EXPLOSION OF LAB TESTING:
Changing the Paradigm with Value-Based Care Leading the Way

BENION S. HORTON, MD, MHA AND
MICHAEL G. LEMIEUX, PH.D.

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INTRODUCTION

Billions of laboratory tests are performed in the United States each year, and data derived from testing heavily influence clinical decisions regarding patient care. The explosion of lab testing carries with it exciting opportunities for precision medicine and personalized care, as well as complexity and uncertainty in ensuring the right test informs the right care, while also further opening the system for potential fraud, waste, and abuse. Attempts to address this problem have been largely unsuccessful to date despite the involvement of multiple organizations and guideline changes. A paradigm shift in laboratory testing likely transcends clinical guidance and will involve a transition from fee-for-service healthcare to value-based reimbursement models.

This white paper explores the explosion of lab testing, and the use of science and evidence-based medicine in determining the right test to influence the right care.

BACKGROUND

The Centers for Disease Control and Prevention (CDC) estimates that around 12 billion diagnostic laboratory tests are performed each year in the United States alone.[1] This is a staggering number that is likely to grow due to the increasing availability of new tests, patient expectations, and providers' fear of diagnostic error.[2] With so many laboratory tests being performed each year, it is of paramount importance to ensure that the right tests are being ordered at the right times, to optimize patient care and clinical outcomes.

Laboratory testing is commonplace in modern medicine, and test results heavily influence clinical decisions. As many as 70% of clinical decisions are guided by a laboratory test result.[3,4] Data from the test proactively inform care and improve patient outcomes. This critical intelligence allows for better decisions, resulting in better care while improving the health of individuals and populations. The testing explosion has brought more options to the market, but not all tests are created equal, making it vital that the appropriate test is ordered based on science and evidence-based medicine, as well as patient need and situation.

Unfortunately, evidence shows that there is considerable misuse of diagnostic testing across many healthcare settings. Misuse includes overordering—20% to 30% of laboratory testing may be unnecessary.[5,6] Providers might overorder tests for fear of missing something; fear of diagnostic error can contribute to the practice of what has been called "defensive medicine," wherein a provider may order a particularly large battery of tests to reduce the threat of malpractice liability.[7] This can result in misuse or overuse of tests. More does not necessarily

mean better, because batteries of tests that aren't tailored to a patient's clinical presentation can result in false-positive or false-negative results and subsequent harm to a patient.[8,9] Failure to order the right test affects about 50% of laboratory orders, which might lead to an incorrect or missed diagnosis.[7]

APPROPRIATENESS OF LAB TESTING BASED ON SCIENCE AND EVIDENCE-BASED MEDICINE

Lab testing and interpretation of results are complex and made even more so as new options continue to flood the market. As new testing options emerge, they should be thoroughly evaluated for sufficient peer-reviewed literature that establishes their analytical and clinical validity, and clinical utility; tests that meet acceptable standards of validity and utility may be considered for clinical use.

When determining appropriate clinical use of a laboratory test, it is also important to consider the characteristics of the testing population. This is because a test's predictive value (the certainty of a positive or negative test result) will vary depending on the prevalence of a disease within a population. Consider an example that assumes the use of a high-quality test with 95% sensitivity and specificity. With a total population size of 1000, the number of individuals in each of the 3 subgroups who are truly positive, is different. Accordingly, the hypothetical test generates more true-positive results for the symptomatic population. In an asymptomatic population, false-positives are more likely to occur, and this trend is exacerbated even further in the case of rare disorders.

1000 people in each population	Symptomatic (30% positive)	Asymptomatic (2% positive)	Rare (0.2% positive) 1 in 500
# With actual condition	300	20	2
# Tested positive	320	69	52
% True positives (Positive Predictive Value)	89%	27.5%	3.6% **(96% wrong!)**

The implication is that one must be aware of disease prevalence and understand the impact that it will have on the positive and negative predictive value of a test. A false-positive result may lead to additional unnecessary testing or treatment, as well as unwarranted fear and anxiety for a patient. A false-negative result, conversely, may delay needed intervention, and increase the likelihood of disease spread within a community.

