LAB TREND REPORT 2023

from Avalon Healthcare Solutions

avalon

CONTENTS

FROM THE DESK OF BILL KERR, MD 3

EXECUTIVE SUMMARY 4

INTRODUCTION 6

- General Market Trends and Avalon Spend and Trend Numbers 6
- Qualitative and Quantitative Current and Future Trends 7
- How Avalon Can Help 8
- Introduction to Routine and Genetic Testing 9

ROUTINE TESTING 9

- Routine Testing by the Numbers 10
- Routine Testing Challenge: Waste 12
- Avalon Programs Address Routine Testing Waste 13
- Routine Testing Challenge: Lab Spend Factors 14
- Avalon Programs Can Address Routine Testing Cost and Price Concerns 18
- Spotlight on HbA1c (Hemoglobin Glycosylated A1c) 19
- Summary of Routine Testing Section 21

GENETIC TESTING 22

- Genetic Testing by The Numbers 22
- Genetic Testing Utilization 26
- Genetic Testing Challenge: Waste 27
- Avalon Can Help Manage Genetic Test Utilization 29
- Genetic Testing Challenge: Price 30
- Avalon Can Help Manage Genetic Test Spend 31
- Legislative and Regulatory Landscape Impacting Genetic Testing 32
- Spotlight on MRD (Minimal Residual Disease) 33
- Summary of Genetic Testing Section 36

FUTURE LAB TESTS: MCED AND PRS 36

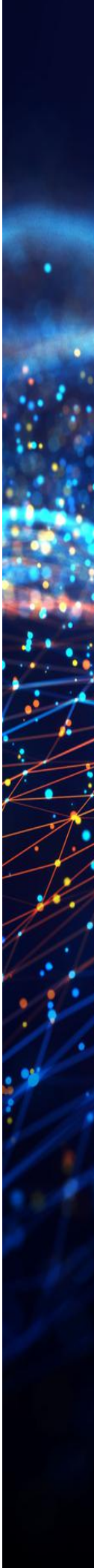
- MCED (Multi-Cancer Early Detection) Tests 36
- PRS (Polygenic Risk Factors) 37
- How Can Avalon Help in Addressing These Two New Technologies? 38

CONCLUSION & TAKEAWAYS 39

FROM THE DESK OF BARRY DAVIS 40

ACKNOWLEDGMENTS 41

REFERENCES 41



FROM THE DESK OF BILL KERR, MD
CEO, AVALON

With the explosion of lab tests in the last few years – a leap forward in both the level of complexity and sheer volume of diagnostics – Avalon is pleased to offer its third Lab Trend Report.

When we launched Avalon 10 years ago, we knew that it was only going to become more difficult for health plans, providers, and patients to determine which test is needed, who can perform it, what price should be paid, and what to do with the result. Improving clinical outcomes is dependent on appropriate lab testing, and this past year was no exception. The right lab test at the right time for the right patient with the right interpretation will lead to more thoughtful treatment plans, which will improve the health care of everyone while creating a more efficient system.

In this report, you will find statistics and analyses that will offer insight into the good news about lab testing trends, as well as the challenges that must be addressed. It is exciting that new, complex lab tests based on the genomic revolution are transforming the way we identify early disease markers in patients so we can better inform care or even prevent diseases. We also explain how new lab testing capabilities – while impressive – are increasing overutilization in the healthcare system. As we all saw during the pandemic with COVID tests being combined with other, sometimes unnecessary lab tests, once again routine lab tests are too often "stuffed" into testing panels or upcoded to more expensive tests that provide no useful additional information to diagnose or treat a patient.

With more than 38 million lives covered by Avalon, we are bringing together the management of lab results at scale and gaining insight into testing trends. We can show where lab tests are under-utilized and where there is waste in the system.

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Thank you for your interest in the Lab Trend Report 2023. We look forward to your feedback.

EXECUTIVE SUMMARY

Innovation in laboratory testing and increased availability of tests are hallmarks of the 2022 American healthcare experience. More accurate molecular tests, the increasing availability of genetic tests, and access to over-the-counter, at-home tests are now common expectations of providers and patients.

Much of the recent progress in diagnostic testing, particularly for respiratory infections, is a reflection of the necessity of invention to prevent the spread of the COVID-19 virus. The evolution was in no small part due to the mandated public and private funding of testing – and to a certain extent, cost controls – to address the public health threat. While this fully funded testing expansion blew wind into the sails of progress, manufacturers felt the decline of testing demand and reduced production capacity soon after the 2020-2021 COVID-19 case surges.

This report bears witness to the shift in lab testing trends in 2022, and how public policy changes and stakeholder expectations served to drive many of these trends. In this report, we examine and show data that illustrates the lab trend spend in 2022, the changes in trends from 2021, and what we expect to change again in the future.

To be sure, it is an unusual time for an industry that is an indispensable part, but sometimes an afterthought, of the healthcare system. Any failure to grasp that testing is a significant factor in determining overall healthcare costs, quality, and outcomes is to ignore that the great majority of patient treatment decisions are guided by lab results. Stakeholders must recognize that lab testing is nothing less than the gateway to appropriate diagnosis and treatment planning.

Accordingly, this report will make clear how important it is to manage lab test costs, now more than ever, as we explore:

- How and why routine tests represent 90% of all lab utilization and 70% of overall spend on labs, the 20 most common tests, and how overuse and unnecessary expense can be avoided.
- Genetic testing and its arrival into the mainstream, how prior authorization and quality differentiation are key to managing new tests – to avoid overuse of unnecessary testing and encourage utilization of only clinically-valid, next-generation sequencing.
- The impact of the public policy landscape that governed an unusual year for lab tests and the great effect legislation and regulation had on market decisions, opportunities, and challenges.

Finally, we will review the lessons learned from Avalon Healthcare Solutions' internal staff and our team of external professional experts during our publicly available presentations and in our thought leadership materials.

The purpose of this report is to share our experience with lab value management solutions in hopes that we will influence the system in the right direction. Avalon is pleased to describe how we are managing the processes to ensure that only necessary and high-quality lab tests at cost-effective prices are commonplace expectations of the American healthcare system.

Key Takeaway Points from the Lab Trend Report 2023 Include:

Overutilization and unnecessary repetition of lab tests are common; routine testing management programs are critical to ensure appropriate utilization and spend.

01 For every office visit, there are ~4 routine tests ordered; the top 4 tests assess and monitor chronic illnesses, with the comprehensive metabolic panel being the #1 ordered test.

02 Laboratory testing affects ~70% of downstream treatment decisions.

03 So-called "panel stuffing" – when labs add tests with no clinical value to panels and bill for them – can add ~$2 per member per month of waste.

Provider consolidation and site of service have a profound effect on lab test costs; identifying outliers and unnecessary price differentials is important to control spend.

Lab test price can vary dramatically depending on where it is performed.

Health systems are incentivized to acquire physician practices and absorb testing volume because they can bill at a higher rate for the same services.

Site-neutral payment reform should eliminate unnecessary disparities in prices.

A steady increase in genetic testing, a mostly manual prior authorization process, and a lack of specific test identification for genetic tests are causing health plans to confront difficult determinations of coverage eligibility, test validity, and utility.

- Despite making up only 10% of lab test utilization, genetic tests make up 30% of lab spend, as more than 10 new genetic tests are introduced every day in the US, reflecting both innovation and premium pricing.
- By November 2022, U.S. physicians could choose from 129,624 genetic tests to order. The growing demand for the early detection of cancer is a clear driver of the growth in genetic testing. In 2022, President Biden re-launched the Cancer Moonshot initiative and Congress established a new federal subagency of the National Institutes of Health - ARPA-H - with $1 billion in funding to support advanced technologies like genetic testing.
- While there is momentum to automate the coverage determination process, genetic tests are still subject to an expensive manual prior authorization process: it is likely that ePA and manual PA will need to live together for a while.
- The lack of specific genetic test codes makes the evaluation of genetic test validity, quality, and utility a real challenge.

Avalon's programs align clinical considerations with cost-effective policies to make sure health plans are covering high-quality, value-based care for their members.

INTRODUCTION

There are several factors driving laboratory spend and market trends. Below we highlight many of them, including increased utilization of laboratory tests, higher prices, consolidation of the laboratory industry, and the consequences of unnecessary lab testing. Avalon policies, as explained below, can help health plans address these factors.

General Market Trends and Avalon Spend and Trend Numbers

Roughly 14 billion clinical laboratory tests are performed every year in the U.S., making them the most utilized medical benefit.[1] Despite accounting for only 2.3 percent of U.S. healthcare expenditures[2], the high percentage of medical decisions that depend on laboratory results[3] underscores how critical they are to patient care.

The demand for clinical laboratory services is reflected in an increase in lab test expenditures over the past few years. In 2021, the Medicare program spent $9.3 billion on laboratory tests, marking a record 17 percent increase from the previous year.[4] The spending increase resulted from a rise in demand for COVID-19 tests, high-priced genetic tests, and chemistry tests. Notably, in 2021, Medicare Part B spent $5.5 billion – or 59% of total test spending – on the top 25 laboratory tests.[5] Still, the total volume of routine tests during the pandemic was lower than in pre-pandemic years, so the expectation is that the demand for routine testing will continue to increase as the healthcare system returns to normal.

Genetic tests, in particular, experienced rapid growth. Between 2012 and 2022, a total of 51,803 new genetic tests were made available in the U.S.[6] Since the government began monitoring Medicare Part B spending on lab tests in 2014, spending on genetic tests has more than tripled.[7] While genetic tests accounted for 20% of all Medicare lab test expenditures, that is primarily due to price and not volume. Of the top 25 laboratory tests, only five were for genetic tests, but the prices far exceeded the other 20 tests. The range for the most-ordered non-genetic test prices in 2021 was $8.46 - $246.92; the range of prices for genetic tests that same year was $508.87-$3,873.00.

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The following is a brief explanation of the factors driving these trends:

Increased Utilization of Laboratory Tests

The increased popularity of laboratory testing during 2022 may be because it helped resolve uncertainty at a time when COVID-19-related medical conditions were confusing and ambiguous. After the second surge of the pandemic, the mysterious “long Covid”[8] condition started to appear, and the demand for at-home diagnostics[9] and more sophisticated tests intensified.[10] Coupled with an aging population of “Baby Boomers” who had a growing incidence and prevalence of diseases, demand for and utilization of laboratory tests increased.[11] Moreover, solutions like genetic sequencing technologies, laboratory automation, and artificial intelligence tools facilitated the ease, scalability, and efficacy of testing, further increasing the value and thus demand for laboratory tests.[12]

Increases in Prices for Laboratory Tests

Macroenvironmental changes and reimbursement policies are also fueling increased lab spend and trend. For example, the acquisition of physician practices by hospital systems is resulting in a shift of lab testing from independent labs to higher-priced patient service settings.[13] Furthermore, Medicare reimbursement for physicians has decreased by 22% from 2001 to 2021.[14] As a result, physicians feel financial pressure to increase the number of primary care visits, thereby increasing the number of lab tests performed, to reach their target income. Finally, disrupters in primary care are further consolidating the market. One example is the acquisition of Oak Street, a Chicago-based

primary care network, by CVS Health for $10.5 billion,[15] making competitive negotiated rates more challenging.

Qualitative and Quantitative Current and Future Trends

Hospitals are Increasingly Integrating Laboratories

To accommodate the rise in laboratory testing demand, more hospitals are joining forces with established laboratory companies, like Quest Diagnostics and LabCorp.[16] For instance, Quest partnered with and even acquired parts of various hospital systems including Summa Health's outreach lab services business,[17] New York Presbyterian,[18] and UMass Memorial Medical Center.[19] LabCorp is managing Ascension's hospital labs in 10 states.[20] Indeed, Quest and LabCorp completed 36 hospital laboratory deals between 2017 and 2019, and both companies have strategic relationships with dozens more hospital labs.[21]

Inappropriate Laboratory Testing

With so many diagnoses dependent on a lab test, perhaps it is unsurprising that there is a large amount of inappropriate –or wasteful – lab testing.[22] Indeed, the rate of inappropriate hospital laboratory testing is 43.9% at the time of admission and 7.4% for subsequent testing.[23] Waste is defined by CMS as the overutilization of services that result in unnecessary costs to the Medicare program.[24] It is well-settled that Medicare Advantage plans are required to operate programs to detect, prevent, and mitigate instances of fraud, waste, and abuse ("FWA"). Such programs are designed to ensure program integrity, by, among other things, verifying the veracity of claims, which necessarily includes determining whether the items and services claimed were actually provided, were provided at the level billed, and otherwise satisfy the plan's medical necessity and other payment requirements. Inappropriate lab test utilization is caused by factors such as a lack of guidance on appropriate use criteria for laboratory tests and unstandardized and decentralized guidelines on diagnostic test ordering.

Studies have long since established that physicians attributed overutilization of laboratory tests to limited understanding of utilization guidelines, unawareness, and feelings of uncertainty.[25] Another example of lab testing waste is "panel stuffing"[26]– when labs add tests to existing lab orders that have no clinical value and then bill for them. Waste caused by panel stuffing in processed claims costs about $2 per member per month. The consequences of inappropriate lab testing include these unnecessary costs, but also lower quality of care.[27]

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Inefficient Prior Authorization Processes

Prior authorizations (PA) account for a significant portion of market spending and hence are a good target area for improving spend and trend. PA processes can be expensive, typically costing around $11 per occurrence – compared to the $0.66 it takes to process claims electronically – and this number continues to rise year after year.[28] According to the CAQH 2019 Index,[29] automating various medical transactions, including PA, could save the healthcare industry $13.3 billion. While manual PA processes are intended to reduce levels of unnecessary care and expenditures, they remain costly and often end up delaying and impeding access to care.

How Avalon Can Help

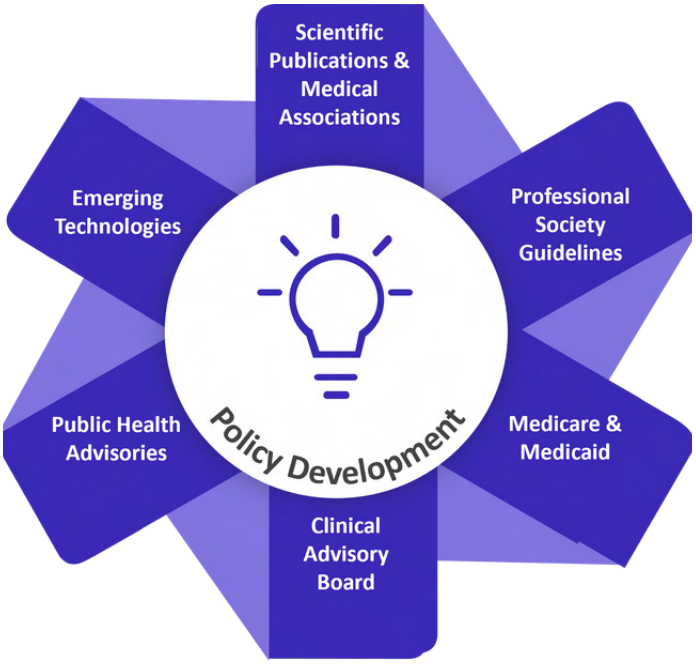
Clinical Advisory Board

Avalon's Independent Clinical Advisory Board (CAB) reviews and evaluates scientific lab policies on a quarterly basis. CAB experts have expertise in fields such as hematology, laboratory science, molecular genetics, and pathology, and bring valuable insights to the table in their review and approval of lab policies to support value-driven care (Figure 1).

Partnering with Independent Labs

Avalon maintains contracts with over 60 independent laboratories, creating a broad network that supports client health plans in all medical areas. Having access to 60 individual network provider relationships and fee schedules and merging these into a single standard reimbursement mechanism is advantageous to both patients and providers.

Figure 1. The Policy Development and Curation Process Has Yielded ~140 Current Policies to Optimize Lab Testing for Avalon Clients



Avalon's dedicated full-time scientists support and maintain ~65 Routine and ~75 Genetic outpatient laboratory policies

All policies are researched, written, and maintained in-house by dedicated science team, including PhDs

Demonstrated conditions of coverage

Each policy has robust scientific rigor, typically ~50 references

Annual updates reviewed and approved by Avalon's Independent Clinical Board

Description: The policy development process includes Avalon's review of the current literature as well as emerging technologies, attention to professional society guidelines, and compliance with government actions by federal payers and public health authorities.

