TITLE: A Review of Published Studies on the Value of Laboratory Medicine

RUNNING HEAD: Value of Lab Medicine

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ABBEVIATIONS:

Centers for Medicare and Medicaid Services (CMS)

Turnaround Time (TAT)

Point-of-Care Testing (POCT)

Hemoglobin (Hgb)

Potassium (K)

Emergency Department (ED)

Length of Stay (LOS)

Sodium (Na)

Chloride (Cl)

Electronic Health Record (EHR)

Centers for Disease Control and Prevention (CDC)

Diagnostic Management Team (DMT

Doctorate of Clinical Laboratory Science (DCLS)

National Accrediting Agency for Clinical Laboratory Science (NAACLS)

Health Care-Associated Infection (HAI)

Multi-Drug Resistant Organisms (MDRO)

National Healthcare Safety Network (NHSN)

Methicillin-resistant Staphylococcus aureus (MRSA)

Antimicrobial Stewardship Programs (ASP)

Drug Susceptibility testing (DST)

Laboratory Response Network (LRN)

Lipid Standardization Program (LSP)

Food and Drug Administration (FDA)

Hepatitis C Virus (HCV)

Chronic Myelogenous Leukemia (CML)

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Abstract: 129

ABSTRACT: In the current healthcare climate, pressures for cost control are extreme. Every sector is required to justify activities and expenditures through demonstrated value to patient outcomes and/or the system as a whole. This review of recent literature, with particular attention to studies published in 2000-2017, was undertaken to reveal what is known about the value of laboratory medicine in terms of patient health outcomes; but limited evidence was available on this topic. Instead, laboratory value was described in more qualitative ways, organized around four themes: 1) providing test results, 2) test consultation, 3) financial value, and 4) knowledge development. This literature review outlines what is currently published with respect to medical laboratory value. This review suggests research opportunities to clarify the quantitative value of laboratory medicine to healthcare.

INTRODUCTION

Laboratory scientists, like other healthcare professionals, are being pressured to demonstrate the value of laboratory medicine; yet data are lacking on improved patient outcomes tied unequivocally to clinical laboratory services, except in very specific instances such as the superiority of serum troponin in the definition of myocardial infarction.[1] Clinicians who strive for positive patient outcomes are key stakeholders who are well positioned to assess the valuable contributions of the laboratory. However, identifying and validating measures that would potentially tease apart the value of laboratory medicine from other healthcare services in achieving desired patient outcomes remain elusive.

This narrative literature review was conducted with a concentration on studies published between 2000 and 2017 regarding the value of laboratory medicine based on the perspective of the various key stakeholders including: patients and family members, clinicians, parent organizations (licensed entities that provide health care services) and healthcare systems, the Centers for Medicare & Medicaid Services (CMS), pharmaceutical industry, and public health. In this narrative review, the working definition for the value of laboratory medicine was considered as patient health outcomes achieved per dollar spent.[2] Authors utilized PubMed, Google Science and Web of Science to conduct the literature search. For the search strategy we used search terms including, "Value of Laboratory" and "Pathology, Clinical" OR "Pathology Department, Hospital" OR "Clinical Laboratory Services"[Mesh] OR "Laboratories, Hospital" and "Diagnostic Tests, Routine" and "Outcome and Process Assessment (Health Care)". While numerous publications addressed the need to identify strategies for defining the value of laboratory medicine, the literature is sparse concerning the application of this definition and did not adequately assess the overall impact of the laboratory within the continuum of health care delivery. The search produced the following number of publications relative to the stakeholder of interest: clinicians (69), parent organizations and healthcare systems (27), public health (26), Centers for Medicare & Medicaid Services (CMS) and pharmaceutical industry (25), and patients and family members (22). Therefore, the following narrative is organized based on four common themes across the perspective of key stakeholders as determined by the literature. Selected studies published prior to 2000 were included in this report for historical context. It is anticipated that the information presented in this review will assist the stakeholders in identifying meaningful measures/metrics for determining the value of laboratory medicine testing and services.