SCIENCE AS THE TRUE NORTH GUIDES AVALON LAB TESTING POLICIES

With science as our true north, Avalon ensures our policies for lab testing follow evidence-based medicine. This foundational element creates stability within the lab ecosystem, guiding health plans and physicians as they navigate the explosion in available lab testing options. Our laboratory policies ensure the right tests are ordered while also educating physicians as to what is most appropriate for a particular population or individual. Avalon's Clinical Advisory Board (CAB) evaluates every new test being considered for inclusion in policy, while continually reviewing and updating Avalon's policies governing test utilization. This group is composed of experts with well-renowned expertise in the fields of hematology, laboratory science, molecular genetics, and pathology. The CAB also responds to inquiries and provider requests for an exception, while bringing their professional knowledge to the Avalon Policy Research Team.

GENETIC TESTING

In the United States, the genetic testing market costs $5.2 billion to $14.8 billion, depending upon the source.[10,11,12] Data from CMS (Centers for Medicare & Medicaid Services) show a significant increase in its compounded annual growth rate (CAGR) for genetic testing from 2015 to 2021, with it making up 20.4% of CMS' total lab test spending by 2021.[13,14]

MEDICARE FEE FOR SERVICE DATA

Year	Total Lab Spending	Genetic Test Spending	% Genetic Test Spending	CAGR Genetic
2015	$6.96 B	$289 MM	4.2%	
2016	$6.77 B	$393 MM	5.8%	36.0%
2017	$7.13 B	$473 MM	6.6%	27.9%
2018	$7.59 B	$969 MM	12.8%	49.7%
2019	$7.68 B	$1.5 B	17.7%	47.3%
2020	$8 B	$1.2 B	15%	<24.0%>
2021	$9.3 B	$1.9 B	20.4%	58.3%

Given the rate of increase, genetic testing deserves particular attention in the discussion on appropriate testing practices. Partly due to the sheer number of new tests that are constantly emerging, market forces can create confusion around genetic test ordering and use, and result in unnecessary care in some populations and emotional distress in individuals. For example:

- **New technology:** New knowledge about genetic involvement with different disorders, and test proliferation, adds to the complexity.
- **Lab panel packaging:** More complex panel combinations can increase waste.
- **Order confusion:** Genetic labs are prone to being misunderstood or misordered.
- **Inconsistent counseling:** Variability exists in when and who provides counseling to a patient and a physician.
- **Increased oversight:** Regulation and compliance mandates will expand.

There will continue to be rapid growth in the genetic testing market, and validated tests can be leveraged to drive precision medicine and personalized care. The flip side, however, demands increasing vigilance to ensure that the right tests are ordered, at the right times, to inform the right care.

HISTORICAL EFFORTS TO STEM THE FLOW OF LABORATORY TESTING MISUSE

Several organizations have taken steps to help ensure proper laboratory test utilization. For instance, in response to some direct-to-consumer (DTC) laboratories using deceptive marketing practices and generating medically unsupported predictions, the U.S. Food and Drug Administration (FDA) declared that all DTC genetic tests are medical devices that require premarket approval.[15] More recently in response to the COVID-19 pandemic, the FDA granted emergency use authorization (EUA) under the Federal Food, Drug, and Cosmetic Act (FDCA) for unapproved diagnostic tests and other medical products necessary to address the crisis. The Clinical Laboratory Improvement Amendments of 1988 (CLIA) provide standards that help to ensure quality laboratory testing that are applicable to approximately 320000 laboratory entities in the United States.[16] Multiple organizations, including the FDA, CDC, and CMS are involved in the enforcement of these standards.

The American Medical Association (AMA) developed coding standards intended to create processes to vet medical activities. Today, the AMA's CPT (Current Procedural Terminology) codes are used by all federal programs and commercial payers, with molecular pathology codes

being added in 1993.[17] The existence of a CPT code indicates the test has been vetted by the CPT Editorial Panel, composed of 17 people, including 11 physicians and representatives from health plans and CMS. Palmetto GBA, a CMS fee-for-service (FFS) claims processing contractor, created Z-Codes for genetic tests 10 years ago to identify and establish coverage determination, test quality assessment, and reimbursement criteria enabling specificity as well as post-service claims editing.[18]