Introduction to Routine and Genetic Testing

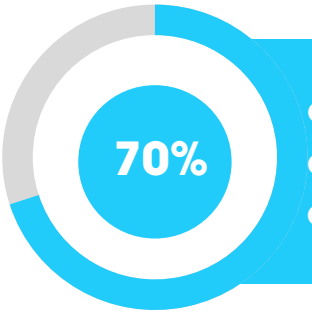
The next two sections on Routine Testing and Genetic Testing further explain these lab trends. Routine tests make up 90% of all testing, as these tests make up the majority of tests performed during the office visit and follow-up monitoring. Yet health plans are seeing an evolution of testing patterns, such as the dramatic effects of COVID testing requirements, as well as more subtle changes in spend and trend in this category. In contrast, genetic testing is new and evolving. Genetic testing may represent a small volume of overall lab testing (10% of all lab tests by utilization), but the relatively high prices of each test and the rapid growth of new technologies make this arena an important one to understand and manage. Below, we address spend and trend for routine and genetic testing and spotlight two examples: the hemoglobin A1C testing (routine test) and minimal residual disease testing (genetic test).

ROUTINE TESTING

Routine lab tests are critical to the overall practice of medicine. The definition of routine testing, as outlined by Avalon and based on the literature, includes the following: routine tests are tests that evaluate health metrics and can be repeated over time to monitor and compare the changing health condition of an individual. These tests are generally less complex and less expensive than genetic tests and are performed more regularly. Routine tests make up ~90% of all lab testing.

According to the CDC, laboratory testing affects ~70% of downstream treatment decisions.[30] As a result, routine lab testing is a high-volume activity; it is also highly variable and prone to waste. Despite an increased interest in and focus on lab tests during the pandemic, there remains a high volume of unnecessary tests that represent avoidable waste, inappropriate billing, and dramatic price discrepancies.

Approximately 70% of total lab test spending is on routine lab tests, mostly due to the high utilization. Once considered plentiful in number but inexpensive in cost, new expensive tests are a growing part of routine testing. For example, urine flow cytometry is replacing inexpensive urine dipstick testing as the preferred method for excluding urinary tract infections. COVID testing introduced a new class of CPT codes and three codes for COVID-19 testing along with a new U code for PCR testing. In addition, place of service continues to count in terms of higher paid amounts for testing in the physician's office and outpatient hospital setting versus the independent lab setting. If the goal is to provide the right test, for the right patient, at the right time, at the right price, then there is a lot of work left to do.



70% of medical decisions are based on lab results.[30]

Whether a medical visit is for an illness or a routine checkup, the primary lab test that will be performed is a blood test. These tests are so indispensable to medicine, that when Elizabeth Holmes claimed that her company, Theranos, would be able to perform hundreds of tests from one drop of blood, she was able to defraud multiple experienced investors and industry leaders who believed it would change the practice of medicine[31]. While there continue to be

legitimate efforts to disrupt the traditional blood testing process,[32] the typical blood test requires 10-15 milliliters of blood and measure lipids, metabolites, proteins, and inflammatory markers. Studies show that approximately 70%, and as high as 88% of all outpatient encounters, include a lab test.[33]

Routine Testing by the Numbers

In 2022, the overall spend on lab tests was $226 per member per year (PMPY), a 15% decrease from $264 PMPY in 2021. This decreased spend is mostly related to decreased spend on COVID-related testing (see Figure 2 below).

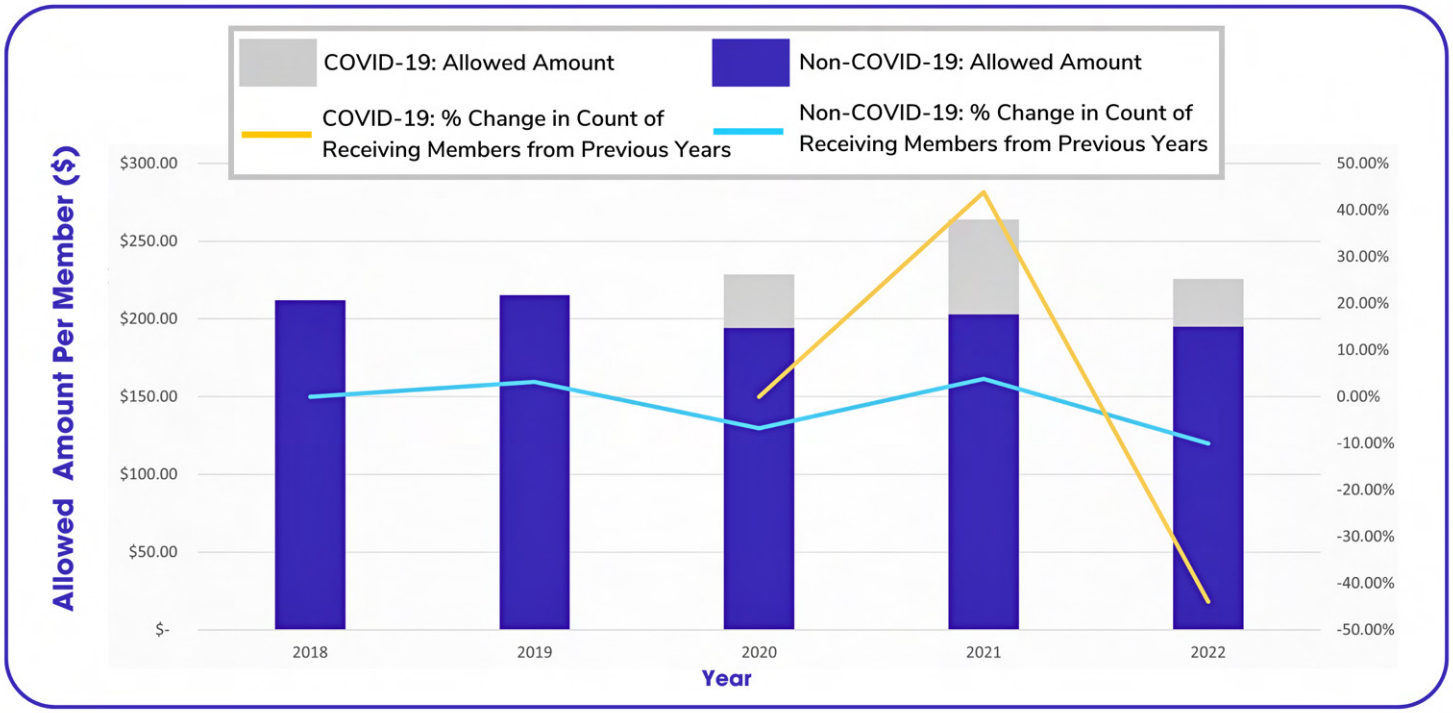
- Non-COVID-related spending is down slightly from peak spending pre-pandemic in 2019 ($215 PMPY), most likely due to muted recovery after the pandemic with a return to office visits as well as active management by Avalon through our services.
- COVID-related spending is down from a peak of $61 PMPY in 2021 that accounted for 23% ($63/$264) of routine test spend, to $31 PMPY in 2022 that accounted for 14% ($31/$226) of routine test spend.

We analyzed routine test management for health plans engaged with Avalon in 2022 to look for patterns of utilization among members. In this subgroup analysis of 7,324,155 members who had at least one routine CPT code procedure over the year, we measured utilization and spend figures (Table 1).

Table 1. Routine Tests Utilization and Spend Figures for 2022

Category	Utilization	Spend
Mean	8	$287
Median	5	$125
Standard Deviation	+12	$796
Quartile 1	2	$54
Quartile 3	11	$287
Intra-quartile Range	9	$233

Figure 2. Trend in Spend for Routine-Testing 2018 – 2022



Description: Non-COVID-related spending is down slightly from peak spending pre-pandemic in 2019 and COVID-related spending is markedly decreasing since 2021.

Key Findings on Routine Testing Utilization:

- The mean number of tests per member (8) was greater than the median number of tests per member (5), suggesting the skewing of test use towards high users.
- The large standard deviation also points to a wide distribution of testing numbers per member: the large interquartile range also underscores the high variation of testing numbers in this population.
- The mean number of encounters over the year was 2, suggesting that there are ~4 routine tests ordered per office visit.
- Health plans may wish to address these outliers in terms of utilization, as they determine what tests could be offered under their coverage policies as part of annual wellness exams and routine monitoring Avalon offers health plans a series of edits through its routine test management tools, utilization management, and outbound physician calls.

Key Findings on Routine Testing Spend:

- The data demonstrate similar findings with respect to skewing towards high-spend members, as the mean spend ($287) is greater than the median spend ($125) here.
- The large standard deviation, as well as interquartile range observed, also underscores the same high variability of pattern of spend as seen in the utilization analysis.

Routine Testing Challenges

Routine Testing Challenge: High Utilization

Roughly 14 billion clinical lab tests are performed every year, making lab testing one of the most utilized medical benefits.[34] In 2022, LabCorp, Quest, Siemens Healthineers, and Hologic all reported a shift away from COVID-19 tests but experienced increased revenue in other areas.[35] When including cytology, perinatal, and blood screening, Hologic's testing catalog as a whole grew by nearly 16%.[36] LabCorp reported a 7.7% drop in revenue in 2022 because of the decrease in demand for COVID-19 diagnostics: this revenue drop was offset by an increase in non-COVID testing business.[37]

We analyzed the top five tests in terms of utilization of routine testing across all Avalon business lines in terms of number of allowed units per 10,000 members. Of note, these figures represent allowed versus ordered test units: the number of ordered tests is higher than the number of allowed tests, as some tests are screened out from the system using Avalon's routine test management program (further explained below).

The results demonstrated the incarnate list of routine tests common to the outpatient setting, including traditional chemistry and organ specific testing (Table 2). The Comprehensive Metabolic Panel, CPT 80053, leads the list and includes measurements for evaluating kidney and liver function as well as metabolic status as described in the test name. The

Complete Automated Blood Count, CPT 85025, is the second most-ordered test and provides information on red cells, white blood cells, and platelet count. The 2022 highest-ranking trends differed only slightly from 2021.

Approximately 70% of total lab test spending is on routine lab tests, mostly due to the high utilization.

Table 2. Routine Test Management Utilization

CPT Code	Utilization Rank	Number of Units/ 10,000 members	Description
80053	Comprehensive Metabolic Panel	3486	Glucose, urea nitrogen (BUN), creatinine, sodium (Na), potassium (K), chloride (CL), carbon dioxide (CO2), anion gap, calcium, total protein, albumin, AST (SGOT), ALT (SGPT), alkaline phosphatase, total bilirubin, GFR (African American), GFR (Others)
85025	Complete Automated Blood Count	3277	White blood cells or "diff" in which the following leukocytes are differentiated: neutrophils or granulocytes, lymphocytes, monocytes, eosinophils, and basophils
80061	Lipid panel	3137	Total cholesterol, serum (82465), lipoprotein, direct measurement, HDL (83718), triglycerides (84478)
83036	Hemoglobin; glycosylated (A1c)	2205	Glycosylated hemoglobin A1, usually determined by ion-exchange affinity chromatography, immunoassay or agar gel electrophoresis
88305	Level IV - Surgical pathology, gross and microscopic examination	2152	Surgical pathology involves the gross and microscopic examination by surgical (e.g., dermatologists) and non-surgical providers (e.g., pathologists) of surgical or biopsy specimens

The Take-Home Points for the Utilization Numbers Outlined Include:

- The top 4 tests represent codes for assessing and monitoring a variety of chronic illnesses as well as codes for tests that are often performed during annual wellness checks.
- The utilization of the CPT 88305 code is not likely generated through primary care and more likely represents a common outpatient procedure for the evaluation of cancer, including skin biopsies, prostate biopsies, and bone marrow biopsies.
- While the metabolic panel test leads as the number one test, all the blood chemistries provided are well aligned and congruent with the broad evaluation of chronic diseases.

Routine Testing Challenge: Waste

In general, overutilization of lab tests is common; one of every five tests performed may be unnecessary. A study performed in 2020 found that repeat testing of normal test results occurred in up to 85% of patients.[38]

In 2022, the federal government began scrutinizing labs that billed Medicare at questionably high levels during the pandemic. For example, the HHS Office of

Inspector General found that 378 labs billed Medicare Part B for add-on tests at a much higher volume, payment amount, or both. The agency reported that one outlier lab regularly billed for a combination of five add-on respiratory tests on almost all of its claims for COVID-19 tests. As a result, the average per-claim Medicare payment to this outlier lab was $666, covering both COVID-19 and add-on tests, compared to an average payment of $89 to all other labs that billed for COVID-19 tests and any add-on tests. As a general rule, billing for add-on tests is allowed, but only when they are medically appropriate. The OIG recommended that CMS investigate these wasteful or potentially fraudulent patterns by some labs.[39]

This wasteful or fraudulent activity was also reflected in the commercial market, due in part to the Congressional mandate to require health plans to pay the listed cash price a non-contracted provider posted on a public website for COVID-19 tests.[40] As a result, health plans were unable to negotiate more affordable COVID-19 testing prices with labs that refuse to become in-network providers, and evidence of price-gouging was widely reported.[41]

Routine testing is also prone to an activity known as "panel stuffing" – when labs add tests with no clinical value to panels and bill for them. This abusive behavior costs billions of dollars every year.[42] An example of this phenomenon is one of the largest tests influencing spend is CPT 80050, which represents the general health panel. This test represents several common outpatient routine tests, including a metabolic panel, a complete blood count, and a TSH level, as several different combinations of CPT codes can combine into 80050. This test is not covered by Medicare: when billing Medicare, the component tests must be billed individually. Avalon can work with its commercial clients to limit the use of panel stuffing as reported here.

Avalon Programs Address Routine Testing Waste:

Avalon's Routine Testing Management (RTM) solution is powered by a proprietary cloud-based clinical lab editing application. Approximately 65 of Avalon's laboratory policies, which are adapted and adopted by Avalon's clients, are partially or fully managed by Avalon. Avalon's RTM solution provides decision advice codes to deny, reduce, or approve claim lines along with references to specific policy detail supporting the decision.

Avalon's RTM solution may be integrated with the payer's adjudication system to automate the review of fixed criteria from lab claims to ensure compliance with the payer's laboratory policies. RTM is highly configurable and can apply various filters according to line of business, place of service, and provider.

For the challenges posed by COVID-19 testing, Avalon and its client health plans communicated early and often. The first step was to inform plans about the evolving testing methodologies, strategies, and accumulating evidence. Avalon commenced internal policy development in 2020 and provided quality updates throughout the pandemic. A new policy is available to clients now for adoption at the end of the Public Health Emergency, including key data on clinical validity and utility data that were used by our Clinical Advisory Board in the policy development phase. Early adoptors of the program, which includes monitoring of COVID tests as well as tests for RSV and influenza A and B, which have surged in 2022 into 2023, have seen 4-6% savings.

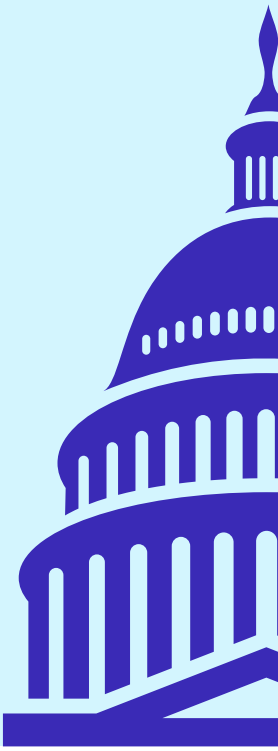
Routine Testing Challenge: Lab Spend Factors

During the Public Health Emergency (PHE), a new collective consciousness emerged about the price of lab tests. First, the demand for COVID-19 tests resulted in a dramatic change in federal and private sector spending. After setting the COVID-19 test price for Medicare at $100 in 2020, the federal government also required the cash price of COVID tests to be posted on labs' websites. These and other activities shone a spotlight on the dramatic range of prices for COVID-19 tests and there was a subsequent backlash against outliers with egregious pricing practices.[43]

With the termination of the PHE, lab providers will face a reduction in reimbursement, payers will be released from the special payment flexibilities, and patients must decipher health plan coverage criteria. One important trend to monitor post-PHE is the increase in multiplex testing – when a combination of COVID and influenza testing is ordered – which is an important trend to monitor.