THEME 1: PROVIDING TEST RESULTS

The 2015 Institute of Medicine's report on Improving Diagnosis in Health Care notes that over the past 100 years, diagnostic testing has become a critical feature of standard medical practice.[3] This report notes that in many cases, diagnostic testing can identify a condition before it is clinically apparent. Laboratory medicine and pathology have been described as "essential element[s] of the health care system," stating that these disciplines are "integral to many clinical decisions, providing physicians, nurses, and other health care providers with often pivotal information for the prevention, diagnosis, treatment, and management of disease."[4]

Reviews of the numbers of conditions and tests used in the diagnostic process further support clinician reliance on laboratory medicine for diagnosis, prognosis, interventions and ongoing treatment of a patient. In an attempt to quantify the range of conditions managed by clinicians, a 2008 study of a large multispecialty practice in Massachusetts found that the practice managed patients with more than 5,600 unique primary diagnoses and 6,400 unique secondary diagnoses. Each clinician in this practice managed a median of approximately 130 unique laboratory test orders, 250 unique primary diagnoses, and 280 unique medications. These numbers were even higher for those clinicians in internal medicine.[5] These findings highlight the increasing complexity of managing patient care including the utilization of clinical laboratory diagnostic testing.[6]

Laboratory professionals have traditionally focused on assuring analytical accuracy in the testing process. For physicians, quality and reliability of results have become an assumed integral component of laboratory testing, "a given" in the process.[7] This perspective may also explain the findings in a study of nursing satisfaction with clinical laboratory services, with accuracy of test

results generating the highest level of satisfaction, despite the fact that it was listed as the second most important service category after stat test turnaround times.[8]

Research on the overall diagnostic accuracy of medical laboratory testing is limited; most literature focuses on particular analytes and diseases. One project with a broader focus identified an error rate in stat laboratory testing in a 1750-bed university hospital of only 0.3% with a distribution of 61.9% pre-analytical, 15% analytical, and 23.1% post-analytical errors.[9] Existing evidence shows that the majority of laboratory errors occur outside of analytical laboratory testing, i.e., occur during the pre-and post-analytical phases.[10] This demonstrates that patient safety may likely be compromised during pre- and post- analytical phases of the Total Testing Process (TTP). Thus, significant value to quality improvement systems can be achieved by integrating clinical laboratory professionals into risk management of patient safety.[11]

The need for faster test turnaround time (TAT) has been a common theme in the literature for the past 30 years and is cited as the preference for clinician satisfaction that has driven much of the proliferation of point-of-care testing (POCT).[12] Conclusions in one literature review were that laboratory TAT continues to be a cause of customer dissatisfaction despite advances in technology and information systems.[13] Comparable findings were reported in a seven year time frame in two physician and nursing satisfaction studies performed by the College of American Pathologists.[7,14]

Despite this ongoing "need for speed", the evidence of improved outcomes that may result from a faster testing process has been contradictory. For example, Steindel et al. examined the timeliness of early morning routine clinical laboratory tests for inpatients in 653 institutions and found little evidence that longer routine test TAT affects patient length of stay (LOS).[15] In contrast, physicians reported unacceptable delays in treatment due to TAT for hemoglobin (Hgb)

and potassium (K) tests in an emergency department (ED) setting.[16] Though the POCT is reported to be more expensive and challenging with regards to regulatory management compared to central laboratory testing, its rapid TAT is considered to be the main contributor to improvement in patient outcomes. Specifically, cardiac markers, the D-dimer test, and rapid urine drugs-of-abuse test have led to decreased ED length of stay.[17,18] In one study in which POCT afforded a modest benefit in the ED, an 87% decrease in TAT through POCT translated to a 41 minute decrease in the LOS for patients who received rapid testing for HCG, urine dipstick, and cardiac markers with high clinician satisfaction with test accuracy.[19] In a more recent analysis of POCT process design in the ED, POCT was associated with statistically significant improvements in three measures: service time, waiting time, and quality of care provided to patients, defined by number of patients who returned within 72 hours.[20] It is important to note, however, that these studies focused on the value of speed but did not suggest that POCT results were more accurate.

