

Synergy between point-of-care testing and laboratory consolidations

Tommaso Trenti

Laboratory Medicine & Pathology Department, Azienda Universitaria Ospedaliera e USL di Modena, Italy

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Corresponding author:

Tommaso Trenti
Laboratory Medicine & Pathology
Department, Azienda Universitaria
Ospedaliera e USL di Modena
via Giardini 1355
Modena I-41126
Italy
E-mail: t.trenti@ausl.mo.it

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ABSTRACT

Central or area laboratories will offer an improved number of diagnostic testing services, where drivers for change will involve chronic disease clinical care for an increasingly older population, new emerging diagnostic technologies and personalized medicine. Higher automation quality and ever more diagnostic field integration will lead to higher productivity by means of an improved throughput. At the same time Point of Care Testing (POCT) site of patient care allows for timely medical assessment, which can lead to improved patient outcomes, more effectiveness and patient satisfaction. POCT test introduction in clinical practice should be assessed by an outcome-based policy to avoid adverse events, failure to diagnose providing appropriate timed treatment. The use of POCT devices does not only require technological considerations for the production and management of acceptable tests possibly managed by central laboratory, but also implicates a shift in diagnostic practice across all health organizations. The interaction between laboratory professionals and clinicians will

be enriched with new methods of evaluation of patient needs in the internet of things and mobile Health worlds, where boundaries between POCT and central laboratory or hospital and primary healthcare will no longer exist and where all data can be shared and disseminated among stakeholders in the healthcare system.



CENTRALIZED, AREA, NETWORK OR HUB AND SPOKE LABORATORY SYSTEMS

Routine central laboratory has developed increasingly automated and effective instrumentation, including clinical chemistry, immunochemistry, common haematology testing and even very complex assays, executed using high throughput instruments following sophisticated automation. In the near future, comprehensive central or area laboratories of consolidated assay testing and larger laboratories will be most probable. The centralized clinical laboratory will offer an improved number of diagnostic testing services, where drivers for change will involve chronic disease clinical care for an increasingly older population, new emerging diagnostic technologies and personalized medicine. Higher automation quality and ever more diagnostic field integration will lead to higher productivity by means of an improved throughput. These goals are drivers for technological and management development of a centralized, area, network or hub and spoke laboratory systems, depending on the healthcare organization. Future health care and laboratory systems will have to deal with similar challenges as we face today, which may be summarized by the concept of “do more with less.” The majority of tests will increasingly be performed in consolidated, high-throughput laboratories, because high analytical performance and cost efficiency cannot be fitted by current Point of Care Testing (POCT) technologies or other diagnostic systems. Current

innovation in laboratory technologies is due to the availability of automation and development of analytical instruments, distributed across all disciplines of laboratory medicine. However, if Laboratory Medicine not only provides medical test results, but also helpful information and knowledge to clinicians and other stakeholders to assist decision making for individual patient optimal health outcome, the value of the laboratory is outside the laboratory. This is and will be of increasing value, as the assessments of the impact of medical testing on health outcomes will be a valuable proposition for laboratory medicine. This involves the correct and appropriate utilisation of delivered medical testing, where health results, operational and/or economic benefits are extended across the full clinical care pathway, focusing the interests of all stake holders (1). This aim is important in creating a leading role for laboratory medicine in the development of an effective and valuable healthcare system, as the most outstanding value in care is measured in terms of patient outcome. In this context, the laboratory achieves its best value when the patient successfully completes the diagnostic clinical care pathway. One of the values of laboratory medicine is based on how medical test results change the speed with which the patient completes the care pathway, by providing timely information, empowering clinicians or other stakeholders to make better and fast decisions about patients’ care (2).

KEY DRIVER TO POCT IMPLEMENTATION

Over the past few decades, POCT has been one of the fastest growing disciplines in clinical laboratory medicine, equivalent and parallel to laboratory centralization. POCT is the execution of testing outside the clinical laboratory, near the patient or at the site of patient care. POCT devices are more widely used, both in acute and chronic patient management, inside the hospitals and in primary healthcare settings.

