September/October 2025

CLN Clinical Laboratory News

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SHEDDING LIGHT ON PERFORMANCE

47%

Percentage of POC HbA1c devices that did not meet IFCC or NGSP criteria

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WE'RE ALL EARS.

It's a bird, it's a plane — it's superRCA!

HbA1c testing for diabetes

ADLM Association for Diagnostics & Laboratory Medicine™ Formerly AACC

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On the cover: Daria Kolosova / iStock

Federal Insider

ADLM urges Congress to provide funding for pediatric reference intervals

The Association for Diagnostics & Laboratory Medicine (ADLM, formerly AACC) has requested that Congress appropriate an additional $10 million for the Centers for Disease Control and Prevention's (CDC) fiscal year 2026 budget to fund the development of quality pediatric reference intervals (PRIs), which are essential for delivering accurate pediatric diagnoses.

Despite the wide availability of reference intervals for adults, PRIs often exhibit poor quality or are nonexistent, ADLM wrote in a letter addressed to House Appropriations Subcommittee on Labor, Health and Human Services, Education, and Related Agencies chair Robert Aderholt (R-Ala.) and ranking member Rosa DeLauro (D-Conn.).

Because laboratories don't have the resources to obtain the necessary samples from healthy children to develop appropriate normal ranges, they rely on intervals derived from samples taken from sick children, which distort the "true" normal range. Although adult reference intervals may be used, these ranges don't reflect the growth and developmental stages of children and can lead to misdiagnosis and inappropriate care, according to ADLM.

To remedy this situation, the CDC proposes collecting clinical samples through its National Health and Nutrition Examination Survey and using its Environmental Health Laboratory to generate reference intervals for children and disseminate the information to clinical laboratories, ADLM noted. However, the agency will need an additional $10 million to initiate and advance this work.

In the letter, ADLM is joined in requesting these funds by numerous organizations committed to ensuring that America's children receive high quality and equitable healthcare.

● REPORT SHOWS HHS SHOULD EVALUATE THE PERFORMANCE OF MEDICAL TREATMENTS

The Department of Health and Human Services (HHS) hasn't completed a thorough evaluation of the success and outcomes of available treatment options for various diseases and conditions, a recent report from the United States Government Accountability Office (GAO) shows.

Comparative clinical effectiveness research evaluates and compares the health outcomes of two or more medical treatments, services, or items, according to the GAO report. In 2010, Congress authorized the establishment of the Patient-Centered Outcomes Research Institute (PCORI) to conduct this research and improve its quality and relevance. Congress also directed HHS to publicly disseminate and help incorporate these research findings into clinical practice. PCORI and HHS were allotted a total of $3.1 billion for fiscal years 2019 through 2024 for this initiative.

HHS disseminated findings from 16 PCORI-funded studies from 2016 to March 2025, according to officials. In 2020, HHS had plans to evaluate its dissemination and implementation portfolio near-term goals and performance measures, GAO reported. However, it remains unclear whether the evaluation will be conducted as planned.

HHS has not requested proposals for evaluations, which officials attributed to delays in leadership changes in August 2024 and March 2025. Further complicating matters, in March 2025, HHS announced staff reductions and a departmental reorganization, which the agency only started to implement in July.

In the report, GAO recommends that the secretary of HHS complete an evaluation of the dissemination and implementation portfolio efforts supported by funding as planned, including the development and implementation of near-term goals and associated measures to regularly assess performance.

● TEXAS LAWS COULD LAY OUT A PATH FOR RED STATE REGULATION OF AI IN HEALTHCARE

Three artificial intelligence (AI) laws affecting hospitals, state agencies, and other healthcare stakeholders were passed by Texas Governor Greg Abbott (R) in June. The laws mandate that providers disclose to patients some instances of when they use AI, meet state standards, and take steps to prevent harmful outcomes. They could serve as a model for other GOP states to follow when regulating AI in healthcare.

The most notable law that Abbott signed, The Texas Responsible Artificial Intelligence Government Act (HB149), or TRAIGA, says private and public sector stakeholders can't use AI to encourage people to self-harm, infringe on constitutional rights, or discriminate against protected classes, among other things. Additionally, providers affiliated with government entities must disclose to patients or their representatives when they use AI for treatment, the bill says. According to Inside Health Policy, this represents a lighter touch than Colorado, which passed a broader bill including private sector AI disclosure requirements as well.

Another one of the bills Abbott signed, SB1188, allows practitioners to use AI for diagnoses so long as they follow Texas Medical Board standards, practice within the scope of their license, and disclose their use of AI to patients. Again, this takes a more hands-off approach than another blue state, Illinois, which recently banned AI from providing mental health and therapeutic decision-making, reported Inside Health Policy.

Additionally, Abbott signed SB1964 into law, which regulates how state agencies and local government use and manage AI systems.

Currently, states are poised to lead in the regulation of AI in healthcare instead of the federal government, because lawmakers in Congress are struggling to pass a comprehensive federal AI bill.

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Bench Matters

What clinical labs should know as pursuit of healthcare fraud accelerates

Jacquelyn Papish

As federal and state enforcers ramp up their pursuit of healthcare fraud, clinical laboratories now sit squarely in the crosshairs. Regulators deploy sophisticated data analytics, artificial intelligence tools, and coordinated task forces to scrutinize billing practices, testing volumes, and referral arrangements, leaving labs with little room for error.

This summer saw the largest-ever national healthcare fraud takedown by the U.S. Department of Justice, with 324 defendants charged in connection with $14.6 billion in alleged fraud (*1*). Lab testing played a key role in the crackdown: Nearly 50 defendants were charged with more than $1 billion in fraudulent claims related to telemedicine and genetic testing schemes. July also brought news of a $114.5 million judgment stemming from a genetic cancer screening conspiracy (*2*).

This enforcement activity isn't likely to slow down any time soon. In fact, the U.S. Department of Justice recently announced two cross-agency efforts — the False Claims Act (FCA) Working Group and the Health Care Fraud Data Fusion Center — that aim to improve information sharing among regulators and better leverage data analytics tools to identify fraudulent activity (*3*).

With coordinated, data-driven enforcement on the rise, here's how clinical labs can avoid becoming an enforcement target.

LAB SERVICE PROVIDERS FACE SIGNIFICANT INVESTIGATIONS

Lab testing — with its high service volumes and standardized billing codes — will likely be an easy target for data-driven healthcare fraud investigations. Case in point: The Barnes & Thornburg 2024 Healthcare Enforcement & Compliance Annual Report found that lab service providers accounted for nearly $240 million in recoveries across 18 civil settlements in fiscal year (FY) 2024 (*4*). Thus far in FY 2025 (with one month left to go), they have accounted for $165 million across 14 civil settlements.

Regulators consistently target medically unnecessary testing, especially urine drug testing, genetic testing, and cancer screenings. Enforcement actions frequently uncover improper arrangements between labs, doctors, marketers, and recruiters, including forged physician orders, kickbacks to telemedicine companies, and misuse of patient information to submit claims for tests that were unnecessary or never performed.

For example, earlier this year, federal regulators reached a $4.425 million settlement with a lab for unnecessary urine drug and hormone tests, a $6 million settlement with a lab submitting claims for medically unnecessary genetic testing involving kickbacks, and a $3.78 million settlement for a lab providing kickbacks to physicians ordering medically unnecessary genetic cancer screenings (*5*, *6*, *7*).

THREE BEST PRACTICES FOR CLINICAL LAB COMPLIANCE

Clinical labs looking to avoid regulatory headaches should ensure that they stay compliant by following these three best practices.

- **Conduct regular audits:** Labs should conduct consistent audits of their ordering and billing processes to catch potential issues before they end up on regulators' radars. What these audits entail will vary according to the lab's volume of testing, available resources, and risk appetite. A busy lab or one that has faced recent government scrutiny might want to consider quarterly audits, for example, and may benefit from a comprehensive prebill audit on all claims rather than just representative sampling.