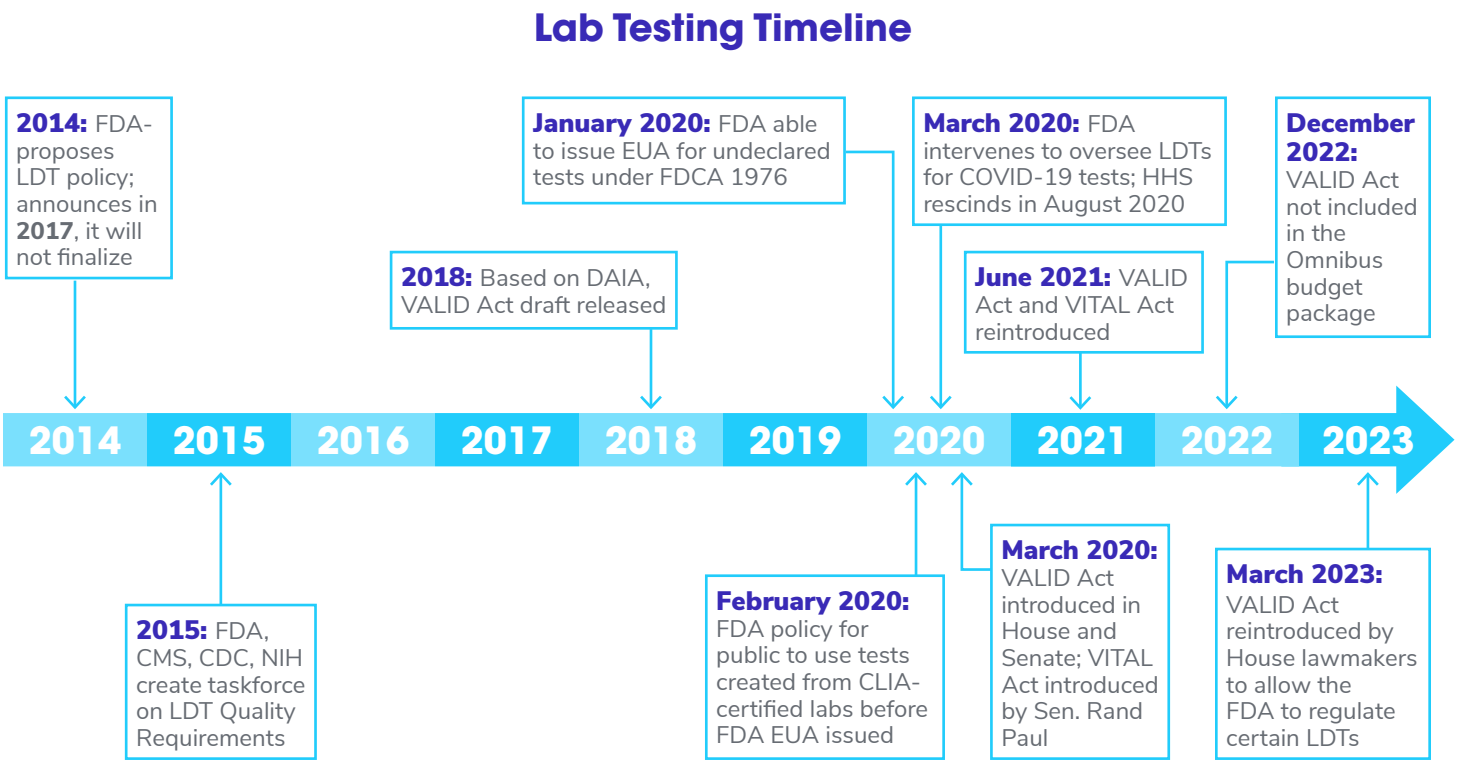

Figure 1: Lab Testing Timeline

Between 1988 and 2014, FDA assumed, but never confirmed or fully tested, its regulatory authority to oversee laboratory developed tests (LDTs). In 2014, FDA proposed for the first time a comprehensive LDT policy to protect patients, promote innovation, and provide clarity regarding its oversight of LDTs.[19]

The FDA's 2014 draft guidance prompted extensive comments and discussions between industry stakeholders and Congress, including the following:

- In 2015, FDA established an Interagency Task Force on LDT Quality Requirements with CMS, the CDC, and the National Institutes of Health (NIH) to assess the necessity of additional oversight.
- In 2015, the College of American Pathologists proposed a legislative framework for LDT oversight.[20]

- In 2016, the American Clinical Laboratory Association drafted a letter to the Office of Information and Regulatory Affairs, Office of Management and Budget, about LDT oversight.
- In 2017, a coalition outlined a regulatory framework for LDTs that subsequently was offered as a draft legislative proposal known as the Diagnostic Accuracy and Innovation Act (DAIA).
- In 2018, FDA provided technical drafting assistance and circulated a revised version of the DAIA.
- In 2018, after feedback from the FDA on DAIA, lawmakers released a discussion draft of a new bill, the Verifying Accurate, Leading-Edge IVCT Development (VALID) Act.

While the FDA and related stakeholders were engaged in this debate, Theranos, a diagnostics start-up that claimed its breakthrough technology could conduct rapid lab tests for a range of conditions using very small amounts of blood, was launched. Theranos opened a CLIA-certified lab in Newark, California, to conduct blood-based tests for a range of conditions.

- In 2013, CLIA inspectors visited Theranos, citing infractions.
- In 2015, Theranos was granted FDA clearance for one of the hundreds of tests it claimed to perform: a simple viral screen for herpes simplex 1.
  - Theranos' CEO, Elizabeth Holmes, published an op-ed in *The Wall Street Journal* where she called for FDA oversight of all LDTs.
- In 2015, FDA subsequently conducted inspections of Theranos and identified several regulatory violations and issued a warning letter to the company. *The Wall Street Journal* subsequently published the first in a series of articles raising questions about Theranos and its technology.
- In 2016, CMS issued a warning to Theranos and revoked the lab's certificate later that year. It subsequently invalidated all the test results Theranos provided to patients, which likely totaled in the hundreds of thousands. The U.S. Securities and Exchange Commission (SEC) investigated Theranos for misleading investors and government officials about its technology and charged the company with fraud in 2018. Theranos shut down later that year.
- In 2018, Theranos' CEO, Elizabeth Holmes, was indicted on multiple counts of wire fraud and conspiracy to commit wire fraud.
- On January 3, 2022, Holmes was found guilty of three counts of wire fraud and one count of conspiracy to commit wire fraud.

A major effort to stem the flow of inappropriate laboratory testing was made in 2012 with the dawn of the Choosing Wisely campaign, a movement to engage physicians and patients in conversations about unnecessary tests, treatments, and procedures.[21] Organized by the American Board of Internal Medicine Foundation in collaboration with the consumer magazine *Consumer Reports*, this initiative began in the United States in 2012 and has since expanded internationally to at least a dozen other countries.[22] Although data suggest that Choosing Wisely has likely impacted certain laboratory testing practices for the better, it has (perhaps unsurprisingly) not solved the whole problem of testing misuse.[23,24,25]

There are several reasons one might reference to explain the inability of previous efforts to ensure appropriate laboratory testing. For one, some laboratories operate outside of any recognized accreditation program and may not maintain necessary standards of quality.[26] Next, CLIA standards do not address the clinical validity of any test.[27] It is important to recognize that independent laboratories are also a major source of testing, which underscores the importance of measures being taken to ensure that the right tests are being performed under the right circumstances. Figure 2 demonstrates that 83.5% of billed units from specific CPT codes in Avalon's book of business in 2020 originated from independent laboratories.[28] Independent lab pricing offers the opportunity to move toward value-based care because tests performed in the hospital setting cost 200% to 400% more, according to Avalon data, making it vital to ensure science guides the performance of the right test in independent lab settings.

