08/14]
196. Rodríguez-Herrera Á, Solaz-García Á, Mollá-Olmos E, et al. Use of the Ultrasound Technique as Compared to the Standard Technique for the Improvement of Venous Cannulation in Patients with Difficult Access. *Healthcare (Basel, Switzerland)* 2022;10(2) doi: 10.3390/healthcare10020261 [published Online First: 2022/02/26]
197. Yalçınlı S, Karbek Akarca F, Can Ö, et al. Comparison of Standard Technique, Ultrasonography, and Near-Infrared Light in Difficult Peripheral Vascular Access: A Randomized Controlled Trial. *Prehosp Disaster Med* 2022;37(1):65-70. doi: 10.1017/s1049023x21001217 [published Online First: 2021/12/07]
198. Tran QK, Flanagan K, Fairchild M, et al. Nurses and Efficacy of Ultrasound-Guided Versus Traditional Venous Access: A Systemic Review and Meta-Analysis. *Journal of Emergency Nursing* 2022;48(2):145-58.e1. doi: <https://doi.org/10.1016/j.jen.2021.12.003>
199. Tran QK, Fairchild M, Yardi I, et al. Efficacy of Ultrasound-Guided Peripheral Intravenous Cannulation versus Standard of Care: A Systematic Review and Meta-analysis. *Ultrasound in medicine & biology* 2021;47(11):3068-78. doi: 10.1016/j.ultrasmedbio.2021.07.002 [published Online First: 2021/08/07]
200. Costantino TG, Parikh AK, Satz WA, et al. Ultrasonography-guided peripheral intravenous access versus traditional approaches in patients with difficult intravenous access. *Ann Emerg Med* 2005;46(5):456-61. doi: 10.1016/j.annemergmed.2004.12.026 [published Online First: 2005/11/08]
201. Bauman M, Braude D, Crandall C. Ultrasound-guidance vs. standard technique in difficult vascular access patients by ED technicians. *Am J Emerg Med* 2009;27(2):135-40. doi: 10.1016/j.ajem.2008.02.005 [published Online First: 2009/04/18]
202. Edwards C, Jones J. Development and Implementation of an Ultrasound-Guided Peripheral Intravenous Catheter Program for Emergency Nurses. *J Emerg Nurs* 2018;44(1):33-36. doi: 10.1016/j.jen.2017.07.009 [published Online First: 2017/08/15]
203. Bagley K. Development and Implementation of an Ultrasound-Guided Peripheral Intravenous Catheter Education Program for Critical Care Nurses. *Dimensions of critical care nursing; DCCN* 2022;41(4):182-89. doi: 10.1097/dcc.0000000000000528 [published Online First: 2022/05/27]
204. McClellan EK, Nakamura RM, Haas W, et al. EFFECT OF PNEUMATIC TUBE TRANSPORT SYSTEM ON THE VALIDITY OF DETERMINATIONS IN BLOOD CHEMISTRY. *Am J Clin Pathol* 1964;42:152-5. doi: 10.1093/ajcp/42.2.152 [published Online First: 1964/08/01]
205. Nybo M, Lund ME, Titlestad K, et al. Blood Sample Transportation by Pneumatic Transportation Systems: A Systematic Literature Review. *Clinical chemistry* 2018;64(5):782-90. doi: 10.1373/clinchem.2017.280479 [published Online First: 2017/12/10]
206. Suchsland J, Winter T, Greiser A, et al. Extending laboratory automation to the wards: effect of an innovative pneumatic tube system on diagnostic samples and transport time. *Clin Chem Lab Med* 2017;55(2):225-30. doi: 10.1515/cclm-2016-0380 [published Online First: 2016/07/01]
207. Papek A, Matthewson B, Whitman E, et al. Comparison of pneumatic tube system with manual transport for routine chemistry, hematology, coagulation and blood gas tests. *Clin Chem Lab Med* 2017;55(10):1537-44. doi: 10.1515/cclm-2016-1157 [published Online First: 2017/04/23]
208. Mullins GR, Bruns DE. Air bubbles and hemolysis of blood samples during transport by pneumatic tube systems. *Clinica chimica acta; international journal of clinical chemistry* 2017;473:9-13. doi: 10.1016/j.cca.2017.08.008 [published Online First: 2017/08/15]
