Review Article

How do we use the data from pre-analytical quality indicators and how should we?

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Abstract: It is impossible to imagine a modern medical laboratory without a structured quality management system in place. Nevertheless, this system usually focuses mostly on the analytical part of the total testing process (TTP), despite being aware of the fact that most errors occur in the pre- and post-analytical phases. There are many reasons possibly explaining this fact, one of them being that extra-analytical processes are hard to grasp, since they occur mostly outside of the laboratory and include many different parties. Despite these obstacles, it is mandatory to keep all steps of TTP, potentially influencing the analytical test result or their interpretation, under meticulous quality control and to improve them as much as possible, involving all health care workers contributing to sample quality. Additionally, it is necessary to collect and evaluate all data in a standardized manner, not only within one laboratory, but nationwide and internationally. This is a perquisite for valid data comparison over time (trend analysis) and benchmarking, the basis for threshold definition and continuous improvement. A widely accepted method to meet all these requirements is the concept of quality indicators (QIs). In this review, we provide an overview over this topic and we discuss an easy to use and freely available tool, aiming to aid laboratories in data collection and comparison: The QIs project of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) Working Group on "Laboratory errors and patient safety" (WG-LEPS). Additionally, we provide practical suggestions on how to successfully implement QIs within any laboratory.

Keywords: Pre-analytical phase; total quality management; quality indicators (QIs); standardization

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Introduction

Safety authorities estimate that about 251,000 patients die every year in the U.S. due to medical errors (1). Comparing this estimation with the respective ranking of the Centres for Disease Control (CDC), make medical errors the third most common cause of death in the U.S. Other authors also highlight the severity of medical errors contributing to patient mortality (2-4). Most studies conclude that beside mistakes in medication and treatment, diagnostic errors are a leading cause of error. Singh *et al.* estimate the rate of diagnostic errors in US out-patients as high as 5.08%, equating to approximately 12 million U.S. deaths per year (5). Bhasale *et al.*, who collected data on incidents of potential or actual harm to general practice patients in Australia, concluded that 34% of all incidents were related to diagnostic errors (6). Although the most common cause in diagnostic incidents might seem to be the missed diagnoses, many other mainly pre- or post-analytical reasons, such as failure in information transfer, poor communication,

specimen collection errors, and even wrong laboratory results, are contributing largely to these numbers (7). This underlines the known fact that only about 15% of errors of the so-called TTP occur in the analytical phase. Of all errors, 62% and 23% take place in the pre- and post-analytical phase, respectively (8). Laboratory test results contribute to the majority of diagnoses and clinical decision making in most health care settings (9). However, there is sparse valid data on the relationship between the laboratory testing process, including pre- and post-analytical errors, and harm related to diagnostic error.

According to a recent OECD (Organization for Economic Co-operation and Development) study, 15% of hospital expenditure and clinical activity in OECD countries can be attributed to treating safety failures (10). Beside other common adverse events, some of the most burdensome include wrong or delayed diagnoses. The annual cost of common adverse events in England is equivalent to 2,000 general practitioners or 3,500 hospital nurses.

These facts indicate that the diagnostic process and the extra-analytical phases hereof in particular need to be improved. Improvement may not only be a financial matter, as costs of prevention typically tend to be far less than the costs of harm, but mostly a concern of patient safety.

Where are we now?

One reason for the above-mentioned fact that a minority of errors within the TTP occur in the analytical phase, is that process steps within this phase usually are under strict quality control. Laboratories are required to adhere to international consensus standardization guidelines such as the EN-ISO 15189 (11), the EN-ISO 17025 (12), the EN-ISO 9001 (13), or to national regulations, such as the German RiliBÄK (Richtlinie der Bundesärztekammer zur Qualitätssicherung laboratoriumsmedizinischer Untersuchungen) (14). Internal (IQA) and external quality assessments (EQA) are an obligatory standard in each laboratory, including defined thresholds (15) and Standard Operating Procedures (SOPs) on causative investigation and further action upon deviation. Additionally, analytical processes are supervised by only few, well-trained health care workers and all processes take place in one single institution: the laboratory.

The exact opposite is true for most extra-analytical process steps. These occur in many different places, mostly outside of the laboratory, involve many parties, such as patients, clinicians, nurses or sample carriers, and include many influencing variables, for instance (16): test selection (17), a process step also referred to as the pre-pre-analytical step (18), patient medication and fasting state, including the time of phlebotomy (19), patients' potential physical activity prior to blood collection (20,21), patient posture during phlebotomy (22,23), biological variability (24-26), as well as sample storage and transport conditions (27,28). Additionally, two of the most frequent pre-analytical errors relate to patient identification errors (29-31) and haemolysed samples (32-35). Reasons for the latter are endless: IV-catheter collection (36), tourniquet time (37), type of collection tube (38), education state of the phlebotomist (39), pneumatic tube transportation (40,41), centrifugation conditions (42), etc. Note that all these influencing factors apply mostly or exclusively to venous blood samples. Covering sample types such as blood cultures (43), cerebrospinal fluid (44), urine (45), body fluids (46) or other samples would go far beyond the scope of this review and are partly covered in separate articles in this issue of the *Journal of Laboratory and Precision Medicine*.