An area of significant value to clinicians occurs post-analytically with the communication of laboratory test results and test information, evaluation, and interpretive information from the laboratory to the clinician using multiple modes of transit (i.e. electronic, verbal, hard copy, etc.). Providing laboratory results within an electronic health record (EHR) has significant potential to provide clinicians with critical information in a timely manner that can contribute to improvements in the care process. However, the large amounts of data currently available within EHRs increase the probability for a clinician to miss a review of relatively important information.[21] The findings of a review by the Australian Clinical Excellence Commission indicated that failures in processes associated with obtaining and using the results of diagnostic testing have the potential to compromise patient safety.[22] Sittig and Singh also suggest that, even with the best information systems (including those that contain advanced notification features),

patients with abnormal diagnostic tests are vulnerable to failures in follow up and tracking follow up in electronic systems.[23] Further, the interpretation of laboratory results in the clinical context by an expert laboratory-based practitioner renders a significant difference to clinical outcomes for individual patients.[24]

Rapid communication of critical results by the laboratory in immediately life threatening or life altering clinical situations are perceived to be of significant value to the clinician and patient outcomes.[25] Identified as one of the highest priority patient safety issues, critical value reporting was incorporated in The Joint Commission National Patient Safety Goals (NPSG.02.03.01) utilized in hospital accreditation programs.[26] However, processes for communicating and acting upon critical results vary widely and are often developed without employing evidence-based practice.[27]

An inarguable source of value in the post-analytic phase of laboratory testing is "reflex" testing, additional testing automatically performed on a specimen subsequent to an initial test result that is inconclusive and meets pre-established criteria. This type of testing reduces overall healthcare costs by increasing efficiency and time to diagnosis, as well as improving patient satisfaction with laboratory services, particularly through fewer specimen collections. Verboeket-van de Venne et al. propose a more advanced form of reflex testing called "reflective testing" to further improve the process of diagnosing and treating a patient, thus enhancing the value of clinical laboratory testing.[28] Reflective testing is defined as add-on tests based on clinical judgement of a laboratory specialist after careful interpretation of laboratory testing results and is more applicable to complex diagnoses. Paterson et al. assessed patient opinion of reflective tests and found that 73% of outpatients and 90% of general practice patients studied were in favor of reflective testing for their own specimens.[29] In another survey, clinicians highly favored the

support received from a laboratory specialist in the post-analytic phase with 75% of respondents indicating that interpretive comments "either help or influence patient management" and 100% of respondents regarding reflective testing as appropriate and valuable.[30]

THEME 2: TEST CONSULTATION

Selecting the right test has become an increasingly difficult challenge given the complexity of patient management, the increase in laboratory testing options, bundling of multiple tests, and advancements in technology. In a 2008 survey of junior physicians in the United Kingdom, only 18% of respondents were confident about requesting 12 common chemistry tests. There was a similar lack of confidence in interpreting the results. For example, only 18% of respondents were confident that they could correctly interpret a hemolyzed sample.[31] A national survey of family medicine and general internal medicine physicians revealed that clinical laboratory tests are ordered in 31.4% of primary care visits; however, the clinicians report uncertainty when ordering tests 14.7% of the time and confusion about interpreting results in 8.3% of the cases in which they ordered tests.[32] In the last 20 years, the number of laboratory tests available to clinicians has doubled to at least 3500 tests without a proportionate increase in medical school curricula. This means that junior physicians are often uncertain over the best use of laboratory tests and may be using them incorrectly on many occasions. Access to consultations from clinical laboratory professionals was cited as one means of reducing this uncertainty.[32] A 2009 report from the Centers for Disease Control and Prevention (CDC) on laboratory medicine noted that there is inadequate attention and emphasis on laboratory testing in the medical school curriculum, even though it plays a central role in medical practice.[33] Molecular and genetic tests are often misunderstood, expensive, and sometimes controversial but play a key role in precision