  As part of these actions, labs should look for questionable practices that could indicate fraud. For example, doctors who consistently order elaborate and expensive panels when simpler and cheaper diagnostic options are available could set off regulators' alarm bells. Similarly, telehealth providers who send patients for testing after brief interactions, particularly when there's no established patient-provider relationship, might not meet the standard for reimbursement and could indicate suspicious activity.
- **Enhance compliance programs:** To protect themselves, labs should ensure that they have a comprehensive compliance program and a dedicated compliance officer to address regulatory issues. Such programs should include clear, accessible policies and updated annual trainings on fraud and abuse laws, the Anti-Kickback Statute, and marketing and referral practices. Additionally, employees should have access to an internal reporting hotline to proactively address potential risks, especially since many FCA claims stem from whistleblower reports. Labs should also be prepared to make self-disclosures to regulators about improper testing or billing as necessary.
- **Maintain robust recordkeeping:** If regulators do flag potentially fraudulent activity, labs should ensure that they have the documentation to support ordering and billing practices. Recordkeeping is essential. Although labs are required to maintain medical records for set periods, they should also develop internal policies for keeping and organizing billing and communications records.

PROACTIVE COMPLIANCE IS KEY

In today's heightened enforcement landscape, labs can no longer afford to rely on reactive compliance efforts. With regulators taking a collaborative, data-driven approach to identifying and prosecuting fraud, labs must invest in robust compliance, from conducting thorough audits to systematizing recordkeeping. Those that do will be well-positioned to thrive even under the regulatory microscope.

For more on genetic testing fraud in particular, see p. 34 of this month's special section on laboratory stewardship.

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The Sample

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Polygenic scores may predict obesity later in life

Recent research describes a polygenic risk score (PGS) reliably associated with adulthood obesity and shows consistent and indicative patterns in early childhood (Nat Med 2025; doi: 10.1038/s41591-025-03827-z).

By 2035, more than half of the global population will be overweight or obese, according to previous research. Obesity often begins during childhood and persists into adulthood. Therefore, predictors available in early life, such as genetic variants, could be valuable. Meanwhile, PGSs that capture an individual's inherited polygenic susceptibility to a trait or disease have shown promise in enhancing disease risk prediction and population screening.

The researchers derived ancestry-specific and multiancestry PGS for BMI and obesity by leveraging the data of more than 5.1 million people from the results of a study by the Genetic Investigation of ANthropometric Traits (GIANT) consortium and 23andMe. The research is the largest genome-wide association study meta-analyses for body BMI. The researchers then tested whether their new PGS was associated with obesity using datasets of the physical and genetic characteristics of more than 500,000 people, including BMI data tracked over time from the Avon Longitudinal Study of Parents and Children (ALSPAC), a world-leading birth cohort study.

The multiancestry score explained 17.6% of BMI variation among UK Biobank participants of European ancestry. For other populations, the multiancestry score accounting for BMI variation ranged from 16% in East Asian Americans to 2.2% in rural Ugandans. In the ALSPAC study, children with higher PGSs showed accelerated BMI gain from age 2.5 years to adolescence, with an earlier second rise in BMI. Adding the PGS to predictors available at birth nearly doubled explained variance for BMI from age 5 onward. Up to age 5, adding the PGS to early-life BMI improved prediction of BMI at age 18.

Higher PGSs were associated with greater adult weight gain. In intensive lifestyle intervention trials, individuals with higher PGSs lost a more modest amount of weight in the first year (0.55 kg per standard deviation) but were more likely to regain it.

Overall, these data show that PGSs have the potential to improve obesity prediction, particularly when implemented early in life, the researchers wrote.

HBA1C POINT-OF-CARE DEVICE PERFORMANCE QUESTIONED

A recent study raises concerns about the analytical performance of HbA1c point-of-care (POC) devices (Clin Chem 2025; doi: 10.1093/clinchem/hvaf059).

An estimated 537 million adults live with diabetes as its worldwide prevalence continues to rise. The World Health Organization and diabetes specialty societies recommend diagnosing and monitoring diabetes with HbA1c. But in low- and middle-income countries (LMICs), access to HbA1c testing often is limited, particularly in rural areas. The situation has driven interest in POC testing for HbA1c. However, POC devices' analytical performance remains poorly understood.

To provide supporting evidence for HbA1c POC selection and improve LMICs' diabetes diagnosis and management, the study's researchers evaluated 19 HbA1c POC devices' analytical performance to determine whether devices met certification criteria and had hemoglobin (Hb) variant interference.

The researchers verified manufacturers' claims about accuracy, imprecision, and interference from Hb variants based on established guidance from the Clinical and Laboratory Standards Institute protocols EP-15-A3 and EP-9-A3, international quality targets, and four certified International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) and National Glycohemoglobin Standardization Program (NGSP) Secondary Reference Measurement Procedures (SRMPs). They assessed all POC devices for performance against both IFCC and NGSP certification criteria.

Only the Afinion 2 and the Quo-Lab devices met both the IFCC criteria and NGSP criteria with all four SRMPs. Twenty-six percent of the devices met only IFCC criteria and 47% did not meet either IFCC or NGSP criteria, despite most of these devices having an IFCC or NGSP certificate at the time of the study. Three devices showed clear interference from Hb variants.

These findings raise questions about the need for further measures to ensure that certified devices can prove consistent performance at regular intervals, rather than at a single time point that is then considered valid for a year.

The researchers noted that their study occurred under optimal laboratory conditions, and device performance may be worse in intended clinical settings.

GENOMIC PROFILING MAY IMPROVE CANCER OUTCOMES

Given the potential benefits of comprehensive genomic profiling (CGP) testing for cancer patients — such as increased rates of targeted therapy without increased treatment-related costs — more CGP testing may improve outcomes, a recent study says (JAMA Netw Open 2025; doi:10.1001/jamanetworkopen.2025.19963).

Clinical guidelines recommend biomarker testing to identify cancer patients who are eligible for targeted therapy. Evidence suggests that biomarker testing rates are below those recommended in guidelines, a situation associated with worse clinical outcomes and overall survival.

To explore the change in rates of CGP testing over time and compare targeted therapy rates and healthcare costs during first-line therapy, the researchers aimed to identify patients with newly diagnosed advanced breast, colorectal, gastric, nonsmall cell lung (NSCL), ovarian, and pancreatic cancer receiving CGP, non-CGP testing, or no biomarker testing in a retrospective cohort study using deidentified data from the Optum Labs Data Warehouse. They identified 26,311 adult patients diagnosed with advanced cancer during a 4-year period from this claims database of longitudinal health information on commercial health plan and Medicare Advantage enrollees. The patients were covered by the plans 12 months before and 6 months after their first advanced cancer diagnosis.

Molecular testing rates were suboptimal. Researchers saw evidence of molecular testing for only 35% of patients. However, testing rates increased across time for most cancer types from 32% in 2018 to 39% in 2021–2022. Patients with NSCL cancer and colorectal cancer with CGP testing were more likely to receive targeted therapy compared with patients who received non-CGP testing, with odds ratios of 1.57 and 2.34 respectively. Costs among patients with CGP showed no statistical difference from those with non-CGP testing for all the cancer types studied.

The authors noted that the study was limited by use of administrative claims, which can be subject to selection bias and do not include biomarker testing results or an algorithm for the testing categories based on procedure codes. As a result, these claims may potentially mischaracterize testing types.

