Opinion Paper

Mario Plebani, Sheri Scott, Ana-Maria Simundic, Mike Cornes, Andrea Padoan, Janne Cadamuro, Pieter Vermeersch, Hikmet Can Çubukçu, Álvaro González, Mads Nybo, Gian Luca Salvagno, Seán J. Costelloe, Rosanna Falbo, Alexander von Meyer, Enrico Iaccino, Francesco Botrè, Giuseppe Banfi and Giuseppe Lippi*

New insights in preanalytical quality

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Abstract: The negative impact of preanalytical errors on the quality of laboratory testing is now universally recognized. Nonetheless, recent technological advancements and organizational transformations in healthcare – catalyzed by the still ongoing coronavirus disease 2019 (COVID-19 pandemic) – have introduced new challenges and promising opportunities for improvement. The integration of value-based scoring systems for clinical laboratories and growing evidence linking preanalytical errors to patient outcomes and healthcare costs underscore the critical importance of this phase. Emerging topics in the preanalytical phase include the pursuit of a "greener" and more sustainable environment, innovations in self-sampling and automated blood collection, and strategies to minimize patient blood loss. Additionally, efforts to reduce costs and enhance sustainability through patient blood management have gained momentum. Digitalization and artificial intelligence (AI) offer transformative potential, with applications in sample labeling, recording collection events, and monitoring sample conditions during transportation. AI-driven tools can also streamline the preanalytical workflow and mitigate errors. Specific challenges include managing hemolysis and developing strategies to minimize its impact, addressing issues related to urine collection, and designing robust protocols for sample stability studies. The rise of decentralized laboratory testing presents unique preanalytical hurdles, while emerging areas such as liquid biopsy and anti-doping testing introduce novel complexities. Altogether, these advancements and challenges highlight the dynamic evolution of the preanalytical phase and the critical need for continuous innovation and standardization. This collective opinion paper, which summarizes the abstracts of lectures delivered at the two-day European Federation of Laboratory Medicine (EFLM) Preanalytical Conference entitled "New Insight in Preanalytical Quality" (Padova, Italy; December 12–13, 2025), provides a comprehensive overview of preanalytical errors, offers some important insights into less obvious sources of preanalytical vulnerability and proposes efficient opportunities of improvement.

Keywords: preanalytical phase; sample collection; errors; innovation; solutions

***Corresponding author: Prof. Giuseppe Lippi**, Section of Clinical Biochemistry, University Hospital of Verona, Piazzale L.A. Scuro, 10, 37134 Verona, Italy, E-mail: giuseppe.lippi@univr.it. https://orcid.org/0000-0001-9523-9054
Mario Plebani and Andrea Padoan, Department of Medicine (DIMED), University of Padova, Padova, Italy; and Laboratory Medicine Unit, University-Hospital of Padova, Padova, Italy. https://orcid.org/0000-0002-0270-1711 (M. Plebani)
Sheri Scott, Nottingham Trent University, Nottingham, UK
Ana-Maria Simundic, Department of Global Medical & Clinical Affairs, Greiner Bio-One, Kremsmünster, Austria; and Faculty of Pharmacy and Biochemistry, University of Zagreb, Zagreb, Croatia
Mike Cornes, Worcestershire Acute Hospitals NHS Trust, Worcester, UK
Janne Cadamuro, Department of Laboratory Medicine, University Hospital Salzburg, Paracelsus Medical University, Salzburg, Austria
Pieter Vermeersch, Clinical Department of Laboratory Medicine, University Hospitals Leuven, Leuven, Belgium
Hikmet Can Çubukçu, Department of Medical Biochemistry, Sincan Training and Research Hospital, Ankara, Türkiye
Álvaro González, Service of Biochemistry, Clínica Universidad de Navarra, Pamplona, Spain
Mads Nybo, Department of Clinical Biochemistry, Odense University Hospital, Odense, Denmark
Gian Luca Salvagno, Section of Clinical Biochemistry, University of Verona, Verona, Italy
Seán J. Costelloe, Department of Clinical Biochemistry, Cork University Hospital, Cork, Republic of Ireland
Rosanna Falbo, Ultraspecialized Laboratory of Clinical Pathology and Substance Abuse, ASST Brianza-Hospital PioXI, Desio, Italy
Alexander von Meyer, Institute for Laboratory Medicine, Barmherzige Brüder Hospital, Munich, Germany
Enrico Iaccino, Department of Experimental and Clinical Medicine, University Magna Graecia of Catanzaro, Catanzaro, Italy
Francesco Botrè, Laboratorio Antidoping FMSI, Federazione Medico Sportiva Italiana, Rome, Italy; and REDs – Research and Expertise on Anti-Doping Sciences, Institute of Sport Science, University of Lausanne, Lausanne, Switzerland
Giuseppe Banfi, Vita-Salute San Raffaele University, Milan, Italy