medicine. The technology and prices evolve rapidly, making it difficult for busy clinicians to stay current with the costs and benefits of any particular test. Physicians who are not geneticists or do not have a strong background in genomics struggle with appropriate ordering and interpretation without guidance from the laboratory.[34] Laboratory professionals clearly have an opportunity to intervene, adding value in the professional development process of clinicians by assisting with education and guidance regarding appropriate laboratory testing.[35]

Inappropriate use of laboratory testing includes both overutilization and underutilization.[36] Over-testing has introduced unnecessary delays in patient care due to the requirement for follow-up of slightly abnormal tests, and increased testing leads to an increase in clinical interventions.[37] A systematic review of studies published in a 15 year period revealed overutilization and underutilization testing rates of 21% and 45%, respectively. Indeed, the overutilization rate was six times higher during initial testing compared to repeat testing.[36] Inappropriate test selection leading to further testing may not only exact a severe financial cost but also have unintended adverse consequences such as potential infection from invasive biopsies and exposure to unnecessary irradiation from inappropriate imaging when tumor marker levels are not appropriately interpreted.

Selection of the "right test" by a provider, as well as the correct interpretation of test results, can be improved through consultation with the appropriate laboratory professional.[38] The use of diagnostic management teams (DMTs) comprised of a group of experts (e.g., pathologists, clinicians, and laboratory professionals) can provide consultations on diagnostic testing, such as selecting the appropriate tests and understanding these results.[39] In addition to assisting with the selection of the "right test," these teams integrate a patient's clinical information to provide a context for the test result, while ensuring that a clinically valuable interpretation is included in the

test result report. Clinicians who participate with laboratory professionals in this process report a favorable view of DMTs, and although perceived high initial costs are a potential barrier, evidence exists that DMTs can lower overall costs.[40]

An unexplored avenue of laboratory value is the addition of the Doctorate of Clinical Laboratory Science (DCLS) practitioner to the profession, either as a solo consultant or member of a DMT. After several years of needs assessment, the consensus of the medical laboratory community was that "the DCLS will assume roles as consultants, educators, and/or administrators to contribute to the common goals of decreasing medical errors, reducing health care costs, and improving patient outcomes".[41] The National Accrediting Agency for Clinical Laboratory Science (NAACLS) established standards for DCLS programs,[42] and the first DCLS graduated in 2018. It will be a few years before the effects of DCLS professionals can be quantified, but the hope is that marked improvements will be reported in laboratory test utilization when DCLS participate more directly in patient care.

Treatment planning conferences for oncology cases (also referred to as tumor boards or molecular tumor boards) are another way laboratory professionals can add value to the provider through selection of the correct tests, interpretation of test results, and participation in care decisions. These conferences serve as a form of case review by a multidisciplinary team of health care professionals to identify best treatment options based on the medical condition. The evidence on whether treatment planning conferences improve patient outcomes has been somewhat contradictory with some studies demonstrating a positive influence,[43] while others reporting no significant improvements on the quality of patient care.[44]

As a generic form of test consultation, many laboratory professional societies have established clinical practice guidelines.[45, 46] Other professional groups have established dozens of

clinical practice guidelines, and many feature laboratory testing prominently.[47, 48] For example, the British Society of Gastroenterology published guidelines on the management of abnormal liver tests; and the American Diabetes Association adopted guidelines for the use of laboratory analysis for the diagnosis and management of diabetes mellitus patients as recommended by the National Academy of Clinical Biochemistry. Therefore, clinical practice guidelines can be interpreted as direct evidence of laboratory value.