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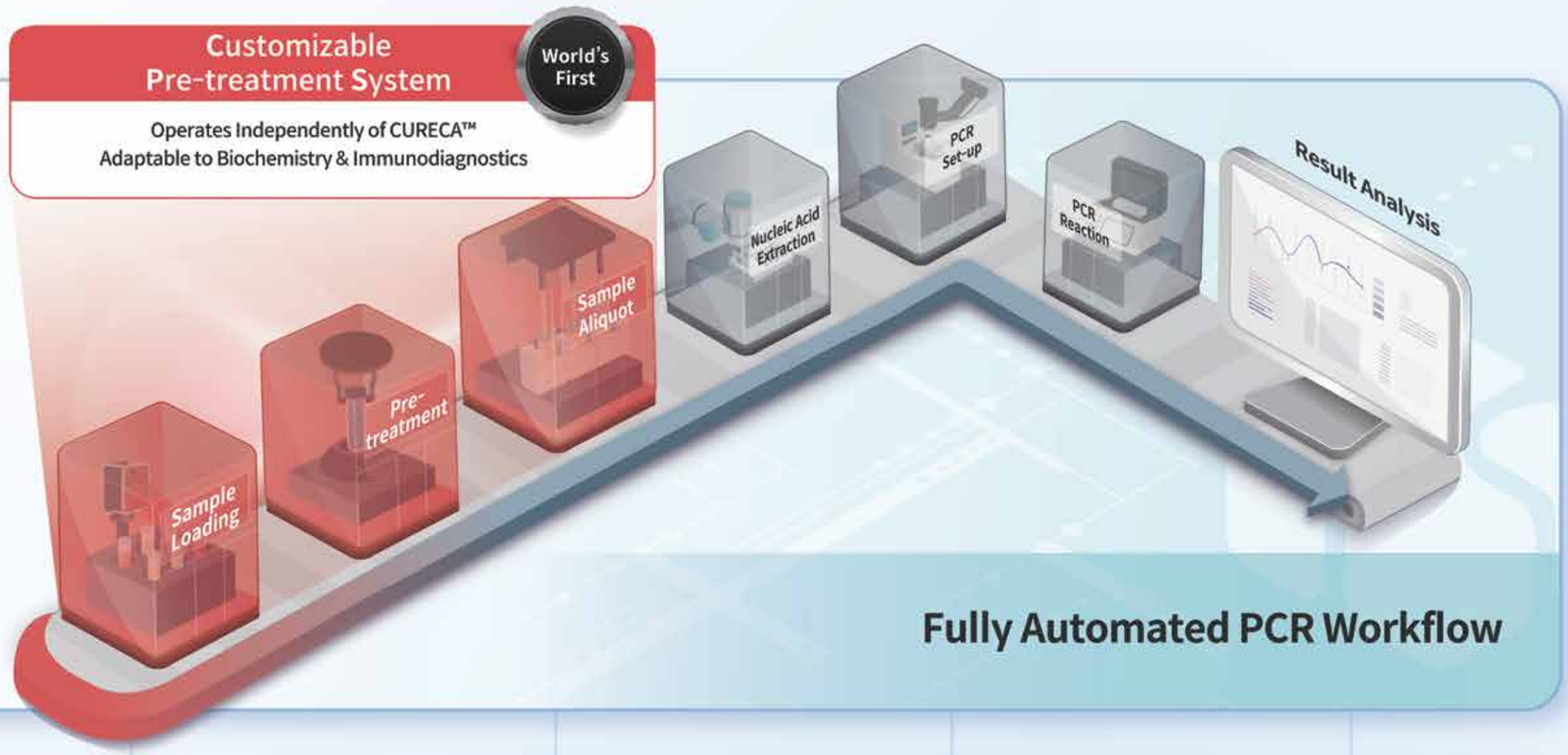

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The case for universal genetic hearing screening in newborns

BY YAAKOV ZINBERG

It could catch more children with hearing loss earlier and guide interventions that potentially prevent delayed development of language and social skills.

Within the first 24 to 48 hours of life, newborn babies are tested for a comprehensive set of serious but treatable genetic and metabolic disorders. Most of these tests are done by labs using dried blood spots taken via heel prick. Babies also undergo one of two tests for hearing loss: the automated auditory brainstem response, which detects electrical activity in the brain in response to a sound stimulus, or the otoacoustic emissions test, which measures the vibrations of the inner ear's hair cells.

Both tests, collectively referred to as physiologic hearing screening, are widely implemented — close to 96% of U.S. newborns were screened in 2022, according to data from the Centers for Disease Control and Prevention — and they catch most babies with deafness and hardness of hearing. Congenital hearing loss is by far the most commonly diagnosed condition on the newborn screening panel.

However, there are instances when current newborn screening methods fail to detect hearing impairments. For instance, babies with mild or later-onset hearing loss may present with normal hearing as newborns but then begin struggling with hearing later in childhood. This can lead to long-term social and developmental consequences.

Given these shortcomings, some experts are calling for all newborns to undergo genetic screening for hearing impairment alongside traditional physiologic testing. They argue that this will help catch more cases of hearing loss as early as possible and enable these children to receive interventions before their development is significantly affected.

THE CURRENT PARADIGM

The Department of Health and Human Services (HHS) publishes the Recommended Uniform Screening Panel (RUSP), which advises states on which disorders they should include on their newborn screening panels. Hearing loss is one of the 37 conditions on the RUSP, and all 50 U.S states follow this recommendation.

Typically, if a newborn fails physiologic screening, they're referred to a clinical audiology center, where more comprehensive testing is performed. This includes a blood test for cytomegalovirus infection, which can be transmitted from mother to baby during pregnancy and is responsible for about 15% of congenital hearing loss cases.

Only if the diagnosis is confirmed at this stage will the baby, in most cases, be referred for genetic screening, according to Anne Giersch, PhD, who studies hearing loss genetics at Brigham and Women's Hospital and Harvard Medical School in Boston. There are more than 120 genes known to be associated with hearing loss, and different genes might be assessed depending on the nature of the condition. If a baby only has high-frequency deafness, for instance, it might not be relevant to look at genetic variants tied to low-frequency deafness.

Even though a diagnosis has been confirmed at this point, genetic testing remains critical because it provides information on the nature and origin of the condition and if and how it might continue to progress. "It helps predict how stable this child's deafness is going to be," Giersch said.

Furthermore, such testing can identify the presence of an underlying condition that might manifest in other ways in addition to hearing loss. "[This] might influence your decision on what sort of language acquisition modality the family chooses," Giersch added. These cases are known as syndromic deafness and account for approximately 30% of all congenital cases. Usher syndrome, for example, is a rare disorder that results in vision and hearing impairment, so if it turns up in a genetic test, sign language should be ruled out as an intervention.

Similarly, there are forms of congenital deafness that affect the cochlear nerve, which would render cochlear implants ineffective.

INSIGHTS FROM GENETIC AND GENOMIC TESTING

Giersch and others worry that if genetic testing is administered only after a baby fails the initial physiologic screen, then those with milder forms of hearing impairment will fall through the cracks. Experts are also particularly concerned about missing late-onset deafness — hearing loss that sets in any time after birth, usually during childhood — which might be more common than congenital deafness.

"Unfortunately, the current paradigm of only doing genetic testing on babies who fail their newborn hearing screen will miss those kids with later-onset deafness," Giersch said.

This is why the Newborn Hearing Screening Working Group of the National Coordinating Center for the Regional Genetics Networks proposed the addition of genetic testing and cytomegalovirus testing to the standard newborn screening regimen all infants undergo. Substantial evidence shows that children who receive hearing interventions before 6 months have much stronger language and speech skills — potentially on par with their hearing peers — compared with those who receive interventions later. Furthermore, this genetic screening would use the same blood spots that are already sampled for other tests on the newborn screening panel.

One of the genes that the group recommends testing for in this context is the mitochondrial gene *MT-RNR1*. Approximately 1 in 500 people carry a mutation in this gene that makes them sensitive to aminoglycoside antibiotics, such that exposure to the drugs could result in ear damage and hearing impairment. These antibiotics are commonly used for treating sepsis in newborns. Although it's rare for a baby with sepsis to also carry this mutation, sequencing for this gene shortly after birth would be a relatively easy way to avoid inadvertently inducing hearing loss.

