

Opinion Paper

Mario Plebani*

Clinical laboratories: production industry or medical services?

DOI 10.1515/cclm-2014-1007

Received October 14, 2014; accepted October 15, 2014; previously published online November 18, 2014

Abstract: The current failure to evidence any link between laboratory tests, clinical decision-making and patient outcomes, and the scarcity of financial resources affecting healthcare systems worldwide, have put further pressure on the organization and delivery of laboratory services. Consolidation, merger, and laboratory downsizing have been driven by the need to deliver economies of scale and cut costs per test while boosting productivity. Distorted economics, based on payment models rewarding volume and efficiency rather than quality and clinical effectiveness, have underpinned the entrance of clinical laboratories into the production industry thus forcing them to relinquish their original mission of providing medical services. The sea change in laboratory medicine in recent years, with the introduction of ever newer and ever more complex tests, including ‘omics’, which impact on clinical decision-making, should encourage clinical laboratories to return to their original mission as long as payments models are changed. Rather than being considered solely in terms of costs, diagnostic testing must be seen in the context of an entire hospital stay or an overall payment for a care pathway: the testing process should be conceived as a part of the patient’s entire journey.

Keywords: clinical laboratory; economies of scale; fee-for-service; personalized medicine; quality; total testing process.

Introduction

The clinical laboratory has recently been defined as ‘the nerve center of diagnostic medicine’ because it provides essential information not only for diagnosis and monitoring, but also for screening, prevention, early diagnosis, tailored treatment and the more effective monitoring of human diseases [1]. Laboratory medicine is the keystone in medical decision-making and in tailoring medicine for the individual patient [2]. Accordingly, the Institute of Medicine (IOM) has now included laboratory services in the 10 Essential Benefits Categories in the US healthcare system [3].

As stated in a number of papers [4, 5] and reports from National Health Departments (e.g. UK and Italy), ‘60%–70% of patients’ diagnoses depend on laboratory tests’ [6, 7]. Yet the contribution of laboratory investigation to making sound medical diagnoses continues to be a controversial issue. Across multiple studies performed in the past, no adverse effects have been associated with a reduction in the number of laboratory tests and no change reported in readmission rates, transfer to intensive care unit, length of stay, and mortality [8, 9]. However, these studies have design bias, and poor transferability; their results are strongly influenced by specific clinical settings and case mixing, and do not include recent advances in laboratory medicine. Since outcome measurements are integral to the development, regulatory approval, and marketing of new drugs, the literature on treatments is abundant while that on diagnostic outcomes is scarce. Of course this dearth is partly due the difficulty involved in demonstrating the outcome of a laboratory test, which is usually temporally remote, and also to the fact that the clinical response to a test result may vary according to the individual physician’s competence, and any further clinical information provided [10]. Furthermore, it is extremely difficult to perform procedures such as randomized controlled trials investigating laboratory tests that are already well established in clinical practice [11]. On discussing the issues of appropriateness and clinical effectiveness of laboratory testing, George D Lundberg, the inventor of

*Corresponding author: Professor Mario Plebani, Department of Laboratory Medicine, University-Hospital of Padua, 35128 Padua, Italy, Phone: +39 0498212792, Fax: +39 049663240, E-mail: mario.plebani@unipd.it

the seminal ‘brain-to-brain loop’ concept, recently stated that ‘thirty-nine years after (the discovery of the concept) these questions, plus the big new one – what outcome that resulted from the tests? – still beg to be answered’ [12]. The lack of evidence of the link between laboratory tests, clinical decision-making and patient outcomes, plus the shortage of economic resources affecting all health-care systems, have compounded the increasing pressure on the organization and delivery of laboratory services. Currently, experienced in laboratories worldwide, consolidation, merger and downsizing are driven by the need to deliver economies of scale, reduce cost per test and improve efficiency and productivity. Since essential stakeholders (administrators and politicians) seem to consider it a ‘mass production facility’, the clinical laboratory is now expected to churn out larger test volumes as cheaply as possible. The aim of this paper is to briefly review the development and evolution of clinical laboratories as a new entity in medical care, to investigate why they have been forced into the production industry, and to design a process that should enable them to reclaim their original mission: to provide a medical service.

Roots and development of laboratory medicine

Laboratory medicine as we now know it, is a relatively young discipline, although it has historical roots, from Hippocrates, who in 300 BC examined urine to diagnose diseases [13, 14], to Bacon, who in the 13th century experimented with optics, which led to the invention of the microscope [15]. However, the value of diagnostic testing was not appreciated until the causative pathogens of diseases, such as cholera, tuberculosis and diphtheria were discovered; the premises of the first clinical laboratory, established in 1896 at John Hopkins Hospital in Baltimore, covered the 144 square feet (13.378 m²) of a room sold for \$50 [16]. Other well-known US clinical laboratories founded in the early 1900s were the William Pepper Laboratory of Clinical Medicine of the University of Pennsylvania and the Children’s Hospital of Columbus, Ohio [17]. Only in the 20th century did clinical laboratories become an established medical entity, and every hospital eventually had an in-house service, the growth between 1969 and 1976 estimated at about 15% a year. An important driver for establishing clinical laboratories as a well-defined medical facility was the regulatory issue. The enactment of the *Clinical Laboratory Improvement Amendments* (CLIA) in 1988, and successive changes in

1997 and 2012, respectively [18], as well as the development of accreditation programs starting from that provided by the College of American Pathology [19] until the more recently developed ISO International Standard [20], and the decision by many payers, including Medicare, to pay only diagnostic tests performed in accredited laboratories represented essential factors for the development of ‘centralized’ clinical laboratories. These factors led to the fairly rapid demise of small diagnostic laboratories overseen particularly by sub-specialists in internal medicine and pediatrics, as before external regulations ‘any graduate student with a pipette and fluorimeter could deliver clinical test results’ [21]. As a consequence, Rex B. Conn highlighted in a paper published in 1978 that ‘during the past 30 years the clinical laboratory has evolved from a small, crowded room in the hospital basement to an organization of marvelous complexity’ [22]. The welcome development of clinical laboratories was due to advances in technology, the discovery and introduction of new diagnostic tests, and the inevitable modifications in medical education and clinical practice (Figure 1), but concern has been expressed regarding the implications of ‘powerful economic stimuli’ in the sphere of laboratory medicine [22].