209. Cadamuro J, von Meyer A, Johannis W, et al. Effect of five different pneumatic tube carrier inserts on mechanical sample stress: a multicentre evaluation. *Clin Chem Lab Med* 2021;59(8):e313-e16. doi: 10.1515/cclm-2020-1818 [published Online First: 2021/03/04]
210. Streichert T, Otto B, Schnabel C, et al. Determination of hemolysis thresholds by the use of data loggers in pneumatic tube systems. *Clinical chemistry* 2011;57(10):1390-7. doi: 10.1373/clinchem.2011.167932 [published Online First: 2011/08/13]
211. Kara H, Bayir A, Ak A, et al. Hemolysis associated with pneumatic tube system transport for blood samples. *Pakistan journal of medical sciences* 2014;30(1):50-8. doi: 10.12669/pjms.301.4228 [published Online First: 2014/03/19]
212. Pasqualetti S, Szöke D, Panteghini M. Heparinate but not serum tubes are susceptible to hemolysis by pneumatic tube transportation. 2016;54(5):785-89. doi: 10.1515/cclm-2015-0751
213. Ellis G. An episode of increased hemolysis due to a defective pneumatic air tube delivery system. *Clinical Biochemistry* 2009;42(12):1265-69. doi: <https://doi.org/10.1016/j.clinbiochem.2009.05.002>

214. Böckel-Frohnhofer N, Hübner U, Hummel B, et al. Pneumatic tube-transported blood samples in lithium heparinate gel separator tubes may be more susceptible to haemolysis than blood samples in serum tubes. *Scand J Clin Lab Invest* 2014;74(7):599-602. doi: 10.3109/00365513.2014.921931 [published Online First: 2014/06/10]
215. Casati M, Intra J, Rossi W, et al. Hemolysis and blood gas analysis: it's time for a change! *Scandinavian Journal of Clinical and Laboratory Investigation* 2022;82(2):138-42. doi: 10.1080/00365513.2022.2034037
216. Wei J, Wu YN, Ling Y, et al. False decrease of high-sensitivity cardiac troponin T assay in pneumatic tube system samples. *Clinica chimica acta; international journal of clinical chemistry* 2019;495:507-11. doi: 10.1016/j.cca.2019.05.027 [published Online First: 2019/06/04]
217. Raimann FJ, Lindner ML, Martin C, et al. Role of POC INR in the early stage of diagnosis of coagulopathy. *Pract Lab Med* 2021;26:e00238. doi: 10.1016/j.plabm.2021.e00238 [published Online First: 2021/06/08]
218. Lippi G, Cadamuro J, von Meyer A, et al. Practical recommendations for managing hemolyzed samples in clinical chemistry testing. *Clin Chem Lab Med* 2018;56(5):718-27. doi: 10.1515/cclm-2017-1104 [published Online First: 2018/01/27]
219. Humble RM, Hounkponou HG, Krasowski MD. The "Rainbow" of Extra Blood Tubes—Useful or Wasteful Practice? *JAMA Internal Medicine* 2017;177(1):128-29. doi: 10.1001/jamainternmed.2016.6834 [published Online First: 2016/11/02]
220. CLH, Hernandez JS, Traub SJ. "Rainbow Draws" in the Emergency Department: Clinical Utility and Staff Perceptions. *J Appl Lab Med* 2019;4(2):229-34. doi: 10.1373/jalm.2018.027649 [published Online First: 2019/10/23]
221. Branco BC, Inaba K, Doughty R, et al. The increasing burden of phlebotomy in the development of anaemia and need for blood transfusion amongst trauma patients. *Injury* 2012;43(1):78-83. doi: 10.1016/j.injury.2010.12.003 [published Online First: 2011/01/05]
222. Cornes M, Simundic AM, Cadamuro J, et al. The CRESS checklist for reporting stability studies: on behalf of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) Working Group for the Preanalytical Phase (WG-PRE). *Clin Chem Lab Med* 2020;59(1):59-69. doi: 10.1515/cclm-2020-0061 [published Online First: 2020/07/28]
223. Doern GV, Carroll KC, Diekema DJ, et al. Practical Guidance for Clinical Microbiology Laboratories: A Comprehensive Update on the Problem of Blood Culture Contamination and a Discussion of Methods for Addressing the Problem. *Clinical microbiology reviews* 2019;33(1) doi: 10.1128/cmr.00009-19 [published Online First: 2019/11/02]