POCT where implemented both in critical care settings/emergency departments and in primary care settings, the assays are performed by nonlaboratory staff. Fast test results at the POCT site of patient care allows for timely medical assessment, which can lead to improved patient outcomes, more effective efficiencies and patient satisfaction (3). Since POCT activities are performed by non-laboratory staff who are unskilled in laboratory practices, one of the main challenges for POCT is the monitoring and management of quality assurance and regulatory compliance. The key driver to POCT implementation is the concept that clinical decision making may be delayed when samples are sent to the clinical laboratory when POCT is able to offer fast results closer to the patient, empowering medical decision making directly. The main endorsement for running POCT depends upon evidence which validates that a timelier result or shorter turnaround time is capable of influencing clinical improvement in decision making, when related with the central laboratory test delivery. In the last four decades, since POCT was adopted for the self-monitoring of blood glucose levels by diabetic subjects, various new POCT methodologies have become accessible, assisting the clinician in obtaining fast results to start treatment more rapidly. POCT seems to reduce pre analytical errors, where in laboratory medicine the higher number of errors happen in this phase (4,5). However, POCT is prone to errors in the analytical phase, due to the management of POCT instruments by staff unskilled in laboratory medicine. Conversely, the analytical phase has the smallest number of errors in laboratory medicine. In some settings, particularly remote rural environments and conditions, a central laboratory would be located at a great distance and the time to availability of some tests would not be acceptable. By contrast, in the Emergency Department, the availability of more rapid results with POCT is

of value, despite the close location of the laboratory. POCT availability is just a means of better care delivery, as other barriers may be important to the implementation of care. Many reviews have applied principles of evidence-based laboratory medicine, seeking high quality systematic reviews and meta-analyses, to find the best possible evidence to support the question of whether POCT gives any advantage in clinical decision making in different scenarios (6) when compared to central laboratory.

THE MAIN THEORETICAL ADVANTAGE OF POCT TO SUPPORT CARE DELIVERY NEARER TO PATIENTS

In primary care there is an increasing focus on the need to encourage a more integrated healthcare attitude to support care delivery nearer to home, to improve not only patient satisfaction but health outcome in primary care. This trend has been matched by a requirement for innovative patient-centred care models (7), driven by the need to decrease rates of inappropriate or unplanned hospital admissions, better care for old patients with long-term chronic conditions and possibly cost containment. One means of realizing care closer to home is the implementation of POCT testing in course of a single routine appointment, supporting the hypothesis that this might decrease additional testing elsewhere, reiteration of visits or further medical appointments due to diagnostic uncertainty. POCT technology improvements have enabled most POCT devices with the knowhow to connect to the laboratory information system (LIS) and electronic medical records (EMR). Therefore POCT performance, when integrated in central medical laboratory activities, are becoming increasingly crucial as hospitals and healthcare systems are undertaking consolidation and harmonization by a continuous interaction (8) to promote the best utilization of diagnostic information and reporting. Some authors

recognize the POCT medical culture as one of the most important characteristics for reducing medical poverty and to design innovative and novel solutions at points of need, worldwide. In this light handheld, pocket-size and connected POCT tools and smartphone diagnostic devices will be used among populations, offering a new vision of healthcare, as an expected element of a highly informed everyday human lifestyle. Practicing point of care in the context of local medical culture is the final frontline and, if positively investigated, will become a 21st Century outstanding achievement (9). It is well recognized that the implementation of POCT is successful when the assay is by itself helpful for the medical decision-making process and does not need additional tests for confirmation from a central laboratory, otherwise the time benefit of POCT is minimal or ineffective. The main theoretical advantage of POCT is early and appropriate aid to diagnosis and treatment, but few studies are available about how POCT results influence clinical decision making. In the case of some immunoassays, POCT results seem to be reliable and accurate, such as for troponin, brain natriuretic peptide and C-reactive protein assays with satisfactory analytical performance together with an excellent feasibility, proposing them to be a consistent tool to be used in clinical practice. However, data and consequently derived evidence regarding clinical outcomes are lacking (10,11). There are many studies highlighting the agreement between POCT and central laboratory in terms of analytical and diagnostic accuracy, but results both on patient management and patient outcomes have not been consistently explored. Evaluation of patient outcomes is a key issue in the decision to implement POCT testing in place of central laboratory testing, and evidence to support this decision making is usually poor (12).

THE DEVELOPMENT OF A VALUE PROPOSITION FOR MEDICAL TESTING IN POCT OR A CENTRALIZED LABORATORY

Some critical steps including key points for discussion and evaluation, have been devised for the development of a value proposition for medical testing in POCT or a centralized laboratory as advised by the IFCC-Emerging Technologies Division (2).

1. What is the unmet clinical need resolved by POCT that cannot be resolved by central laboratory?

The unmet need of the medical test under investigation requires precise and clear definition of the clinical presentation, test impact and the setting of care, as for example the timely delivery of troponin to rule out suspected acute coronary syndrome or myocardial infarction, inside or outside the hospital setting. [13].