Distorted economics

In his seminal paper, Rex B. Conn wrote that ‘hospital accounting practices have had a profound influence on the development of clinical laboratories and how they are managed because revenues are highly leveraged to true laboratory costs’, and therefore ‘modest changes in work load accompanied by even more modest changes in actual costs are reflected by large changes in gross revenues’ [22]. Calculating the cost of a laboratory test or test panel has always been a challenging task. Clearly the cost of testing in the laboratory must be distinguished from the charges (reimbursement) to the outside payer; since several variables are affecting this issue, it has been common policy to calculate reimbursements due on the basis of charges and/or cost, depending on the payers involved. For example, laboratory tests performed in an emergency setting, on Sundays and public holidays, are much more expensive than those performed according to schedule on weekdays. Yet scarce consideration has been given to these and other variables influencing the costs. The fee-for-service model for reimbursing laboratory tests performed for both inpatients and outpatients has been the only one used for many decades.

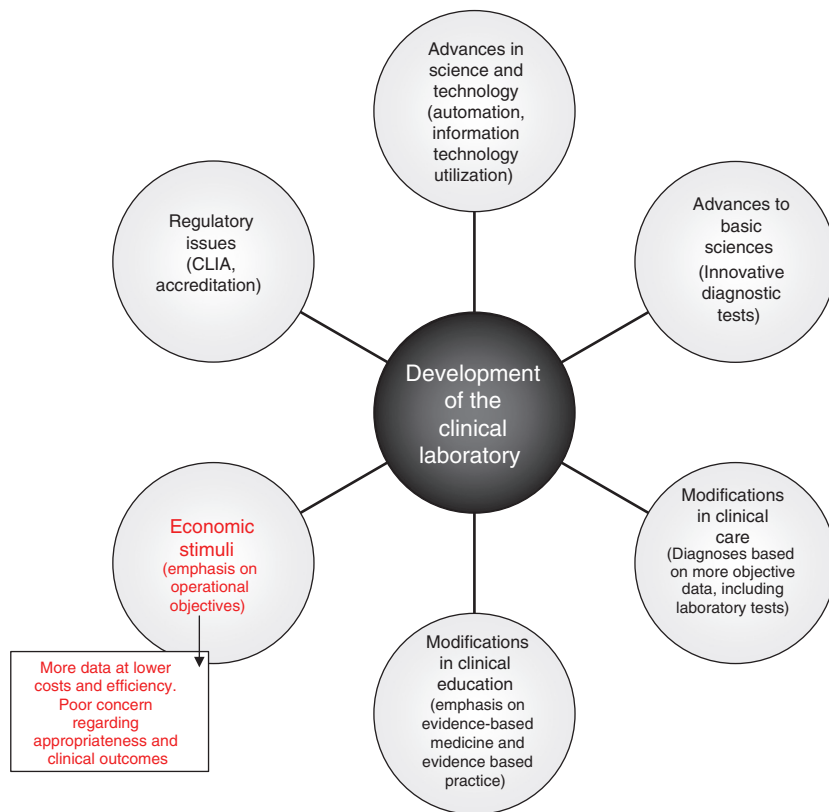


Figure 1 Drivers of developments of the clinical laboratory and their effects.

According to this widely accepted model, and other similar types of contracts, laboratory tests are billed directly to the payer and can generate large profits, the charges usually being significantly higher than the true costs [23]. Hospitals considered laboratories convenient profit centers that could be used to support deficit-producing hospital operations (e.g., intensive care units and emergency departments). In fact, room charges could not be inflated beyond reason because charges in various hospitals could be compared, and patients could compare the charges to those in a first class hotel. However, charges for laboratory tests were small dollars amount (little-ticket technologies), and no user knew how much a laboratory test was worth [24]. As recently stated by Charles M. Strom, ‘the hospital laboratory became a cash cow with potential to generate large profits’ [21]. While the fixed per diem reimbursement rate for hospitalization did set rigid boundary conditions on the revenue available to operate a hospital, there was no limit to the number of laboratory procedures that could be performed on the patient involved. According to Rex B. Conn, ‘no hospital accounting system is so inelegant that profit from the laboratory appears as a discreet figure in a financial statement’ [22]. In the beginning, hospital laboratories had a virtual monopoly in providing services for their own hospitalized

patients, and financial considerations prohibited measures aimed at more economical utilization of laboratory testing. Later on, because hospital laboratories were the bellwethers in setting laboratory charges, the field was attractive to large independent laboratories which could easily perform the same tests and sell their services at a much lower price [24]. Only after the introduction of the diagnosis-related group (DRG) system in the late 1980s [25, 26] were charges for laboratory testing on inpatients rolled up into a single overall fee for the entire hospital admission based on the patient’s diagnosis. This, in turn, has dramatically changed the scenario as the hospital is paid the same overall fee regardless of how many, or how few, tests are performed during the inpatient stay [27]. The DRG system, originally implemented in a small number of hospitals in New Jersey in 1983, was introduced in hospitals throughout in the US in the late 1980s, and later imposed on other countries. However, the distorted economics had already caused extensive damage, and strongly influenced not only the behavior of laboratory professionals and care operators, but also the development of automation and related technologies. In addition, reimbursement for outpatient care is still based on fee-for-service in most countries and the transition to global payments for episodes of care, the so-called, Diagnostic

Clinical and Therapeutic Pathway (PDTA), has long been delayed and it is still widely debated.