The next logical step is to establish that improved outcomes follow implementation of the guidelines. However, some authors have noted that this is a challenge. The American College of Cardiology/American Heart Association Task Force published a thoughtful paper on how to establish outcomes when practice guidelines are used but noted that these studies have not been conducted due to a lack of consensus on how to measure outcomes.[49] Misra et al. reached a similar conclusion in their discussion of implementing and assessing laboratory practice guidelines but also emphasized that the usefulness of the information generated is dependent on the inclusion of the laboratory professional in the development of the guidelines.[50]

Despite the paucity of studies regarding the outcomes of clinical practice guidelines after implementation, it is logical to assume that the value of these guidelines are demonstrated. First, most practice guidelines are based on evidence from outcomes of previous studies, and the strength of that evidence is evaluated by experts prior to a recommendation being adopted. For example, to establish "Molecular Biomarkers for the Evaluation of Colorectal Cancer" guidelines, Sepulveda et al. reviewed more than 4000 articles.[51] In another study, Kim et al. performed outcome modeling on a large population data set and demonstrated that the adherence to the new cervical cancer screening guidelines would improve healthcare and add value.[52] While indirect proof of potential value, this does constitute evidence of the value derived from practice

guidelines related to laboratory testing; and more robust evidence is likely to come when there is consensus on valid evaluation models. Despite the data and evidence driven nature of practice guidelines, they are essentially passive in nature, thus, requiring physicians to both read and actively incorporate their recommendations into practice. A more aggressive use of practice guidelines, however, is through incorporation into clinical decision support within EHRs. Using the capabilities of the EHRs and associated analytics to measure outcomes related to actions, the potential exists for quantifying the impact and value of practice guidelines on the care process.

THEME 3: FINANCIAL VALUE

Laboratories affect value through the decisions that influence both outcomes and costs. Unfortunately, most studies on diagnostic tests focus on analytical or clinical performance. Very few studies have produced data on patient outcomes. Teasing out just the laboratory's contribution is difficult because the patient's outcome is a product of many factors. As a result, it is difficult to evaluate potential interventions. For example, a recent study showed how laboratory monitoring could improve the follow-up of patients with potential chronic kidney disease.[53] Although one can infer that such practice leads to an improvement in outcomes, the study did not explicitly measure them.

Traditionally, the value of the laboratory has been viewed in terms of efficiency in response to test requests, minimizing the cost required to respond to test requests with acceptable levels of quality, delivery, and flexibility. However, a focus on just operational efficiency obscures the total value of the laboratory. To be effective, clinicians must order the correct test, interpret the test correctly, and take the appropriate action.[54] These complex tasks are subject to error that has two consequences. First, inappropriate testing directly increases costs, especially if

it results in wasteful follow-up testing. Second, inappropriate testing can delay diagnosis and therapy resulting in downstream negative effects on patient outcomes, including clinically unimportant incidental findings and harm that ensues from inappropriate follow-up testing. Thus, laboratory professionals can play a substantive role in enhancing value by providing timely services that improve test utilization, such as monitoring test order requests for consultation to identify opportunities for improvement.[55]

Similar to manufacturing and service operations, the effectiveness of a laboratory depends on the alignment between the competitive priorities (i.e., low cost, high quality, fast delivery, flexibility, and ancillary services) and the operation strategies of the parent organization.[56] Laboratory professionals make explicit choices (technology selection, capacity, range of services) that can directly influence the organization's operating capabilities and, hence, may affect the overall functions of the laboratories. Existing literature suggests that laboratory testing has become a commodity,[57] particularly since POCT results are perceived to be as reliable in some cases as those coming from a central laboratory. In other words, test results generated by different sources may be perceived to have equivalent quality and value to clinicians. For example, a blood glucose result from a POCT device used in the home is seen as the same as from one generated from a central laboratory. In a commodity business, the outputs are standard, affording little opportunity for management to differentiate by positioning the organization along these competitive priorities since all outputs are considered to be of equal quality. Studies that refute this notion are sparse; therefore, this is prime territory for further research.