2. What is the clinical pathway in which the POCT is implemented?

The evaluation should focus on how test results improve clinical decision-making, patient management, medical appointments (urgent and non-urgent) and care process efficacy and efficiency. The appraisal should evaluate the clinical setting and report on how POCT medical test results are used, if the test is intended for diagnosis, for monitoring disease progression or for prognosis. Its position and role in the clinical pathway should be defined, such as whether it is a new test, an additional test, a replacement test or if it is used in patient triage. The clinical decision influenced by the medical test result and its impact on patient management needs to be clearly outlined, such as whether POCT testing is used to guide a therapeutic or other intervention.

3. What are the POCT test benefits vs central laboratory test?

The benefits of timed medical test assay to resolve the patient clinical need by robust and well demonstrated data, possibly based on clinical trials of POCT medical tests under evaluation, should be studied. The potential benefits derived from introducing POCT testing is of pivotal importance and should include the measurement of clinical, operational and economic outcomes, highlighting the reduction in time for patients to complete the clinical care pathway. Potential harms arising from the use of POCT medical test should be also identified.

4. Who are the POCT stakeholders?

The stakeholders, including the patient, the clinical team including laboratory medicine the healthcare purchaser and healthcare policy-makers should be identified. Analyses of costs and benefits need to include the impact for each of these actors and stakeholders. Utilisation of health economic outcomes research is needed to guide the introduction of POCT new tests based on a firm foundation of evidence.

The principles of health technology assessment (HTA) are already applied in laboratory medicine and POCT evaluation so promoting efficacy, efficiency in POCT implementation when necessary, by attention to productivity through technology and process innovations (14). In the evolution of HTA appraisal, as in the case of POCT, patients need to be involved, particularly at the early stages (15) in terms of care value perception. Areas for improvement include aim, setting, and focus on the full health system effects (16). Further POCT test introduction in clinical practice may be assessed by an outcome-based policy on testing-related diagnostic errors (17) for a more active selection of useful biomarkers to avoid adverse events, failure to diagnose providing appropriate timed treatment. In this light

the development of high-quality recommendations on POCT versus central laboratory testing may result in common framework to promote harmonisation and risk management in diagnostic pathway as reported in Table 1.

The Test Evaluation Working Group (WG-TE) of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM) proposed an outcome-focused approach that can be used to evaluate any medical test, irrespective of the purpose and role of testing to identify clinical management decisions, linking biomarker testing to health outcomes (18). A patient-centred method that can be used in POCT test assessment is The Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to assess both the certainty in evidence and to develop recommendations (19). Desirable and undesirable effects need to be judged in comparison to the old or traditional laboratory test due to a new POCT testing. The use or misuse of tests for a specific clinical presentation in different professional settings affects equity of access to clinical care (20), test the cost-effectiveness of interventions should include the evaluation of the impact outside the laboratory and the downstream consequence. The great challenge is to identify the overall health care cost and not only the plan cost of the test itself (21).

THE USE OF POCT DEVICES IMPLICATES A SHIFT IN DIAGNOSTIC PRACTICE ACROSS ALL HEALTH ORGANIZATION CLINICAL GOVERNANCE IN LABORATORY MEDICINE

The use of POCT devices does not only require technological considerations for the production and management of acceptable tests, but also implicates a shift in diagnostic practice across all health organizations. A new design for a chronic care model supports the integration of POCT in primary healthcare by an iterative scheme

Table 1 Relationships between clinical-laboratory harmonization in the total testing process and the outcome-based approach in the case of POCT

Outcome-based approach to testing-related diagnostic errors	POCT vs central laboratory harmonization in laboratory medicine
Source: Processes external to the laboratory	Initial and/or final steps of the total diagnostic process (outside the laboratory) POCT vs Central Lab
<ul style="list-style-type: none"> ▶ An inappropriate test is ordered POCT vs Central Laboratory ▶ An appropriate test is not ordered POCT vs Central Laboratory ▶ An appropriate test result is misapplied both Central Laboratory and POCT 	<ul style="list-style-type: none"> ▶ Selection of references biomarkers POCT vs Central Laboratory <ul style="list-style-type: none"> ▶ Appropriateness in POCT test request ▶ Appropriate Test timed interpretation and decision to be acted <ul style="list-style-type: none"> ▶ References population data base
Source: Internal processes (within the laboratory)	Internal processes (within the laboratory or managed laboratory POCT)
<ul style="list-style-type: none"> ▶ An appropriate test is ordered, but a delay occurs somewhere in the total testing process, POCT value ▶ The result of an appropriately ordered test is inaccurate due to an unacceptable POCT or Central Laboratory Management 	<ul style="list-style-type: none"> ▶ Evaluation of pre-analytical sources and pre-analytical quality both in POCT and Central Laboratory ▶ Harmonization of currently available assays and analytical control practice by POCT testing and Central Laboratory