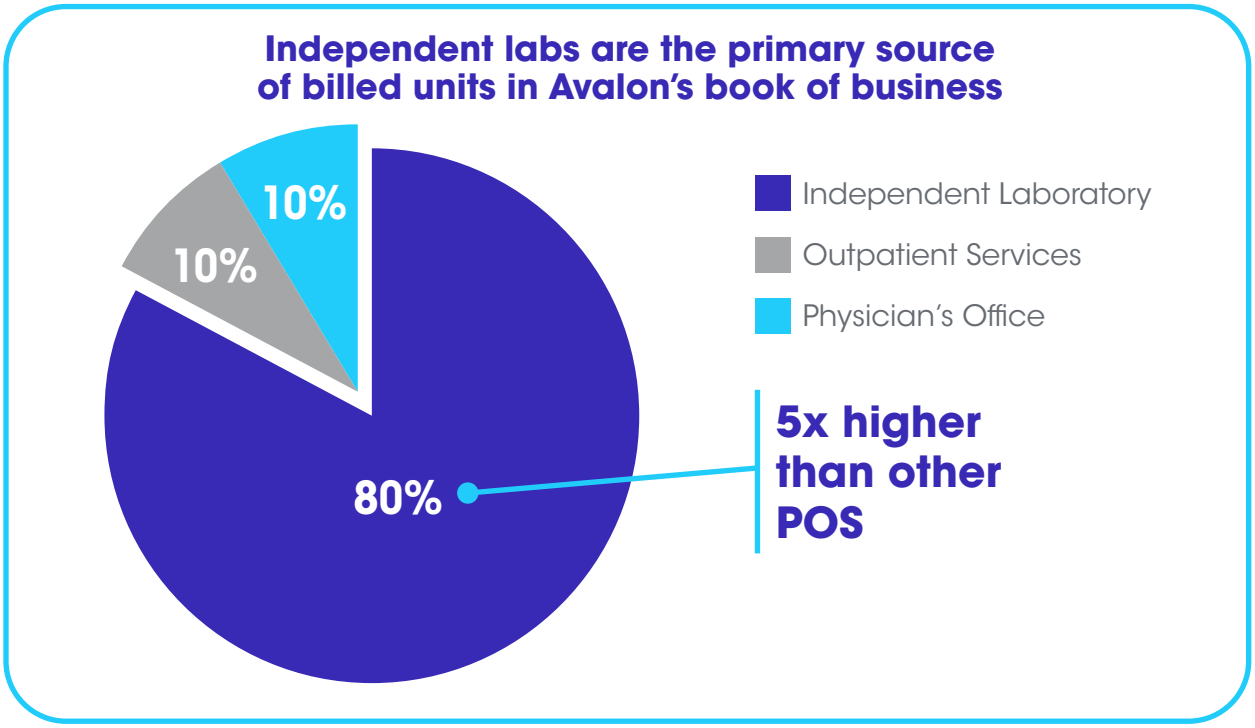

Figure 2: Independent laboratories dominate the testing landscape, and 80% of Avalon's billed units originated from independent labs in 2020.

There is also evidence suggesting that guidelines, such as those of the Choosing Wisely campaign, may not be sufficient to curb clinical practice in the absence of other forces. For instance, a recent study compared the efficacy of recommendations versus payment policy change in reducing the use of low-value laboratory testing. The authors found an almost immediate 93% reduction in low-value vitamin D screening following a payment policy change that eliminated reimbursement for that test. In stark contrast, the release of Choosing Wisely recommendations only resulted in a minor reduction in the rate of increase of vitamin D screens.[29]

VALUE-BASED CARE SETS A NEW LABORATORY TESTING STANDARD

A transition from FFS healthcare to value-based reimbursement models is one key to eliminating laboratory testing overuse. In an analysis of waste and low-value healthcare services, the Washington Health Alliance stated, "We need to keep our collective 'foot on the gas' to transition from paying for volume to paying for value in healthcare," and "The concepts of 'choosing wisely' and shared decision-making must become the bedrock of patient-provider communications."[30]

An emphasis on value-based healthcare is a hallmark of the world's first Lab Insights Company, Avalon Healthcare Solutions. Avalon is working to change the paradigm of laboratory testing through the implementation of medical policies that are grounded in science, and the delivery of a new model that intelligently analyzes data in real time and provides decision advice codes to approve, deny, or reduce claim lines along with references to specific policy detail to support those decisions.

There are several complex conditions, such as chronic kidney disease, diabetes, liver disease, mental health, and cancer, which have wide variability in treatment and outcomes. For example, let's examine how this new model could potentially drive improved results for type 2 diabetes (T2D) patients.