THEME 4: CONTRIBUTIONS TO KNOWLEDGE DEVELOPMENT AND CHANGE IN HEALTHCARE

In addition to diagnostic and disease management information, laboratory medicine affords value through providing knowledge for research and development that impacts public health, policy development, and management of and direction for better therapy through precision medicine. The evolution of technology, molecular epidemiology, precision medicine, and bioinformatics, collectively, has contributed to the increase in value of laboratory services, especially in public health, since the 1960s.[58] Considered the cornerstone of public health practice, surveillance methods aimed at health care-associated infections (HAI), multi-drug resistant organisms (MDRO), reporting of adverse events, natural disasters, and biochemical/chemical threats have improved with advances in information technology.[4,59] Reduction in infections associated with healthcare devices including surgical site infections, ventilator-associated pneumonia, central line-associated bloodstream infections and catheter-association urinary tract infections is a significant outcome of the National Healthcare Safety Network (NHSN) population-based surveillance program.[60]

Information generated from population-based surveillance programs enables the CDC to develop practice guidelines for the prevention of antibiotic-resistant infections in healthcare settings, in the community, and in food.[60] Dissemination of these guidelines resulted in decreases in HAI, such as methicillin-resistant *Staphylococcus aureus* (MRSA).[61] The CDC's National Antimicrobial Resistance Monitoring System for Enteric Bacteria supported by all 50 states in the US, serves to protect populations from resistant infections by providing information related to patterns of emerging resistance in select bacteria transmitted through food.[60] Laboratory services play a key educational role in proper usage of antibiotics through antimicrobial stewardship programs (ASPs), a surveillance system implemented at the institutional level. Beardsley et al.

reported the financial impact of an 11-year ASP at an 880-bed medical center as an average cost savings of $920,070 to $2,064,441 per year.[62]

Advanced molecular testing has influenced HAI, patient health outcomes, hospital LOS, number of days in isolation, patient satisfaction, antibiotic stewardship, and health care economics, all of which can be used as variables to measure the value of laboratory medicine and ultimately influence policy development affecting larger population units.[63] However, the value can also be assessed by measuring the impact of new technology on clinical decision making. Since 2009, the CDC offers its service for the molecular detection of drug resistant *Mycobacterium tuberculosis* to reduce TAT when testing for this organism. Slower phenotypic methods were most often used for drug susceptibility testing (DST) by Public Health Laboratories (PHL) prior to the initiation of this program. Yakrus, Metchock, and Starks reported results of a satisfaction survey of this service administered to 43 PHL.[64] Of the 81% PHL who participated in the study, 97% were satisfied with the TAT for receiving test results. However, 60% of PHL reported clinicians seeking some form of assistance in the interpretation of the molecular testing results indicating the importance laboratory's consultative role, especially with new technology.

The history of medical laboratory research shows consistently improved healthcare over time, and this will likely continue. Dowdle et al. illustrate several examples of laboratory medicine's impact on public policy and regulations in reducing the rate of infectious disease due to advances in laboratory technology.[58] Genomic sequencing identified the first outbreak of circulating vaccine-derived poliovirus which led to the recommendation of replacing live with inactivated virus in the vaccines. Identification of hepatitis B surface antigen through advanced technology and subsequent development of a vaccine is another example of reduction in disease rates due to laboratory services. Standardization of methodology by PHLs enabled the creation of