Introduction

The negative influence of preanalytical variables on the accuracy and reliability of laboratory results is widely acknowledged within the scientific community. Nevertheless, contemporary advancements in technology and the evolving organizational landscape of healthcare systems, catalyzed by the still ongoing COVID-19 pandemic, present novel obstacles and potential avenues for enhancing the quality of laboratory testing. This collective opinion paper, which contains the abstracts of the lectures given at the two-day European Federation of Laboratory Medicine (EFLM) Preanalytical Conference entitled "New Insight in Preanalytical Quality" (Padova, Italy; December 12–13, 2025) (Table 1), provides a comprehensive overview on preanalytical errors, offers some important insights into less obvious sources of preanalytical vulnerability and proposes efficient opportunities of improvement, representing the last contribution in a series of articles written in connection with the six earlier editions of this meeting [1–6] (Table 2).

Value-score for clinical laboratories

The concepts of value-based medicine (VBM) and value-based laboratory medicine (VBLM) are attracting increasing interest in improving healthcare quality, sustainability, and safety. Laboratory medicine is well positioned to support the transition to value-based healthcare, as it contributes to improving clinical outcomes and healthcare sustainability by reducing time to diagnosis, enhancing diagnostic accuracy, providing effective guidance for tailored therapies and monitoring, as well as for supporting screening and wellness care [7]. However, the perception of the value of laboratory medicine is still limited to the extent that it has been defined as a "profession without a face", often lacking visibility to patients and the public. Following the publication of a 10-point manifesto for implementation of VBLM [8], a new EFLM initiative is to develop a value-score for clinical laboratories which is based on: (i) traceability in the total testing process; (ii) level of automation (number of manual procedures); (iii) laboratory performance on quality indicators; (iv) data management and quality of laboratory information; and (v) interaction with clinicians and multidisciplinary initiatives. Although the value of laboratory medicine continues to expand and evolve, driven by rapid technological advancements, greater efforts are needed to break down silos and enhance the visibility and integration of laboratory data into broader clinical and healthcare decision-making processes [9].

Table 1: Program of the European Federation of Laboratory Medicine (EFLM) Preanalytical Conference "New Insight in Preanalytical Quality" (Padova, Italy; December 12–13, 2025).

Friday, December 12 2025	
Sustainability and preanalytical phase	
Chairs: Alexander Von Meyer (Germany), Snezana Jovicic (Serbia), Tomris Ozben (Türkiye)	
08:45–09:00	Welcome and introduction, Mario Plebani (Italy)
09:00–09:20	"Greener" and more sustainable preanalytical phase, Sheri Scott (UK)
09:20–09:40	How can labs minimize patient blood loss? Ana-Maria Simundic (Croatia)
09:40–10:00	Good patient blood management improves cost, patient outcome and sustainability, Michael Cornes (UK)
The role of digitalization and AI in improving preanalytical phase	
Chairs: Giuseppe Banfi (Italy), Tomas Zima (Czech Republic)	
10:30–11:00	Value-score for clinical laboratories, Mario Plebani (Italy)
11:00–11:30	Patient related outcomes and cost of preanal errors, Giuseppe Lippi (Italy)
11:30–12:00	Digitalization and artificial intelligence in preanalytical phase, Andrea Padoan (Italy)
13:30–14:00	Tube transportation: Benefits, Drawbacks and Monitoring, Janne Cadamuro (Austria)
14:00–14:30	Patient and sample identification and exact time of venous blood collection, Pieter Vermeersch (Belgium)
14:30–15:00	The role of AI in preanalytical phase – use cases, Hikmet Can Çubukçu (Türkiye)
Alternatives to classical venous blood collection	
Chairs: Joao Tiago Guimares (Portugal), Klaus Peter Kohse (Germany)	
15:00–15:30	Self-sampling benefits and challenges, Alvaro González (Spain)
15:30–16:00	The future of blood collection – robotic phlebotomy and other possibilities, Mads Nybo (Denmark)
16:00–16:30	Preanalytical challenges in decentralized laboratory testing, Gian Luca Salvagno (Italy)
Saturday, December 13 2025	
Various preanalytical challenges – past, present and today	
Chairs: Dalius Vitkus (Lithuania), Pilar Fernandez Calle (Spain)	
09:00–09:30	Closing the Gap on Haemolysis, Sean Costelloe (Ireland)
09:30–10:00	Preanalytical phase in urine collection, Rosanna Falbo (Italy)
10:00–10:30	Sample stability – study design and reporting, Alexander von Meyer (Austria)
10:30–11:00	Liquid biopsy: preanalytical changes, Enrico Iaccino (Italy)
Interactive session – let us talk about preanalytics	
11:30–12:00	Roundtable: Pre-analytical challenges in anti-doping context – Discussants: Mario Plebani (Italy), Francesco Botrè (Italy), Giuseppe Banfi (Italy) Chair: Giuseppe Lippi (Italy)
12:00–13:00	Preanalytical cases – interactive session, Chair: Ana-Maria Simundic (Croatia)
13:00–13:10	Closing remarks, Mario Plebani (Italy), Alexander von Meyer (Germany)