Another possibility is to sequence a baby's entire exome or genome. Although whole exome or genome sequencing isn't commonly done in clinical settings right now, it could prove beneficial in cases where a genetic panel doesn't turn up anything unusual, since there may be hundreds of genes associated with deafness that haven't been discovered yet.

"Genomic sequencing would be useful when you've got a very rare form of deafness and that gene is not on the panel," Giersch said. "Or maybe it's never been associated with deafness before." If the baby carries an unusual variant, you might then also sequence the parents. If they don't have the variant and are not hearing impaired, you might begin to suspect that it's causative.

A POTENTIAL MODEL IN CHINA AND OBSTACLES IN THE U.S.

Thus far, evidence supporting the efficacy of newborn genetic hearing screening has come mostly from China, where several clinical trials have assessed a panel of hearing-associated genes in newborns. Across the trials, investigators looked at 20 variants in four genes and independently found that they could identify the genetic cause behind each case of a failed physiologic test. They also were able to predict which babies among those who passed physiologic testing were likely to develop later-onset deafness or hardness of hearing.

While these results are encouraging and back the idea of implementing genetic testing in newborn hearing screening, it's unclear if they translate to American populations,

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Unfortunately, the current paradigm of only doing genetic testing on babies who fail their newborn hearing screen will miss those kids with later-onset deafness.

which have different genetic backgrounds than those in China. To achieve similar results in the U.S., a screening panel would need to have more than four genes, which adds to the cost and complexity of interpreting the results.

Regardless, clinical studies like these, along with basic research, have informed what's included in the RUSP.

Historically, the Advisory Committee on Heritable Disorders in Newborns and Children (ACHDNC), a volunteer group of experts convened by HHS, would make recommendations based on the latest evidence that would heavily influence updates to the RUSP. For example, 20 years ago, newborns weren't screened for lysosomal storage diseases because these conditions weren't really detectable or treatable, which is a requirement for inclusion in the RUSP, said Dennis Dietzen, PhD, the division chief of pathology and laboratory medicine at Phoenix Children's Hospital in Phoenix. After advances in research enabled treatments for some of these disorders, ACHDNC recommended some of them, which were added to the RUSP and are tested for today.

One could have imagined ACHDNC meeting in the not-too-distant future to weigh the merits of genetic screening for hearing loss in newborns. Unfortunately, as part of a campaign to downsize and restructure HHS, the Trump administration disbanded the committee in April, effectively freezing the RUSP as it currently is.

"To throw this committee away, it lacks a lot of foresight, in my opinion," Dietzen said. "It's frustrating, because medical science does not stand still." Public health departments in every state are free to make their own decision about what's in their panel and don't have to follow the RUSP. "But for the most part, that committee was seen as an unconflicted panel of experts, and their recommendations were usually adopted without much controversy," Dietzen noted. If the RUSP no longer undergoes continuous updates, states will be left without an important standard for care, potentially leading to health disparities.

"Every baby born in every state ought to be treated in the same way — that was the whole idea behind forming this group in the first place," Dietzen added.

In spite of the loss of ACHDNC, there are still reasons to be optimistic about the advancement of newborn hearing screening. More clinical trials that take a look at genetic testing are underway and the early data is positive. This is the first step toward making universal genetic hearing screening a reality — and giving children with hearing challenges a better chance at the best possible outcomes.

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Genomic sequencing would be useful when you've got a very rare form of deafness and that gene is not on the panel.

An innovative test known as superRCA that detects very small amounts of cancer-causing mutations won the 2025 ADLM Disruptive Technology Award.

Taking cancer monitoring and care to the next level

BY KAREN BLUM

Linus Bosaeus, CEO of Rarity Bioscience, had just exited the stage at ADLM 2025 after presenting about his company's superRCA assay and was catching up with colleagues when he got the good news: The audience vote had come in, naming his product as the fan favorite of this year's ADLM Disruptive Technology Award competition. The official judges' vote came in shortly after, echoing the audiences' choice and confirming Rarity Bioscience as the winner of the award.

"I was surprised because it was so quick," Bosaeus said, "but I guess that was good. I didn't have to stand there and be nervous."

SuperRCA is an ultrasensitive multiplex assay that detects very small amounts of DNA sequence variants, such as mutations, in tissue and blood samples. In fact, it can detect one single nucleotide out of 100,000 wild-type DNA molecules. As explained by Bosaeus, it converts DNA into fluorescent particles and enables detection of mutations using conventional flow cytometry, and it can be performed in most laboratories using existing equipment. Currently, the technology is targeting detection of minimal residual disease (MRD) in cancers during or after treatment.

"In the follow-up setting, you no longer have a tumor to biopsy, so you're relying on a liquid biopsy — a blood sample," Bosaeus said. "For that, you need a very sensitive test, because your mutation levels are supposedly zero. You're measuring from the ground up. You also need something inexpensive that you can do frequently.

> "...you need a very sensitive test, because your mutation levels are supposedly zero. You're measuring from the ground up."

"In an acute leukemia, your relapse can happen in weeks or months, so it's really quick," he added. "You need to have a test that is available close to patients and that gives you a result, ideally, the same day. If a patient receives a bone marrow transplant or undergoes some specialized treatment, getting that measurement is critical."

SuperRCA is such a test. It returns results in 5 hours and 40 minutes, he said, and 96 samples can be run in one go.

THE INS AND OUTS OF SUPERRCA

The superRCA technology combines rolling circle amplification (RCA) and padlock probes in a novel way for highly specific nucleic acid sequences detection. This method generates a relatively large, self-contained structure that can be analyzed using microscopy or automated flow cytometry. RCA is an isothermal amplification method that uses a circular DNA template to produce large amounts of DNA from a small initial sample. Padlock probes are short DNA oligonucleotides with segments at the 3' and 5' ends that are complementary to a target region.

Here's a more detailed explanation of how superRCA works from Rarity Bioscience's website (raritybioscience.com): DNA is extracted from a sample of whole blood, bone marrow, or tissue. Then, DNA sequences of interest that are known to be mutated in malignant cells are enriched by a limited pre-PCR (~10 cycle) amplification. The enriched sample then undergoes a ligase-mediated circularization of one strand. Next, the circularized strands containing the target region are amplified by the first RCA step. This is followed by a genotyping padlock probe ligation and a highly specific, second RCA step in which the second RCA encircles the first RCA product to form large super-RCA structures that can be analyzed by flow cytometry. Finally, the super-RCA products can be enumerated as mutant- or wildtype-specific using fluorophore-labeled hybridization probes and recorded as individual, fluorescent objects in a standard flow cytometer. For multiplex assays, analysis is done similarly using multiple fluorophores and wavelengths.

"What we are doing differently is that we are applying padlocks on an already preamplified target," Bosaeus said. "We use an RCA in the first step, and then apply the padlock and do a second RCA. So we call the technology superRCA because we do it twice. This allows us to make extremely large particles and get a very high fluorescent intensity.

"The initial idea was just to increase fluorescent intensity, to reduce signal to noise for any type of assay," he added. "Serendipitously, it was discovered that by doing it this way, we actually get a very good allele distinction, basically getting increased specificity over, for example, PCR-based technologies."

Because the assay can be run on standard flow cytometry equipment, the company has earned a lot of attention from more resource-limited countries in southern Europe, South America, and elsewhere that may not have digital PCR or other advanced technologies, Bosaeus said. "That's an interesting observation that we didn't really expect or foresee."