Conclusions and Observations to Consider with PHE Ending Include:

- Health plans are no longer obligated to reimburse labs for COVID-19 testing at 100% of billed charges.
- Member cost share is back. This includes the ability of the health plan to pay out-of-network providers within the defined member benefits (e.g., no reimbursement or at an increased cost share).
- Plans should monitor the utilization of respiratory panels.
- Plans should carefully review a lab's claims history utilization and composition of services on claims before adding the lab to the participating network.
- Labs that purchased new PCR machines to conduct COVID-19 testing are now seeking new uses for this capacity.



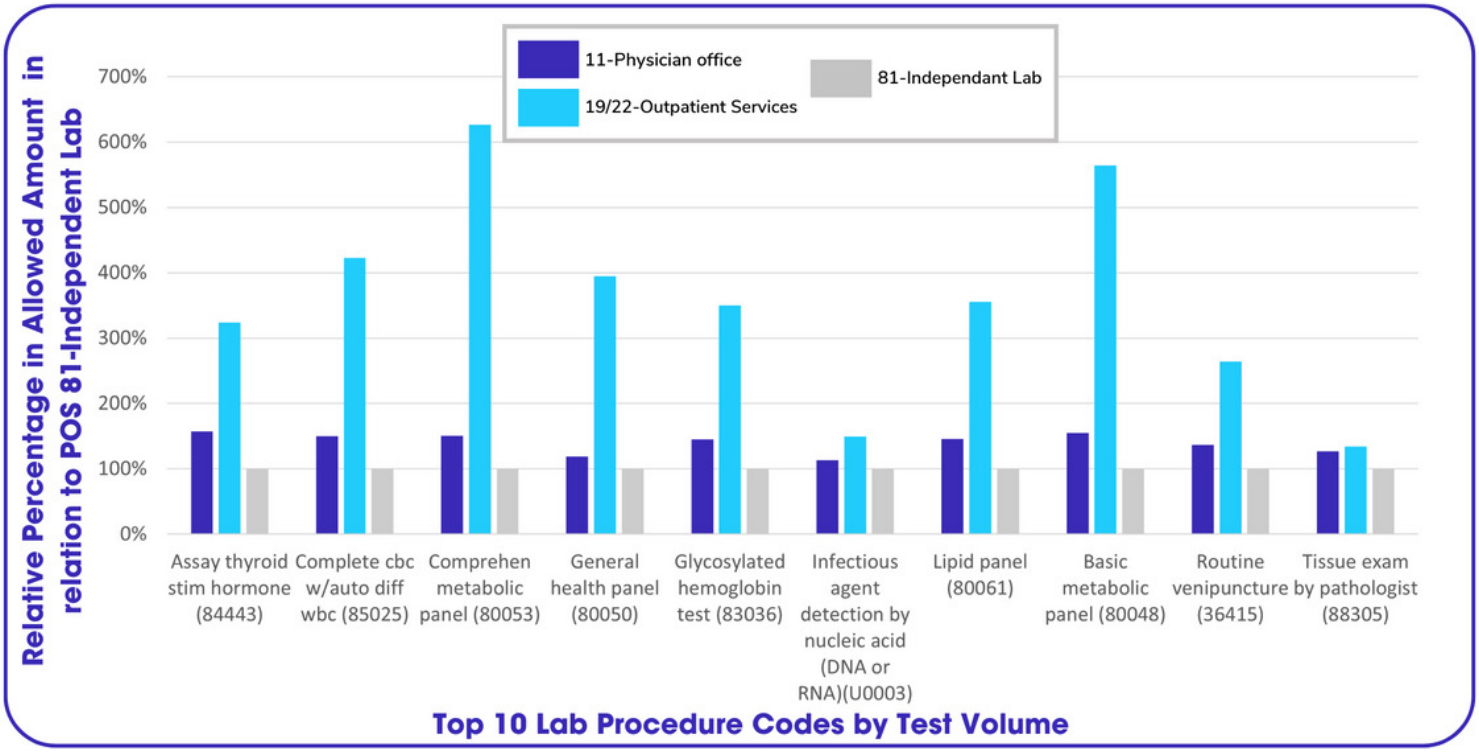
A lab test price can vary dramatically depending on where it is performed. Both public and private insurance tend to pay a higher rate for lab tests when performed at a hospital outpatient department rather than an independent lab. Indeed, employer-based insurance typically pays 3 times more for clinical lab tests when billed by hospital outpatient departments compared to identical tests billed by physician offices and independent laboratories.[44]

Negotiated rates paid by health plans for a metabolic panel can range from $20 - $400 depending on where you live.[45] The price for a comprehensive metabolic panel in 2019, for example, ranges from $8.85 to $19.56 when billed by an independent lab or physician's office, but can be between $47.13 and $214.20 when billed by a hospital outpatient lab.[46] The average cash price for self-pay patients is $155 for the same test,[47] while Quest offers one for purchase for $49 + $6 physician service fee,[48] and other at-home test companies offer the test for $99 or more.[49]

For the top 10 routine tests by paid amounts, the

physician office and outpatient services (usually hospital-based labs) were higher than the independent lab setting (Figure 3). The biggest differences were noted for the comprehensive metabolic panel measurement (CPT 80053) and complete blood count (85025) with automated differential measurement, which were also the top two tests in terms of utilization. Furthermore, the increased costs associated with these routine tests in the hospital setting do not provide added quality here. This combination of scenarios, high utilization of testing, and high differential price per setting, compounds the costs for health plans and their members.

Figure 3. Percent Difference in Average Allowed Payment for Independent Labs for 2022's Top 10 Procedure Codes



Description: When comparing lab charges for common routine tests, the outpatient services site (generally hospital labs) and physician office settings were more expensive than the reference independent lab (set at 100%).

Hospital outpatient departments have traditionally commanded a higher rate of pay due to the heavier regulatory burden associated with a greater complexity of services than physicians offer in freestanding office settings.[50] With many hospitals buying independent physician practices, however, the outpatient departments are frequently located off-campus from the primary hospital setting. Indeed, by the start of 2022, 52.1% of physicians were employed by hospitals or health systems, allowing the higher-tiered payment rates for lab services to be more frequent.[51] As these "outpatient" departments operate exactly as the former independent physician's offices they once were, hospitals can no longer justify these higher payments. The current landscape incentivizes hospital systems to continue to acquire physician practices and absorb testing volume. Increasingly, policymakers and key influencers are urging Congress to pass site-neutral payment reform to eliminate unnecessary disparities in prices.[52]

In a recent report, the HHS Office of Inspector General (OIG) flagged a surge in Medicare spending on lab tests. In 2015, there were $289 million in payments to labs, but by 2019, the total was $1.36 billion.[53] These costs are expected to continue to rise as price disparity in lab testing is impacted by where the test is performed; hospital lab fees cost more than independent labs or physician office orders.

A new federal law demonstrates another factor driving the decision-making of where a lab test should be generated. Beginning in 2022, the No Surprises Act prohibits hospitals that participate with a health plan but utilize non-participating labs from balance billing a patient for the lab's diagnostic services – whether the lab tests are ordered to support emergency or non-emergency services.[54] The No Surprises Act, however, applies only to hospitals and specific facilities, not doctor's offices. As a result, any charges for labs that are ordered by a physician's office that exceed the amount the insurance covers may be billed to the patient, because these are not protected from balancing billing by the No Surprises Act.[55] Accordingly, out-of-pocket expenses and the amount that can be reimbursed to a lab will depend on who by and where from a lab test is ordered.

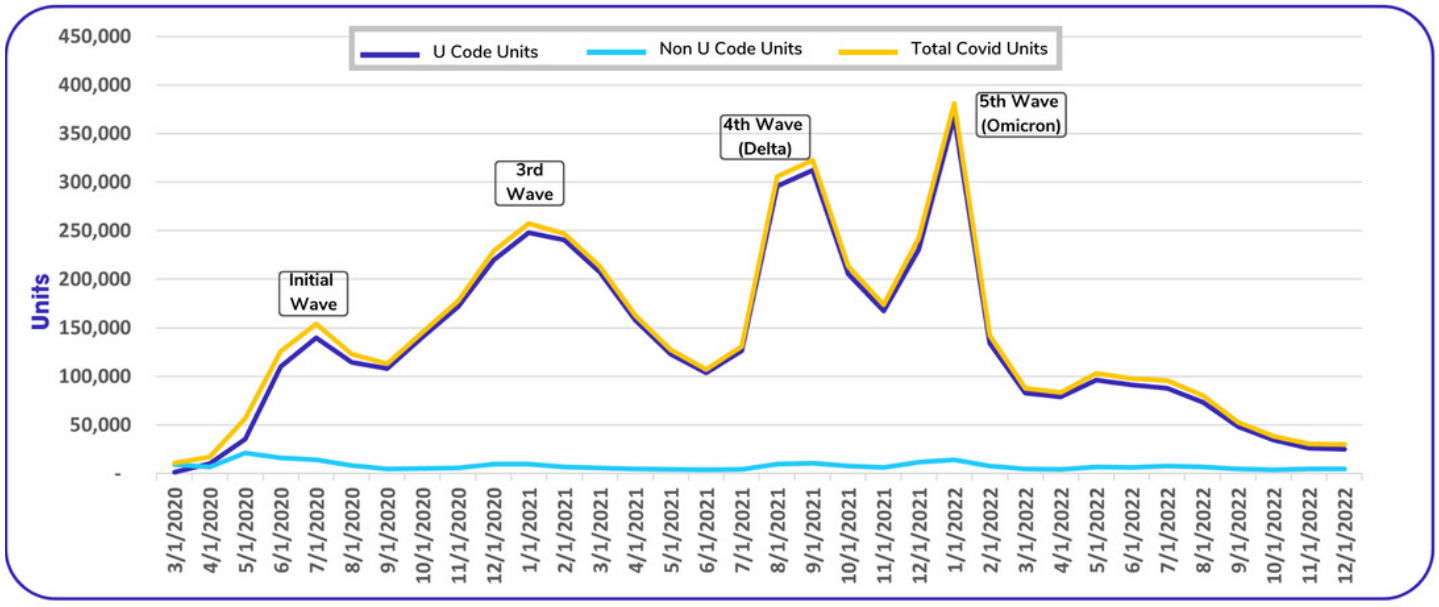
Out of the ~80 million lab tests that Avalon managed in 2022, we identified the top five routine lab tests with the highest prices across all business lines in terms of per member per year spend (PMPY) (Table 3). Of note, these figures represent allowed versus ordered lab spend, as tests are screening out from the system using the Avalon routine management tool, as described above, such that the spend for allowed testing is less than the spend for ordered testing. The results demonstrated a similar list of routine tests common to the outpatient setting: CPT 88305, CPT 80053, and CPT 80061 are on both lists. This scenario is most likely due to the large volume of test ordering for the relatively inexpensive CPT 80053 and CPT 80061 codes as well as the high price per code associated with pathology testing CPT 88053. However, there are two new tests on the spend list described below that are worth noting. The first is CPT 80050, as described above, which represents several tests.

Table 3. Routine Test Management Spend

CPT Code	Utilization Rank	PMPY Spend	Description
88305	Level IV – Surgical pathology, gross and microscopic examination	$19.74	Surgical pathology involves the gross and microscopic examination by surgical (e.g., dermatologists) and non-surgical providers (e.g., pathologists) of surgical or biopsy specimens
U0003	Infectious agent detection by nucleic acid (DNA or RNA), SARS-CoV-2	$13.32	Infectious agent detection by nucleic acid (DNA or RNA), severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) (Coronavirus disease [COVID-19]), high throughput screening
80053	Comprehensive metabolic panel	$9.87	Glucose, urea nitrogen (BUN), creatinine, sodium (Na), potassium (K), chloride (CL), carbon dioxide (CO2), anion gap, calcium, total protein, albumin, AST (SGOT), ALT (SGPT), alkaline phosphatase, total bilirubin, GFR (African American), GFR (Others)
80050	Complete health panel	$6.76	Comprehensive metabolic panel (80053), blood count, thyroid stimulating hormone (TSH) (84443), and complete blood count (CBC) (85025)
80061	Lipid panel	$6.54	Total cholesterol, serum (82465), lipoprotein, direct measurement, HDL (83718), triglycerides (84478)

The second highest routine lab test is PCR/high throughput screening tests associated with COVID-19 testing, represented by the special pandemic code U0003, at $13.32 PMPY. This code was introduced in 2020 and quickly appeared in the top 5 for lab spend. The lab spend for this code decreased 57% from $30.86 in 2021: this trend is depicted in detail below (Figure 4).

Figure 4. Covid-19 Testing Monthly Paid Units per 1000 Members by Type of Test



Description: Peaks and valleys of COVID test spend were associated with waves of the pandemic, with the current spending consistent with decreased incidence of COVID in the community setting.

The Take-Home Points for the Spend Numbers Outlined Include:

Consolidation of hospital and physician practice groups increases the health plan medical spend due to new rates for the same services. A lab test price can vary dramatically (up to several fold differences) depending on where it is performed. Site neutral payment legislation may reduce the disparity between site of service.

COVID consumed almost as much spend as pathology code 88305, but is expected to materially decline in 2023 and beyond.

The results demonstrated a similar list of routine tests common to the outpatient setting: CPT 88305, CPT 80053, and CPT 80061 are on both utilization and spend lists.

CPT 80050 represents several tests not congruent with each other and may represent panel stuffing.

The second highest spend for routine lab tests is PCR/high throughput screening tests associated with COVID-19 testing, which represents a newly introduced test.

Avalon Programs Can Address Routine Testing Cost and Price Concerns:

Avalon works closely with its clients to identify outliers and egregious pricing practices in routine testing. As noted above, there are wide variations in lab test costs depending upon the site of service. Avalon contracts with over 60 independent laboratories creating a broad network that supports client health plans. Excess laboratory spend can be avoided through point-of-service optimization. Programs that drive utilization to independent labs can achieve marked cost savings in an administrative manner that is a natural combination with other measures to improve utilization overall.

Excess laboratory spend can be avoided through point-of-service optimization. As noted above, wide variations in cost per test are noted when comparing the independent lab with other choices of physician offices and hospital outpatient services. Most patients and consumers are not aware of this and their potential savings. Payers should pursue programs that drive utilization to independent labs that can achieve marked cost savings in an administrative manner that is a natural combination with other measures to improve utilization and spend overall.

Routine Testing - Spotlight on HbA1c:

Since the publication of the Diabetes Control and Complications Trial (DCCT) results in 1993, routine assessment of HbA1c has become a standard of care for patients with diabetes. Accurate assessment of glycemic control is essential to ongoing management of diabetes and titration of therapy. Such testing can (1) help health care professionals (2) find prediabetes and counsel patients about lifestyle changes to help delay or prevent type 2 diabetes; (3) diagnose type 2 diabetes, and (4) work with patients to monitor the disease and help make treatment decisions to prevent complications.