Effects of distorted economics

Thanks to ‘distorted economics’, the main goals for both laboratory professionals and *in vitro* diagnostic (IVD) manufacturers became higher throughput and productivity in order to reduce the cost per test and improve efficiency. Financial considerations that precluded measures designed to achieve the more appropriate, evidence-based use of laboratory services promoted an efficiency-oriented generation of laboratory instrumentations. Technological advances created a clinical laboratory infrastructure with a significantly expanded capacity to accommodate high volume testing with an expanding test menu; it was increasingly affected by redundancy and showed little concern for true clinical effectiveness.

The paradigm of the above trend is the application to automation of one of the most impressive inventions in the field of clinical chemistry: the continuous-flow autoanalyzer. This innovative approach to automation reduced, in minutes rather than hours (or days), the need to complete an analysis without the direct involvement of the personnel [28] and it was the first clinical analyzer to incorporate a computer. The system evolved, with the generation of the sequential multiple analyzers (SMA, e.g., SMA 6/60 and 12/60), until the final analyzer called sequential multiple analyzer with computer (SMAC). These systems increased throughput and rapidity while reducing the need for huge sample volumes, providing test panels based on the availability of analytical methods rather than answers to specific clinical questions. The so-called ‘SMA or SMAC profiles’, which simultaneously yielded up to 20 biochemical parameters, met the increasing demand for laboratory tests, but reinforced the idea that laboratories are purely technological facilities and providers of commodities. With this generation of analyzers the cost of the test profile was lower than the additional costs of individual tests, the cost of the single reagent being scarcely influent compared with the cost of the analyzer and the saving of the personnel’s time. In addition, the concept of test panel provided by these analyzers was attractive to most physicians thanks to the inherent oversimplification of test requesting; in many institutions, the older generation of clinicians still tends to request the ‘SMAC or SMAC profile’ even though this instrument has long been defunct.

Although panel testing has been promoted to reduce order variety by clinicians [29], the fixed series of

laboratory tests applied to a broad category of patients with quite different diseases increased inappropriate utilization and wasted laboratory resources [30]. High-volume, multiple-test analyzers have gained ground because they meet the needs of laboratories with an increasing workload of basic chemical tests, but they have forced laboratories to follow the production industry model. Currently, core laboratories are increasingly designed to perform a large volume of tests at the lowest possible cost (economies of scale). As core laboratories continue to evolve and maximize efficiency, they no longer feel the need to reduce testing and maximize appropriateness. In fact, ‘the reward structure for a core laboratory is the polar opposite of that for controlling test utilization’ [31]. Test utilization is rewarded by reducing unnecessary testing and associated costs while increased core laboratory test volume maximizes test capacity, efficiency, and justifies any increase in the demand for resources (e.g., personnel, reagents, new instrumentation). If the test capacity is not ‘maximized’, there is ‘wastage’, instruments and personnel standing idle [31]. These diametrically opposed reward systems have led to tension between laboratory medicine principles of clinical appropriateness and laboratory management principles of efficiency and cost-effectiveness (Table 1).

As highlighted by Rex B. Conn, ‘in this economic environment laboratories may be staffed and instruments purchased on the basis of the projected revenues rather than on the basis of considered medical judgment regarding the requirements for cost-effective patient care’ [22]. As automation of increased workload and complex workflows became increasingly dominant, clinical laboratory Directors are faced with issues, such as total quality management (TQM), certification and accreditation, Lean, Six-Sigma and other management systems, while losing sight of their original mission to provide valuable information for improving quality of care and patient safety [32].

Table 1 Principles of laboratory medicine versus principles of industrial management.

Principles of laboratory medicine	Principles of industrial management
– Appropriateness (in requesting tests and interpreting results)	– Throughput and productivity
– Quality in the total testing process	– Cost per test
– Patient-centered service	– Efficiency
– Patient safety	– Revenue
– Valuable clinical outcomes	

Centralization or decentralization of clinical laboratories

As the pace of technological advancements in laboratory medicine accelerated, the extensive use of automation and other mass-production techniques enabled operators to guarantee the timely release of results despite the impressive increase in test requesting and workload. However, this achievement had two pitfalls: one, the progressive autonomy from the clinical context incurring the risk of inappropriate test requesting and the misleading interpretation and utilization of laboratory information, the other, the perception of laboratory services as a commodity or ‘mass-produced unspecialized products’ to be evaluated solely on the basis of cost while overlooking quality [33]. Together, these trends caused clinical laboratories act as insular departments, focusing almost exclusively on their silos while neglecting any proactive and interactive relationship with clinics. Moreover, the larger, faster and more expensive laboratory instruments that became available precipitated economic pressures for centralization. As the focus was on economies of scale and the lowest possible cost per test and productivity, the final organizational design hinged upon a few centralized laboratories with enormous, high-speed analyzers performing dozens of tests on each and every specimen. In theory, centralization or decentralization of clinical laboratories should proceed concertedly according to the logic of patient needs, care organization, technologic developments and economic constraints, but the above-described inappropriate financial considerations have thwarted this much needed process.