the Lipid Standardization Program and PulseNet for foodborne disease surveillance, cluster-detection, and outbreak investigations. Referred to as one of the most important achievements of PHL, identification of lead in gasoline as a major source of lead exposure using atomic absorption analyses provided evidence for policy to remove lead from gasoline in industrialized countries throughout the world. Subsequently, this policy resulted in a significant reduction in the percentage of children with lead toxicity.[65] The development of laboratory methods to quantify serum cotinine (major nicotine metabolite) led to the regulation of tobacco products usage in public areas.[66] A decrease in cotinine levels in nonsmokers by approximately 70% was cited as a result of implementing the smoking restriction. State mandated newborn screening programs developed and performed by PHLs have led to early diagnosis and management of more than 50 diseases. PHLs also assist in mitigating the adverse outcomes related to natural disasters and biochemical threats by ensuring access to laboratory testing and providing a mechanism for communication among public and private laboratories.[4] For example, during the 2001 anthrax attacks, the establishment of the Laboratory Response Network (LRN) and the use of sequencing and subtyping techniques were instrumental in confirming organism identification and differentiating cases of intentional attacks from natural exposure.

The pharmaceutical industry is becoming increasingly dependent on laboratory tests in the development of new drugs and the salvage/repurposing of therapeutics that had been abandoned prior to developments in pharmacogenomics.[67] The Food and Drug Administration (FDA) uses viral load test data as an evidence base for recommendations for therapeutic management of many infectious viral diseases including cytomegalovirus, hepatitis B virus, and hepatitis C virus (HCV).[68-70] One study estimated a single HCV viral load test in a single medical management decision pathway was valued at over $2000 per patient.[71] In the field of companion diagnostics,

where tests determine the efficacy and dosage of a drug for a particular patient, it is estimated that over 100 drugs are in clinical trials with diagnostics listed as either part of primary or secondary outcome measures or as inclusion or exclusion criteria. Co-development of these tests with the drugs is so important that the FDA has issued a guidance document developed from all three device and drug centers: Center for Drug Evaluation and Research, Center for Devices and Radiological Health, and Center for Biologics Evaluation and Research.[72]

A commonly cited example of the interplay between patient laboratory data and pharmaceutical discovery/implementation is the development of imatinib for treatment of chronic myelogenous leukemia (CML), which increased the five-year survival rate for CML patients from less than 50% to 89%.[73] Imatinib therapy is now used in treating other serious malignant disorders, based on tests for kinase pathway mutations and modified by mutation analysis of the patients' constitutional Cytochrome P450 metabolic genes.[74] Instead of characterizing and treating cancers only by anatomic site, genetic characterization of tumors by clinical and research laboratories is directing patients into more effective therapy. "Basket studies," where patients are cohorted into therapy groups based on shared mutations regardless of anatomic site, are now funded internationally; and encouraging results are beginning to be published.[75] Beyond just the pharmaceutical industry, cooperation between the medical laboratory and developers of new tests, new analytical platforms, and other research studies continues to contribute significantly to knowledge advancement and subsequently improved patient outcomes and community health.

DISCUSSION

The quest to demonstrate value within healthcare is one that will continue to grow as both developed and developing countries come face to face with the reality of the increasing costs

necessary to provide quality care and maintain the health of their populations. The days of relying upon data-sparse narratives to describe a sector or service's value or contribution to the healthcare process are quickly coming to an end. Despite an ever changing landscape of healthcare policy both in the US and internationally, the concept of applying data-driven science to the art of medicine in order to improve value will likely continue to grow as countries seek to control costs.

Quantifying the actual contributions of laboratory medicine, however, remains somewhat elusive. Medical laboratory tests supply clinicians with actionable information that is integral to aiding medical management decisions, facilitating development of new therapies, steering infection control, and guiding public health strategies. Although a laboratory test may provide an accurate, timely, or even less invasive diagnosis compared to other diagnostic methods, these attributes do not automatically translate to value-improved therapeutic management, improved outcome, or cost-effectiveness of care in general.[76] Clinical utility studies that document the degree to which the actual use of a test leads to improved treatment decisions and consequently improved patient outcomes, or, more generally, cost-effectiveness of provided care are required. Sadly, there are few published studies of this type. Advances in healthcare analytics which permit the examination of "big data" may eventually permit reliable conclusions as to the value of the laboratory. One author suggests that while directly connecting laboratory testing to patient outcomes and actual dollars saved is ideal, it may be too ambitious given the multitude of factors that contribute to outcomes.[77] He suggests evaluating easier to determine "intermediate" outcomes such as time to diagnosis, accuracy of diagnosis, completeness of diagnosis and "missed opportunities." Whatever outcomes are selected for study, it is critically important that

laboratory professionals develop methods to quantify and effectively communicate the relevant value of laboratory services.