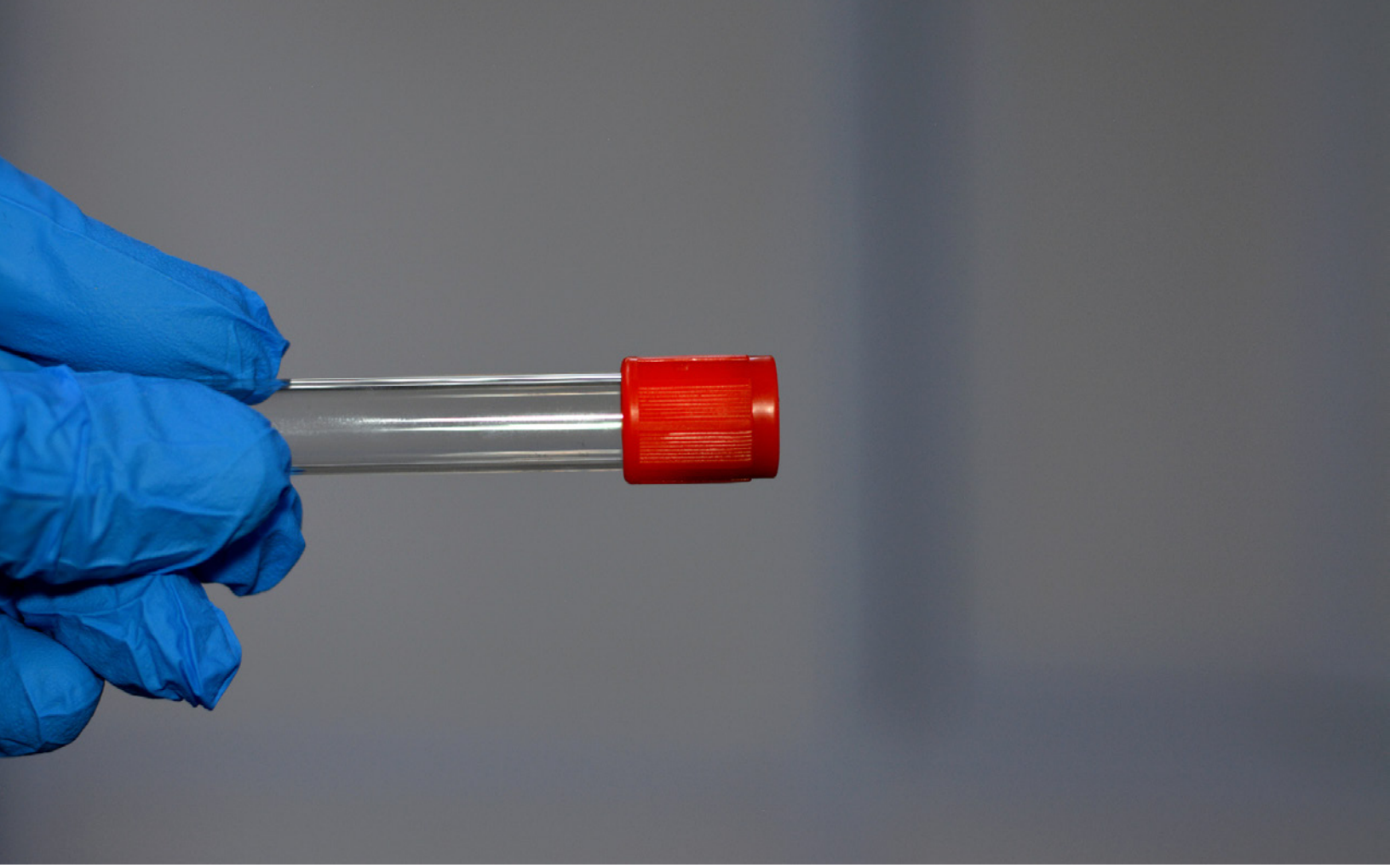
Hemoglobin glycosylated (A1c) testing, CPT code 83036, is usually determined by ion-exchange affinity chromatography, immunoassay, or agar gel electrophoresis. In 2022, this was the fourth-most ordered lab test with 2205 units/10,000 members. It is possible that this number represents both overutilization as well as underutilization of testing. Data sharing from the health plan to Avalon in terms of diagnosis codes and lab test values may allow for more understanding of testing and patient outcomes.

Furthermore, it is recommended that patients over age 45 or patients under 45 who are overweight get a baseline HbA1c test.[56] The USPSTF recommends screening overweight or obese adults ages 40-70 years for abnormal blood glucose, with a grade B recommendation.[57] Avalon is well-positioned to help meet this goal by providing plans with up-to-date information and patient level information on test ordering regardless of the location of the testing as well as the healthcare provider providing the test.

In addition, the recommendation of the American Society for Clinical Pathology and the American Society for Clinical Laboratory Science is “don’t repeat HbA1c testing in stable patients within 3 months of a previous result.” As the lifespan of a HbA1c is approximately 90–120 days, and the full effects of a patient’s change in behavior, diet, or newly adjusted medications will not be fully appreciated until all previous HbA1c in circulation are replaced (~90 days).[58] Therefore, testing at time intervals earlier than 3 months may not allow enough time to pass to reach the expected target by the clinician. Testing at 6-month intervals may be considered when glycemic targets are consistently achieved.

Furthermore, conditions that change the life span of red blood cells, such as recent blood loss, sickle cell disease, erythropoietin treatment, hemodialysis, or transfusion, can change A1C levels. A falsely high A1C result can occur in people who are very low in iron; for example, those with iron-deficiency anemia NIH external link. Other causes of false A1C results include kidney failure or liver disease. If the patient is of African, Mediterranean, or Southeast Asian descent or has family members with sickle cell anemia or a thalassemia NIH external link, an A1C test can be unreliable for diagnosing or monitoring diabetes and prediabetes.[59] Avalon can help identify patients for whom HbA1c testing is inappropriate.

With respect to price, glycosylated hemoglobin, testing was 45% more expensive ($13.50) in the physician office setting (setting 11) and 250% more expensive ($32.53) in the outpatient service setting (settings 19 and 22) versus the reference independent lab setting ($9.29). Avalon is working with its health plan customers to address these disparities in price.



The Take-Home Points from the Spotlight on HbA1c:

- HbA1c is the fourth most ordered routine test.
- It would be valuable to understand the results of HbA1c testing. Health plans may wish to address outliers in terms of utilization; furthermore, health plans may wish to encourage such test use as part of annual wellness exams.
- A clearer opportunity to detect waste is the evaluation of frequency of HbA1c testing: testing every 3 months represents the minimum interval between testing, given the life of the red cells is approximately 90 days. Avalon's current policy, which incorporates the American Society for Clinical Pathology and American Society for Clinical Laboratory Science recommendations, already addresses this theme.
- The price for this routine test varies greatly by place of service. Avalon can help health plans with their strategies to optimize the cost of testing by selecting preferred locations for such testing.

Summary of Routine Testing Section:

In this section, we recognized the overall 2022 spend on lab tests is $226 PMPY, a 15% decrease from $264 PMPY in 2021. This overall spending amount is driven by many challenging factors, including:

- High utilization – the Comprehensive Metabolic Panel ranked as the #1 ordered test.
- Waste is prevalent and very expensive in the routine testing area.
- Place of service has profound effects on costs: testing in hospital laboratories provides increased cost without providing increased quality for routine testing.
- High costs and prices were a direct result of the pandemic as were the proliferation of relatively inexpensive at-home lab tests. These costs are coming down with the decreased incidence of COVID infections in the US.
- HbA1c test monitoring provides a robust opportunity and example of how Avalon can help health plans think about their coverage policies for wellness exams and routine monitoring. Avalon's clients have adopted policies that address the frequency of testing.
- Avalon's Routine Testing Management solution can help identify outliers and egregious pricing practices in routine testing.

GENETIC TESTING

Genetic testing, which can provide information about an individual's risk for certain medical conditions is becoming more complicated and more common.[60] Genetic tests are tests that study genes and the way certain traits or conditions are passed down from one generation to another. With recent advances, genetic tests also now include biomarkers and direct tumor testing which can help the presence of a genetic mutation that can determine tumor type and provide information on the tumor's susceptibility to targeted drugs. Payers are faced with an increasing number of requests to cover genetic testing, determining whether it is appropriate under the circumstances amid an uncertain landscape.

Not long ago, single-gene tests were the norm; now, there are more than 10 new tests being developed every day that are more complex – analyzing more than one gene using advanced technology. With the field of molecular pathology evolving from an imprecisely defined discipline to a firmly established medical subspecialty that plays an essential role in patient care, the training, certification, and licensure requirements for directing and performing testing in a molecular diagnostics laboratory have evolved too. Both the American Board of Medical Genetics and the American Board of Pathology now certify lab techs and lab directors for molecular pathology licenses. Although MGP certification is not a CLIA requirement for a laboratory director, it provides the opportunity to gain additional experience and ability in directing a molecular diagnostics laboratory. The utility of all of these new tests continues to be in question, but the growth and sophistication of the genetic testing market is undeniable.

Indeed, genetic tests are increasingly being used to inform the use of a specific medication – called "companion diagnostics."[61] Targeted oncology therapy approvals and their companion diagnostics, in particular, are growing rapidly. For example, a companion diagnostic test may identify whether a patient's tumor has a specific gene change or biomarker that is targeted by the drug. The list of FDA-approved companion diagnostics is longer every year.[62]

The significant reduction in the costs of writing DNA is fueling significant advances in biotech and enabling the increase in genetic screening: the cost of a human genome sequence decreased from an estimated $1 million in 2007 to $1,000 in 2014, and today it is approximately $600.[63] As technology advances and the price for genetic testing decreases, it is possible that DNA sequence information will become a common part of a patient's medical records.

Genetic Testing by the Numbers

As of August 2017, there were approximately 75,000 genetic tests on the U.S. market.[64] The rapid development of genetic tests led to the creation of the Genetic Testing Registry, maintained by the National Institutes of Health, to provide information on genetic tests and the corresponding laboratories.[65] By

November 2022, a total of 129,624 genetic tests in the U.S. were submitted to the genetic testing registry, over 90% of which are for clinical rather than research purposes.[66]

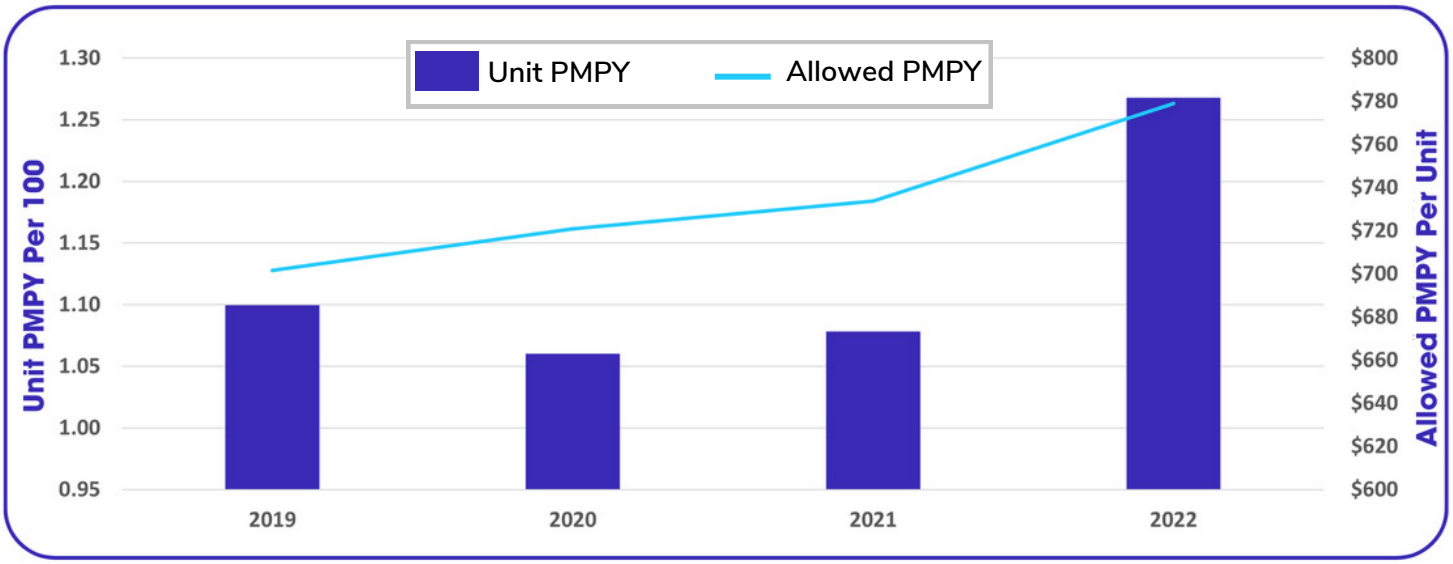
In 2020, the U.S. genetic testing market reached $4.38B and is expected to grow to $10B by 2027.[67] The growing demand for the early detection of cancer is a clear driver of the growth in genetic testing. Indeed, in 2022, President Biden re-launched the Cancer Moonshot initiative because of recent progress in cancer diagnostics and therapeutics.[68] Not long after announcing the initiative's goal of reducing the death rate from cancer by 50% over the next 25 years, a new federal subagency of the National Institutes of Health – ARPA-H – was created, with $1 billion in starter funding, in part to support the Cancer Moonshot goal.[69] Accordingly, companies are focusing on the adoption of advanced technologies to cater to the demand of processing large datasets as well as efforts to make genetic testing reach a larger population.

The federal health programs are also seeing an uptick in genetic testing. In 2021, Medicare Part B spending on four categories of high-priced genetic tests increased by 56%, from $1.2B in 2020 to $1.9B in 2021, exceeding pre-pandemic spending levels. Overall, the volume of genetic tests that Medicare Part B paid for increased by 55%, from $1.8M in 2020 to $2.8M in 2021.[70] Total spending on these genetic tests accounted for 20% of Medicare spending for lab tests in 2021.

These trends and activities mean that molecular techniques are becoming both more advanced and more commonly used. Faster turnaround times are enabling doctors to receive highly precise and specific information quickly, making decisions about genetic testing and subsequent treatment even more challenging for payers to make speedy coverage determinations. Given the exponential growth, a mostly-manual prior authorization process, and a lack

In 2020, the U.S. genetic testing market reached $4.38B and is expected to grow to $10B by 2027.[67]

FIGURE 5. Analysis of Avalon's Annual Growth Rate for the Past 4 Years in Genetic Test Spend is ~19%



Description: Both utilization (left Y-axis) and spend (right Y-axis) have increased versus 2019, the baseline year. Both saw double-digit increases from 2021 to 2022.

of specific test identification for genetic tests (discussed further below), health plans are confronting tricky determinations of coverage eligibility, test validity, and utility.

We analyzed utilization and spend for genetic tests among Avalon clients across all books of business. The results (Figure 5) demonstrated the utilization increased from 1.10 units of testing in 2019 to 1.27 units of testing in 2022, representing a 15% increase. Overall costs PMPY rose from $702 in 2019 to $779 in 2022, representing an 11% increase. Utilization and spend figures in Avalon's book of business compare favorably with the Medicare population, as described above.

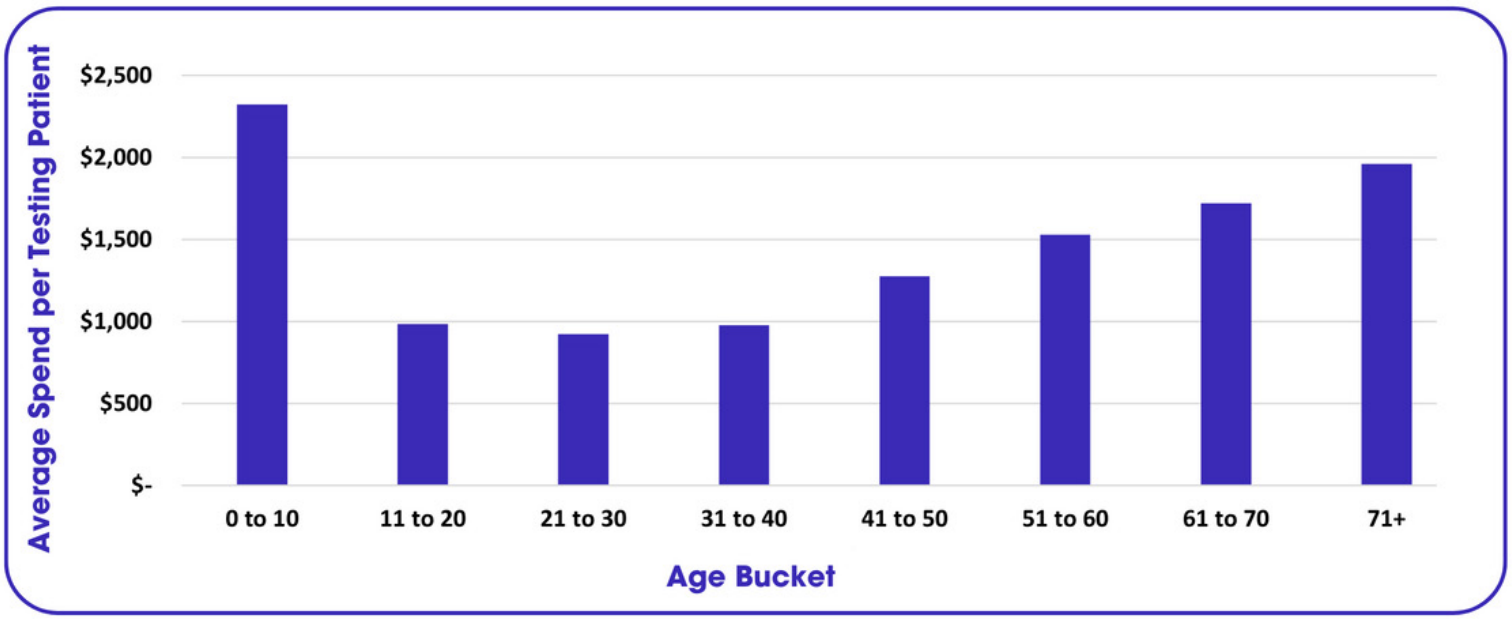
We analyzed genetic test management for health plans who were enrolled in Avalon's genetic test management program in 2022 to look for patterns of use among members. In this subgroup analysis of 85,634 members who had at least one genetic test over the year, we measured utilization and spend figures (Table 4).