The commonly held assumption that *bigger is better* cannot be applied to laboratory medicine. First, although there may be a production line within the laboratory, we must never lose sight of the fact that laboratory medicine should be considered first and foremost a service industry, trading in information and coping with multiple, complex client interactions [34]. The diagnostic process, calling for interaction between the clinical laboratory, the requesting physician and the patient, is continuously evolving, and the inherent ethical, organizational and economic aspects deserve greater consideration [35]. In recent years, an increasing number of papers and initiatives are promoting a more rational utilization of laboratory services with a focus on managing upstream demand and downstream interpretation of laboratory results to safeguard quality and patient safety in the ‘brain-to-brain loop’ [36]. Examples of debatable issues include direct access to laboratory tests, and the direct reporting of laboratory results

to the patient [37], aspects that, in the era of genomics, highlight the need for an approach based on ethics and patient safety, rather than on economics. For example, the notification of critical values has been described as a time-consuming and expensive activity that should be outsourced to call centers [38]. Yet critical results, which are frequently unexpected, may call for a change in treatment and can result in significant clinical benefit if issued promptly, and accompanied by clinical advice from laboratory professionals [39]. Second, although at first glance economies of scale appear to reduce costs, the relationship between cost and increasing volume is complex, and certainly not linear. Our group found that the trend towards a decrease in total costs – due to an increase in test volumes – attained statistical significance only for quantities of up to about 1,100,000 tests per year. For 1,800,000 tests and more, the cost per test appeared to range from 1.5 to 2.0 € irrespective of the different volumes [40]. As in other fields of production, the law of diminishing returns applies to increasing volume beyond a certain point; in clinical laboratories in particular it differs according to several variables, including the complexity of the main organization, number and types of specialty in the hospital, number of production facilities of the laboratory, different case mix, and the inpatients/outpatients ratio [41]. Third, several studies performed in clinical settings, ranging from primary care to internal and emergency medicine, demonstrate the unacceptable rates of errors in test request and interpretation of results, as well as their association with diagnostic errors [42–44]. The dichotomy between the clinical world and the mere production of laboratory data is not only costly, but also conducive to ineffective and potentially risky care. An increasing body of evidence demonstrates the substantial downstream costs of laboratory testing due to inappropriate request and result interpretation, as the clinical work-up of ‘supposedly’ abnormal results takes up the time of physicians and may prompt further radiological studies and unnecessary further laboratory testing [24]. As highlighted by Knowles and Barnes, ‘...clipping a few cents off the cost of a routine blood test will yield little benefit if it is the wrong test, done at the wrong time for the wrong reasons’ [34]. Fourth, evidence provided in recent years demonstrates that pre-analytical errors account for about 70% of errors in laboratory testing [45, 46]. One of the major assumptions of centralization of clinical laboratories is the safe transportation of biological samples. However, recently reported data demonstrate that the safe transportation of biological samples necessitates a careful control of time and temperature variables, together with the use of appropriate, costly logistic solutions that call for the attention of both

collection centers and laboratory staff [47, 48]. In addition, available literature on sample transportation and quality is based on data collected on samples from healthy blood donors or from cohorts with a high prevalence of values within the reference range. Samples from patients behave differently and might evidence clinically significant differences after transportation, as has recently been clearly demonstrated for some hematological parameters as well as for basic biochemical tests [49–51]. Finally, a further hazard in the factory approach to laboratory medicine is the prospect of disruptive innovation. Research into the life cycle of innovation in a number of different industries shows a common pattern: initially ‘sustaining innovation’ prompts organizations to consolidate and centralize around expensive and complex technologies that require high volumes and high profit margins to sustain them before simpler, more user friendly technologies are designed in order to bring the solution closer to the end user (disruptive innovation) [52]. The new generation of point-of-care testing (POCT) should provide an adequate answer to the development of disruptive innovation, which was foreseen a decade ago [53]. Advances made in miniaturization and connectivity have led to the availability of devices with micrometer-sized features designed to perform a range of assays and to integrate all of their steps onto a single small device—the so-called lab-on-a-chip [54]. This in turn is expected to allow the continuous expansion of the near-patient testing (NPT) option. In general, POCT and NPT involve small, transportable analytical devices that facilitate the quick generation of results to enable prompt diagnostic and interventional decisions. The use of POCT, particularly in some Institutions, may significantly reduce the turnaround times and limit the number of tests referred to the main clinical laboratories. As reported by Jani and Peter [55], particularly in areas of limited resources, ‘classic diagnostic technologies are not well suited to meeting the expanded testing needs. Laboratory tests require complex infrastructure, skilled technicians, and a stable supply of electricity. Traditional testing is usually performed in remote laboratories which increases the cost and inconvenience of accessing health care and leads to a high number of patients who leave the system before a diagnosis is established’ [55]. The rise of POCT is thus expected to expand access to medical services, improve health outcomes, and facilitate the sustainability of disease-control programs. However, most laboratory professionals perceive POCT as an ‘alien’ and dangerous alternative to traditional laboratory services, while it should be a typical issue of clinical governance in laboratory medicine [56]. Odysseus navigated between Scylla and Charybdis, and laboratory professionals seem

to be navigating between a rock and a hard place: totally automated and focused factories and the widespread introduction of decentralized and POCT options [33, 57].