224. Wilson ML. Principles and procedures for blood cultures; approved guideline 2007:53.
225. Towns ML, Jarvis WR, Hsueh PR. Guidelines on blood cultures. *Journal of microbiology, immunology, and infection = Wei mian yu gan ran za zhi* 2010;43(4):347-9. doi: 10.1016/s1684-1182(10)60054-0 [published Online First: 2010/08/07]
226. Self WH, Speroff T, Grijalva CG, et al. Reducing blood culture contamination in the emergency department: an interrupted time series quality improvement study. *Acad Emerg Med* 2013;20(1):89-97. doi: 10.1111/acem.12057 [published Online First: 2013/04/11]
227. Plato FD, Fontana C, Gherardi G, et al. Collection, transport and storage procedures for blood culture specimens in adult patients: recommendations from a board of Italian experts. 2019;57(11):1680-89. doi: doi:10.1515/cclm-2018-1146
228. Weinstein MP. Blood culture contamination: persisting problems and partial progress. *J Clin Microbiol* 2003;41(6):2275-8. doi: 10.1128/jcm.41.6.2275-2278.2003 [published Online First: 2003/06/07]
229. Boyce JM, Nadeau J, Dumigan D, et al. Obtaining blood cultures by venipuncture versus from central lines: impact on blood culture contamination rates and potential effect on central line-associated bloodstream infection reporting. *Infect Control Hosp Epidemiol* 2013;34(10):1042-7. doi: 10.1086/673142 [published Online First: 2013/09/11]
230. Garcia RA, Spitzer ED, Beaudry J, et al. Multidisciplinary team review of best practices for collection and handling of blood cultures to determine effective interventions for increasing the yield of true-positive bacteremias, reducing contamination, and eliminating false-positive central line-associated bloodstream infections. *Am J Infect Control* 2015;43(11):1222-37. doi: 10.1016/j.ajic.2015.06.030 [published Online First: 2015/08/25]
231. Arenas M, Boseman GM, Coppin JD, et al. Asynchronous Testing of 2 Specimen-Diversion Devices to Reduce Blood Culture Contamination: A Single-Site Product Supply Quality Improvement Project. *J Emerg Nurs* 2021;47(2):256-64.e6. doi: 10.1016/j.jen.2020.11.008 [published Online First: 2021/01/13]
232. Rupp ME, Cavalieri RJ, Marolf C, et al. Reduction in Blood Culture Contamination Through Use of Initial Specimen Diversion Device. *Clinical Infectious Diseases* 2017;65(2):201-05. doi: <http://dx.doi.org/10.1093/cid/cix304>
233. Bell M, Bogar C, Plante J, et al. Effectiveness of a Novel Specimen Collection System in Reducing Blood Culture Contamination Rates. *J Emerg Nurs* 2018;44(6):570-75. doi: 10.1016/j.jen.2018.03.007 [published Online First: 2018/04/25]
234. Plebani M, Sciacovelli L, Aita A, et al. Harmonization of pre-analytical quality indicators. *Biochem Med (Zagreb)* 2014;24(1):105-13. doi: 10.11613/bm.2014.012 [published Online First: 2014/03/15]
235. Plebani M. Performance specifications for the extra-analytical phases of laboratory testing: Why and how. *Clin Biochem* 2017;50(10-11):550-54. doi: 10.1016/j.clinbiochem.2017.02.002 [published Online First: 2017/02/09]
236. Cadamuro J, Gaksch M, Mrazek C, et al. How do we use the data from pre-analytical quality indicators and how should we? 2018;3(4)
237. Lukić V. Laboratory Information System - Where are we Today? *Journal of medical biochemistry* 2017;36(3):220-24. doi: 10.1515/jomb-2017-0021 [published Online First: 2017/07/14]
238. Stotler BA, Kratz A. Determination of turnaround time in the clinical laboratory: "accession-to-result" time does not always accurately reflect laboratory performance. *Am J Clin Pathol* 2012;138(5):724-9. doi: 10.1309/ajcphyb9oqrm8dx [published Online First: 2012/10/23]
239. Yeste MLL, Mas ARP, Muñoz LG, et al. Management of post-analytical processes in the clinical laboratory according to ISO 15189:2012. Considerations about the management of clinical samples, ensuring quality of post-analytical processes, and laboratory information management. 2021;2(3):373-80. doi: doi:10.1515/almed-2021-0044
240. Medicine IFoCCaL, Group W. MODEL OF QUALITY INDICATORS: EFLM; 2016 [Available from: [https://www.eflm.eu/upload/docs/ISO15189\\_audit\\_of\\_IVDRcompliantLDTs.pdf](https://www.eflm.eu/upload/docs/ISO15189_audit_of_IVDRcompliantLDTs.pdf) accessed 11/07/2023.