A BRIGHT IDEA

The product builds on technology developed at Sweden's Uppsala University by Ulf Landegren, MD, PhD, a professor of immunology, genetics, and pathology. Landegren had commercialized RCA and padlocks for other applications and spun out several different companies, including Olink Proteomics, Bosaeus said. When Lei Chen, PhD, Rarity's co-founder and chief technology officer, was a doctorate student working under Landegren, the techniques were largely applied to proteins. But Chen had the idea to try to apply the technology to nucleic acids using the double RCA approach.

"[As] with all the great inventions, this was not supposed to work," Bosaeus said. Landegren told Chen it had been tested before and couldn't be done. "But Dr. Chen didn't take no for an answer and got data to prove that it can actually work." Chen has worked on these techniques for the past 10 years.

Rarity Biosciences was established 4 years ago and began offering the assays for research collaborations about 2.5 years ago, Bosaeus said. While they considered different readout platforms, they ultimately went with flow cytometry because it is the most readily available instrument in hematology and pathology, he said. The company now has ongoing research collaborations for about 10 cancer types, including leukemia, lymphoma, glioblastoma, melanoma, and lung and colorectal cancers. "We [also] just launched our first off-the-shelf kits at the end of last year, enabling decentralized use," he said.

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WHAT THE STUDIES SHOW

The company has been part of several impactful peer-reviewed studies that Bosaeus presented at the meeting. One showed how super-RCA could help monitor leukemia patients through detection of sequence variants and early disease recurrence (Nat Commun 2022; doi: 10.1038/s41467-022-31397-y). One demonstrated that superRCA could be used to monitor colorectal cancer patients by analyzing hotspot mutations in cell-free DNA and identifying changes in mutant allele frequency in patients with clinical relapse (Cancers 2024; doi.org/10.3390/cancers16030549). A third used superRCA to measure *IDH1/2* mutations as biomarkers for detection of MRD in patients with acute myeloid leukemias (Blood Adv 2025; doi.org/10.1182/bloodadvances.2025016726).

Another study of over 330 patients that's still in press used superRCA to improve diagnostic screening and classification of clonal mast cell disease.

"Even though we are sort of early-stage, we have run thousands of retrospective biobank samples," Bosaeus said. "Anything that is mutation-driven, we can analyze."

Overall, published papers demonstrate superRCA's sensitivity to be 10–100 times that of digital PCR, Bosaeus said. The tool can be helpful in monitoring cancer patients, he said, such as when you need to determine if a patient experiencing residual mutations after a third round of chemotherapy should go on for a fourth, or receive a complementary treatment. Following bone marrow transplant — a treatment for many leukemias — the test could detect early so-called relapsing mutations (i.e., those that return) so that clinicians can gain time to adjust treatment accordingly. The technology also can be helpful in early detection of drug resistance, he said, allowing clinicians to switch treatments. "You enable precision medicine by having more frequent, accurate diagnostics," he said.

The other award finalists were Chemeleon, for its BINDS-AMI assay, and MagIC Lifescience, for its MagChipR platform.

The proprietary binding-induced nanostructure dynamic surface (BINDS) assay is an instrument-free diagnostic platform that enables rapid, high-sensitivity biomarker detection, delivering results in under 2 minutes. Chemeleon's lead product targets acute myocardial infarction (AMI) by detecting and quantifying cardiac troponins with 99.2% sensitivity and 90.5% specificity.

The MagChipR platform is an ultra-fast PCR system with high multiplexing capability that delivers lab-quality pathogen and antimicrobial susceptibility results in under 20 minutes. The technology enables same-visit diagnosis and treatment. MagChipR's first commercial application targets the rising epidemic of sexually transmitted infections, offering a single-test panel for *Chlamydia trachomatis, Neisseria gonorrhoeae* (NG), *Trichomonas vaginalis,* and *Mycoplasma genitalium* (MG). If NG or MG are detected, the platform performs antimicrobial susceptibility testing using high-resolution melt analysis.

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Navigating

hemoglobin A1C measurements for diabetes care

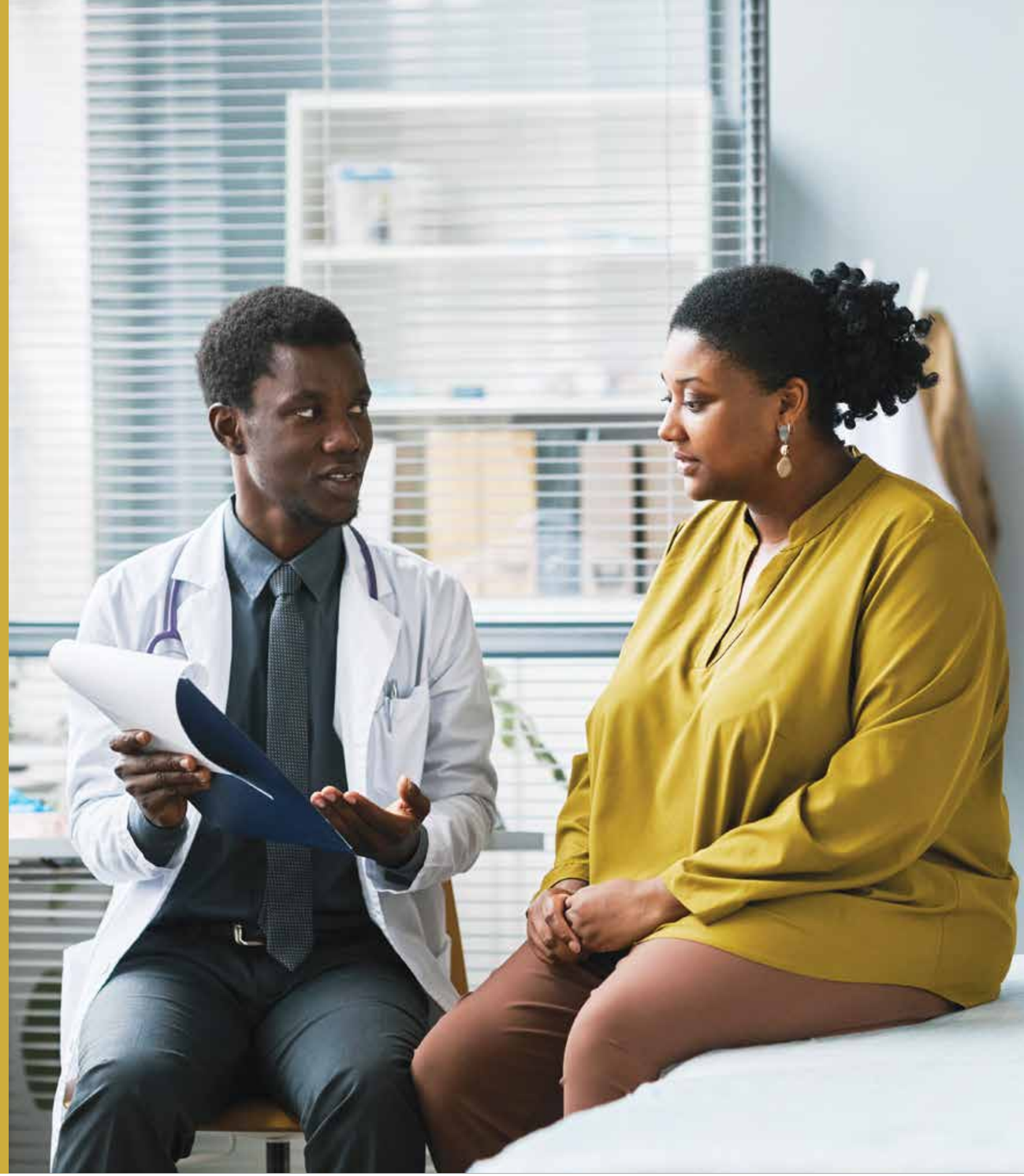
Not all HbA1c tests are the same, and neither are all patients with diabetes.