When it comes to T2D, there are key process measures that improve outcomes such as: an annual A1c test, annual lipid profile, and biannual health checkups. Each of these process measures serves as a quality-of-care indicator. Healthcare providers ideally perform these activities during patient visits. When we look at healthcare visit data, we can view quality-of-care indicators, such as whether providers are performing all three process measures for T2D, or just one or two of them. There is a remarkable difference in cost per member, slightly more than twice as much, when only one quality process measure is followed, compared to the high-quality category of members who received better care. Drilling down into the lab data allows

us to examine patient-provider patterns and how they are delivering patient care. We can see whether the provider adjusts treatment decisions based on lab values and what the impact is to the patient. This is more than data. It's actionable, lab-driven insights to enable a better basis for alignment of goals in value-based contracts.

By connecting traditional process reviews with lab values and outcomes, we believe health plans and providers can dramatically move the needle on realizing value-based care success. Lab values are leading indicators. They may help modify disease progression before it happens. Previously in healthcare, the flag for identifying risk was prior hospitalization(s), which is a good performance measure for a program, but not a proactive or leading measure. Lab results are quite unique in this manner, in that they are emergent indicators.

The explosion of testing options within the lab ecosystem makes ensuring the right test produces the right data, so that the right intelligence can inform the right care vital to improving the health of populations and individuals.

Learn more about how Avalon's innovation solutions and policies guide health plans and providers in unlocking the power of Lab Insights. Visit www.avalonhcs.com or contact avalon-info@avalonhcs.com.

ABOUT THE AUTHORS

Benion S. Horton, MD, MHA
Vice President, Medical Director at Avalon Healthcare Solutions

Benion S. Horton, MD, MHA, is a physician leader with proven experience in practice management, staff development, quality improvement, and patient safety initiatives. For more than 20 years he has maintained a special focus on the advancement of evidence-based treatment policies and protocols. As Avalon's Medical Director, Dr Horton supervises physician utilization management review for laboratory testing, focusing primarily on genetic testing requests for health plan clients. He participates in internal policy development and review, acting as clinical liaison to the company, and is an ambassador for Avalon's clients through program development, implementation, and value achievement.

Prior to joining Avalon, Dr Horton was a physician executive at Atrium Health, Carolinas Healthcare System Medical Group. He was also a Clinical Assistant Professor at UNC School of Medicine in Chapel Hill, North Carolina. Dr Horton earned his undergraduate and medical degrees at Mercer University and his Master of Healthcare Administration at the University of North Carolina, Chapel Hill.

Michael G. Lemieux, PhD
Medical Policy Manager at Avalon Healthcare Solutions

Michael G. Lemieux joined Avalon Healthcare Solutions in 2021 and serves as Manager of Medical Policy. Dr Lemieux is an experienced PhD-level molecular biologist with a demonstrated history of improving access to scientific information and evidence-based healthcare. As manager, Dr Lemieux oversees the Medical Policy Team and leads Avalon's new technology review process.

Prior to joining Avalon, Dr Lemieux worked with Pfizer's Rare Disease Research Unit and Bristol-Myers Squibb's Study Strategy and Planning team, served as a quality control scientist, and managed the Scientific Support team at a global plasmid distribution laboratory. Dr Lemieux's professional interests include leveraging scientific data to improve clinical outcomes, expanding access to evidence-based healthcare and medical communication. Dr Lemieux earned his undergraduate and doctorate degrees at the University of Connecticut.

ABOUT AVALON HEALTHCARE SOLUTIONS

Avalon Healthcare Solutions is the world's first and only Lab Insights company, bringing together our proven Lab Benefit Management solutions, lab science expertise, digitized lab values, and proprietary analytics to help healthcare insurers proactively inform appropriate care, reduce costs, and improve clinical outcomes. Working with health plans across the country, the company covers more than 37 million lives, and delivers 7% to 12% outpatient lab benefit savings. Avalon is pioneering a new era of value-driven care with its Lab Insights Platform that captures, digitizes, and analyzes lab results in real time to provide actionable insights for earlier disease detection, ensuring appropriate treatment protocols, and driving down overall cost.

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Avalon Healthcare Solutions
3405 W Dr Martin Luther King Jr Blvd, Suite 200
Tampa, FL 33607
813-751-3800