241. Medicine IFoCCaL. IFCC; [Available from: <http://www.ifcc-mqi.com> accessed 2022 may 2022.

242. Meier FA, Souers RJ, Howanitz PJ, et al. Seven Q-Tracks monitors of laboratory quality drive general performance improvement: experience from the College of American Pathologists Q-Tracks program 1999-2011. *Archives of pathology & laboratory medicine* 2015;139(6):762-75. doi: 10.5858/arpa.2014-0090-CP [published Online First: 2015/06/02]
243. Badrick T, Gay S, Mackay M, et al. The key incident monitoring and management system - history and role in quality improvement. *Clin Chem Lab Med* 2018;56(2):264-72. doi: 10.1515/cclm-2017-0219 [published Online First: 2017/08/05]
244. Preanalytic Benchmark Database OGLMKC: Referenzinstitut für Bioanalytik; 2023 [Available from: <https://www.rfb.bio/cgi/haemolysisLogin>] (accessed Jan 2023).
245. Florkowski C, Don-Wauchope A, Gimenez N, et al. Point-of-care testing (POCT) and evidence-based laboratory medicine (EBLM) - does it leverage any advantage in clinical decision making? *Crit Rev Clin Lab Sci* 2017;54(7-8):471-94. doi: 10.1080/10408363.2017.1399336 [published Online First: 2017/11/25]
246. Kendall J, Reeves B, Clancy M. Point of care testing: randomised controlled trial of clinical outcome. *BMJ (Clinical research ed)* 1998;316(7137):1052-7. doi: 10.1136/bmj.316.7137.1052 [published Online First: 1998/04/29]
247. Kocher KE, Meurer WJ, Desmond JS, et al. Effect of testing and treatment on emergency department length of stay using a national database. *Acad Emerg Med* 2012;19(5):525-34. doi: 10.1111/j.1553-2712.2012.01353.x [published Online First: 2012/05/19]
248. Asha SE, Chan AC, Walter E, et al. Impact from point-of-care devices on emergency department patient processing times compared with central laboratory testing of blood samples: a randomised controlled trial and cost-effectiveness analysis. *Emergency medicine journal; EMJ* 2014;31(9):714-9. doi: 10.1136/emered-2013-202632 [published Online First: 2013/06/12]
249. Zenlander R, von Euler M, Antovic J, et al. Point-of-care versus central laboratory testing of INR in acute stroke. *Acta neurologica Scandinavica* 2018;137(2):252-55. doi: 10.1111/ane.12860 [published Online First: 2017/10/27]
250. Loten C, Attia J, Hullick C, et al. Point of care troponin decreases time in the emergency department for patients with possible acute coronary syndrome: a randomised controlled trial. *Emergency medicine journal; EMJ* 2010;27(3):194-8. doi: 10.1136/emj.2008.069427 [published Online First: 2010/03/23]
251. Goldstein LN, Wells M, Vincent-Lambert C. Doctors' perceptions of the impact of upfront point-of-care testing in the emergency department. *PLoS One* 2018;13(12):e0208655. doi: 10.1371/journal.pone.0208655 [published Online First: 2018/12/14]
252. Murray RP, Leroux M, Sabga E, et al. Effect of point of care testing on length of stay in an adult emergency department. *The Journal of emergency medicine* 1999;17(5):811-4. doi: 10.1016/s0736-4679(99)00107-9 [published Online First: 1999/09/28]
253. McIntosh BW, Vasek J, Taylor M, et al. Accuracy of bedside point of care testing in critical emergency department patients. *Am J Emerg Med* 2018;36(4):567-70. doi: 10.1016/j.ajem.2017.09.018 [published Online First: 2017/09/19]
254. Ivaska L, Niemelä J, Leino P, et al. Accuracy and feasibility of point-of-care white blood cell count and C-reactive protein measurements at the pediatric emergency department. *PLoS One* 2015;10(6):e0129920. doi: 10.1371/journal.pone.0129920 [published Online First: 2015/06/04]