We note that the average lab spend per member who underwent at least one genetic test was $1,168, (which makes up 10% of utilization). In contrast, the average spend per member who had at least one routine test was $287 (which makes up 90% of utilization) (Table 1). These figures underscore the premium pricing of genetic testing and their contribution to lab spend.

Table 4. Genetic Tests Utilization and Spend Figures for 2022

Category	Utilization	Spend
Mean	1	$1,168
Median	1	$700
Standard Deviation	+3	$1,656
Quartile 1	1	$440
Quartile 3	2	$1,183
Intra-quartile Range	1	$743

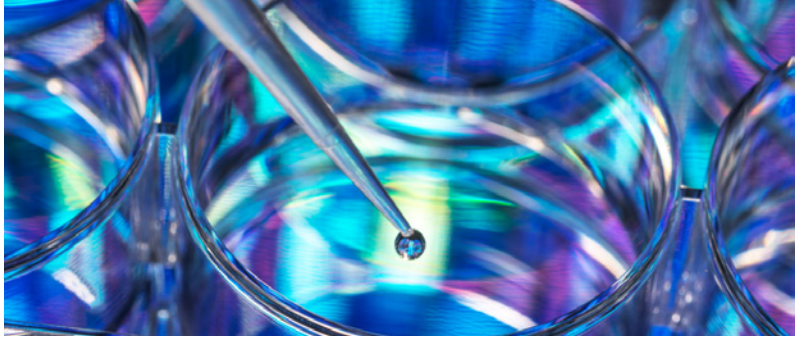
Figure 6. Average Spend on Genetic Testing Varies Dramatically by Age Group



Description: For patients who had at least one test in 2022, the average spend across all age groups shows variation from $2,322 for patients 0-10 years of age to $921 for patients 21-30 to $1,959 for patients 71 and older.

Key findings on Genetic Testing Utilization:

- The mean number of tests per member (1) was the same as the median number of tests per member (1), a pattern of utilization without the skewing of test use towards high users seen in routine testing.
- A long tail is noted, with some very high users undergoing as many as 55 tests per year in this population. Potential interventions could be targeted towards this tail to better understand the cause of a large number of tests in a very small group of members.
- The mean number of encounters was 1, suggesting that there is ~1 genetic test ordered per office visit for genetic tests. This number is in contrast with the 4 routine tests ordered per office visit. These encounter results suggest a different set of potential investigations and interventions, with a goal to assess the quality of testing and the ability to substitute one genetic test for another and yet allow for achievement of the same clinical need.



Key Findings on Genetic Testing Spend:

- The data demonstrate a similar pattern as seen with utilization. The difference between mean spend ($1,168) and median spend ($700) is not likely due to large number of tests by high users, but rather due to variation in price across the genetic test procedure codes.
- The first quartile spend of $440 (associated with 1 genetic test) seems parallel in case to the third quartile spend of $1,183 (associated with 2 genetic tests) and supports the theme of variable pricing of genetic tests: a doubling of tests leads to a tripling of spend.
- Across all lines of business, Avalon can provide health plans with this information, which may be helpful as a predictor of usage based on a plan's membership.

By November 2022, a total of 129,624 genetic tests in the U.S. were submitted to the genetic testing registry, over 90% of which are for clinical rather than research purposes.[66]

Medicare Part B spending on four categories of high-priced genetic tests increased by 56%, from $1.2B in 2020 to $1.9B in 2021.[70]

Overall, the volume of genetic tests that Medicare Part B paid for increased by 55%, from $1.8M in 2020 to $2.8M in 2021.[70]

Genetic Testing Utilization - Most Common CPT Procedure Codes

Molecular diagnostic testing and laboratory developed testing are rapidly evolving areas that present billing and coding challenges. Due to the rapid changes in this field, the CMS Clinical Laboratory Fee Schedule pricing methodology does not account for the unique characteristics of these tests. These challenges have led to services being incorrectly coded and improperly billed.

We analyzed the top tests in terms of utilization of genetic testing in 2022 across all Avalon business lines in terms of number of allowed units per 10,000 members (Table 5). Of note, these figures represent allowed versus ordered test units: the number of ordered tests is higher than the number of allowed tests, as tests are screened out from the system based on criteria set by health plans and reinforced by Avalon.

The results demonstrated the incarnate list of genetic tests used for prenatal and early infant care. Code 81420 provides risk assessment for the most common autosomal trisomies, sex chromosome aneuploidies, and also provides fetal gender. All newborns in the United States are now screened for cystic fibrosis, generally under CPT code 81220. Prenatal genetic carrier screening is reimbursable for certain analyses of spinal muscular atrophy and cystic fibrosis is classified as code 81329, SMN1 (survival of motor neuron 1, telomeric). Code 81479 represents the grab bag that is unclassified representing an assortment of laboratory derived tests without further description, making such tests difficult to document and even more challenging to manage. F5 (Coagulation Factor V)(eg Hypercoagulability) gene analysis, Leiden Variant CPT code 81241 is used to identify the cause of pregnancy loss. The 2022 highest-ranking genetic tests by utilization differed only slightly from 2021.

Table 5. Genetic Test Utilization - Top 5 tests in 2022

CPT Code	Utilization Rank	Number of Units /10,000 members	Description
81420	Fetal chromosomal aneuploidy	29.26	Fetal chromosomal aneuploidy (e.g., trisomy 21, monosomy X) genomic sequence analysis panel, circulating cell-free fetal DNA in maternal blood, must include analysis of chromosomes 13, 18, and 21.
81220	Cfr gene com variants	16.95	CFTR (cystic fibrosis transmembrane conductance regulator) gene analysis; common variants
81329	SMN1 gene dos/deletion alys	8.5	SMN1 (survival of motor neuron 1, telomeric) gene analysis; dosage/deletion analysis, includes SMN2 (survival of motor neuron 2, centromeric) analysis, if performed
81479	Unlisted molecular pathology	5.46	Unlisted molecular pathology procedure
81241	F5 gene	4.79	F5 (Coagulation Factor V)(eg Hypercoagulability) gene analysis, Leiden Variant

The Take-Home Points on Utilization of Genetic Testing Include:

- The results demonstrated that maternal and fetal tests make up 4 out of top 5 codes on genetic test utilization: given this finding, there is likely little that can be done to address these tests which represent standard of care monitoring. That being said, Avalon can prevent duplicate testing and help ensure that testing is well aligned well with the health plan coverage rules.
- The major opportunity for intervention is addressing the CPT procedure code 81479, which is rising due to increased number of new tests in the marketplace well as uptake of recently marketed tests.
- The 2022 highest-ranking genetic tests by utilization differed only slightly from 2021.

It is the responsibility of Medicare Administrative Contractors (MACs) to process Medicare claims that are medically reasonable and necessary and coded correctly. MACs may reject screening services such as pre-symptomatic genetic tests and services used to detect an undiagnosed disease or disease predisposition because they are not a Medicare benefit and are not covered. For people with a cancer diagnosis, Medicare policies for coverage of genetic testing for an inherited mutation vary based on where you live.

Medicare allows limited coverage of genetic testing.[71] Medicare covers panel testing when:

- The patient has pretest genetic counseling with a genetics professional who does not work for a testing laboratory.
- The patient has a post-test genetic counseling appointment with a genetics professional who does not work for a testing laboratory.
- The patient has a cancer diagnosis and meets the BRCA testing criteria listed above.
- The genetic test will affect their cancer treatment options.
- All of the genes included in the test panel are relevant based on their personal and family history.
- The patient also meets criteria for at least ONE other hereditary cancer syndrome for which NCCN guidelines provide clear genetic testing criteria and management recommendations (e.g., LiFraumeni syndrome, Cowden syndrome, or Lynch syndrome).

Medicare coverage of multigene panel testing is available in all Medicare regions, although eligibility for this testing varies by MAC policies. First Coast Service Options and Novitas Solutions MACs have more narrow testing policies. Broader coverage is available under Noridian Healthcare Solutions, Palmetto, Wisconsin Physicians Service Insurance, and CGS Administrators.

Providers are required to use a procedure code that most accurately describes the service being rendered. If the genetic tests are not represented by a procedure code, the unlisted molecular pathology procedure code 81479 is used.[72] With 81479 being the default unspecified code for molecular testing, there has been tremendous growth in its utilization over the last few years. From 2020 to 2021, CMS reported an expenditure increase of 40%, from $290M to $409M, related to 81479 billings, the largest contributor to the $2.8B in CMS's Molecular Pathology spending in 2021. Claims billed with CPT code 81479 are reviewed by payers on a case-by-case basis and initially denied pending additional information.

Genetic Testing Challenge: Waste

The greater access and ease of genetic testing make it

vulnerable to potential fraud, waste, and abuse. For example, in 2022, a federal jury convicted a Georgia man for submitting over $463 million in genetic lab tests that Medicare beneficiaries did not need by paying bribes to obtain doctors' orders for authorizing the tests.[73] Also in 2022, the Department of Justice announced criminal charges against 36 defendants of $1.2 billion in alleged fraudulent schemes involving cancer genetic testing and other services. The Center for Program Integrity of CMS took administrative actions against 52 providers involved in similar schemes (Figure 7).[74]

in 2022, a federal jury convicted a Georgia man for submitting over $463 million in genetic lab tests that Medicare beneficiaries did not need by paying bribes to obtain doctors' orders for authorizing the tests.[73]

Figure 7. Fraud in Genetic Testing Reached $1.2B


THE UNITED STATES DEPARTMENT of JUSTICE

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JUSTICE NEWS

Department of Justice

Office of Public Affairs

FOR IMMEDIATE RELEASE Wednesday, July 20, 2022

Justice Department Charges Dozens for $1.2 Billion in Health Care Fraud

Nationwide Coordinated Law Enforcement Action to Combat Telemedicine, Clinical Laboratory, and Durable Medical Equipment Fraud

FRAUD

The Department of Justice today announced criminal charges against 36 defendants in 13 federal districts across the United States for more than $1.2 billion in alleged fraudulent telemedicine, cardiovascular and cancer genetic testing, and durable medical equipment (DME) schemes.

The nationwide coordinated law enforcement action includes criminal charges against a telemedicine company executive, owners and executives of clinical laboratories, durable medical equipment companies, marketing organizations, and medical

More than $1.2 BILLION

Alleged fraudulent telemedicine, cardiovascular and cancer genetic testing, and DME schemes

13 U.S. Federal Districts

36 Defendants

Description: In July 2022, the Department of Justice announced criminal charges against 36 defendants in 13 federal districts across the United States for more than $1.2 billion in alleged fraud schemes, including cardiovascular and cancer genetic testing.[74]

In addition to wasteful, abusive, and/or fraudulent claims, genetic tests are being ordered despite a lack of medical necessity or clinical utility. Genetic tests are being performed on individuals without proper justification for the test, given the individual's circumstances, which add little value to a patient's care but profoundly affect the costs of providing the insured benefit. There is a lack of consensus on how to operationalize clinical utility, leading to inconsistent determinations of value and coverage across labs, providers, and payers – which translates into a substantial variation in test coverage and access.[75]

Avalon Can Help with Genetic Test Utilization:

Avalon provides its health plans information on test quality, such as analytic validity, clinical validity, and clinical utility, as well as other metrics applicable to help health plans develop coverage policies to meet their needs. This information is summarized by Avalon internally and reviewed externally with its scientific, expert-led Clinical Advisory Board. As outlined in detail below, Avalon leverages emerging industry standard DEX™ Diagnostics Exchange Test Identification Codes (DEX Z-Code™) to identify discrete test quality and ensure consistent coding as well as provides automated policy enforcement through NCQA-certified prior authorization programs.

Health plans benefit from Avalon's programs in several ways:

- Greater compliance with state Medicaid and Medicare Advantage coverage rules.
- Higher Net Promoter Scores as auto-approvals increase.
- Ensure that ordered tests meet quality standards.
- Prevent fraud, waste, and abuse through Avalon's Genetic Test Management programs.
- Increased accuracy between tests authorized and tests covered during claim adjudication.
- The tables below address the top 5 compliant prior authorization codes as well as the top 5 non-compliant codes (Tables 6 and Tables 7, respectively).

Table 6. Top 5 Codes Approved by Prior Authorization

Procedure Description	Percent of Total Units Determined Compliant
SMN1 GENE DOS/DELETION ALYS (81329)	9.65%
Cftr gene com variants (81220)	8.56%
Hrdtry brst ca-rlatd dsordrs (81432)	7.58%
Hrdtry brst ca-rlatd dsordrs (81433)	7.56%
Unlisted molecular pathology (81479)	3.51%

Table 7. Top 5 Codes Determined to Be Noncompliant by Prior Authorization

Procedure Description	Percent of Total Units Determined Non-Compliant
Unlisted molecular pathology (81479)	9.72%
Hrdtry brst ca-rlatd dsordrs (81432)	4.10%
Hrdtry brst ca-rlatd dsordrs (81433)	4.08%
Cftr gene com variants (81220)	2.13%
SMN1 GENE DOS/DELETION ALYS (81329)	2.10%

Genetic Testing Challenge: Price

The price of genetic tests is relatively high, with an average payment of $666 per test in 2021.[76] The number of procedure codes for genetic tests increased to 365 in 2021, representing an additional 31 codes to the 334 procedure codes that Medicare Part B paid for in 2020. Prices ranged from $509 to $3,873 across three molecular pathology procedure codes and two multianalyte assays with algorithmic analysis procedure codes. For example, Medicare Part B spent $282.2M on 141,146 units of a specific molecular pathology code (81408). Volume for this test increased by 36% in 2021 and had the highest change in volume and spending for genetic tests.

We identified the top genetic lab tests with the largest spend and highest prices in 2022 across all business lines in terms of per member per year spend (PMPY) (Table 8).

The results demonstrated a similar list of genetic tests common to the outpatient setting: CPT 81420 and CPT 81220 are on both lists. This scenario is most likely due to the large volume of test ordering for this prenatal and early infant care. However, there are three new tests on the spend list described below that are worth noting. Oncology breast gene expression profile CPT 81519 represents a test for detecting genes associated with breast cancer recurrence. BRCA 1&2 gen full seq dup/del CPT code 81162 represents a test to measure a mutation associated with a higher risk of breast, ovarian, and other cancers. Exome sequence analysis CPT 81416 represents exosome sequencing of families to optimize the interpretation of the variants detected in the patient.

Table 8. Genetic Test Management Spend

CPT Code	Utilization Rank	Spend/10,000 members	Description
81420	Fetal chromosomal aneuploidy	$2.18	Fetal chromosomal aneuploidy (e.g., trisomy 21, monosomy X) genomic sequence analysis panel, circulating cell-free fetal DNA in maternal blood, must include analysis of chromosomes 13, 18, and 21.
81220	Cfr gene com variants	$0.94	CFTR (cystic fibrosis transmembrane conductance regulator) gene analysis; common variants
81519	Oncology breast gene expression profile	$0.81	Oncology (breast), mRNA, gene expression profiling by real-time RT-PCR of 21 genes, utilizing formalin-fixed paraffin embedded tissue, algorithm reported as recurrence score
81162	BRCA mutations	$0.77	BRCA1 (BRCA1, DNA repair associated), BRCA2 (BRCA2, DNA repair associated) (e.g., hereditary breast and ovarian cancer) gene analysis; full sequence analysis and full duplication/deletion analysis (i.e., detection of large gene rearrangements)
81416	Exome sequence analysis	$0.44	Exome (e.g., unexplained constitutional or heritable disorder or syndrome); sequence analysis, each comparator exome (e.g., parents, siblings)

Unlisted molecular pathology CPT 81479 was ranked sixth at 0.38 PMPY for 2022. Of note, this CPT procedure increased 22% in spend in 2022 versus 2021, which is consistent with newly introduced genetic tests and their early code classification as 81479.

Overall, the 2022 highest-ranking genetic tests by spend differed only slightly from 2021.

The Take-Home Points for Spend on Genetic Tests Include:

- The spend and trend results demonstrated a similar list of genetic tests common to the outpatient setting as described in the genetic test utilization section above: CPT 81420 and CPT 81220 are on both lists.
- Two new oncology tests – tests for breast cancer recurrence and the BRCA genes – represent two new codes that are distinguished by their high costs and associated spend figures.
- The unlisted molecular pathology code represents a grab bag test code, described as unlisted molecular pathology procedure and mentioned in the utilization section, ranked sixth on the spend list.
- The 2022 highest-ranking genetic tests by spend differed only slightly from 2021.