Diabetes mellitus, a chronic metabolic disorder characterized by persistent hyperglycemia, affects millions of people worldwide and poses significant health and economic challenges. An accurate diagnosis plays a crucial role in helping patients receive treatment as soon as possible to prevent complications. Traditional testing of patients' glycemic status involves either measuring their blood glucose levels or assessing the amount of hemoglobin A1c (HbA1c) in their blood.

Assessing the relative concentration of HbA1c offers several advantages over direct glucose measurement. Most notably, it correlates effectively with the average concentration of serum glucose over a period of 2–3 months (*1*, *2*), whereas glucose evaluations can provide insight only into a patient's glucose status at the time of blood collection. For that reason, the American Diabetes Association (ADA) recommends the use of HbA1c as an indicator of long-term glycemic control in patients with diabetes mellitus, as well as for the screening and diagnosis of the disease, with a cutoff value of 6.5% (*1*) (See Table 1).

Given the importance of HbA1c in managing diabetes, it's important for clinical lab professionals and healthcare providers to understand how results can be influenced by various factors, including analysis methods, clinical conditions, and other variables. Selecting the best approach requires careful assessment of each patient's needs.

BY ALINA GABRIELA SOFRONESCU, PHD, NRCC, FADLM



ABOUT HBA1C

HbA1c is produced by the non-enzymatic addition of a glucose molecule to the easily accessible N-terminal valine residue on the β chain of the hemoglobin A (HbA) molecule. Because no enzymatic limitation exists, the production of HbA1c reflects the exposure of HbA to the glucose level in the cellular environment in a directly proportional relationship. The higher the glucose level, the higher the HbA1c. However, stabilization (Amadori rearrangement) of hemoglobin's glycated structure (such as reversable Schiff base, also known as labile-HbA1c) requires a continuous and lengthy exposure of HbA to glucose (stable-HbA1c with clinical significance) (*3*). Therefore, HbA1c correlates with the mean level of blood glucose over the life span of erythrocytes and HbA, which is 106±21 days (*4*, *5*). Nevertheless, depending on the method, the labile-HbA1c may or may not be included in the measurement and calculation of stable-HbA1c.

Because the process of glycation is not enzymatically mediated but based on the biochemical properties of the -NH groups of amino acids and the aldehyde group of glucose and how they react with each other, there is no site-specific attachment of glucose to HbA. As such, glycation, the attachment of glucose residues at amino groups, can occur at any amino group or amino acid that is accessible to glucose. Although N-terminal valine residue on the β chain of HbA is the most accessible position in the HbA molecule, 85% of total glycated HbA is represented by HbA1c. However, additional hemoglobin glycated species, such as HbA1a1, HbA1a2, and HbA1b, also can be formed. Together, they are defined as the total glycated HbA. This is what the charge-based methods and electrophoresis actually evaluate.

Glycation of the N-terminal residue changes the structure and decreases the positive charge of HbA, allowing separation and quantification of glycated versus nonglycated HbA in clinical laboratories (*6*).

TYPES OF HBA1C ANALYSIS

Methods of HbA1c analysis fit into two broad categories: Methods based on the separation and quantification of the glycated hemoglobin due to its different molecular charge in relationship with the nonglycated hemoglobin, and methods based on the identification of structural changes of the hemoglobin post glycation and quantification. The former category includes capillary electrophoresis-high performance liquid chromatography (CE-HPLC, e.g., Bio-Rad) and electrophoresis (e.g., Sebia Capillaries). The latter includes immunoassays (various manufacturers), boronate affinity chromatography (Trinity Biotech), and mass spectrometry (*7*).

CE-HPLC AND ELECTROPHORESIS ASSAYS

This method is able to quantitate HbA1c by separating it from HbA because glycation of the N-terminal valine decreases the positive charge. However, charge-based methods are susceptible to interference from nonglucose adducts such as carbamylation in uremia and acetylation, and structural changes from Hb variants that alter net charge. That affects the migration profile with electrophoresis or retention time with CE-HPLC of hemoglobin variants, which may migrate or coelute concurrently with HbA1c or HbA, causing incorrect interpretation. Currently, more than 1,000 human hemoglobin variants (alpha, beta, gamma, or delta variants) have been described. They result from point mutations that cause amino acid substitutions. Depending on their charge, these variants can lead to false increases or decreases in HbA1c (*7*).

Although these methods are not affected by most common Hb traits, such as Hb AS (the sickle cell trait) and Hb AC, they are not completely excluded from interference due to certain hemoglobin variants (*11*). Proper resolution and peak identification of HbA1c, HbA, and interfering variants is critical for accurate quantification (e.g., %HbA1c=AUC of HbA1c / AUC of total Hb) (*7*, *10*). However, labile-HbA1c can interfere with HbA1c measurements and often requires pretreatment.

Table 1: Comparison of glucose and HbA1c testing modality, advantages, and limitations.

Glucose evaluation	HbA1c evaluation
Fasting	No fasting necessary
Multiple draws (e.g., oral glucose tolerance test)	One draw
Reflects immediate glycemic level	Reflects long-term glycemic level (2-3 months)
No hemoglobin variant interferences	Hb variants can interfere
Standardized and reference methods established	In process of standardization A complex International Federation of Clinical Chemistry and Laboratory Medicine reference method has been developed

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IMMUNOASSAYS

This form of testing uses antibodies that target N-terminal glycated amino acids (generally the first four monoacids) on the β chain to quantify HbA1c. Labs calculate the HbA1c percentage based on the HbA1c and total Hb concentrations (*11*, *12*, *13*). Thus, any factor that prevents glycation or any amino acid substitution in the β-chain N-terminal epitope may hinder antibody binding, leading to falsely low or undetectable HbA1c values. This may occur, for example, in patients with hemoglobin variants such as HbS, which is present in people with sickle cell disease, and HbC, an inherited mutation.

Depending on the specificity (antibody recognition), glycated species resulting from hemoglobin variants may or may not be included in the measurements. Additionally, patients with high levels of fetal hemoglobin (HbF >10%), such as sickle-cell patients treated with hydroxyurea or individuals with a genetic condition in which they continue to produce HbF into adulthood, are prone to falsely low HbA1c value by immunoassay, since HbF lacks the β chain targeted by most assays. Although HbF is included in the calculation of the %HbA1c (%HbA1c=HbA1c/total Hb), HbF β chains share limited homology with the β-chain N-terminus, resulting in poor cross-reactivity with antibodies in most immunoassays (*14*). These assays were never harmonized and thus vary in sensitivity to hemoglobin variants, which leads to discrepancies across platforms.

Methods of HbA1c analysis fit into two broad categories: Methods based on the separation and quantification of the glycated hemoglobin ... and methods based on the identification of structural changes of the hemoglobin post glycation and quantification.

BORONATE AFFINITY CHROMATOGRAPHY (BAC)

In this method, boronic acid reacts with cis-diol groups created by glycation, thereby allowing glycohemoglobins such as HbA1c to be very specifically separated from HbA (2). Due to the design of the assay, BAC is virtually free of interferences from hemoglobin variants. However, elevated HbF (>20%) can still lead to spurious results for the reasons mentioned above. Further, rare Hb variants with excessive glycation, such as Hb Himeji, also can interfere with boronate affinity chromatography (*15*). Still, BAC (Trinity Biotech) remains the method with the highest specificity for HbA1c currently on the market. This test specifically measures HbA1c and does not include other hemoglobin glycated species.

Thanks to its high specificity, BAC results correlate better than any other method with results obtained using the mass spectrometry-based reference method from the International Federation of Clinical Chemistry and Laboratory Medicine (IFCC) mentioned below (*8*). It should also be noted that Abbott developed a point-of-care testing (POCT) instrument for robust evaluation of HbA1c that is based on this method (the Abbott Afinion HbA1 assay).