Often when we depend on a product or service that has been so readily obtainable that it may be considered a commodity, its true value may not be realized until it is no longer available. The intrinsic value of laboratory testing is the pivotal information afforded to health care providers for improving prevention, diagnosis, treatment and management of a patient; evaluating a clinical trial; identifying or predicting an outbreak; as well as the many other contributions previously noted. Some professionals and researchers have suggested we measure the value of that information by building scenarios with and without the laboratory test information.[71] A common language used is health economics, the study of the functioning of healthcare systems and behaviors affecting health, but few methodologies have been developed specifically around the value of the laboratory information. Health economic outcomes can be measured in lives/years saved, money saved or money invested per specific outcome. Forward thinking health economists have suggested that decision theory and the value of information would be useful for this conversation.[78-80] The work has been limited, and the conversation is complex. However, as value-of-information is becoming more useful in making decisions about extending or ceasing clinical trials, the methods are streamlining and the vocabulary is becoming more familiar.[81] It is important that laboratory professionals adapt and build on such work in order to raise the awareness of laboratory medicine's value, so that the discussion of the contributions of laboratory services and information are relevant, effective, understandable and recognized.

The laboratory sector is certainly no exception in having to respond to healthcare's quest to demonstrate value and manage costs. The worldwide laboratory community has started to recognize this struggle and the need to work together to develop a new narrative to objectively

demonstrate the value the laboratory brings healthcare. A number of laboratory organizations and groups have started to propose recommendations on how laboratory medicine can collectively focus efforts on value to develop that narrative.

The International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) has developed recommendations on how to maximize the value of laboratory medicine in five areas including: improved utilization of existing and new tests, definition of new roles for laboratory professionals that are focused on optimizing patient outcomes, development of standardized protocols for prospective patient-centered studies, benchmarking of existing and new tests with commonly accepted measures of effectiveness, and agreed upon definitions and validation of effectiveness measures for articles submitted for publication.[82] Progress in these areas is thought to be essential in helping laboratory medicine enhance value.

The American Association of Clinical Chemistry (AACC) published a position paper echoing similar themes including increased use of evidence-based test protocols, the creation of clinical decision support systems, and expanded clinician education.[83] The paper outlines recommendations on areas to engage the US Congress and federal agencies, as well as actions the laboratory and clinical community can take to "further streamline the healthcare delivery system and result in better patient outcomes." Ideally, this document can be used as a model to create a more global position paper representing a consensus from the entire medical laboratory community that would drive additional studies.

Another group of laboratory professionals seeking to provide laboratory guidance is Project Santa Fe. The Project's "Clinical Lab 2.0" seeks to help laboratories transition from volume-based to value-based healthcare by moving from a transactional to integrative model of laboratory services.[84] The intent is to address not only how laboratories can impact quality and

outcomes but also how those efforts impact costs as part of the overall value equation of health outcomes achieved per dollar spent. As part of the effort, Project Santa Fe members have embarked on demonstration projects to support their recommendations.

In order for laboratories to maintain and further improve upon past contributions to value-based healthcare, the laboratory community must work together to objectively demonstrate the value of the laboratory and share that information via the literature both within the laboratory community and especially outside of it. Laboratory organizations and groups have helped start that process by proposing a course forward. It is up to laboratory leadership to embrace and participate in those efforts, develop new ones and keep a data-driven, outcomes-focused laboratory value narrative front and center at all levels in the laboratory community.

Disclaimer: The findings and conclusions of this article are those of the authors and do not necessarily represent the views of the CDC.

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