Avalon Can Help Manage Genetic Test Spend:

As the number of genetic lab tests grows, payers struggle to determine the clinical validity and utility due in no small part to the lack of test management and oversight and lack of specific test identification. The incorporation of specific genetic test codes into Avalon's policies aligns clinical and payment policy with genetic test evolution – ensuring the right test is provided for the right care.

Avalon's Precision Genetic Test Management (PGTM) solution leverages the MolDX® Program, administered by PALMETTO GBA®, on non-specific CPT codes. More specific codes, known as DEX Z-Codes™, are assigned by the MolDX® Program to better establish coverage and reimbursement for molecular tests.[77] Under the PGTM program, unspecified codes, such as 81479, will require authorization and billing with a DEX Z-Code™ identifier obtained through the MolDX® program. This process helps make sure that payers know exactly what test is performed and pays for only appropriate testing.

Specific to genetic testing, the incorporation of the MolDX® Z-Codes™ into Avalon's policies aligns clinical and payment policy with genetic test evolution – ensuring the right test is provided for the right care. There is inherent importance of genetic test specificity in lab testing and its potential impact on lab science across all fields. With 1 in 3 tests being ordered incorrectly, Avalon's PGTM solution directly address this problem in genetic testing.

Legislative and Regulatory Landscape Impacting Genetic Testing

Legislative Proposals Support Genetic Testing

In early 2023, a bipartisan bill was introduced in the U.S. Senate that would increase access to genetic testing for Medicaid-eligible patients[78]. Almost one-third of low-income Medicaid beneficiaries have been diagnosed with depression; genetic testing would be ordered for patients suffering from a mental health condition. The bill would require CMS to provide states with best practices to improve outcomes for Medicaid-eligible individuals with major depressive disorder (MDD) or other mental health conditions to help increase access to genetic testing to better inform their treatment options.

On March 9, 2023, the Reducing Hereditary Cancer Act was reintroduced in Congress[79]. It would expand Medicare's coverage to include guideline-recommended genetic testing for certain mutations that increase cancer risk. The bill would apply to those who have a personal or family history of hereditary cancer or a known hereditary cancer mutation in their family.

A Federal Rule Will Automate the Prior Authorization Process: Impact on Lab Testing

There is serious momentum for electronic prior authorization as the federal government prepares to mandate payers and providers to utilize technology and software to better communicate about coverage requests and determinations.

On April 27, 2022, the HHS OIG released a report on Medicare Advantage coverage denials, concluding that Medicare Advantage plans denied prior authorization requests by:

- Using plan clinical criteria that are not part of Medicare coverage rules.
- Requesting unnecessary documentation.
- Making manual review errors and system errors.

In August 2022, CMS also released a request for information, seeking feedback on how to improve Medicare Advantage for stakeholders. More than 4,000 comments were filed, including those from Avalon, in response. As the only company currently producing a lab trend report, the CMS request for

information provided Avalon an opportunity to speak directly to the insights we have uncovered in the annual report.

Recommendations included:

- Improving the prior authorization processes.
- Making lab testing cost-effective and reducing medically unnecessary testing (e.g., detecting and preventing avoidable waste).
- Implementing innovative coding and quality assessment techniques to incentivize value-based care.

On December 13, 2022, CMS released a 402-page proposed rule to require health plans and encourage providers to automate prior authorization. The electronic prior auth (ePA) rule, if finalized, would require payers to automate the prior auth process with a new FHIR-based API and offers an incentive to providers to use the new ePA API. The required information available through the API would include documentation that the provider sends to the payer to support a coverage decision, like laboratory results and diagnostic reports.[80] A final rule is expected in 2023.

In its 2024 Medicare Advantage and Part D Policy Changes Final Rule,[81] CMS clarified that MA plans must make medical necessity determinations that are no more restrictive than Traditional Medicare's national and local coverage policies and approved by a plan's medical director. CMS also referred to the proposed electronic prior authorization rule about how the agency will be standardizing prior authorization processes in the future.

Genetic Testing - Spotlight on MRD (Minimal Residual Disease):

Measurable or minimal residual disease (MRD) testing is used to see if the cancer treatment is working and to guide further treatment plans. MRD testing is mainly used in blood cancers (leukemia, lymphoma, and myeloma), but is being studied in solid tumors as well. An MRD negative result means that no disease was detected after treatment.

MRD testing can be used to:

- Diagnose cancer progression, recurrence, or relapse before there is clinical, biological, or radiographical evidence of progression, recurrence, or relapse.
- Detect tumor response to therapy by measuring the proportional changes in the amount of available circulating tumor DNA.

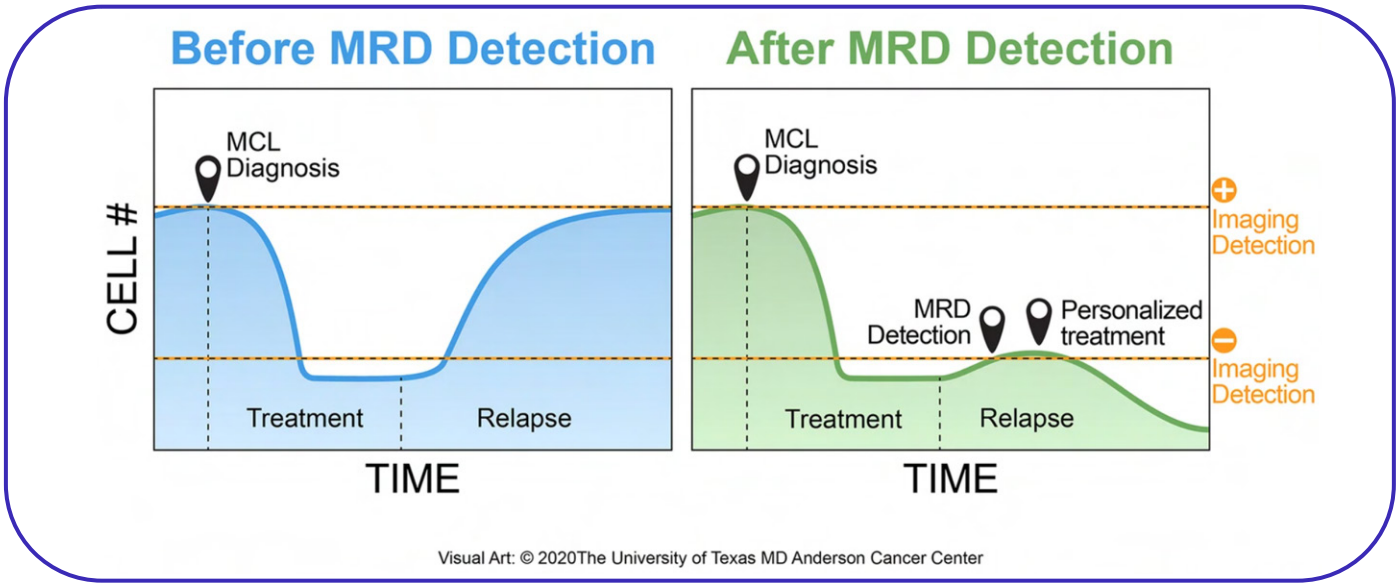
Information from MRD testing may be used for prognostic purposes, treatment strategies among different agents, or avoidance of unnecessary diagnostic or therapeutic intervention.

MRD tests use highly sensitive methods: the literature suggests that minimum residual disease (MRD) is closely associated with disease recurrence, thus identifying specific genetic and molecular alterations as novel MRD detection targets using ctDNA (circulating tumor DNA) has been a major focus. The most widely used tests to measure MRD are flow cytometry, polymerase chain reaction (PCR), and next-generation sequencing (NGS). These methods are designed to be sensitive enough to detect one cancer cell among one million normal cells.

MRD tests using blood and other bodily fluids provide advantages over current standard of care methods. In contrast to traditional tissue biopsies, so-called “liquid biopsies” are non-invasive, easy to repeat, and provide a real-time tumor picture. Furthermore, standard biopsies can be plagued with

sampling bias and intratumor heterogeneity that led to false negative results and other inaccurate information. Lastly, MRD test measuring ctDNA can be used in patients in whom tissue is not available for a repeat biopsy. In contrast to radiographic methods which require millions of cells to make a tumor big enough to show up on an imaging test. MRD tests are designed to go to the level of the single cancer cell. These findings outline the advantages of MRD in evaluating tumor progression (Figure 8).[82–83]

Figure 8. Measurement of Treatment Effect and Tumor Relapse Before and After MRD Methods (Jung et al, 2020)



Description: General overview of minimal residual disease detection. The figure shows two scenarios emphasizing the importance of MRD detection after initial treatment of mantle cell lymphoma. When MRD detection is not performed, there is no indication of how effective the treatment was on the tumor, and relapse may eventually occur (left). If MRD diagnosis confirms a positive result, the patient can be prescribed to a more personalized treatment to prevent any future relapses (right)

Given all these features, the global MRD market is estimated at $1.2B in 2022 and expected to rise to $2.3B in 2027.[84] Most of the current market is focus on hematological tumors: the market is expected to move to solid tumors as well. Yet despite the theoretical and realized opportunity associated with MRD testing, several challenges exist.[85]

- In plasma, ctDNA levels tend to be variable and low, resulting in a variable detection threshold.
- Negative ctDNA may be due to low copy number detection rather than the absence of ctDNA. The limited sensitivity of the ctDNA analysis is a critical challenge, particularly in patients with resected early-stage cancer, when plasma ctDNA levels are low. False negatives are inevitable due to the influence of biological variables such as mucinous histology, low DNA-shedding tumor, and hidden micrometastasis.
- Other challenges include streamlining the MRD testing workflow, navigating a lack of standardized detection approaches, and selecting diagnostic testing technology that is sensitive and accurate enough to optimize the MRD testing process.

Avalon can help health plans identify diagnostic labs that meet the analytical and clinical validity benchmarks needed for accurate tests. Furthermore, Avalon has developed coverage criteria for MRD that highlights multiple methodologies corresponding to multiple CPT codes.

- For individuals with multiple myeloma (MM), chronic lymphocytic leukemia (CLL), or small lymphocytic lymphoma (SLL), minimal residual disease (MRD) testing by multiparameter flow cytometry or next-generation sequencing (NGS) MEETS COVERAGE CRITERIA.
- For individuals with acute myeloid leukemia (AML) or acute lymphoblastic leukemia (ALL), MRD testing by multiparameter flow cytometry, PCR-based techniques, or NGS MEETS COVERAGE CRITERIA.

CMS has opined that MRD testing can be used to accurately predict disease recurrence or progression before clinical or radiographical evidence is evident (establishing molecular recurrence) and performs better than other established methods for disease surveillance such as serial CEA monitoring, physical exams, imaging or flow cytometry.[86] Under a local coverage determination finalized by Medicare Administrative Contractor PALMETTO GBA® in 2021, any MRD test that successfully passes a technical assessment by MolDX® and sufficiently demonstrates clinical validity and utility for its intended use case can gain coverage.[87]

The Take-Home Points from the Spotlight on MRD Include:

- MRD testing offers multiple advantages compared to radiological or tissue-based methods currently in practice, but it is not yet the standard. As MRD testing improves, health plans can expect to replace traditional radiological monitoring methods with lower-cost blood tests.
- Not all MRD tests are created equal. Many differ with respect to their definitions of minimal residual disease, test performance characteristics such as sensitivity and specificity as well as clinical utility, and readiness for prime use in the solid tumor space where less evidence is available versus the liquid tumor space.
- Payers may note that the cost of radiology services for oncology disease and treatment monitoring costs may go down with the advent and spread of MRD tests. Plans may thus save costs outside of lab services with this investment in blood tests.
- Avalon can help health plans manage and optimize the use of MRD testing in oncology. Coverage policies are currently in place for testing by two diagnostic companies. Avalon will continue to monitor the evolving science and evidence development in this area and provide results of its findings to health plans so such health plans can make informed decisions on coverage.

Summary of Genetic Testing Section:

Genetic tests are increasing in number so rapidly that health plans need help monitoring the newly developed tests as well as managing claims to ensure appropriateness of testing. Sophisticated molecular techniques are becoming both more advanced and commonly used. While genetic tests currently constitute only ~10% of lab utilization, the spend on genetic testing is increasing rapidly accounting for 30% of total lab dollars, similar to the pattern seen in specialty pharmaceuticals.

Avalon's LBM process offers payers an opportunity to adopt laboratory policies for genetic tests that will track and manage unspecified codes and help identify clinical utility, and the flipside of clinical utility (i.e., avoidable waste). Health plans that take advantage of this process can adopt faster and improved coverage and payment decisions for genetic tests.

FUTURE TESTS: MCED AND PRS

This section addresses the future of newly marketed tests or lab tests under development. Both multi-cancer early detection (MCED) tests and polygenic risks scores (PRS) address preventative strategies and are considered screening tests.

The characteristics of a good screening test are relevant to review here. The preclinical phase of a disease starts with the onset of the disease process and lasts until signs and symptoms appear, which is when the clinical phase begins. It is this asymptomatic period in which screening may be helpful. The detectable preclinical phase is the interval during which the disease is detectable by screening, but the patient is still asymptomatic. During this period, if there is a critical point at which intervention is more effective than if started after the clinical phase begins, then it is worthwhile to conduct screening tests.[88]

The screening test for the disease must be capable of detecting a high proportion of disease in its preclinical, asymptomatic phase state and must have high test performance with preferably 90% or greater sensitivity and specificity. A highly sensitive test means that there are few false negative results, and thus fewer cases of the disease are missed. The specificity of a test is its ability to designate an individual who does not have a disease as negative. A highly specific test means that there are few false positive results.[89] Further characteristics of a screening test include logistical considerations such as being widely available and widely available at a reasonable cost as well as health-related considerations such as being safe to administer and associated with demonstrated improved health outcomes. Two particular technologies – multi-cancer early detection (MCED) tests and polygenic risk score (PRS) – are outlined below.

MCED (Multi-Cancer Early Detection) Tests

What is MCED?

MCED (multi-cancer early detection) tests are a type of liquid biopsy that use a sample of blood to identify specific biologic signals released by cancer cells into the blood.[90] Specifically, a common type of liquid biopsy on the market focuses on cell-free DNA to search for abnormal patterns of DNA methylation, which help to identify cancer cells and the tissue of origin.[91–92]

Why is it relevant?

Currently, there are proven screening tests for some types of cancer (including breast, cervical, colorectal, prostate, and lung) which have shown clinical

effectiveness and are generally covered by health plans. The goal is early detection of cancer, as cancers that are found early are often easier to treat and tend to have better outcomes. Unfortunately, many cancers do not have proven early-detection screening tests. In fact, about 70% of all cancer deaths come from cancers for which there are currently no proven screening tests. These cancers are often diagnosed at an advanced stage when they can be harder to treat[93]. Currently, the pan-cancer testing space includes a small handful of large, prominent players, and large clinical trials are underway to address the clinical validity of these tests.[94]

What is the opportunity to improve patient care?

Most of the makers of these MCED tests claim that they are not meant to replace screening tests currently in use (such as mammograms for breast cancer, Pap tests and HPV tests for cervical cancer, stool tests and colonoscopy for colorectal cancer, the PSA blood test for prostate cancer, and low-dose CT scans for lung cancer). Instead, MCED tests might supplement current screening tests as well as help find other cancers for which there are no proven screening tests.

What are the challenges?

There are several potential harms associated with MCED testing. The test could reduce advanced-stage cancer, but not reduce mortality. In addition, there is a need to be compliant with the diagnostic workup if a positive MCED test result is seen. Lastly, there is risk of anxiety in a person who received a positive result before the workup as well as after the workup when cancer is ruled out, given the false negative rate of the diagnostic workup of cancer and with respect to future risk.

There are also multiple unanswered questions. What will be the costs of these tests under development? Does early intervention result in better patient outcomes? What is the required frequency for such testing? Specifically, if the patient has a negative MCED test result in 2023, what is the rate of future testing that is required?

While this technology is in its infancy, health plans would be wise to monitor this space, as these genetic tests used for screening have the potential for replacing higher cost and/or more invasive screening methods of today. Conversely, it will also be important for health plans to proactively address desired use criteria for their members given the ease of use and potential overuse of simple blood tests to screen for cancer.

PRS (Polygenic Risk Factors)

What is a PRS?

