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Opinion

Quality in laboratory medicine: 50 years on

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ABSTRACT

The last 50 years have seen substantial changes in the landscape of laboratory medicine: its role in modern medicine is in evolution and the quality of laboratory services is changing. The need to control and improve quality in clinical laboratories has grown hand in hand with the growth in technological developments leading to an impressive reduction of analytical errors over time. An essential cause of this impressive improvement has been the introduction and monitoring of quality indicators (QIs) such as the analytical performance specifications (in particular bias and imprecision) based on well-established goals. The evolving landscape of quality and errors in clinical laboratories moved first from analytical errors to all errors performed within the laboratory walls, subsequently to errors in laboratory medicine (including errors in test requesting and result interpretation), and finally, to a focus on errors more frequently associated with adverse events (laboratory-associated errors). After decades in which clinical laboratories have focused on monitoring and improving internal indicators of analytical quality, efficiency and productivity, it is time to shift toward indicators of total quality, clinical effectiveness and patient outcomes.

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1. Introduction

Over the past 50 years, the clinical laboratory and its professionals have been facing the challenges of rapid technologic development, scientific advances, and the changing medical landscape of disease as well as the approach to diagnosis and therapy. Although founded centuries ago, laboratory medicine is a relatively young as an academic discipline, being established in the early twentieth century, and only after the Second World War were modern clinical laboratories established. [1]. The famous song by Bob Dylan "The times they are a-changing" aptly evokes the rapid growth and the dramatic changes seen in the discipline over the last 50 years. Laboratory testing, originally practiced in small laboratories with few manual tests performed, now calls for highly automated and integrated facilities performing millions of tests every year.

2. Technological advancements and quality improvement: progress in tandem

The evolving landscape of clinical laboratories affects not only the menu and volume of tests, but also their accuracy and the quality of laboratory information. The major developments in instrumentation, including automation [2], introduction of computers [3], use of monoclonal antibodies and of polymerase chain reaction (PCR) [1], which has brought molecular diagnostics into the forefront of diagnostic testing, has walked in conjunction with the emerging need for programmes aiming to evaluate and improve quality. In the early 1950s Levey and Jenning introduced into clinical laboratories the principles of statistical quality control, as well as control charts and procedures based on the mean and range of duplicate measurements obtained for a single sample [4]. With the advent of computers and quality control software, multi-rule charts have become widely available [5]. In 1947, the seminal work of Belk and Sunderman paved the way for the development of external quality assurance (EQA)/proficiency testing (PT) schemes to enable the clinical laboratory to make benchmark and performances comparisons [6].

The need to control and improve quality in clinical laboratories has grown hand in hand with the growth in technological developments leading to an impressive reduction of analytical errors over time. In 1947, Belk and Sunderman reported a percentage of 16.2% of errors, most of them being major errors. Converting the data from that study to part per million, this suggested metrics allowing comparison with other error rates in our society, yielded an unacceptable result rate of 162,116 per million laboratory tests (ppm). Fifty years later, Witte and Colleagues reported an analytical error rates of 447 ppm (0.0447%), thus highlighting an impressive improvement in laboratory analytical quality [7]. This 100-fold reduction of analytical errors was due to the great improvements made in assay standardization, automation, utilization of informatics, and training of laboratory personnel. However, another essential cause of this impressive improvement has been the introduction and monitoring of quality indicators such as the analytical performance specifications (in particular bias and imprecision) based on well-established goals. Internal quality control (IQC) and External

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Quality Assurance/Proficiency tests (EQA/PT) are the tools used by clinical laboratories to verify the achievement of the analytical goals, and the indicators are the intra- and inter-laboratory comparative performances [8].