Hospital versus commercial laboratories

An important influence on laboratory testing, initially in the US and thereafter in other Countries, was the massive growth of independent, for-profit laboratories. These facilities started to provide, in addition to analytical operations, courier service to doctor’s offices, as well as to other care institutions including hospitals, and returned results via computer or fax with short turnaround times. According to these features, diagnostic testing came to be increasingly view as a commodity and laboratories results at lower costs became more attractive to managers not trained in science or medicine [24]. Distorted economics have generated debate regarding the possible competition between academic/hospital-based and commercial laboratories. In theory, academic/hospital-based laboratories should be non-profit providers of patient-centered services, while the main goal of profit-sector is to assure operational efficiency. However, as the distorted economics led to significant revenues for laboratory services, not only commercial but also hospital laboratories became ‘a cash cow’ with the potential to generate large profits [22]. The debate regarding the possible advantages and disadvantages of the two ‘phenotypes’ of clinical laboratories, and whether the use of private companies should increase or decrease health care costs focused on mere efficiency issues such as the cost per test. Comparing costs in hospital laboratories to those in private laboratories is at best difficult because of the differences between these two types of service providers [58]. Hospital-based laboratories provide more ‘stat’ services, are open on nights, Sundays and public holidays and do more esoteric and reference work. In addition, they play a vital role in translational medicine, and educate medical students, laboratory technicians, house staff, post-doctoral fellows and other care operators. Yet several attempts have been made to compare their costs, despite the caveats. In 1994, the Ontario Hospital Association emphasized the ‘massive reserve capacity in the hospital laboratories ... a fully staffed evening shift could absorb the private laboratories workload without difficulty’ [59]. There is excess capacity in public hospitals worldwide, especially for automated analyses and routine tests, but the extent of the excess has not been established. In addition, the method of

determining cost on the basis of marginal costs of extra-staff, and reagents is not advocated by the private laboratory industry, which aims to compare the discrete unit cost of providing tests. However, even on calculating costs by using the latter method, compelling evidence obtained in Ontario shows that money can be saved by using hospitals to process community laboratory work [60, 61].

No evidence is available to demonstrate that outsourcing laboratory services to the private sector assures that costs are contained while quality and clinical effectiveness are preserved. In fact, academic and commercial laboratories can coexist in a mutually beneficial relationship based on cooperation and competition on quality if they, as well as policy makers and administrators, recognize their different role and missions. In particular, the vital role to play in translational medicine and education of medical students should be taken into account when evaluating the costs of academic/hospital laboratories [62]. However, given the formidable sea change of laboratory medicine experienced in recent years, a paradigm shift in evaluating the value of laboratory services is urgently required.

The changing face of clinical laboratories

The sea change experienced by laboratory medicine in the last few decades is the fruit of both technological and scientific progress. As shown in Table 2, both these drivers of progress have led to significant changes and improvements.

The shortened turnaround times achieved thanks to technological developments has made results available in real-time and dramatically improved the diagnosis and treatment of patients admitted to emergency departments and intensive care units. The availability of pivotal diagnostic information (e.g., blood-gas, electrolytes, disease biomarkers) at the point of care, and within a few minutes, allows clinicians to make evidence-based medical decisions and to immediately prioritize the treatment of patients [30]. This has changed the clinicians'

mind-set forever. On the other hand, the extraordinary advancements in our understanding of the molecular and biochemical bases of human diseases have paved the way for the introduction into the clinical practice of a new generation of laboratory tests for earlier and more accurate diagnoses, as well as for the identification of important risk factors. Innovative and more effective laboratory tests such as cardiac troponin I and T have, for example, changed the paradigms for the diagnosis of acute coronary syndrome and the same improvements have been achieved for hematological and many other disorders. Even greater expectations are based on the introduction of 'omics' (e.g., genomics, proteomics, transcriptomics, metabolomics), and the translation of 'omics' into clinical practice gives laboratory professionals the opportunity to make their role and value more visible [33]. On the basis of this prediction, V. Roy emphasized the crucial role of laboratory tests in modern medicine in stating 'in the era of molecular medicine, more and more diagnoses will be made by laboratory tests in asymptomatic patients. The goal is to make the diagnosis before clinical signs or symptoms resulting from organ damage become evident' [63]. The medical community and policy makers, who underestimated the importance of the above issue, have been slow to grasp the paradigmatic change in laboratory tests. Only recently this aspect received the attention it deserves. In commenting on an article concerning genetic testing, Tom Walley underlined the evidence that 'recent technological developments have created a new generation of laboratory diagnostics, which promise to provide better ways of detecting diseases and monitoring response to treatment' [64]; he stressed the need for a careful evaluation of the tests themselves, starting from the purpose, the clinical context in which they are to be used and adopting the ACCE framework based on a) analytical validity, b) clinical validity, c) clinical usefulness, and d) any ethical, social or legal implications [65]. This framework has been conceived and suggested for evaluating all types of diagnostic tests, not only 'omics' [66]. Many other contributions available in the literature confirm the importance not only of improving the regulatory framework for diagnostic tests, but also the need for laboratorians to assure clinical advice and consultations to the patient's medical

Table 2 Improvements in modern laboratory medicine (from reference [30], modified).