Another reason for errors occurring more frequently in the extra-analytical phases of the TTP is the fact that despite phlebotomy guidelines (47-51) and the EN-ISO 22870 for Point of Care Testing (POCT) (52), quality management in the these phases, including defined goals and regulations, are scarce, since respective literature in this field is limited. Even if guidelines are available, these regulations are often not known or not adhered to (53-55).

Imagining that guidelines would exist for every pre-analytical step and further assuming that these recommendations would be adhered to, there still is no consensus on how to measure the quality of the respective process steps. These metrics, however, are mandatory to properly monitor and react to deviations. Already in the early 1940s W. Edwards Deming proposed the concept of continuous improvement by endlessly repeating four simple steps: Plan – Do – Check – Act (PDCA cycle) (56). If you remove one of these steps, for example the monitoring part (Check), the whole system of improvement collapses. The EN-ISO 15189 standard requests laboratories to improve quality in a similar way (11), by demanding them to develop plans to implement improvement and to monitor and document the quality of pre-examination-, examination and post-examination procedures (57). Based on a quote of Robert S. Kaplan, the inventor of the Balanced Scorecard, one could summarize: you cannot manage/improve what you don't measure.

How can we improve?

Similar to the analytical phase, we are in need of IQA and EQA schemes for the extra-analytical part of the total testing process (TTP). Measurement of haemolysis, icterus and lipaemia, so called HIL-indices, is a good example. Many modern high-throughput laboratories are using automated methods, so called serum indices, to detect these pre-analytical influencing factors (58). Subsequently these measurements are used to validate the test results from the respective sample by defining the material as haemolytic, lipaemic or icteric, eventually deleting specific parameters from the report or even cancelling the entire report (59). However, up to this date there are no commercial quality controls available for either of these index measurements. Thankfully, at least more and more EQA programs are currently evolving for serum index measurements.

Even if adequate IQA schemes for serum index analyses would exist, laboratories are still required to control and improve the quality of the remaining steps in the pre- and post-analytical processes. Unlike the serum indices, these steps can't be quantified by analytical procedures. Hence, other metrics are necessary. One possibility are so called Key Performance Indicators (KPIs) (60). They are derived from lean management, a concept originally developed by the car manufacturer Toyota, subsequently adapted and applied to a variety of industries including healthcare and medical laboratories (56). KPIs are a way of quantifying errors within any system and may be applied to a variety of processes within any organization, such as production (analytics), finances, customers, employees, etc. Within the pre-analytical phase, KPIs could be measurements of the amount of misidentified samples, or the amount of wrong sample containers. However, retrieving such KPIs may create a huge workload. Therefore, it is of utter importance to define the requirements of KPIs beforehand, asking the following questions:

- What do I intend to do with the outcome of the KPI?
- Does the outcome help in improving the quality of my process?
- How easy will it be to measure the KPI?
- How often has the KPI to be measured in order to be of value?
- Who is going to measure the KPI or is it possible to automate it?
- What are the desired thresholds for acceptable performance of the KPI?
- How often will the KPI be evaluated and who performs these evaluations?
- What actions will be taken upon deviation from defined goals?
- Is the KPI comparable to those of other laboratories?

The key to successful implementation of KPIs, in order to monitor and improve the quality of extra-analytical process steps, is to standardise their retrieval and evaluation similar to SOPs in the analytical phase of the testing process. Hence, KPIs have to be consistent, meaning they have to be gathered always in the same manner on a regular basis (daily, weekly, monthly, quarterly), in order to spot trends and deviations at an early stage. Outcomes of KPIs have to be communicated properly internally within the laboratory staff and externally whenever necessary for improvement. Finally, the best KPI is of minor use if it is not comparable. Take haemolysis measurement as an example. The variety of instruments, measuring haemolysis indices and reporting them either in a dichotomous, ordinal or in continuous way, combined with the heterogeneity in defining a cut-off for haemolytic specimen, makes comparisons between laboratories difficult, if not impossible (61). Subsequently, a single laboratory will not be able to define an e.g., 3% haemolysis rate at a cut-off of 0.3 g/L of free haemoglobin, measured on a COBAS instrument as high or low quality. Consequently, laboratories measuring KPIs for the extra-analytical phases need to do so in the exact same manner.

What tools do we have?