255. Jarvis P, Davies T, Mitchell K, et al. Does rapid assessment shorten the amount of time patients spend in the emergency department? *British journal of hospital medicine (London, England; 2005)* 2014;75(11):648-51. doi: 10.12968/hmed.2014.75.11.648 [published Online First: 2014/11/11]
256. Kankaanpää M, Holma-Eriksson M, Kapanen S, et al. Comparison of the use of comprehensive point-of-care test panel to conventional laboratory process in emergency department. *BMC Emergency Medicine* 2018;18(1):43. doi: 10.1186/s12873-018-0198-x
257. Larsson A, Greig-Pylypczuk R, Huisman A. The state of point-of-care testing: a European perspective. *Uppsala journal of medical sciences* 2015;120(1):1-10. doi: 10.3109/03009734.2015.1006347 [published Online First: 2015/01/28]
258. ISO. ISO 15189:2022. 2022
259. Goldstein L, Wells M, Vincent-Lambert C. A Randomized Controlled Trial to Assess the Impact of Upfront Point-of-Care Testing on Emergency Department Treatment Time. *Am J Clin Pathol* 2018;150(3):224-34. doi: 10.1093/ajcp/aqy042 [published Online First: 2018/06/23]
260. Bargnoux AS, Beaufile O, Oguike M, et al. Point-of-care creatinine testing in patients receiving contrast-enhanced computed tomography scan. *Clinica chimica acta; international journal of clinical chemistry* 2018;478:111-13. doi: 10.1016/j.cca.2017.12.025 [published Online First: 2017/12/23]
261. Han JH, Jang S, Choi M-O, et al. Point-of-care coagulation testing for reducing in-hospital delay in thrombolysis. 2019;26(4):218-24. doi: 10.1177/1024907918799938
262. Hight M, Conklin K, Archer B, et al. Implementing Point-of-Care Troponin Testing in the Emergency Department: Impact on Time to Result. *J Emerg Nurs* 2021;47(2):299-304. doi: 10.1016/j.jen.2020.06.014 [published Online First: 2020/12/15]
263. Collinson PO, Saenger AK, Apple FS. High sensitivity, contemporary and point-of-care cardiac troponin assays: educational aids developed by the IFCC Committee on Clinical Application of Cardiac Bio-Markers. *Clin Chem Lab Med* 2019;57(5):623-32. doi: 10.1515/cclm-2018-1211 [published Online First: 2018/12/12]
264. Ferraro S, Dolci A, Panteghini M. Fast track protocols using highly sensitive troponin assays for ruling out and ruling in non-ST elevation acute coronary syndrome. *Clin Chem Lab Med* 2017;55(11):1683-89. doi: 10.1515/cclm-2017-0044 [published Online First: 2017/03/28]
265. Roffi M, Patrono C, Collet JP, et al. 2015 ESC Guidelines for the management of acute coronary syndromes in patients presenting without persistent ST-segment elevation: Task Force for the Management of Acute Coronary Syndromes in Patients Presenting without Persistent ST-Segment Elevation of the European Society of Cardiology (ESC). *European heart journal* 2016;37(3):267-315. doi: 10.1093/eurheartj/ehv320 [published Online First: 2015/09/01]
266. Spagnolello O, J Reed M, Dauncey S, et al. Introduction of a ROTEM protocol for the management of trauma-induced coagulopathy. 2021;23(4):308-21. doi: 10.1177/1460408620957919
267. Ganter MT, Hofer CK. Coagulation monitoring: current techniques and clinical use of viscoelastic point-of-care coagulation devices. *Anesthesia and analgesia* 2008;106(5):1366-75. doi: 10.1213/ane.0b013e318168b367 [published Online First: 2008/04/19]



268. Hawkins R. Measurement of Whole-Blood Potassium--Is It Clinically Safe? *Clinical chemistry* 2004;49:2105-6. doi: 10.1373/clinchem.2003.027227
269. Nigro M, Valli G, Marchionne ML, et al. Is There a Risk of Misinterpretation of Potassium Concentration from Undetectable Hemolysis Using a POCT Blood Gas Analyzer in the Emergency Department? 2023;59(1):66.