– Shortened turnaround time (<i>real-time results</i>) thanks to developments in analytical instruments and information technology
– Availability of <i>more effective tests</i> (strongly influencing the clinical decision-making process)
– Biomarkers for an <i>early diagnosis</i> and risk factors for <i>disease prevention</i>
– The era of ' <i>omics</i> ' (e.g., genomics and proteomics)
– The <i>nature of errors</i> in laboratory medicine and testing-associated diagnostic errors

team to improve the appropriateness in test request, result interpretation and utilization. It was predicted that the ‘development of significant genetic advances to clinical practice (would) take generations’ [67] but clinical laboratories may play a relevant role in realizing the promise of genomics and proteomics, offering their expertise and willingness for translating research insights and new biomarkers into standardized laboratory tests and reliable clinical information [68]. For example, next-generation sequencing (NGS) technology, which has been embraced for its ability to revolutionize genetic testing owing to its massively high-throughput nature, is replacing the previous gold standard, Sanger sequencing. However, assuring the quality of NGS requires sound guidelines, as well as monitoring of performance metrics and external quality assessment programs and laboratory professionals should play a central role in addressing these issues [69]. In particular, there is the need for a comprehensive view of the diagnostic testing cycle, the so-called ‘brain-to-brain loop’ [70], to avoid the risk of a wild request of ‘omics’ testing outside the appropriate clinical context. Although the sea change in laboratory testing has already been experienced, further developments and understanding will only be achieved in the next few years. However, to counteract the current perception of clinical laboratories as simple ‘mass production facilities’ and overcome their marginal role in clinical care, a paradigmatic shift should be achieved also in the payment models. Diagnostic testing can no longer be considered in terms of the cost of the procedure but in the overall context of the total cost of a hospital stay or a bundled payment for a care pathway: the testing process should be conceived as a part of the whole patient journey [71]. Companion diagnostics, for which tests are an integral part of the intervention, [72] are a drop in the ocean, if we mean to promote and reward a more appropriate role of laboratory testing in the care pathway. ‘Value-based’ payment models that would hold providers accountable for the outcomes and costs of care delivery, rather than solely volume, are finally emerging as a remedy to a payment model that has long undervalued total quality, care coordination, and appropriateness. The current evidence of the need to reduce testing-related diagnostic errors, assuring quality in the total testing process and adopting a new outcomes-based approach in laboratory medicine [73] must pave the way to obviating the risk of relegating clinical laboratories to a ‘back office’ function. To regain their pivotal role, laboratory medicine and laboratorians must be firmly reintegrated into the care pathway. For this to be achieved, a paradigmatic change must be made to the core curricula and training programs of medical students, as already outlined in the

literature [74, 75], more emphasis being placed on the knowledge and skills required to provide valuable clinical advice and consultancy in test request and result interpretation. Transforming clinical laboratories from a business model based on cost and volumes of test performed (the ‘silo model’) to an essential source of information for high-quality care and an outcomes-oriented facility is the only possible remedy for the workforce shortage experienced worldwide [76]. To circumvent this progressive and silent workforce shortage, academic and professional organizations must promote valuable training programs, and provide continuing education and mentoring to upgrade the competencies of the personnel thus ensuring management and improvement in all steps of the testing process in close cooperation with all other care operators and patients themselves. Teaching consultative skills is a pre-requisite for changing both the function and the role of the clinical laboratory.

Conclusions

The clinical laboratory is essential to health care. Medical diagnoses and treatments rely on the accurate and timely issuing of laboratory test results, and the trend towards preventive and personalized care necessitates more complex and effective tests and biomarkers. In the past, growth in automation boosted productivity, timeliness and analytical performances but it primarily benefited the laboratory stakeholder (the silo model) rather than end-users. Few studies have demonstrated the impact of technological developments on the entire care pathway and patient outcome. These developments hand in hand with distorted economics, have led to the consolidation of laboratory services and their organization as focused factories that, thanks to their goal of maximizing productivity and revenues, churn out huge volumes rather than provide useful clinical information. However the sea change in laboratory medicine, with the introduction of more complex and effective tests, including genetic tests, should lead the clinical laboratory back to its original mission of providing a true and proper medical service – and playing a more effective role in the patient’s journey. This will be possible only if a paradigmatic change is made to payment models whereby diagnostic testing will no longer be considered in terms of the cost of the procedure but within the overall context of the total cost of a hospital stay or a bundled payment for a care pathway. By linking the dramatic advances in the test menu to modified payment models we will assure a bright future

not only to laboratory medicine, but also and above all to patients and healthcare systems.

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Financial support: None declared.

Employment or leadership: None declared.

Honorarium: None declared.

Competing interests: The funding organization(s) played no role in the study design; in the collection, analysis, and interpretation of data; in the writing of the report; or in the decision to submit the report for publication.