To monitor the quality of laboratory processes, KPIs are being used in the analytical process for a long time, referred to as quality indicators (QIs) (62-65). Such QIs might be performance criteria regarding IQA or EQA measurements or the implementation of new assays to match clinical requirements. As the importance of standardization of the neglected extra-analytical part of laboratory testing became evident, these QIs were later applied to the pre- and post-analytical phases (18,66). However, although the EN-ISO 15189 standard for medical laboratories requires the implementation of QIs for all stages of the TTP, no consensus exists to this date.

The Education and Management Division (EMD) of the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) has established a Working Group on "Laboratory errors and patient safety" (WG-LEPS), whose mission it is to stimulate studies on the topic

Table 1 Quality indicators concerning key processes as proposed by the IFCC WG-LEPS (69)

Pre-analytical phase
Misidentification errors
Inappropriate test requests
Test transcription errors
Unintelligible requests
Incorrect sample type
Incorrect fill level
Unsuitable samples for transportation and storage problems
Contaminated samples
Hemolyzed sample
Clotted samples
Inappropriate time in sample collection
Intra-analytical phase
Test uncovered by an IQC
Unacceptable performances in IQC
Test uncovered by an EQA-PT control
Unacceptable performances in EQA-PT schemes
Data transcription errors
Post-analytical phase
Inappropriate turnaround times
Incorrect laboratory reports
Notification of critical results
Interpretative comments

IFCC, International Federation of Clinical Chemistry and Laboratory Medicine; WG-LEPS, IFCC Working Group on "Laboratory errors and patient safety".

or errors in laboratory medicine, to collect available data on this topic, and to recommend strategies and procedures to improve patient safety (67). One of the projects of the WG-LEPS is aiming to harmonise the use of QIs in laboratory medicine, thereby closing the mentioned gap of a missing consensus on what and how to measure (68). In order to do so, the WG-LEPS has proposed and revised a model of quality indicators (MQI) for pre-analytical, intra-analytical and post-analytical processes (*Table 1*), all categorized in distinct priority levels, including guidelines on how to measure them (16,18,69). Additionally, the working group implemented an online platform (http://www.ifcc-mqi.com) for laboratories to document respective QI-measurements from their site, thereby providing an easy solution for intra-laboratory trend analyses as well as for national and international benchmarking. As performance criteria this model suggests using the 25th and 75th percentile of the QIs data collected during the previous year as limits for individual laboratory evaluations (69). An individual result lower than the 25th percentile of value distribution, would then represent a performance of high quality, results between the 25th and 75th percentile would be of medium and those above the 75th percentile of low performance.

Additionally, there are some separate projects with similar intentions. In the US, for example, laboratories have the possibility to participate in a College of American Pathologists' (CAP) Q-Tracks program, in which participants are required to collect data on seven extra-analytical errors according to defined methods (70). In Australia, the "Key Incident Monitoring and Management System" (KIMMS) started in 2008. Using this system, laboratories are able to document eighteen pre-analytical and three post-analytical incidents (process defects) and episodes (occasions at which incidents may occur) and to calculate individual incident rates. This system further uses the Failure Mode Effects Analysis (FMEA) to assign quantified risk to each incident type (71). In Germany and Austria, a database solely for haemolysis data has been introduced in the end of 2017 (https://www.rfb.bio/cgi/haemolysisLogin), making it possible to perform ward specific trend-analyses and national and international comparisons, similar to the MQI project of the WG-LEPS.

Are these tools used?

Despite the criteria defined by the EN-ISO 15189 (*[…]the laboratory shall establish QIs to monitor and evaluate performance throughout critical aspects of pre-examination, examination and post-examination processes[…]*) and the availability of some standardised QIs, including a guideline on how to measure them, the number of clinical laboratories participating in benchmarking programs is rather limited. This gap led to the term "quality indicators paradox" (72). The best and easiest system is not of much use if it is not utilized.

To overcome the paradox, a series of initiatives have been promoted. In particular, the European Federation of Laboratory Medicine (EFLM) has established a Task Force on "Performance specifications for the extra-analytical phases" (TFG-PSEP) with the aim of identifying reliable performance specifications for the extra-analytical phases.

The first initiative of the TFG-PSEP was to survey clinical laboratories on the use of extra-analytical phase QIs (73). 98.7% of respondents believed extra-analytical QIs to be important and 90.1% indeed had one or more QIs implemented in their laboratory. However, the number and types of QIs varied significantly across laboratories and only 17.5% of participating institutions used the standardised QIs provided by the WG-LEPS, making it hard, if not impossible to benchmark performance properly. While nearly all of the responding laboratories were aware of the fact that the EN-ISO 15189 requires the implementation of QIs also for extra-analytical steps of the TTP, only 52% knew of the initiative of the WG-LEPS and the respective website. As the main reason for not collecting QIs, respondents of the survey mostly mentioned the lack of a laboratory information system (LIS) to support data collection. First approaches to overcome this issue have already been undertaken (74).