Table 2: Title, venue and dates of the seven European Federation of Laboratory Medicine (EFLM) preanalytical conferences.

- 1st EFLM Conference on Preanalytical Phase: "Preanalytical quality improvement: from dream to reality". Parma (Italy), 1–2 April, 2011.
- 2nd EFLM Conference on Preanalytical Phase: "Preanalytical quality improvement: in quality we trust". Zagreb (Croatia), 1–2 March, 2013.
- 3rd EFLM Conference on Preanalytical Phase: "Preanalytical quality improvement. In pursuit of harmony". Porto (Portugal), 20–21 March, 2015.
- 4th EFLM Conference on Preanalytical Phase: "Improving quality in the preanalytical phase through innovation". Amsterdam (The Netherlands), 24–25 March, 2017.
- 5th EFLM Conference on Preanalytical Phase: "Preanalytical challenges - time for solutions". Zagreb (Croatia), 22–23 March, 2019.
- 6th EFLM Conference on Preanalytical Phase: "Preanalytical quality improvement - an interdisciplinary journey". Online only Conference, 15–18 March, 2022.
- 7th EFLM Conference on Preanalytical Phase: "New insights in pre-analytical quality". Padua (Italy), 12–13 December, 2025.

"Greener" and more sustainable preanalytical phase

The preanalytical phase of laboratory testing, encompasses three key elements; sample collection, handling, and transportation. This phase of the patient sample pathway is crucial for ensuring accurate and timely patient results. Current evidence presents the pre-analytical phase as a significant source of both error and carbon impact [10]. With growing concerns for the impacts of climate change on public health and healthcare delivery, the clinical laboratory is reviewing current practice and seeking new ways of working, with the key aim to improve its ecological footprint, while maintaining a quality-driven service. Clinical laboratories are implementing circular economy principles by adopting reusable and biodegradable materials for sample collection and transportation, thus reducing the volume of plastic laboratory waste progressing to landfill [11]. Laboratories are also reducing greenhouse gas emissions by utilizing energy-efficient equipment and by considering sustainable quality improvement strategies, lean processes to reduce the carbon footprint of preanalytical activities. Digital tools are being used for sample tracking and data management, reducing the need for paper, while education and training strategies are being used to promote climate health awareness, thus supporting and empowering healthcare professionals to question established norms and adopt and implement greener practices. Growing evidence presents a requirement for healthcare laboratory professions to work with clinical colleagues to develop diagnostic stewardship principles, reducing unnecessary testing [12]. By providing a comprehensive overview of current strategies and practical recommendations, it is aimed that best practice can be shared among the global clinical laboratory community. Drawing on case examples from practice, it is time to explore and share successful strategies to reduce error and waste within the preanalytical phase, further decreasing the global carbon footprint of clinical laboratories.

How can labs minimize patient blood loss?

Hospital-acquired anemia significantly affects hospitalized patients. Excessive blood collection for laboratory diagnostics is a major contributing factor outside surgical and intensive care unit (ICU) departments, leading to extended hospital stays and increased costs [13]. Implementing patient blood management (PBM) strategies is essential to mitigate these issues and improve patient outcomes. Key strategies for minimizing blood loss include demand management, the use of low-draw and capillary tubes [14], consolidation of laboratory equipment and point-of-care testing (POCT). By ensuring that only essential tests are ordered, healthcare providers can reduce the frequency and volume of blood draws. Converting to low-volume tubes and capillary tubes, remains one of the key strategies in effective PBM, and this approach helps in reducing the overall volume of blood collected from patients. Low-draw tubes are particularly beneficial in settings where frequent blood tests are necessary, such as the ICU, while capillary blood tubes are suitable for pediatric patients and those at increased risk of iatrogenic anemia [15]. Consolidation of laboratory equipment is a long-term PBM strategy, which further helps reduce the need for separate blood samples for different tests, thereby minimizing the overall volume of blood collected from patients. The benefits of implementing PBM strategies include improved patient outcomes and substantial cost savings through reducing the cost of consumables and waste management expenses. Moreover, there are also some sustainability-related benefits, such as reduced amount of plastic waste. Last but not least, through implementing PBM interventions, laboratory services can increase their operational efficiency, streamline laboratory processes, and reduce turnaround time (TAT). Reducing the amount of blood collected for diagnostic testing is ISO 15189 requirement and laboratories need (i) to have a system in place to ensure that optimal sample volume is collected from patients, (ii) to monitor and periodically review the volume of blood collected from patients, and (iii) take necessary measures to minimize patient blood loss.