Although virtually no analytical interference affects HbA1c evaluation in patients with common hemoglobin variant traits regardless of the method, this is not the case in patients who have both β-globin alleles affected by mutation. This includes homozygous mutations such as Hb SS-sickle cell disease and Hb CC-hemoglobin C disease, or compound heterozygous mutations, such as Hb SC. Although the process of hemoglobin glycation still occurs, leading to formation of glycated variant hemoglobins, these patients do not have HbA and therefore do not produce HbA1c.

MASS SPECTROMETRY

The IFCC developed a mass-spectrometry–based technique for measuring HbA1c. Because of its higher specificity for evaluating the glycated N-terminal valine of the HbA β chain, the IFCC approved mass spectrometry as the international reference method for evaluating HbA1c. This approach involves a two-step process. First, the hemoglobin (glycated and nonglycated) is digested by the endoproteinase Glu-C to shorter polypeptides. Second, the glycated and nonglycated N-terminal hexapeptides of the β chain are separated and quantitated either by liquid chromatography-mass spectrometry (LC-MS) with electrospray ionization or by a two-dimensional approach using HPLC and capillary electrophoresis with UV-detection.

Both principles give identical results, and HbA1c is measured as the ratio between the glycated and nonglycated hexapeptides. The calibrators of this method consist of a mixture of highly purified HbA1c and HbA0 and represent an important step toward standardization of HbA1c testing. Precision and accuracy were high for this method, which was virtually free of any analytical interference. Although this method is considered the basis of the uniform standardization of HbA1c routine assays worldwide, it is not routinely used in clinical laboratories due to the complexity of the analytical steps involved, the prohibitive cost of a mass spectrometer, and the complicated nature of its installation and operation (*6*).

POINT-OF-CARE TESTING

Most of the POCT instruments used for evaluating HbA1c are based on immunoassay and are thus subject to the limitations of that technique, as well as significant performance variability due to reagents' lot-to-lot variability (*17*). Further, the Food and Drug Administration (FDA) has authorized most POCT HbA1c instruments for monitoring HbA1c levels in patients with known diabetes and not for diagnostic purposes.

However, recently, the Afinion 2 HbA1c Dx cartridges received FDA-approval as a moderate complexity tool for diagnosing diabetes mellitus and helping to identify patients at high risk for developing it.

The wide range of methods clearly contributes to significant analytical variability. The availability of numerous FDA-approved HbA1c testing platforms on the market further complicates this issue.

SPECTROENZYMATIC METHOD

A spectroenzymatic method for HbA1c also was developed recently. In this method, the hemoglobin in the sample is first oxidated using sodium nitrite, which results in the formation of methemoglobin. Measurements at 505/800 nm are used to determine the concentration of total hemoglobin. After this step, protease cleaves the connection between leucine and histidine at the N-terminal end of the β-chain, which leads to the formation of a glycated dipeptide fragment. This glycated dipeptide then undergoes a reaction with fructosyl peptide oxidase, resulting in the production of hydrogen peroxide. Subsequently, under the action of peroxidase, hydrogen peroxide reacts with a specific die. The concentration of HbA1c in the sample can be measured through spectrophotometric evaluation of the resulting complex. The HbA1c content and its percentage in total hemoglobin is then calculated by measuring the absorbance at 660/800 nm.

Currently, this method is not used routinely for HbA1c lab testing. However, one study has shown that it produces results with comparable accuracy to those obtained using the IFCC method and that it also demonstrates limited susceptibility to interferences (*18*). Because of its demonstrated high level of specificity and accuracy, it is possible that it might become a common method in the future.

VARIATIONS IN TESTING METHODS

Several factors influence the selection of HbA1c testing methods in clinical laboratories, including cost, patient demographics, existing equipment, performance characteristics, and available resources. There is an intense effort to standardize HbA1c testing. About 99% of U.S. clinical laboratories use methods certified by the National Glycohemoglobin Standardization Program (NGSP), which aims to align HbA1c results with those of the Diabetes Control and Complications Trial (DCCT) and the United Kingdom Prospective Diabetes Study.

These landmark studies established clear connections between HbA1c levels and outcomes in patients with diabetes. The NGSP Certified Network Laboratories employ methods that are calibrated and traceable to those used in the DCCT. By comparing results with the NGSP network, both manufacturers and clinical laboratories can ensure their glycated hemoglobin measurements align with DCCT standards, increasing the likelihood of meeting the College of American Pathologists' (CAP) survey requirements.

The wide range of methods clearly contributes to significant analytical variability. The availability of numerous FDA-approved HbA1c testing platforms on the market further complicates this issue. Currently, according to ADA, the precision goals for HbA1c measurement are to have a coefficient of variation (CV) of <1.5% for intralaboratory tests and <2.5% for interlaboratory measures (using at least two control samples with different HbA1c levels), and ideally no measurable bias (*19*, *20*).

According to the most recent CAP survey of HbA1c challenges released in January, 29 methods from over 1,000 participating laboratories achieved this criterion on proficiency testing, representing most of the available products on the market. Some methods, such as ARKRAY Adams HA-8190V, had a CV<1.5%. Eight other methods performed at a bias <2%, including the Biorad D-100, Sebia Cappilarys, Siemens Atellica, Tosoh, Trinity Biothec Premier, and all three Abbott methods. A few methods did not meet the ADA criteria, performing at a CV > 2.5% or even >3% (Roche cobas, Siemens DCA Vintage, Vitros Chemistry Systems, and Beckman AU Systems). Like other CAP challenges, the survey evaluated the results against the NGSP and IFCC reference method target and considered acceptable results within ±6% of the target value.

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BIOLOGICAL AND CLINICAL FACTORS

In addition to method-specific analytical issues, correct evaluation of HbA1c also depends on biological and clinical factors (*7*). Conditions that shorten the lifespan of red blood cells (RBCs), such as hemolysis and anemia, result in lower HbA1c levels because of insufficient exposure time to glucose, regardless of glycemia. Similarly, decreases in the number of RBC or the quantity of hemoglobin will lead to a decrease in glycation time. This can occur with numerous conditions, including iron-deficiency anemia, hemolytic disease, splenomegaly, B12/B9 deficiency, renal disease, and ineffective erythropoiesis. Patients with these conditions will have falsely low HbA1c independent of the glucose concentration (*20*, *21*).

Medical conditions that increase the life span or number of RBCs, including chronic kidney disease, inefficient erythropoiesis, or repeated transfusions, will lead to an increase in glycation time. Therefore, patients will have falsely elevated HbA1c independent of the glucose concentration (*20*, *21*).

Although certain analytical limitations can be overcome by using alternative methods or assays — for example, fructosamine in patients with complex hemoglobinopathies — clinical conditions should be considered for accurate evaluation of glycemic level (*7*, *21*, *22*).

Many other factors can interfere with effective glycation of HbA independent of the

concentration of plasma glucose and age. These include various conditions such as liver and biliary diseases with hyperbilirubinemia, alcohol addiction, and pregnancy; supplements such as vitamins C and E; and medication such as opiates used in pain management, which negatively modulate the process of glycation and endocrine glycemic control (*7*).

CONCLUSION

Although HbA1c measurement is a powerful tool in diabetes management, the accurate interpretation of results is extremely complex. Without assessing the full context, results could be interpreted overconfidently. Before selecting a tool, healthcare professionals should carefully consider analytical, pathophysiological, and other factors that could affect the accuracy of measurement for every patient.

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How UNIVANTS is inspiring labs to break down healthcare silos to transform patient care

BY KIMBERLY SCOTT

Igniting clinical excellence

To create transformational change within healthcare organizations, clinical labs must build new, interdisciplinary partnerships — something the UNIVANTS of Healthcare Excellence awards program has highlighted since its inception in 2018.