References

- Cortelyou-Ward K, Rotarius T, Liberman A, Trujillo A. Hospital in-house laboratories: examining the external environment. *Health Care Manag (Frederick)* 2010;29:4–10.
- Plebani M, Lippi G. Personalized (laboratory) medicine: a bridge to the future. *Clin Chem Lab Med* 2013;51:703–6.
- Institute of Medicine Committee on defining and Revising Essential Health Benefits Package for Qualified Health Plans. Report on essential health benefits: balancing coverage and costs. Washington, DC: National Academic Press, October 7, 2011.
- Forsman RW. Why is the laboratory an afterthought for managed care organizations? *Clin Chem* 1996;42:813–6.
- Becich MJ. Information management: moving from test results to clinical information. *Clin Leadership Manag Rev* 2000;14:296–9.
- Report of the Review of NHS Pathology Services in England. An Independent Review for the Department of Health. London: Department of Health, 2006:6.
- Linee di indirizzo per la riorganizzazione dei servizi di Medicina di Laboratorio nel Servizio Sanitario Nazionale. Available from: http://www.agenas.it/innov_sperim_sviluppo/Riorganizz-Medicina_Laboratorio.Pdf. Accessed 2 September, 2014.
- Dixon RH, Laszlo J. Utilization of clinical chemistry services by medical house staff. *Arch Int Med* 1974;134:1064–7.
- Peterson MC, Holbrook JH, Von Hales D, Smith NL, Staker LV. Contributions of the history, physical examination, and laboratory investigation in making medical diagnoses. *West J Med* 1992;156:163–5.
- Price CP, St John A. Innovation in healthcare. The challenge for laboratory medicine. *Clin Chim Acta* 2014;427:71–8.
- St John A, Price CP. Measures of outcome. In: Price CP, Christenson RH, editors. Evidence-based laboratory medicine. AACC Press: Washington DC, 2003:55–75.
- Lundberg GD Adding outcome as the 10th step in the brain-to-brain laboratory test loop. *Am J Clin Pathol* 2014;141:767–9.
- Berger D. A brief history of medical diagnosis and the birth of the clinical laboratory. Available from: <http://www.academia.dk/Blog/wp-content/uploads/KlinLabHist/LabHistory1.pdf>; 1999. Accessed 22 June, 2012.
- Armstrong JA. Urinalysis in Western Culture: a brief history. *Kidney Int* 2007;71:384–7.
- Doesschate GT. Oxford and the revival of optics in the thirteenth century. *Vision Res* 1962;1:313–42.
- Delwiche FA. Mapping the literature of clinical laboratory science. *J Med Libr Assoc* 2003;91:303–10.
- Kricka LJ, Savory J. A guide to the history of clinical chemistry. *Clin Chem* 2011;57:1118–26.
- Clinical Laboratory Improvement Amendments (CLIA). Available from: <http://www.cdc.gov/clia/Regulatory/default.aspx>. Accessed 10 August, 2014.
- College of American Pathologists. Accreditation and Laboratory Improvement. Available from: <http://www.cap.org/apps/cap.portal>. Accessed 10 August, 2014.
- ISO 15189:2012. Medical laboratories – Requirements for quality and competence. Geneva, Switzerland: International Organization for Standardization, 2012.
- Strom CM. Changing trends in laboratory testing in the United States. *Clin Lab Med* 2012;32:651–64.
- Conn RB. Clinical laboratories: profit center, production industry or patient-care resource? *N Engl J Med* 1978;298:422–7.
- Huck A, Lewandowski K. Utilization management in the clinical laboratory: an introduction and overview of the literature. *Clin Chim Acta* 2014;427:111–7.
- Conn RB, Snyder JW. Charges in the American health care system: crisis in the clinical laboratory. *Clin Chim Acta* 1997;267:33–49.
- Fetter RB, Shin Y, Freeman JL, Averill RF, Thompson JD. Case mix definition by diagnosis related groups. *Med Care* 1980;18:1–53.
- Fetter RB, Freeman JL. Diagnosis related groups: product line management within hospitals. *Acad Manage Rev* 1986;11:41–54.
- McMillan D. Calculating cost savings in utilization management. *Clin Chim Acta* 2014;427:123–6.
- Skegg LT Jr. an automatic method for colorimetric analysis. *Am J Clin Pathol* 1957;28:311–23.
- Werner M. Appropriate utilization and cost control of the hospital laboratory: panel testing and repeat order. *Clin Chim Acta* 1995;233:1–17.
- Plebani M. The changing face of clinical laboratories. *Clin Chem Lab Med* 1999;37:711–7.
- Ng VL. Utilization management in the core laboratory. *Clin Chim Acta* 2014;427:154–7.
- Plebani M, Zaninotto M, Faggian D. Utilization management: a European perspective. *Clin Chim Acta* 2014;427:137–41.
- Plebani M, Lippi G. Is laboratory medicine a dying profession? Blessed are those who have not seen and yet have believed. *Clin Biochem* 2010;43:939–41.
- Knowles S, Barnes I. Lean laboratories: laboratory medicine needs to learn from other industries how to deliver more for less. *J Clin Pathol* 2013;66:635–7.
- Wijeratne N, Benatar SR. Ethical issues in laboratory medicine. *J Clin Pathol* 2010;63:97–8.
- Plebani M, Panteghini M. Promoting clinical and laboratory interaction by harmonization. *Clin Chim Acta* 2014;432:15–21.
- Plebani M, Laposata M, Lundberg GD. The brain-to-brain loop concept for laboratory testing 40 years after its introduction. *Am J Clin Pathol* 2011;136:829–33.
- Liebow EB, Derzon JH, Fontanesi J, Favoretto AM, Baetz RA, Shaw C, et al. Effectiveness of automated notification and customer