Good patient blood management improves cost, patient outcome and sustainability

It has been widely reported that cumulative phlebotomy volume is an independent risk factor for hospital-acquired anemia (HAA). It has been estimated that for every 50 mL of phlebotomy volume, the risk of HAA increases by 18 %. Moreover, with modern analytical platforms and the reduced sample volume required, the volume of blood taken can be 40 times greater than the volume needed to perform the tests [16]. Despite this, healthcare providers have continued to take the same-size blood tubes for decades. It is also estimated that the healthcare sector contributes 4.4 % of global net emissions, with an excess of 14 billion kg of plastic produced each year and that 25 million liters of blood are discarded annually in the Western world, 4 times the volume transfused [17]. Considering the above, it is time for a change, and laboratories have a moral and professional obligation to work more sustainably, more efficiently, and provide better patient outcomes. The simple act of using blood tubes that are smaller than current will reduce the weight of waste plastic and blood that needs to be incinerated, will reduce the volume of blood taken from patients and hence reduce related complications, will reduce the volume of packaging and space required, will lower the carbon footprint and will be less expensive [18]. All this with no or minimal impact on the total testing process. The only obstacle to this is ensuring that blood tubes remain compatible with automation. Estimations indicate that there would be an approximate reduction of up to 45 % in the volume of waste produced with additional significant cost savings depending on local agreements. Moreover, it is estimated that the carbon footprint of phlebotomy-related plastic waste could be reduced by up to 40 %.

Patient-related outcomes and cost of preanalytical errors

It is now undeniable that preanalytical errors significantly affect the accuracy of *in vitro* diagnostic test results. Errors occurring in the manually-intensive preanalytical procedures of the total testing process may jeopardize the analytical performance, resulting in far-reaching consequences. In fact, these errors not only compromise diagnostic reliability, but can also influence clinical decision-making, leading to adverse patient outcomes and generating considerable economic burdens on healthcare systems. According to reliable literature, up to 15 % of all preanalytical errors can result in moderate to critical impacts on patient outcomes [19]. These findings are corroborated by a seminal survey published by Carraro and Plebani [20], who showed that as many as 25 % of preanalytical errors can adversely affect clinical outcomes. These consequences can range from relatively benign issues, such as the need for sample recollection, to more severe complications, such as inappropriate transfusions or unnecessary ICU admissions [20]. Besides clinical implications, preanalytical errors may also contribute to enhanced healthcare expenditures, encompassing costs related to sample redraws, repeat testing, instrument downtime, extended hospital stays, inappropriate use of invasive diagnostic procedures, and management of complications arising from errors. A comprehensive evaluation of preanalytical specimen errors in North American and European healthcare settings revealed that preanalytical errors can account for up to 0.23–1.2 % of total hospital operating costs [20]. For example, in clinical practice, the financial impact of preanalytical errors may approach $1.2 million per year for a hospital with approximately 650 beds. Specifically concerning hemolysis – the most prevalent preanalytical error – it has been estimated that hemolyzed samples may contribute to around 1.4 % of the total cost of hospital blood drawing expenditure [21]. In conclusion, the burden of preanalytical errors extends beyond their direct impact on analytical quality, representing a significant source of adverse clinical outcomes and economic strain on healthcare.