270. Duhalde H, Skogö J, Karlsson M. Point-of-care hemolysis detection in blood gas specimens directly at the emergency department. *Scand J Clin Lab Invest* 2019;79(5):283-87. doi: 10.1080/00365513.2019.1612089 [published Online First: 2019/05/09]
271. O'Hara M, Wheatley EG, Kazmierczak SC. The Impact of Undetected In Vitro Hemolysis or Sample Contamination on Patient Care and Outcomes in Point-of-Care Testing: A Retrospective Study. *J Appl Lab Med* 2020;5(2):332-41. doi: 10.1093/jalm/jfz020 [published Online First: 2020/05/24]
272. Nichols JH, Alter D, Chen Y, et al. AACC Guidance Document on Management of Point-of-Care Testing. *J Appl Lab Med* 2020;5(4):762-87. doi: 10.1093/jalm/jfaa059 [published Online First: 2020/06/05]
273. Altman DE, Clancy C, Blendon RJ. Improving Patient Safety — Five Years after the IOM Report. *N Engl J Med* 2004;351(20):2041-43. doi: 10.1056/NEJMp048243
274. Wagar EA, Tamashiro L, Yasin B, et al. Patient safety in the clinical laboratory: a longitudinal analysis of specimen identification errors. *Archives of pathology & laboratory medicine* 2006;130(11):1662-8. doi: 10.5858/2006-130-1662-psitcl [published Online First: 2006/11/02]
275. Panagioti M, Khan K, Keers RN, et al. Prevalence, severity, and nature of preventable patient harm across medical care settings: systematic review and meta-analysis. 2019;366:l4185. doi: 10.1136/bmj.l4185 %j BMJ
276. Zhan C, Miller MR. Excess length of stay, charges, and mortality attributable to medical injuries during hospitalization. *Jama* 2003;290(14):1868-74. doi: 10.1001/jama.290.14.1868 [published Online First: 2003/10/09]