Polygenic risk score (PRS), or polygenic scores, represent a single value estimate of an individual's common genetic liability to a phenotype, calculated as a sum of their genome-wide genotypes, weighted by corresponding genotype effect size estimates (or Z-scores) derived from summary statistic genome-wide association studies (GWAS) data.[95] The GWAS data compare groups with a certain disease to a group without the disease. The PRS thus represents a relative risk (e.g., 3 times the average risk) for a person to develop a specific disease.

Why is it relevant?

Many inherited diseases are monogenic and thus can be traced to variants in a single gene. For example, cystic fibrosis, a progressive genetic disease, is caused by variants in the cystic fibrosis transmembrane conductance regulator (CFTR) gene on chromosome 7. In contrast, complex diseases that represent the majority of chronic diseases, such as cardiovascular disease, diabetes, and osteoporosis as well as multiple forms of cancer occur as a result of multiple genomic variants, paired with environmental and lifestyle. These diseases are thus referred to as polygenic diseases. There are roughly 4 to 5 million such genomic variants in an individual's genome. These variants may be unique to that individual or occur in others as well. Some variants increase the risk of developing diseases, while others may reduce such risk; others have no effect on disease risk[96].

It will be important for health plans to proactively address desired use criteria for their members given the ease of use and potential overuse of simple blood tests to screen for cancer.

What is the opportunity to improve patient care?

Adding genomic risk to standard non-heredity risks can aid in the risk stratification process. For example, an integrated risk tool that combines polygenic risk with a standard risk calculator for cardiovascular disease outperformed current risk stratification tools and offered greater opportunity for early interventions.[97] Given the plummeting costs of genetic tests, future iterations of risk tools used in usual care for chronic diseases could be enhanced with the addition of a person's polygenic risk for a variety of common disorders and led to enhanced and personalized prevention strategies.

The majority of genomic studies to date have examined individuals of European ancestry. Because of this issue, there may not be adequate data about genomic variants from other populations.

What are the challenges?

The majority of genomic studies to date have examined individuals of European ancestry. Because of this issue, there may not be adequate data about genomic variants from other populations for calculating a polygenic risk score in those populations.

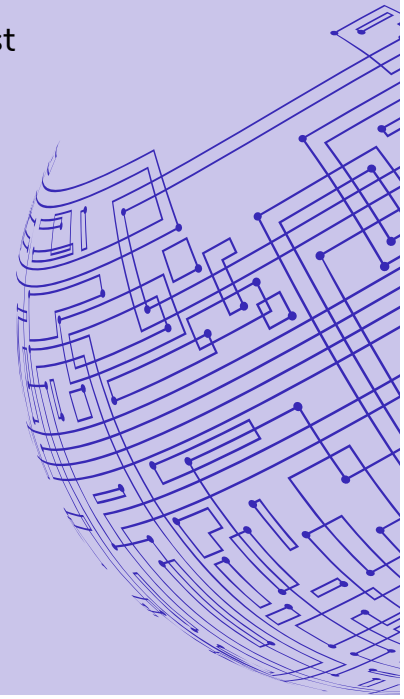
Absolute risk differs from relative risk. Relative risk such as a 3 times increased risk may be hard to integrate into clinical practice and change management strategy. It is the absolute risk that is usually used to guide physician management practices.

In a recent systematic review of the existing evidence for the clinical utility of PRS, 22 of the 591 articles reviewed provided strong evidence of clinical validity, but not a single article demonstrated clinical utility.[98]

How Can Avalon Help Health Plans Address these New Technologies?

Avalon can help health plans with their determination of appropriate coverage for these tests for their members. In the policy development phase, Avalon does a deep dive into the clinical validity and clinical utility of new and evolving blood tests.

Clinical validity studies focus on answering the question, “Does the test measure what is intended to measure?” For MCED tests, the question is whether the test result identifies cancer as measured against gold standard technologies such as tissue biopsy and standard of care screening tests? For PRS tests, the question is whether the test result identifies patients at higher risk that are likely to develop the target condition in the represented time interval?



Clinical utility studies focus on answering the question, “Does the test result lead to a change in patient behavior of health care provider decision making, and/or does this change lead to better outcomes?” These studies are needed to establish the addition on the lab test to the usual care pathway for the patient and the healthcare provider in a way to justify the logistics and costs of their implementation and use.

Conclusion:

The purpose of the Lab Trend Report 2023 is three-fold: to provide a resource of the statistics and analyses about lab testing trends, to comment on the potential future of lab testing, and to help payers understand how to better manage the quality and costs of this changing arena. Routine testing is heavily relied on to inform medical treatment plans, which means there are real challenges in making sure tests are well-utilized, not unnecessarily repeated, and appropriately priced. The future lies in lab tests that are the gateway to the early identification and prevention of disease, but there is no standard practice for ordering genetic tests or agreed-upon criteria for their general validity, utility, or coverage eligibility. Avalon's lab benefit management programs for payers can help align clinical considerations with cost-effective policies to make sure only high-quality, value-based lab tests are provided to their members.

From the Desk of Barry Davis

Chief Growth Officer, Avalon

Avalon's third Lab Trend Report continues our trend of defining and leading the Lab Benefit Management industry. Our mission is to leverage laboratory science, innovation, and technology to bring novel insights on the latest lab trends and to provide solutions to payers.

Every day, we work to help our clients reduce waste in routine testing and assist with the challenging arena of genetic test decision-making. Avalon is launching new services to assist payers with value-based care. By digitizing laboratory results and integrating them into our advanced analytics, Avalon can provide earlier disease detection to drive treatment protocols and reduce the per-member cost of healthcare.

Avalon knows that managing your lab benefit means much more than managing unit cost. If you would like to discuss your Lab Benefit Management strategy or see how Avalon's solutions can help your organization, please reach out to me.

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ACKNOWLEDGMENTS

The 2023 Lab Trend Report would not have been possible without significant contributions from many reviewers and content providers. Specifically, Avalon greatly appreciates the material contributions of Julie Barnes, Dr. Mark Monane, Dr. Jason Bush, Joanna Stefaniak, Michele Bennett, Holly Simmons, Steve Morgan, Barry Davis, Michele Norton, and Asmaa Habiballah.

REFERENCES

1. Strengthening Clinical Laboratories. Centers for Disease Control and Prevention. November 15, 2018. Accessed May 26, 2023. https://www.cdc.gov/csels/dls/strengthening-clinical-labs.html.

2. AACC. Laboratory medicine: Advancing quality in patient care. Accessed May 26, 2023. https://www.aacc.org/advocacy-and-outreach/aacc-policy-reports/2015/laboratory-medicine-advancing-quality-in-patient-care.

3. Strengthening Clinical Laboratories. Centers for Disease Control and Prevention. November 15, 2018. Accessed May 26, 2023. https://www.cdc.gov/csels/dls/strengthening-clinical-labs.html.

4. Medicare Part B Spending on Lab Tests increased in 2021, driven by higher volume of covid-19 tests, genetic tests, and chemistry tests. OEI-09-22-00400 12-19-2022. December 19, 2022. Accessed May 26, 2023. https://oig.hhs.gov/oei/reports/OEI-09-22-00400.asp.

5. As required by the Protecting Access to Medicare Act of 2014 (PAMA), the HHS Office of Inspector General performs an annual review of the top 25 laboratory tests. Monitoring Medicare Payments for Clinical Diagnostic Laboratory Tests - Mandatory Review. December 17, 2018. Accessed May 26, 2023. https://oig.hhs.gov/reports-and-publications/workplan/summary/wp-summary-0000108.asp.

6. Halbisen AL, Lu CY. Trends in Availability of Genetic Tests in the United States, 2012-2022. Journal of Personalized Medicine. April 6, 2023. Accessed May 26, 2023. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC10142561/#:~:text=Of%20the%2051%2C803%20new%20genetic,in%20the%20US%20are%20diagnostic.

7. Medicare Part B Spending on Lab Tests increased in 2021, driven by higher volume of covid-19 tests, genetic tests, and chemistry tests. OEI-09-22-00400 12-19-2022. December 19, 2022. Accessed May 26, 2023. https://oig.hhs.gov/oei/reports/OEI-09-22-00400.asp.

8. Long Covid or Post-Covid Conditions. Centers for Disease Control and Prevention. December 16, 2022. Accessed May 26, 2023. https://www.covid.gov/longcovid/definitions.

9. Research and Markets. Clinical Laboratory Service Market Research Report 2022: A $280+ billion market by 2030 - growing prevalence of target diseases coupled with rising demand for early disease diagnostic tests. GlobeNewswire News Room. December 9, 2022. Accessed May 26, 2023. https://www.globenewswire.com/en/news-release/2022/12/09/2570900/28124/en/Clinical-Laboratory-Service-Market-Research-Report-2022-A-280-Billion-Market-by-2030-Growing-Prevalence-Of-Target-Diseases-Coupled-With-Rising-Demand-For-Early-Disease-Diagnostic-T.html.

10. Wilson S, Steele S & Adeli, K. Innovative technological advancements in laboratory medicine: Predicting the lab of the future, Biotechnology & Biotechnological Equipment, BIO, April 18, 2022. 36:sup1, S9-S21, DOI: 10.1080/13102818.2021.2011413.

11. Role of the clinical laboratory in response to an expanding geriatric population. ASCLS. https://ascls.org/expanding-geriatric-population/. April 8, 2021. Accessed May 26, 2023.

12. Maher L, Miller D. The future of diagnostic testing is in the home. Cardinal Health. https://www.cardinalhealth.com/en/essential-insights/the-future-of-diagnostic-testing-is-in-the-home.html. July 8, 2022. Accessed May 26, 2023.

13. Whaley CM, Zhao X, Richards M, Damberg CL. Higher Medicare spending on imaging and lab services after Primary Care Physician Group vertical integration. Health Affairs. 2021;40(5):702-709. doi:10.1377/hlthaff.2020.01006

14. Shryock T. Physician payment outlook. Medical Economics. https://www.medicaleconomics.com/view/physician-payment-outlook. January 31, 2023. Accessed May 26, 2023.

15. CVS Health to acquire Oak Street Health. Oak Street Health. https://investors.oakstreethealth.com/news/news-details/2023/CVS-Health-to-Acquire-Oak-Street-Health/default.aspx. February 8, 2023. Accessed May 26, 2023.

16. Scott K. To outsource or not to outsource. AACC. https://www.aacc.org/cln/articles/2017/april/to-outsource-or-not-to-outsource-hospitals-face-touch-decisions-when-it-comes-to-lab-services. April 1, 2017. Accessed May 26, 2023.

17. Quest Diagnostics completes acquisition of Outreach Lab services business of Summa Health. Quest Diagnostics Newsroom. https://newsroom.questdiagnostics.com/2022-11-28-Quest-Diagnostics-Completes-Acquisition-of-Outreach-Lab-Services-Business-of-Summa-Health. November 28, 2022. Accessed May 26, 2023.

REFERENCES

18. Quest Diagnostics partners with NewYork-Presbyterian Hospital to broaden access to lab services in New York and tri-state area and beyond; Quest to acquire Select Lab Service assets, NewYork-Presbyterian to own, Operate Hospital Labs. Industry Intelligence. https://www.industryintel.com/consumer-wellness/news/quest-diagnostics-partners-with-newyork-presbyterian-hospital-to-broaden-access-to-lab-services-in-new-york-and-tri-state-area-and-beyond-quest-to-acquire-select-lab-service-assets-newyork-presbyterian-to-own-operate-hospital-labs-158495943408. February 14, 2023. Accessed May 26, 2023.

19. Quest Diagnostics to acquire Clinical Outreach Laboratory from UMass Memorial Medical Center; plan to build "lab of the future." UMass Memorial Health. https://www.ummhealth.org/umass-memorial-medical-center/quest-diagnostics-acquire-clinical-outreach-laboratory-umass-memorial-medical-center-plan-build-%E2%80%98lab. Accessed May 26, 2023.

20. Pifer R. Ascension inks strategic relationship with Labcorp, expanding testing capabilities. Healthcare Dive. https://www.healthcaredive.com/news/ascension-strategic-relationshi-labcorp-testing/618635/. February 10, 2022. Accessed May 26, 2023.

21. Bonislawski A. Pace of hospital lab acquisitions likely to remain steady, industry observers say. 360Dx. https://www.360dx.com/clinical-lab-management/pace-hospital-lab-acquisitions-likely-remain-steady-industry-observers-say. November 3, 2022. Accessed May 25, 2023.

22. Vrijsen BEL, Naaktgeboren CA, Vos LM, van Solinge WW, Kaasjager HAH, Ten Berg MJ. Inappropriate laboratory testing in internal medicine inpatients: Prevalence, causes and interventions. Ann Med Surg (Lond). 2020;51:48-53. Feb. 7, 2020. doi:10.1016/j.amsu.2020.02.002

23. Conroy M, Homsy E, Johns J, et al. Reducing unnecessary laboratory utilization in the medical ICU: A fellow-driven quality improvement initiative. Critical Care Explorations. 2021; 3(7). doi:10.1097/cce.0000000000000499

24. Medicare Managed Care Manual Chapter 21 – Compliance Program Guidelines and Prescription Drug Benefit Manual Chapter 9 - Compliance Program Guidelines, https://www.cms.gov/Regulations-and-Guidance/Guidance/Manuals/Downloads/mc86c21.pdf

25. Hickner J, Thompson PJ, Wilkinson T, et al. Primary care physicians' challenges in ordering clinical laboratory tests and interpreting results. J Am Board Fam Med. 2014; 27(2):268-274. doi:10.3122/jabfm.2014.02.130104

26. Kerr B. Eliminate lab test panel stuffing to support value-based care. MedCity News. https://medcitynews.com/2022/12/eliminate-lab-test-panel-stuffing-to-support-value-based-care/. December 20, 2022. Accessed May 25, 2023.

27. Korenstein D, Chimonas S, Barrow B, Keyhani S, Troy A, Lipitz-Snyderman A. Development of a Conceptual Map of Negative Consequences for Patients of Overuse of Medical Tests and Treatments. JAMA Intern Med. 2018;178(10):1401-1407. doi:10.1001/jamainternmed.2018.3573

28. Finnegan J. Costs of prior authorizations increase for physician practices at an "alarming" rate. Fierce Healthcare. https://www.fiercehealthcare.com/practices/costs-prior-authorizations-increase-for-physician-practices-at-alarming-rate. January 22, 2020. Accessed May 25, 2023.

29. Streamlining the business of Healthcare. CAQH. https://www.caqh.org/about/press-release/caqh-2019-index-133-billion-33-percent-healthcare-administrative-spend-can-be. January 21, 2020. Accessed May 25, 2023.

30. Forsman RW. Why is the laboratory an afterthought for managed care organizations? Clin Chem. 1996;42(5):813-816.

31. Tracing the scandal of Theranos founder Elizabeth Holmes. The Wall Street Journal. Accessed May 25, 2023. https://www.wsj.com/news/collection/theranos-coverage-ea13b200.

32. Koong L. Stanford researchers claim to create "Theranos that works." The Stanford Daily. January 21, 2023. Accessed May 25, 2023. https://stanforddaily.com/2023/01/20/stanford-researchers-theranos-that-works/.

33. Zhi M, Ding EL, Theisen-Toupal J, Whelan J, Arnaout R. The landscape of inappropriate laboratory testing: a 15-year meta-analysis. PLoS One. 2013;8(11):e78962. 2013; doi:10.1371/journal.pone.0078962; Rohr U-P, Binder C, Dieterle T, et al. The value of in vitro diagnostic testing in medical practice: A status report. PLOS ONE. 2016;11(3). doi:10.1371/journal.pone.0149856

34. Strengthening Clinical Laboratories. Centers for Disease Control and Prevention. November 15, 2018. Accessed May 25, 2023. https://www.cdc.gov/csels/dls/strengthening-clinical-labs.html.

35. Quest Diagnostics reports fourth quarter and full year 2022 financial results; provides guidance for full year 2023. Quest Diagnostics Newsroom. February 2, 2023. Accessed May 25, 2023. https://newsroom.questdiagnostics.com/2023-02-02-QUEST-DIAGNOSTICS-REPORTS-FOURTH-QUARTER-AND-FULL-YEAR-2022-FINANCIAL-RESULTS-PROVIDES-GUIDANCE-FOR-FULL-YEAR-2023.

36. Hologic announces preliminary revenue results for first quarter of fiscal 2023. Hologic, Inc. - Hologic Announces Preliminary Revenue Results for First Quarter of Fiscal 2023. January 8, 2023. Accessed May 25, 2023. https://investors.hologic.com/press-releases/press-release-details/2023/Hologic-Announces-Preliminary-Revenue-Results-for-First-Quarter-of-Fiscal-2023/default.aspx.