Digitalization and artificial intelligence in preanalytical phase

The preanalytical phase is a critical determinant of laboratory quality, accounting for up to 70 % of laboratory errors [22]. Artificial intelligence (AI) and digitalization have recently emerged as transformative tools that can enhance several steps of the preanalytical phase, including test requests, sample collection, handling, and reducing human and procedural errors. Among the approaches for improving test appropriateness, demand management strategies could be advanced from basic algorithms to machine learning (ML) and natural language processing models, trained using patient demographic and clinical/laboratory parameters or previous testing strategies. The utility of these tools can potentially reduce the underuse/overuse of laboratory tests. AI-driven image recognition and machine learning algorithms can detect in real-time improper sample labeling, hemolysis and clotting, ensuring early error management before sample processing, lowering the risk of diagnostic errors. Moreover, delta-check technology can be modified by

incorporating advanced models with better performances based on hematological and/or biochemical tests. Despite that, AI implementation in the preanalytical phase faces several challenges, many of which remain unresolved. The variability of preanalytical collection conditions and the lack of standardized methods to evaluate these parameters limit the development and integration of AI algorithms into laboratory routines. Datasets not promptly collected for AI applications (or simply clinical data are not available to laboratory professionals) and misuse of information could also lead to ineffective models [23]. Integration complexities with existing laboratory information systems (LIS), poor informatics capabilities and lack of cloud computers also limit widespread adoption of AI, as recently found in an EFLM survey on 195 participants from laboratories across Europe [24]. Finally, ethical concerns, including data privacy and potential biases in AI algorithms, raise issues regarding the management of patients' data and regulatory compliance.

Monitoring sample transport condition and innovative tools

A shortcoming of laboratory diagnostics, from the clinician's point of view, is the time from test order to result availability. When analyzing the cause hereof, the process that contributes the most to prolonged TAT is sample transport, especially in larger healthcare settings [25]. Suggestions to improve the TAT are manifold, one of which is the transport via pneumatic tube systems (PTS). Although PTS transportation may drastically shorten the TAT, concerns regarding sample quality due to potential trauma must be acknowledged. Depending on several variables, sample integrity might be influenced (e.g., by hemolysis), including the subsequent bias in test results [26]. These variables include the length and speed of the PTS, the distribution centers, curves, acceleration and deceleration, as well as the type of exit from the PTS, the analytical methods, the laboratory analyzers, sample pre-processing and reagents used for testing. Approaches to reduce mechanical trauma include lowering the speed or wrapping the samples into a suitable insert within the PTS tube [27]. According to the ISO 15189:2022, *the laboratory shall establish and periodically evaluate the adequacy of sample transportation systems*. This task may seem easier than it really is. Data loggers that can monitor acceleration, temperature, humidity, and pressure may be used, but the above-mentioned variables may differ substantially, even within the same hospital, PTS line or even time of day. Hence, findings from published studies on sample transport and its effect on sample integrity cannot be directly adopted into the local setting. Laboratories need to perform their own validation studies, simulating as many different transportation scenarios as possible, including a periodic re-evaluation. Ideally, the laboratory should participate in an external quality assessment (EQA) scheme on sample transport. Although regulations on the obligations of laboratories with regard to sample transportation are already in place, recommendations on how to comply with these are still missing.

Patient ID, sample labelling and time of collection – Pieter Vermeersch (BE)

Patient and sample misidentification are recognized as important causes of avoidable serious patient harm in healthcare. National and international standards such as ISO 15189:2022 require unequivocal patient and sample identification and "identification errors" is one of the most frequently monitored laboratory key performance indicators together with turn-around-time, and hemolysis rate [28]. Although the prevalence of identification errors in clinical laboratories is relatively low (≤0.1 % of samples) and most errors are identified before results are reported, the potential adverse consequences are serious with an estimated 10–20 % of these errors resulting in serious patient harm [29]. Detecting identification errors remains one of the most challenging tasks in laboratory medicine. Point-of-care testing poses a particular challenge in this regard. Lack of accurate knowledge of the time of venous blood collection, in contrast, is not generally considered a significant problem. The ISO 15189:2022, for example, only requires "recording of the collection date, and, when relevant, recording of the collection time" even though knowledge of the time of venous blood collection is essential to verify analyte stability and can be clinically important for result interpretation. An EFLM survey in 2017 found that 70 % of participating laboratories did not have information about the exact blood collection time upon receiving samples [30]. Most laboratories also fail to monitor the TAT from the time of sampling, but rather from the time of sample reception. The use of digital solutions such as patient identification bands for inpatients and outpatients, pre-barcoded tubes and a computerized physician order entry (CPOE) system that can establish an unequivocal link between the patient, the order and the tubes and record the exact time of sample collection are solutions that could help reduce the risk of misidentification and improve quality in the preanalytical phase.