277. Boone DJJA, Assurance Q. Is it safe to have a laboratory test? *Accred Qual Assur* 2004;10:5-9.
278. McGlynn EA, Asch SM, Adams J, et al. The quality of health care delivered to adults in the United States. *The New England journal of medicine* 2003;348(26):2635-45. doi: 10.1056/NEJMsa022615 [published Online First: 2003/06/27]
279. Cheng CM. Hospital systems for the detection and prevention of adverse drug events. *Clinical pharmacology and therapeutics* 2011;89(6):779-81. doi: 10.1038/clpt.2010.356 [published Online First: 2011/05/20]
280. Da Rin G. Pre-analytical workstations: a tool for reducing laboratory errors. *Clinica chimica acta; international journal of clinical chemistry* 2009;404(1):68-74. doi: 10.1016/j.cca.2009.03.024 [published Online First: 2009/03/24]
281. Plebani M. Errors in clinical laboratories or errors in laboratory medicine? *Clin Chem Lab Med* 2006;44(6):750-9. doi: 10.1515/cclm.2006.123 [published Online First: 2006/05/30]
282. Salvagno GL, Lippi G, Bassi A, et al. Prevalence and type of pre-analytical problems for inpatients samples in coagulation laboratory. *Journal of evaluation in clinical practice* 2008;14(2):351-3. doi: 10.1111/j.1365-2753.2007.00875.x [published Online First: 2008/03/08]
283. Seemann TL, Nybo M. Continuous quality control of the blood sampling procedure using a structured observation scheme. *Biochem Med (Zagreb)* 2016;26(3):337-45. doi: 10.11613/bm.2016.037 [published Online First: 2016/11/05]
284. Erdal EP, Mitra D, Khangulov VS, et al. The economic impact of poor sample quality in clinical chemistry laboratories: results from a global survey. *Annals of clinical biochemistry* 2017;54(2):230-39. doi: 10.1177/0004563216651647 [published Online First: 2016/05/12]
285. Lundberg GD. Acting on significant laboratory results. *Jama* 1981;245(17):1762-3. doi: 10.1001/jama.1981.03310420052033 [published Online First: 1981/05/01]
286. Plebani M. Quality indicators to detect pre-analytical errors in laboratory testing. *The Clinical biochemist Reviews* 2012;33(3):85-8. [published Online First: 2012/08/30]
287. Huf W, Mohns M, Garmatiuk T, et al. Benchmarking diagnostic laboratory performance: Survey results for Germany, Austria, and Switzerland. *Wiener klinische Wochenschrift* 2022;134(3):174-81. doi: 10.1007/s00508-021-01962-4
288. Clark DM, Silvester K, Knowles S. Lean management systems: creating a culture of continuous quality improvement. *Journal of clinical pathology* 2013;66(8):638-43. doi: 10.1136/jclinpath-2013-201553 [published Online First: 2013/06/13]
289. Almasi S, Rabiei R, Moghaddasi H, et al. Emergency Department Quality Dashboard; a Systematic Review of Performance Indicators, Functionalities, and Challenges. *Archives of academic emergency medicine* 2021;9(1):e47. doi: 10.22037/aaem.v9i1.1230 [published Online First: 2021/08/19]
290. Venkatesh AK, Hajdasz D, Rothenberg C, et al. Reducing Unnecessary Blood Chemistry Testing in the Emergency Department: Implementation of Choosing Wisely. *Am J Med Qual* 2018;33(1):81-85. doi: 10.1177/1062860617691842 [published Online First: 2017/07/12]
291. Gupta P, Thomas M, Sbetan N, et al. A Quality Improvement Initiative to Reduce Rejected Laboratory Samples and Enhance Specimen Acceptability. *Joint Commission journal on quality and patient safety* 2021;47(8):519-25. doi: 10.1016/j.jcjq.2021.04.005 [published Online First: 2021/06/07]
292. Al-Hamad A. Successful Reduction of Blood Culture Contamination in an Emergency Department by Monitoring and Feedback. *The Open Microbiology Journal* 2019;13:279-85. doi: 10.2174/1874285801913010279
293. Sandberg S, Fraser CG, Horvath AR, et al. Defining analytical performance specifications: Consensus Statement from the 1st Strategic Conference of the European Federation of Clinical Chemistry and Laboratory Medicine. *Clin Chem Lab Med* 2015;53(6):833-5. doi: 10.1515/cclm-2015-0067 [published Online First: 2015/02/27]
294. Sciacovelli L, Panteghini M, Lippi G, et al. Defining a roadmap for harmonizing quality indicators in Laboratory Medicine: a consensus statement on behalf of the IFCC Working Group "Laboratory Error and Patient Safety" and EFLM Task and Finish Group "Performance specifications for the extra-analytical phases". *Clin Chem Lab Med* 2017;55(10):1478-88. doi: 10.1515/cclm-2017-0412 [published Online First: 2017/07/09]

Blood sampling prior to performing laboratory measurements is one of the most frequent interventions performed in managed care. In the emergency department, obtaining rapid, high-quality test results to inform patient management is a mainstay. However, it is noteworthy that the majority of errors associated with laboratory testing are not analytical in nature, but occur in the preanalytical phase, particularly during blood sample collections. Three European scientific societies - EUSEM, EUSEN and EFLM - collaborated jointly to produce these recommendations for the preanalytical phase.