process, to optimize a care model based on dynamic integration of POCT into the network of care delivery to optimize the benefit of the diagnostic test performed. This care model design is based on the integration of POCT through the connectivity with primary care providers according to clinically approved guidelines. Therefore, the POCT results are managed by the clinical central laboratory, not only as technology assurance but also in the diagnostic information

process. Laboratory medicine specialists are likely to take a lead in organizing and managing multidisciplinary teams and to undertake this clinical diagnostic processes in terms of clinical governance (22). The brain-to-brain loop describes the process from the physician's decision to request a diagnostic test up to the action due to the reported result. The integration of all diagnostic laboratory test, POCT or central laboratory test performed, into the care pathways,

by digitalization of care will have an important impact on this process. Effective chronic disease management needs the involvement of multi-disciplinary teams, stimulating and encouraging a continuum between primary, secondary and tertiary sectors. New clinical governance framework may be based on an integrated diagnostic framework, where POCT and central laboratory data are fully combined with all patient data to allow not only traditional policy and programme of quality assurance, risk management, technology assessment but also integrated for shared disease management.

THE DIGITALIZATION OF HEALTHCARE AND LABORATORY MEDICINE

The interaction between laboratory professionals and clinicians will be enhanced by digitalization, internet of things and mobile Health worlds, where borders between POCT and central laboratory will no longer exist. The availability of diagnostic Artificial Intelligence (AI) support utilizing POCT results coupled by laboratory data may be of value at the hospital admission promoting an accurate and fast diagnosis fostering the expected outcome or assuring the best possible care at home after discharge from hospital. Now and in the near future, new generation of electronic medical record systems digitally connecting information from POCT, Central or area Laboratory and patient homes, is an emerging healthcare model as proposed by the report from the IFCC-Emerging Technologies Division (2). The central laboratory robotization, POCT extension strategy, big data and algorithmic recording and reporting by artificial intelligence will drive the presence of another brain-to-brain loop or the so-called Lundberg cycle, defined as the “Artificial Intelligence Brain” (23). Currently health care debate leads to a healthcare reorganization strategy where the hospitals are devoted to the emergencies and intensive

care management while chronic patient care is decentralized in community hospitals or near patient health structures or patient home managed by GP and/or nurses. In this light the laboratory diagnostic test may be a driver for best medical decision based on the interaction with all patient data derived by clinical history when available. This may be of value in home to hospital care as in the case of patient with acute disease, or in hospital to home in the case of low-level intensive care as in patient with chronic disease. The future balance between testing in central laboratories and testing at the point of care is difficult to predict accurately (24) as POCT or near-patient testing is now starting to look to laboratory testing with new mobile devices and online services in a new context of home bedside care or self-care.

The rise of AI and machine learning can allow the combination of data from different hospital settings, POCT, central laboratories and healthcare sites to promote the “learning” of predictive models (25,26) as distributed learning.

The availability of large population medical datasets opens the way to approaches based on the analysis of data to generate diagnostic hypotheses that can be confirmed by further test inside laboratory or outside. POCT area datasets merged by population diagnostic records derived by area or network laboratory data are means to develop real-word AI diagnostic support tools to improve the management of chronicity in primary near patient care. In this light the use of POCT technologies offer an opportunity to promote the best use of laboratory results even in absence of skilled physicians. This approach may be operated in remote, primary and secondary diagnostics.

In **remote diagnostic** to obtain information on symptoms and signs that can allow establishing the degree of urgency and the requirements for diagnostic tests, like POCT, based on data

already known possibly in primary care. This will also increase the positive predictive value for the POCT tests by pre-screening for patients that are more likely to have the condition assessed by POCT.

In primary diagnostics as reliable and cost competitive primary diagnostics support tool for common diseases by simplifying the diagnostic process. The AI may be helpful to advise still rare or uncommon diseases streamlining the process of obtaining the right diagnosis reducing the delays in the diagnosis.

In secondary and tertiary diagnostics by the application of AI integrated with secondary diagnostics tools, such as ECG, imaging, and all available population clinical data set. AI or diagnostic support tool will help to identify patients, who either do not get a diagnosis or in situation where the diagnosis is particularly difficult. This approach enables clinicians to make a diagnosis with increased accuracy significantly improving patient journey identifying complex cases where a precise diagnosis is difficult.

Synergies on Laboratory Medicine Department basis between POCT results with all real patient diagnostic data available as present in area Laboratory Information System repository will unlock AI based potential diagnostics support tools, providing quicker and more accurate and less expensive diagnosis.

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