The role of artificial intelligence in preanalytical phase – use cases

The preanalytical phase of clinical laboratory testing, encompassing processes from test ordering to sample preparation, is highly susceptible to errors that can compromise patient safety. AI and ML have emerged as powerful tools to address these vulnerabilities, with several use cases reported in the literature and implemented in commercial products [31]. Neural networks have been successfully employed for clot detection in coagulation testing with high accuracy, leveraging standard coagulation parameters. Similarly, various ML models, including extreme gradient boosting and deep learning techniques, have shown superiority over traditional methods in identifying specimen mix-ups and wrong blood in tube errors using complete blood count data and chemistry analytes. Beyond error detection, AI has been applied to optimize sample dilution in specialized assays, identify chemical manipulation in urine samples, and automate the assessment of serum quality by classifying hemolysis, icterus and lipemia. Moreover, AI-driven approaches are being explored to improve test utilization and ordering, reducing unnecessary tests and ensuring appropriate investigations [32]. Robotic systems integrating convolutional neural networks are also showing promise in automating tube handling and labeling, minimizing manual errors [33]. The translation of these research findings into commercial solutions is evident in several innovative products. Autonomous phlebotomy devices use AI-powered imaging for precise vein detection, improving first-stick success rates. Advanced optical character recognition enhanced with ML is used to digitize handwritten orders, reducing transcription errors. Intelligent preanalytical automation platforms incorporate AI for comprehensive specimen checks, including volume, barcode matching, and clot detection, as well as dynamic sample routing. POCT devices use AI to detect hemolysis. Moreover, AI-based clinical decision support systems assist in optimizing test ordering and flagging potential anomalies. These different applications underscore the transformative role of AI in enhancing efficiency, reducing errors, and ultimately improving the quality of laboratory diagnostics in the preanalytical phase.

Self-sampling benefits and challenges

Capillary blood is routinely used in POCT and neonatal screening. Capillary blood collection has several advantages over venous blood, such as being minimally invasive and, as a self-sampling procedure, does not require trained staff. It could be particularly beneficial for patients with difficult venous access, fragile blood vessels, or those who need frequent testing. It may also improve the availability of healthcare in certain areas or for patients with difficult access to phlebotomy centers. In addition, there are lower costs associated with the overall blood collection process. In recent years, capillary blood testing has been increasingly used in direct-to-consumer laboratory testing, usually associated with lifestyle or sports [34]. However, its integration into routine healthcare in clinical laboratories remains limited. To achieve this, results and reference ranges should be similar or comparable between capillary and venous blood. Several articles suggest that many routine measurands render similar results [35]. However, some important pre-analytical issues need to be addressed to ensure sample quality. Appropriate collection techniques are essential to obtain sufficient volume for analyses and to minimize the risk of hemolysis and contamination. Thus, it is crucial to have a robust and standardized extraction device [36]. Correct sample identification, stability and traceability should be ensured throughout the process. In addition, sample tubes received in clinical laboratories should be compatible with the fully-automated analyzers introduced in the routine, avoiding manipulation or pipetting. These analyzers should be adapted to the new types of samples, in particular by reducing the dead volume. Although extensive efforts are still needed from laboratory and *in vitro* diagnostics industry, the use of capillary blood will undoubtedly bring enormous benefits to the healthcare system and patients and will change some paradigms of clinical care.

The future of blood collection (robotic phlebotomy)

Phlebotomy plays a crucial role in clinical diagnostics, but unfortunately, the availability is challenged by the increased demands and shortage of phlebotomists. Alternative sampling possibilities are therefore increasingly being considered, among these self-sampling, sampling at general practitioners, and the use of robots. The latter has been studied for years [37], but due to technical and psychological barriers, only one study has evaluated an automated ultrasound-guided phlebotomy device in humans [38]. In recent years, a number of possible devices have emerged, but only one has been CE-marked and is available for a clinical setting so far. At present, a multicenter study on this

device is under publication and will hopefully elucidate strengths and limitations. Importantly, there are also a number of possible caveats and challenges, mainly psychological and organizational matters, to deal with.