- service call centers for timely and accurate reporting of critical values: a laboratory medicine best practices systematic review and meta-analysis. *Clin Biochem* 2012;45:979–87.
39. Piva E, Pelloso M, Penello L, Plebani M. Laboratory critical values: automated notification supports effective clinical decision making. *Clin Biochem* 2014;47:1163–8.
 40. Barletta G, Zaninotto M, Faggian D, Plebani M. Shop for quality or quantity? Volumes and costs in clinical laboratories. *Clin Chem Lab Med* 2013;51:295–301.
 41. Lippi G, Mattiuzzi C. Testing volume is not synonymous of cost, value and efficacy in laboratory diagnostics. *Clin Chem Lab Med* 2013;51:243–5.
 42. Hickner J, Graham DG, Elder NC, Brandt E, Emsermann CB, Dovey S, et al. Testing process errors and their harms and consequences reported from family medicine practices: a study of the American Academy of Family Physicians National Research Network. *Qual Saf Health Care* 2008;17:194–200.
 43. Gandhi TK, Kachalia A, Thomas EJ, Puopolo AL, Yoon C, Brennan TA, et al. Missed and delayed diagnoses in the ambulatory setting: a study of closed malpractice claims. *Ann Intern Med* 2006;145:488–96.
 44. Kachalia A, Gandhi TK, Pupolo AL, Yoon C, Thomas EJ, Griffey R, et al. Missed and delayed diagnoses in the emergency department: a study of closed malpractice claims from 4 liability insurers. *Ann Emerg Med* 2007;49:196–205.
 45. Plebani M. The detection and prevention of errors in laboratory medicine. *Ann Clin Biochem* 2010;47:101–10.
 46. Plebani M, Sciacovelli L, Aita A, Padoan A, Chiozza ML. Quality indicators to detect pre-analytical errors in laboratory testing. *Clin Chim Acta* 2014;432:44–8.
 47. Zaninotto M, Tasinato A, Padoan A, Vecchiato G, Pinato A, Sciacovelli L, et al. An integrated system for monitoring the quality of sample transportation. *Clin Biochem* 2012;45:688–90.
 48. Zaninotto M, Tasinato A, Padoan A, Vecchiato G, Pinato A, Plebani M. Effects of sample transportation on commonly requested laboratory tests. *Clin Chem Lab Med* 2012;50:1755–60.
 49. Kalpatthi R, Thompson B, Lu M, Wang WC, Patel N, Kutlar A. Comparison of hematologic measurements between local and central laboratories: data from the BABY HUG trial. *Clin Biochem* 2013;46:278–81.
 50. Da Rin G, Lippi G. The quality of diagnostic testing may be impaired during shipment of lithium-heparin gel tubes. *Clin Chem Lab Med* 2014;52:1633–7.
 51. Henriksen LO, Faber NR, Moller MF, Nexø E, Hansen AB. Stability of 35 biochemical and immunological routine tests after 10 hours storage and transport of human whole blood at 21° C. *Scand J Clin Lab Invest* 2014;74:603–10.
 52. Christensen CM, Bohmer R, Kenagy J. Will disruptive innovations cure health care? *Harv Bus Rev* 2000;78:102–12.
 53. Plebani M. Charting the course of medical laboratories in a changing environment. *Clin Chim Acta* 2002;319:87–100.
 54. Fortina P, Kricka LJ. Nanotechnology: improving clinical testing? *Clin Chem* 2010;56:1384–9.
 55. Jani IV, Peter TF. How point-of-care testing could drive innovation in global health. *N Engl J Med* 2013;368:2319–24.
 56. Pearson J. Point-of-care-testing and clinical governance. *Clin Chem Lab Med* 2006;44:765–7.
 57. Plebani M, Lippi G. Point of care testing: evolving scenarios and innovative perspectives. *Clin Chem Lab Med* 2014;52:309–11.
 58. Sutherland R. The effect of for-profit laboratories on the accountability, integration, and cost of Canadian health care services. *Open Med* 2012;6:e166–70.
 59. Response to Laboratory Services Review External Advisory Subcommittee Social Contract Study summary report. Toronto (ON): Ontario Hospital Association, 1994.
 60. Hospitals In-Common Laboratory Inc. Report of the Chairman of the Board and President to the Annual Meeting on June 22, 1983, D. Murray Young. Archives of Ontario, RG10-247, container #8, Acc.28303, B212503.
 61. McQueen MJ, Bailey AJ. A cost accounting prototype in the clinical laboratory: the Hamilton Health Sciences Laboratory Program. *Clin Diagn Today* 1993;29–33.
 62. Plebani M. The changing scenario in laboratory medicine and the role of laboratory professionals in translational medicine. *Clin Chim Acta* 2008;393:23–6.
 63. Roy V. Crucial role of laboratory tests in modern medicine. *Am J Med* 2008;121:e27.
 64. Walley T. Evaluating laboratory diagnostic tests. *Br Med J* 2008;336:569–70.
 65. Haddow J, Palomaki G. ACCE: a model process for evaluating data 4 on emerging genetic tests. In: Khouri M, Little J, Burke W, editors. *Human genome epidemiology*. Oxford: Oxford University Press, 2004:217–33.
 66. Plebani M. Evaluating laboratory diagnostic tests and translational research. *Clin Chem Lab Med* 2010;48:983–8.
 67. Bell JI. The double helix in clinical practice. *Nature* 2003;421:414–6.
 68. Plebani M, Laposata M. Translational research involving new biomarkers of disease. *Am J Clin Pathol* 2006;126:169–71.
 69. Baudhuin LM. Quality guidelines for next-generation sequencing. *Clin Chem* 2013;59:858–9.
 70. Lippi G, Favaloro E, Plebani M. Direct-to-consumer testing: more risks than opportunities. *Int J Clin Pract* 2011;65:1221–9.
 71. Kassirer JP. Imperatives, expediency, and the new diagnosis. *Diagnosis* 2014;1:11–3.
 72. Blair ED. Molecular diagnostics and personalised medicine. *Per Med* 2010;7:143–61.
 73. Epner PL, Gans JE, Graber ML. When diagnostic testing leads to harm: a new outcomes-based approach for laboratory medicine. *BMJ Qual Saf* 2013;(Suppl 2):ii6–10.
 74. Scott MG, Smith BR, Wu AH, Young IS, Plebani M, Chiu RW. How well are we raining the next generation of clinical pathologists and clinical laboratory directors? A global perspective. *Clin Chem* 2012;58:491–5.
 75. Wilson ML. Learning to be a consultant. *Am J Clin Pathol* 2014;142:284–5.
 76. Cortelyou-Ward K, Ramirez B, Rotarius T. The laboratory workforce shortage: a managerial perspective. *Health Care Manag (Frederick)* 2011;30:148–55.