3. Analytical versus total quality

In 1997, the same issue of the Journal containing the above cited study by Witte and co-workers featured a study by Plebani and Carraro showing that the great majority of errors resulted from problems in the pre-analytical (68.2%) or post-analytical phases (18.5%), while analytical errors accounted for only 13.3% of total mistakes [9]. The study design of this paper allowed the authors to discover not only analytical errors performed "within the laboratory walls" but also mistakes due to patient/sample misidentification, poor quality of biological samples as well as data transcription and notification. This paper changed the perspective of studies aiming to evaluate quality in clinical laboratories, the focus shifting from internal processes to a patient-centred viewpoint to assure quality and safety in the final laboratory information provided. Further papers confirmed the vulnerability of the extra-analytical phases of the testing cycle, stressing the need for a wider control of all steps of the loop [10–13]. The vulnerability of extra-analytical phases should be predicted in view of the complexity of the processes, the existence of different operators, the lack of a well identified process owner and the evidence that most errors are performed in the boundaries between the laboratory and the clinic. In pre-pre-analytical steps the procedures for test requesting, sample collection, handling and transportation were a neglected issue even though they strongly affect the quality of biological specimens and, in turn, the accuracy of analytical results. In the final steps of the loop, the evidence collected in the last decades on poor/delayed acknowledgment of laboratory reports, errors in interpretation and utilization of laboratory information shows the correlation between missed, wrong and delayed diagnoses and patient harm. In this context, the evolving landscape of quality and errors in clinical laboratories moved first from analytical errors to all errors performed within the laboratory walls, subsequently to errors in laboratory medicine (including errors in test requesting and result interpretation), and finally, to a focus on errors more frequently associated with adverse events (laboratory-associated errors), as shown in Fig. 1 [8]. Historically, in laboratory medicine efforts to improve diagnosis and therapy have been directed toward improving diagnostic technology – higher volumes and more accurate laboratory tests – but previously reported data emphasized the need to re-evaluate the seminal concept of the "brain-to-brain loop". According to this concept, the generation of any laboratory test result consists of nine steps, comprising ordering, collection, identification (at several stages), transportation, separation (or preparation), analysis, reporting, interpretation, and action [14,15]. In an editorial published 20 years later, the father of this seminal concept, George D. Lundberg, emphasized that the final step (i.e. action undertaken on the patient and based on laboratory information) was not great enough, stating that "clinicians and laboratorians should all be concerned about the effects of that laboratory test and whether the performance of it was useful for the patient or for the public's health", thus stressing the need for an outcomes research agenda [16]. The concept of quality in laboratory medicine is therefore evolving from the focus on internal processes to the real impact of laboratory information on patient care and/or in assuring a healthy status to (any individual and) the entire population. In this sense, the testing process has been defined as "*a set of interrelated or interacting activities that transform biologic patient sample materials into laboratory results and information to ultimately assure the most appropriate clinical outcomes*" [8].

4. Changing the paradigm

According to the prophetical view expressed by Michael E. Porter "health care is shifting focus from the volume of services delivered to the value created for patients, with "value" defined as the outcomes achieved relative to the costs" [17]. This is also applicable to laboratory medicine. After decades in which clinical laboratories have focused on monitoring and improving internal indicators of analytical quality, efficiency and productivity, it is time to shift toward indicators of total quality, clinical effectiveness and patient outcomes. The paradigm adopted in the past 50 years has led to a gap between the laboratory and clinic, with an increased risk of inappropriateness, and a consolidation of analytical work in megastructures oriented only toward achieving a greater turnover of volumes, and decreasing cost per test and generating a vision of laboratory services as simple commodities [18]. In other words, the business model involved in the delivery of laboratory services is primarily designed, managed, and executed in individual units or silos. These units are driven by internal activities of the discipline and managed according to performance metrics that match the discipline itself – rather than the product of the services to improve clinical pathways, clinical and economical outcomes and patient safety [19]. Clinical laboratory professionals must enhance their mission: rather than being a factory model focused almost exclusively on providing accurate, timely test results at the lowest possible cost, laboratories should expand their mission to one of rapidly and efficiently enabling the accurate diagnosis of conditions, the selection of appropriate treatments and the effective monitoring of health status [20]. In addition, consensus has been achieved on the evidence that the value of a diagnostic test cannot simply be measured by its accuracy, but depends on how it affects patient health, and the downstream consequences of testing on patient outcomes [21,22].

Changing the paradigm thus appears to be necessary in assuring the survival of our discipline in the context of the dramatic changes in healthcare, increasing economic pressures and, first and foremost, the evidence that breakdowns in the testing cycle, in particular test ordering and interpretation, poor follow-up and tracking of diagnostic information cause wrong, delayed or missed diagnoses and incur the risk of moderate to severe harm. Recently published papers highlight the evidence of delayed or missed follow-up of abnormal findings for laboratory tests translating into patient adverse events [23]. In particular, missed or delayed follow-up of prostatic cancer antigen (PSA) and faecal occult