Preanalytical challenges in decentralized laboratory testing

Decentralized laboratory testing, encompassing POCT, near-patient testing (NPT) and patient self-testing (PST), refers to laboratory diagnostics performed at or near the site of patient care. Decentralized laboratory testing represents an emerging boundary in laboratory medicine, offering the potential to enhance accessibility and reduce TAT for clinical laboratory results in both high-income and low-to-middle-income countries [39]. Despite these advantages, the expansion of decentralized laboratory testing necessitates careful oversight to prevent unregulated implementation. Establishing appropriate clinical governance, particularly in managing the preanalytical phase, is essential. The preanalytical phase is particularly vulnerable to errors, primarily due to a lack of standardization, with reported error rates ranging from 60 to 70 % [40]. The introduction of decentralized laboratory testing presents novel preanalytical challenges that can significantly affect the accuracy and reliability of laboratory results, many of which remain insufficiently explored. A comprehensive evaluation of critical preanalytical factors – including patient preparation and identification, sample collection, handling, storage, and transportation – is imperative. Blood sample collection, particularly capillary sampling, requires meticulous attention to device selection and technique to minimize variability and error [41]. Implementing quality indicators is essential for assessing performance and identifying primary error sources within the preanalytical phase. Moreover, evaluation and enhanced training of personnel involved in delocalized sample collection are crucial, ensuring that the staff conducting tests outside traditional laboratory settings possesses the necessary competencies. Key challenges in decentralized laboratory testing also include ensuring accurate patient identification and preparation, maintaining sample integrity across diverse testing environments and providing sufficient training for non-laboratory personnel. Ultimately, the establishment of standardized protocols and rigorous quality control measures is vital to ensuring the reliability of decentralized laboratory testing results and optimizing patient care outcomes [41].

Closing the gap on hemolysis

Hemolysis can erroneously impact laboratory results and compromise patient care [42]. Effective detection, monitoring, and mitigation of hemolysis is not uniform across European medical laboratories [43], as there are several key barriers to implementation. Firstly, laboratories may use subjective and inaccurate visual inspection to detect and quantify hemolysis, even in some cases, where spectrophotometric or digital image-based methods are locally available. Secondly, transforming hemoglobin concentration from automated methods into ordinal hemolysis indices (OHI) compresses a continuous spectrum of severity in limited broad categories. Using OHI can limit the application of exact assay-specific tolerances, resulting in the withholding of analytically valid results. Moreover, technological or operational factors may prevent routine hemolysis detection and categorization across all relevant assays or testing locations, such as NPT. In addition, hemolysis indices are not always subject to internal quality control or EQA. Laboratories do not always monitor hemolysis rates across requesting locations or communicate identified issues to stakeholders. The ISO15189:2022 highlights rigorous risk assessment and management, reinforcing the need for proactive control of preanalytical risks such as hemolysis as part of the laboratory quality management system [44]. Finally, laboratories face an evidence gap when implementing, verifying, or validating hemolysis cutoffs for use in management processes. Manufacturer-provided information on the magnitude and direction of hemolysis interference is often insufficient and rarely considers the full range of hemolysis severity encountered in routine service. Therefore, laboratories may rely on potentially overly conservative manufacturer thresholds, consult (or await) peer-reviewed guidance, or conduct independent validations. Depending on the study design, the latter is resource-intensive, expensive, and requires insight into the specific mechanism(s) of hemolysis interference for the analyte under consideration, which may be poorly understood. Closing these gaps requires coordinated input from manufacturers, EQA providers, and the broader professional community to improve analytical quality and patient outcomes.

Preanalytical phase in urine collection

In an effort to improve urinalysis preanalytics, the EFLM Urinalysis Guideline 2023 [45] affirms the need to support

physician requests for urinary tract infections (UTIs) and non-infectious kidney or urological disorders with medical evidence. The quality and cost-effectiveness of urine tests should be addressed through strategic discussions on suitable routine and special workflows. Patients must be empowered to learn how to obtain the highest quality specimens possible and actively participate in the diagnostic decision-making process. Laboratories must provide guidance on how to control posture, diuresis and physical activity [1, 45]. The reported urine density aids in evaluating the given concentrations (particle analysis, chemistry). Additionally, laboratories must provide instructions on how to physically prevent contamination, using a goal of less than 15 % polymicrobial growth in urine culture at 10^4 colony-forming units (CFU)/mL (10^7 colony-forming bacteria (CFB/L)) as a quality indicator at the laboratory level. This will determine a continuous reduction of non-diagnostic specimens. Urine specimen collection methods, such as single catheterization, suprapubic aspiration, or post-operative urostomy, should be reviewed with healthcare professionals. A novel method for urine collection in infants is the Quick-Wee [46]. General requirements are proposed for containers used for urine collection and transportation. End-user must be informed about the proper use of disposable primary containers and the steps involved in transferring the specimen into the secondary container. Microbial contamination should be prevented in the parts of the container and its cap that come into contact with the urine sample. To evaluate the acceptability of specimens in the laboratory and clinical units, electronic hospital and regional information systems must allow the recording of the actual time of urine collection. The EFLM Guideline specifies procedures for specimen preservation during transportation, and criteria for successful preservation are given [45]. Non-preserved specimens should be analyzed within 2–6 h after voiding.