37. Labcorp announces 2022 fourth quarter and full-year results. Labcorp. February 16, 2023. Accessed May 25, 2023. https://ir.labcorp.com/news-releases/news-release-details/labcorp-announces-2022-fourth-quarter-and-full-year-results.

38. Vrijsen BEL, Naaktgeboren CA, Vos LM, van Solinge WW, Kaasjager HAH, ten Berg MJ. Inappropriate laboratory testing in internal medicine inpatients: Prevalence, causes and interventions. Annals of Medicine and Surgery. 2020;51:48-53. doi:10.1016/j.amsu.2020.02.002

REFERENCES

39. Labs with questionably high billing for additional tests alongside COVID-19 tests warrant further scrutiny. U.S. Department of Health and Human Services Office of Inspector General. December 2022. Accessed May 26, 2023. https://oig.hhs.gov/oei/reports/OEI-09-20-00510.pdf.

40. Price transparency: Requirements for providers to make public cash prizes for COVID-19 diagnostic testing. Centers for Medicaid and Medicare Services. 2020. Accessed May 26, 2023. https://www.cms.gov/files/document/covid-ffs-price-transparency-faqs.pdf.

41. Park A. Senators request FTC investigation into "unfair, Deceptive and harmful" Covid test price gouging. Fierce Biotech. January 20, 2022. Accessed May 26, 2023. https://www.fiercebiotech.com/medtech/senators-request-ftc-investigation-unfair-deceptive-and-harmful-covid-test-price-gouging.

42. Shrank W.H., Rogstad T.L., Parekh N. Waste in the US health care system: estimated costs and potential for savings. J. Am. Med. Assoc. 2019;322(15):1501–1509. doi: 10.1001/jama.2019.13978.

43. AHIP E&C price gouging statement. America's Health Insurance Plans. February 2, 2022. Accessed May 26, 2023. https://www.ahip.org/resources/ahip-e-c-price-gouging-statement.

44. Price markups for clinical labs. Health Cost Institute. July 2022. Accessed May 26, 2023. https://healthcostinstitute.org/images/pdfs/HCCI_Issue_Brief_FINAL.pdf.

45. Sanger-Katz M. They want it to be secret: How a common blood test can cost $11 or almost $1,000. The New York Times. April 30, 2019. Accessed May 26, 2023. https://www.nytimes.com/2019/04/30/upshot/health-care-huge-price-discrepancies.html.

46. Chang J, Sen AP, Boccuti C. Health Care Cost Institute and Westhealth. Issue brief: price markups for clinical labs: employer-based insurance pays hospital outpatient departments 3X more than physician offices and independent labs for identical tests. https://healthcostinstitute.org/images/pdfs/HCCI_Issue_Brief_FINAL.pdf. July 2022. Accessed May 26, 2023.

47. Turquoise Health. Basic metabolic panel. https://turquoise.health/services/basic-metabolic-panel/. Accessed May 26, 2023.

48. Quest. Comprehensive metabolic panel (CMP). https://www.questhealth.com/product/comprehensive-metabolic-panel-cmp-10231M.html. Accessed May 25, 2023.

49. Shoemaker S. Verywell Health. Best at-home metabolism tests of 2023. https://www.verywellhealth.com/best-at-home-metabolism-tests-5212225. March 31, 2023. Accessed May 25, 2023.

50. Committee for a Responsible Federal Budget. Equalizing medicare payments regardless of site-of-care. https://www.crfb.org/papers/equalizing-medicare-payments-regardless-site-care. February 23, 2021. Accessed May 25, 2023.

51. Physicians Advocacy Institute. PAI-Avalere health report on trends in physician employment and acquisitions of medical practices: 2019-2021. http://www.physiciansadvocacyinstitute.org/PAI-Research/Physician-Employment-and-Practice-Acquisitions-Trends-2019-21. Updated April 2022. Accessed May 25, 2023.

52. Committee for a Responsible Federal Budget. Site-neutral payments would lower private health costs, encourage competition. https://www.crfb.org/blogs/site-neutral-payments-would-lower-private-health-costs-encourage-competition. February 14, 2023. Accessed May 25, 2023.

53. Office of Inspector General. Data brief: despite savings on many lab tests in 2019, total medicare spending increased slightly because of increased utilization for certain high-priced tests. OEI-09-20-00450. https://oig.hhs.gov/oei/reports/OEI-09-20-00450.pdf. December 2020. Accessed May 25, 2023.

54. 42 U.S.C. § 149.120.

55. Centers for Medicare & Medicaid Services. Frequently asked questions (FAQs) about consolidated appropriations act, 2021 implementation- federal independent dispute resolution system, notice and consent, applicability. https://www.cms.gov/CCIIO/Resources/Regulations-and-Guidance/Downloads/Guidance-IDR-NC-FAQ.pdf. Accessed May 25, 2023.

56. Centers for Disease Control and Prevention. All about your A1C. https://www.cdc.gov/diabetes/managing/managing-blood-sugar/a1c.html. September 30, 2022. Accessed April 8, 2023.

57. Siu AL; U S Preventive Services Task Force. Screening for abnormal blood glucose and type 2 diabetes mellitus: U.S. preventive services task force recommendation statement. Ann Intern Med. 2015;163(11):861-868. doi:10.7326/M15-2345

58. American Family Physician. Don't repeat A1C testing in stable patients within three months of a previous result. https://www.aafp.org/pubs/afp/collections/choosing-wisely/525.html. Accessed April 8, 2023.

59. National Institute of Diabetes and Digestive and Kidney Diseases. The A1C test & diabetes. https://www.niddk.nih.gov/health-information/diagnostic-tests/a1c-test. April 2018. Accessed April 8, 2023.

60. Sun R, Hernandez-Bousard T, Kurian A. Home. Centers for Medicare & Medicaid Services. Genetic Testing: Fraud, Waste & Abuse. July 2020. Accessed May 27, 2023. https://www.cms.gov/files/document/hfpp-genetic-testing-fwa-white-paper.pdf.

61. US Food and Drug Administration. Companion diagnostics. https://www.fda.gov/medical-devices/in-vitro-diagnostics/companion-diagnostics. December 7, 2018. Accessed May 26, 2023.

REFERENCES

62. US Food and Drug Administration. List of cleared or approved companion diagnostic devices. https://www.fda.gov/medical-devices/in-vitro-diagnostics/list-cleared-or-approved-companion-diagnostic-devices-in-vitro-and-imaging-tools. Accessed May 23, 2023.

63. Shin Y. Whole Genome Sequencing Cost 2023. 3billion. December 29, 2022. Accessed May 26, 2023. https://3billion.io/blog/whole-genome-sequencing-cost-2023.

64. Trends in Genetic Tests Provided Under Medicare Part B Indicate Areas of Possible Concern. U.S. Department of Health & Human Services Office of Inspector General. December, 2021. Accessed May 26, 2023. https://oig.hhs.gov/oas/reports/region9/92003027.pdf.

65. About the Genetic Testing Registry. National Center for Biotechnology Information. Accessed May 26, 2023. https://www.ncbi.nlm.nih.gov/gtr/docs/about/.

66. Halbisen AL, Lu CY. Trends in Availability of Genetic Tests in the United States, 2012–2022. Journal of Personalized Medicine. 2023;13(4):638. doi:10.3390/jpm13040638

67. U.S. Genetic Testing Market Size, Share & COVID-19 Impact Analysis, By Technique (PCR, DNA Sequencing, Microarrays and Others), By Application (Cardiology, Oncology, Pharmacogenomics, Cognitive Dysfunction, Pathogenomics, and Others), By Payer (Public Health Insurance, Private Health Insurance, and Out-of-Pocket), By End-User (Hospitals, and Independent Laboratories) & Forecast, 2020-2027. Fortune Business Insights. 2021. Accessed May 26, 2023. https://www.fortunebusinessinsights.com/u-s-genetic-testing-market-105034

68. Fact sheet: President Biden Reignites Cancer Moonshot to End Cancer as We Know It. The White House. February 2, 2022. Accessed May 26, 2023. https://www.whitehouse.gov/briefing-room/statements-releases/2022/02/02/fact-sheet-president-biden-reignites-cancer-moonshot-to-end-cancer-as-we-know-it/.

69. Advanced Research Projects for Agency for Health (ARPA-H). National Institutes of Health. Accessed May 26, 2023. https://www.nih.gov/arpa-h.

70. Data Brief: Medicare Part B Spending on Lab Tests Increased in 2021, Driven By Higher Volume of COVID-19 Tests, Genetic Tests, and Chemistry Tests. U.S. Department of Health and Human Services Office of Inspector General. December, 2022. Accessed May 26, 2023. https://oig.hhs.gov/oei/reports/OEI-09-22-00400.pdf.

71. Does Medicare Cover Genetic Testing? Medicare.org. Accessed May 26, 2023. https://www.medicare.org/articles/does-medicare-cover-genetic-testing/

72. Billing and Coding: Molecular Pathology and Genetic Testing. CMS.gov Centers for Medicare & Medicaid Services. October 1, 2022. Accessed May 26, 2023. https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleId=58918&ver=44.

73. Lab Owner Convicted in $463 Million Genetic Testing Scheme to Defraud Medicare. Department of Justice Office of Public Affairs. December 14, 2022. Accessed May 26, 2023. https://www.justice.gov/opa/pr/lab-owner-convicted-463-million-genetic-testing-scheme-defraud-medicare

74. Justice Department Charges Dozens for $1.2 Billion in Health Care Fraud: Nationwide Coordinated Law Enforcement Action to Combat Telemedicine, Clinical Laboratory, and Durable Medical Equipment Fraud. Department of Justice Office of Public Affairs. July 20, 2022. Accessed May 26, 2023. https://www.justice.gov/opa/pr/justice-department-charges-dozens-12-billion-health-care-fraud.

75. Walcott SE, Miller FA, Dunsmore K, Lazor T, Feldman BM, Hayeems RZ. Measuring clinical utility in the context of genetic testing: a scoping review. European Journal of Human Genetics. 2020;29(3):378-386. doi:10.1038/s41431-020-00744-2

76. Medicare Part B Spending on Lab Tests Increased in 2021, Driven By Higher Volume of COVID-19 Tests, Genetic Tests, and Chemistry Tests. Department of Health and Human Services Office of Inspector General. December 19, 2022. Accessed May 26, 2023. https://oig.hhs.gov/oei/reports/OEI-09-22-00400.asp.

77. https://www.palmettogba.com/

78. Introduce Legislation to Give States Better Resources to Improve Medicaid Care. Sherrod Brown: US Senator for Ohio. March 10, 2023. Accessed May 26, 2023. https://www.brown.senate.gov/newsroom/press/release/sherrod-brown-scott-introduce-legislation-give-states-better-resources-improve-medicaid-care.

79. Reducing Hereditary Cancer Act, H.R. 1526, 118th Congress, January 12, 2023.

80. Medicare and Medicaid Programs; Patient Protection and Affordable Care Act; Advancing Interoperability and Improving Prior Authorization Processes for Medicare Advantage Organizations, Medicaid Managed Care Plans, State Medicaid Agencies, Children's Health Insurance Program (CHIP) Agencies and CHIP Managed Care Entities, Issuers of Qualified Health Plans on the Federally-Facilitated Exchanges, Merit-Based Incentive Payment System (MIPS) Eligible Clinicians, and Eligible Hospitals and Critical Access Hospitals in the Medicare Promoting Interoperability Program. Department of Health and Human Services Centers for Medicare & Medicaid Services. December 13, 2022. Accessed May 26, 2023. https://public-inspection.federalregister.gov/2022-26479.pdf.

81. Centers for Medicare & Medicaid Services. Medicare Program; Contract Year 2024 Policy and Technical Changes to the Medicare Advantage Program, Medicare Prescription Drug Benefit Program, Medicare Cost Plan Program, and Programs of All-Inclusive Care for the Elderly. https://www.federalregister.gov/documents/2023/04/12/2023-07115/medicare-program-contract-year-2024-policy-and-technical-changes-to-the-medicare-advantage-program. Published April 12, 2023. Accessed May 25, 2023.

REFERENCES

82. McDole J. Raising the Bar in MRD Testing. The Pathologist. https://thepathologist.com/diagnostics/raising-the-bar-in-mrd-testing. Published September 22, 2022. Accessed April 8, 2023.

83. Jung D, Jain P, Yao Y, Wang M. Advances in the assessment of minimal residual disease in mantle cell lymphoma. J Hematol Oncol. 2020;13(1):127. 2020 Sep 24. doi:10.1186/s13045-020-00961-8

84. Markets and Markets. Minimal Residual Disease Testing Market. https://www.marketsandmarkets.com/Market-Reports/minimal-residual-disease-testing-market-215386038.html. Published December 2022. Accessed April 8, 2023.

85. Peng Y, Mei W, Ma K, Zeng C. Circulating Tumor DNA and Minimal Residual Disease (MRD) in Solid Tumors: Current Horizons and Future Perspectives. Front Oncol. 2021;11:763790. 2021 Nov 18. doi:10.3389/fonc.2021.763790

86. Centers for Medicare & Medicaid Services. MolDX: Minimal Residual Disease Testing for Cancer. https://www.cms.gov/medicare-coverage-database/view/lcd.aspx?lcdId=38779&ver=4. Accessed April 8, 2023.

87. Centers for Medicare & Medicaid Services. Billing and Coding: MolDX: Minimal Residual Disease Testing for Hematologic Cancers. CMS. https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleId=59004. Accessed April 8, 2023.

88. Herman C. What makes a screening exam "good"? Virtual Mentor. 2006;8(1):34-37. 2006 Jan 1. doi:10.1001/virtualmentor.2006.8.1.cprl1-0601

89. New York State Department of Health. Disease Screening – Statistics Teaching Tools. New York State. https://www.health.ny.gov/diseases/chronic/discreen.htm. Published April 1999. Accessed May 11, 2023.

90. Patel J. What Are Multi-Cancer Early Detection Tests and How Might They Impact the Future of Cancer Screening?. Cancer.Net. https://www.cancer.net/blog/2022-10/what-are-multi-cancer-early-detection-tests-and-how-might-they-impact-future-cancer-screening. Published October 25, 2022. Accessed April 22, 2023.

91. Nicolaus P. Pan-Cancer Testing: A Closer Look at Different Technology Approaches. DiagnosticsWorld. https://www.diagnosticsworldnews.com/news/2022/04/05/pan-cancer-testing-a-closer-look-at-different-technology-approaches. Published April 5, 2022. Accessed April 22, 2023.

92. Liu MC, Oxnard GR, Klein EA, Swanton C, Seiden MV; CCGA Consortium. Sensitive and specific multi-cancer detection and localization using methylation signatures in cell-free DNA. Ann Oncol. 2020;31(6):745-759. doi:10.1016/j.annonc.2020.02.011

93. American Cancer Society. Multi-cancer Early Detection (MCED) Tests. https://www.cancer.org/healthy/find-cancer-early/multi-cancer-early-detection-tests.html. Published June 30, 2022. Accessed April 9, 2023

94. S Nicolaus P. Super early Detection: Pan-Cancer Tests Aim to Catch Cancer Earlier than Ever. DiagnosticWorld. https://www.diagnosticsworldnews.com/news/2022/03/16/super-early-detection-pan-cancer-tests-aim-to-catch-cancer-earlier-than-ever. Published April 5, 2022. Accessed April 24, 2023.

95. Choi SW, Mak TSH, O'Reilly PF. Tutorial: a guide to performing polygenic risk score analyses. Nat Protoc. 2020;15:2759-2772. https://doi.org/10.1038/s41596-020-0353-1

96. National Human Genome Research Institute. Polygenic risk scores. https://www.genome.gov/Health/Genomics-and-Medicine/Polygenic-risk-scores. Published August 11, 2022. Accessed April 24, 2023.

97. Riveros-Mckay F, Weale ME, Moore R, et al. Integrated Polygenic Tool Substantially Enhances Coronary Artery Disease Prediction [published correction appears in Circ Genom Precis Med. 2021 Aug;14(4):e000085]. Circ Genom Precis Med. 2021;14(2):e003304. doi:10.1161/CIRCGEN.120.003304

98. Kumuthini J, Zick B, Balasopoulou A, et al. The clinical utility of polygenic risk scores in genomic medicine practices: a systematic review. Hum Genet. 2022;141(11):1697-1704. doi:10.1007/s00439-022-02452-x