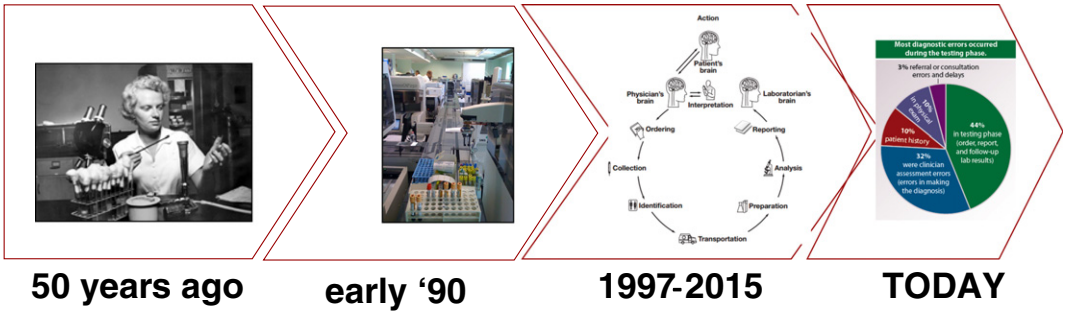

Fig. 1. The evolving landscape of quality and errors in laboratory medicine. 50 years ago, the introduction of internal quality control and external quality assurance programs; early '90, impressive reduction of analytical errors; 1997–2015, errors in the total testing cycle; Today, laboratory-associated diagnostic errors.

blood test (FOBT) were found to be associated with significant incidence of a diagnosis of suspected cancer (1048 out of 291,773 cases) and 47 high-grade cancers [24]. In primary care settings, problems with diagnostic tests accounted for 47.4% of diagnostic errors and many other reports confirm a comparable incidence of patient harm due to laboratory-associated errors in different clinical settings [25–27]. The increased awareness of medical errors with the movement for patient safety promoting safer health care through system solutions has led to increased attention on diagnostic errors as an important source of preventable harm. The recently issued IOM report in the Quality Chasm series, "Improving Diagnosis in Health Care" focuses specifically on the problem of diagnostic error, and emphasizes that diagnostic errors constitute an important and underestimated safety concern, and that it is a professional and moral imperative for all health care operators to address this issue [28]. In particular, it calls for laboratory professionals to be actively involved as partners in the diagnostic team , and for payment reform to cover the time spent on providing clinical advice and consultation. The take-home message for laboratory professionals is largely based on the framework of the total testing process, and the realization that so many diagnostic errors reflect problems in the pre- and post-analytical phases of testing. Now that laboratories have achieved such an impressive record of quality in the analytical phase of testing, it is time for the laboratory to help address these other problems, many of which occur outside the laboratory walls.

5. Tools for change

Measurement science, an evolving field, is under increasing pressure thanks to the demand for accountability, performance measures reports and value-based indicators [29]. The purposes of measurement are to: a) establish the incidence and nature of errors, mistakes and defects; b) determine the causes and risks of errors; c) evaluate interventions; d) provide education and training; and 5) guarantee accountability [28]. In laboratory medicine, measurement based on appropriate analytical performance specifications as quality indicators has led to impressive improvement in quality and error reduction. While these quality indicators (QIs) have been available for 50 years, in the extra-analytical phase the developments and utilization of reliable QIs is still in its infancy. However, harmonized performance indicators are a valuable tool, enabling the clinical laboratory to document and monitor all procedures and processes in the testing cycle, and to provide inter-laboratory comparative performances (benchmark) [30–33]. Laboratories attending the College of American Pathologists Q-Tracks program have achieved a significant decrease in defect rates following their use of performance quality indicators, regular collection of data, and issuing of reports [34]. However, process measurement should be linked and integrated with outcomes measurement encompassing the whole testing cycle, as recently proposed by Epner and Colleagues [35]. Examples of outcomes measures are, for instance, delays in result communication and testing-related delays, frequency of sample recollection episodes, and misapplication of test results. However, there is a need for standardization for performance quality indicators, just as there is for outcomes measurement [36].

Diagnostic and laboratory-associated diagnostic errors can be grouped into two categories: system-related and cognitive errors [37]. Quality indicators are valuable tools for reducing and addressing system-related errors. To ensure that effective efforts are made to reduce diagnostic errors, QIs (performance and outcome measures) should be linked to cognitive interventions aiming to: a) enhance medical knowledge and experience, particularly in test requesting and interpretation; b) improve clinical reasoning, if necessary using decision support such as an algorithm and/or expert systems [37,38]. In particular, there is increasing consensus on the need to update medical curricula by paying more attention to laboratory medicine and the issues of test requesting and interpretation of laboratory results [39].

6. Conclusions

The last 50 years have seen substantial changes in the landscape of laboratory medicine: its role in modern medicine is in evolution and the quality of laboratory services is changing. The better understanding gained of the molecular basis of human disease, the identification of risk factors and disease prediction as well as the advent of personalized medicine has paved the way for an upsurge in the demand for more numerous and more reliable laboratory tests. In view of the fact that added value underpins the ultimate quality of laboratory information, the changing face of quality, initially based on analytical performances, is now shifting to quality in the total testing process, thus including control over, and improvement in, the extra-analytical phases. Laboratory professionals must always be actively involved as partners in the diagnostic team, and must assure cooperation and advice in order to improve upon clinical pathways and patient outcomes [40].

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