Sample stability – study design and reporting

Sample stability is a critical factor in ensuring the accuracy and reliability of laboratory results, yet historically, it has been a significant source of variability due to the lack of standardized methodologies. The EFLM Working Group for the Preanalytical Phase (WG-PRE) addressed this challenge through the Checklist for Reporting Stability Studies (CRESS) initiative, a comprehensive framework designed to standardize and harmonize stability study design, reporting, and evaluation. The CRESS initiative provides three key manuscripts for stability studies. The first CRESS manuscript introduced a checklist for reporting stability studies, ensuring transparency and comparability across publications [47]. The second provided a practical guide for conducting high-quality stability studies, detailing methodology, sample handling and data analysis [48]. The last manuscript established a structured approach to evaluate and grade published stability studies based on 20 criteria, with weighted scoring to assess study quality [49]. The implementation of CRESS will significantly improve the quality of stability data, enabling laboratories to make evidence-based decisions tailored to their local settings. By creating a centralized database of graded stability information, the initiative aims to enhance patient safety through reliable laboratory results.

Liquid biopsy: preanalytical changes

Liquid biopsy is emerging as a powerful tool in clinical diagnostics, offering non-invasive access to molecular biomarkers for cancer and other diseases. Among its components, extracellular vesicles (EVs) – nanosized particles released by cells – stand out for their role in intercellular communication and their rich cargo of proteins, nucleic acids, and lipids. However, the clinical translation of EV-based liquid biopsy remains limited, largely due to preanalytical variability undermining result consistency and reliability [50]. These errors – arising during sample collection, handling, storage and processing – can significantly compromise EV integrity and yield. Improper blood draw techniques, delayed processing, or inadequate storage may lead to EV degradation, contamination by non-vesicular particles (e.g., lipoproteins), or artificial vesicle aggregation. Such factors obscure biomarker detection and reduce diagnostic sensitivity and specificity. Variability in centrifugation protocols, anticoagulant choice, and isolation methods further exacerbate inconsistencies, limiting inter-laboratory reproducibility and clinical confidence. As a result, the integration of EV assays into routine workflows remains slow [50]. Addressing these challenges requires automation of EV purification and characterization. Automated platforms – such as microfluidic devices or robotic systems – minimize human error, ensure consistent sample handling, and reduce contamination risks [51]. Likewise, high-throughput technologies such as automated flow cytometry, single-particle analysis, and advanced imaging can standardize the profiling of EV subpopulations, each with distinct biological roles and biomarker signatures [52].

These innovations enhance reproducibility, scalability and diagnostic accuracy. In parallel, the adoption of universal preanalytical guidelines – defining variables such as sample type, collection tubes, and processing timelines – will help harmonize procedures across institutions. In conclusion, minimizing preanalytical variability through automation and standardization is key to unlocking the full clinical potential of EV-based liquid biopsies. These advancements will strengthen biomarker reliability and accelerate their adoption in diagnostics and personalized medicine.

Preanalytical challenges in anti-doping context

Preanalytical challenges in the anti-doping context offer substantial hurdles to ensuring the integrity, reliability and reproducibility of antidoping tests [53]. The preanalytical phase, which is especially vulnerable to errors, may introduce variability in biological matrices, potentially leading to deviations in analytical test results and complicating interpretation or even abrogating the validity of doping test outcomes [54]. A key concern in this context is the heterogeneity of the biological matrix used for testing. Factors such as unvoluntary contamination, hydration status, circadian rhythms, metabolic rate, strenuous exercise and inter-individual physiological variations can influence the concentration of several analytes in urine and blood samples. Environmental conditions such as temperature fluctuations, humidity, and light exposure can also contribute to degrading substances or altering sample composition, leading to false-positive or false-negative test results [54]. The lack of standardized preanalytical procedures across different anti-doping laboratories and jurisdictions further exacerbates these challenges. Although international organizations such as the World Anti-Doping Agency (WADA) have established practical guidelines, disparities in adherence, sample handling protocols and analytical methodologies remain. Nevertheless, the constantly evolving nature of doping strategies – marked by the emergence of novel performance-enhancing substances and techniques – necessitates continuous innovation in both preanalytical and analytical methodologies. Therefore, addressing preanalytical challenges in anti-doping necessitates a multifaceted approach, combining improved standardization of sample collection, handling and storage, continuous education and training of antidoping agents and implementation of innovative technologies, such as AI-assisted analysis, which may further strengthen the reliability of doping test results [54, 55]. Ultimately, ensuring the integrity of anti-doping tests is essential for maintaining fairness in sports, but also for protecting athletes' rights and public trust in the global anti-doping framework.

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