Outcome studies of data from laboratories participating in the MQI project seem promising, despite variability amongst laboratories concerning some QIs (75-77). However, additional efforts need to be undertaken to ensure that more clinical laboratories are participating in this important strive for standardization and improvement. In order to define a roadmap for harmonization of QIs, the IFCC WG-LEPS and the EFLM TFG-PSEP have published a consensus document, including the revised MQI as well as planned future achievements (69). Amongst other targets, the consensus document seeks the involvement of national scientific societies, accreditation bodies and EQA providers of different countries, as means for disseminating the MQI project. In addition, a "national coordinator" shall be appointed, coordinating and managing the MQI project in each country (69).

In the US Q-Track project the number of laboratories, some of them participating as long as 18 years, varies between 97 and 159, depending on the QIs they subscribed to (70). In the Australian KIMMS, 69 laboratories were participating by 2016. The system is holding data from over 200 million episodes and a total incident count for the QIs measured of 2.9 million (71). The comparably young German/Austrian haemolysis database collected about 2.3 million datasets from 20 laboratories so far and will hopefully be further expanding.

To elaborate more on the question how European laboratories handle pre-analytical quality and whether respective QIs are measured and evaluated periodically, the EFLM Working Group on the Preanalytical Phase (WG-PRE) has issued a survey among EFLM countries, whose first results will be published in the near future.

How should QIs be used?

As mentioned above, establishing QIs to monitor and evaluate performance throughout the TTP is mandatory to ensure quality management. As there is no consensus document detailing the process of QI implementation, we want to provide a list of proposals on how introduce pre- and post-analytical QIs into a medical laboratory:

- First, select QIs according to your needs, answering the questions in the section "How can we improve?" Additionally, take the priority level from the MQI project into account of each QI (69). Those QIs ranked as top priority are considered as mandatory by the WG-LEPS and the TFG-PSEP.
- Try to standardise and automate the collection of your QIs within your LIS. In case the LIS does not support an automated QI collection or the data are not available in the LIS, a respective software, fitting the IFCC MQI project standards was recently introduced and is freely available (74).
- Appoint staff members responsible for collection and evaluation of QI data.
- Implement a documentation system allowing you to properly evaluate QIs over time (e.g., by using a Levey-Jennings-plot or similar). Since such a system already is in place (http://www.ifcc-mqi.com), we highly recommend using this platform, as it allows you to compare individual QIs nationally and internationally.
- Define performance specification thresholds for each QI. If participating in the MQI project, criteria from the annual evaluation of data of all participating laboratories may be used. Derived from these data the 25th and 75th percentiles are calculated as respective thresholds for the following year (69). Preliminary results of these calculations from the past years were recently published (75,76).
- Define schedules after which QIs are evaluated on a regular basis (daily, weekly, monthly, quarterly, etc.), including an automatic notification system.
- Evaluate your data on:
  - Threshold limit violations;
  - Trends (is the QI worsening within my threshold limits?);
  - Comparison of your data nationally and internationally.

These evaluations should be performed as an overall analysis. Additionally, ward-specific sub-analyses may be necessary for distinct improvement efforts [e.g., amount of hemolyzed samples from wards collecting blood through IV catheters (36)].

- Define which actions should be taken upon exceeding the defined thresholds, following a PDCA cycle. For example, if haemolysis rates or identification errors worsens on a single ward, employees of this ward might benefit from an educational intervention. If the turn-around-time (TAT) worsens, sub-analysis of all respective timestamps would be necessary, to identify the process step where time is lost. The respective part of the process then will need to be reviewed and altered accordingly.
- Document all of the above points in a SOP and communicate them to all involved parties within and outside of the laboratory.

A well-organized medical laboratory is comparable to a well-designed web portal like Google. It is very plain and concise to the customer/clinician, showing exactly what is asked for in a high quality and as fast as possible, but very complex in the backend. Despite the fact that the laboratory usually only gets attention when it breaks down, laboratory specialists often report that clinicians or nurses are deeply impressed when getting a peek behind the curtain, realizing the available medical diagnostic expertise and all the highly organized and standardized processes, including quality management. Another similarity is the fact that whatever you put into the process has a major impact on the outcome ("garbage in – garbage out"). For medical laboratories, this means that the test result is just as good as the quality of the sample it was obtained from. When having in mind that 85% of errors within the TTP occur in the extra-analytical phases (8), one should assume that laboratories are eager to keep these parts under meticulous quality control. Interestingly, the opposite is the case, although the awareness about its need is evident and respective tools are freely available—expanding the "Quality indicator paradox " (72). Despite all reasons for this fact, laboratories need to take action immediately and start implementing internal quality control schemes to the pre- and post-analytical processes as soon as possible using standardized QIs, involving all parties contributing to these processes.

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Footnote

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