A session held July 29 at ADLM 2025 (formerly the AACC Annual Scientific Meeting & Clinical Lab Expo) explored trends among UNIVANTS winners and examined what it takes to make lasting improvements to patient care. UNIVANTS is a partnership of eight health-centered organizations: the Association for Diagnostics & Laboratory Medicine (formerly AACC), Abbott, Modern Healthcare, the International Federation of Clinical Chemistry and Laboratory Medicine, the European Health Management Association, Healthcare Information and Management Systems Society, the National Association for Healthcare Quality, and the Institute of Health Economics.

UNIVANTS has recognized more than 80 initiatives from 32 countries. These include efforts to identify kidney disease in indigenous communities early enough to slow the progression of disease, to improve the perioperative pathway for people with diabetes, and to combat barriers to screening for sexually transmitted diseases.

Octavia Peck Palmer, PhD, FADLM, vice chair of health equity and associate professor in the departments of pathology, critical care medicine, and clinical and translational science at the University of Pittsburgh School of Medicine, came away from the July 29 session feeling inspired, she said.

"The biggest takeaway for me was to think about different partnerships I should be cultivating when I am thinking about how to improve patient lives," Palmer said. "I'm now thinking about how to partner with payors to identify and fill healthcare gaps, which means understanding what the payors need."

Developing partnerships is a central tenet in the UNIVANTS program. The awards program recognizes teams that collaborate across disciplines and transform healthcare delivery and, ultimately, patient lives. To be considered for recognition, clinical care initiatives must involve at least three disciplines, including laboratory medicine or pathology. The highest rated clinical care initiatives involve at least five disciplines, according to the UNIVANTS applicant guide.

Christine Schmotzer, MD, pathologist-in-chief and executive vice chair at University Hospitals Cleveland, said it is critical for labs to partner with other departments within their health system to have a substantial effect on practices.

85
Best practices recognized by UNIVANTS since the awards program began in 2018.

Involving clinicians is particularly important, she stressed.

Schmotzer, who was one of the presenters at the July 29 session, was part of a team that was recognized by UNIVANTS in 2022 for an initiative that increased the accuracy of prescription compliance monitoring through enhanced drug testing support. In addition, she has served independently as a judge for the program.

Khosrow Shotorbani, MBA, MLS(ASCP), president and CEO of Project Santa Fe Foundation and founder and CEO of Lab 2.0 Strategic Services LLC, also attended the session and said it reiterated the importance of partnerships in driving change.

"It's about getting out of the lab and locking arms with clinicians, helping to design care models of the future, and measuring the key performance indicators that matter in terms of outcomes," he said. "Partnerships are essential. Clinical laboratories can't drive change alone."

DEFINE AND DELIVER DATA

Another key to developing and implementing successful initiatives is data, Schmotzer said. To have a successful demonstration of outcomes, it's important to define your data strategy in advance, she advised. Define goal-oriented data by first identifying the problem you are trying to solve and then determine what data might support the assessment of the outcomes you are trying to demonstrate. The data might be qualitative or it might be quantitative.

Part of your data strategy should be to source non-lab data at the beginning of the project, she advised. This includes data related to revenue cycles, payors, electronic health record usage, patient access encounters, pharmacy, accountable care organization metrics, market share, and operations.

Palmer agreed that gathering and analyzing data is a big part of making transformational change. "We need to think about who holds the data in our organizations, how they are using that data, and how we can access it," she said. "We need to understand how to interrogate the data so that it leads to a better healthcare experience."

FOCUS ON PROCESS

Initiatives do not have to address something new or exciting to be successful, said Schmotzer, who noted that even something as simple as glucose testing can be improved through a new process.

Palmer agreed, noting that successful initiatives don't necessarily have to involve a new test or a new diagnostic tool.

"How do we use the tools we already have?" she asked. "How do we ensure we are using diagnostic tools correctly and appropriately and how do we ensure that the people who need these tools can get access to them? There's a whole host of medically underserved individuals. We can do better."

One example of this is an initiative implemented by Kaiser Permanente Southern California to improve management of patients with high low-density lipoprotein cholesterol (LDL-C). Clinical guidelines are clear that high-intensity statins are effective at reducing LDL-C; however, they are underutilized among adults with LDL-C equal to or greater than 190 mg/dL. By implementing electronic health record-directed algorithms that recommended treatment, the organization, which was a 2024 top UNIVANTS winner, saw a 6% improvement in high-intensity statin prescription orders for patients with LDL-C at or above 190 mg/dL and a 22.2% relative increase in the proportion of patients who improved their LDL.

32
Number of countries represented in UNIVANTS recognitions.

Previous page and here: natrot / iStock

"Whether it's new or old, or whether there are guidelines that exist or not, putting a governed process in place to make sure that the best practice actually gets implemented is where a lot of the impact is," Schmotzer said. "And it always takes a spark of creativity."

ALL LABS ARE LOCAL

Although many of the applications submitted to UNIVANTS address global health issues, Schmotzer stressed that it's important to keep in mind who your lab is serving. She cited a 2022 winning initiative out of Malaysia in which women were empowered to self-sample for human papillomavirus (HPV) testing, which resulted in an increase in the number of women testing positive for HPV and then being linked to treatment. Because it can be difficult for women in Malaysia to travel to a clinic to get tested for HPV, this initiative solved a problem specific to that country.

Schmotzer encouraged potential future UNIVANTS applicants to determine what problems there are in their local area and consider designing initiatives to tackle those challenges.

APPLICATIONS ARE OPEN NOW

UNIVANTS is currently accepting applications for the 2026 awards, according to Tricia Ravalico, executive lead for the program. The deadline for submissions is November 15. Applications can be made through the UNIVANTS website at www.univantshce.com. The website also contains a plethora of useful resources, such as best practice examples, helpful hints, templates, and checklists.

The program is open to all healthcare professionals. The UNIVANTS of Healthcare Excellence program is agnostic to products and platforms. In fact, manufacturers' names or any direct product names may not be included in any part of the application process.

29%
The percentage of new countries represented in UNIVANTS recognitions in 2025.

Shotorbani and Palmer encourage teams that have implemented successful initiatives to apply for the award. Even if your team doesn't win, the feedback you receive is worthwhile, they said.

"UNIVANTS is becoming a blueprint of how we are manufacturing a sustainable future," Shotorbani said. "We can no longer build the Taj Mahal of healthcare and wait for the sick to arrive. We have to meet patients where they are."

Find more information about UNIVANTS at www.univantshce.com.

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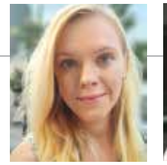


BY ASHLEY R. RACKOW, PHD, DABCC, NRCC,
AND SABRINA V. SOUTHWICK, MS, LCGC

Expanding access to molecular diagnostics in maternal-fetal medicine: A case study

Numerous discoveries in molecular diagnostics have driven a sudden expansion of the field, presenting significant challenges for clinical implementation. Even with robust institutional systems in place, the decision to implement or authorize new genetic testing is multi-factorial, with consideration given to the test itself, the performing laboratory, anticipated volume, clinical utility, professional society guidelines, and costs for patients and healthcare systems. Insufficient data in any of these areas may delay or prevent the adoption of innovative medicine.

The prenatal genetic testing landscape has experienced particularly rapid advancements. It has evolved from traditional karyotyping to fluorescence in situ hybridization and microarray, to noninvasive cell-free DNA screening, and now even includes advanced molecular diagnostic techniques like fetal whole exome and whole genome sequencing (fWES and fWGS, respectively). Although sequencing methods have been foundational to advancing research, the real-world clinical application of fWES and fWGS is still debated. These tools are not currently recommended for routine care, but there is increasing recognition among providers and healthcare entities that there are clinical scenarios where fWES and fWGS can improve diagnostic yield (*1*).

At Johns Hopkins University, we took a multidisciplinary, stewardship-based approach to identifying the most appropriate use of fWES and fWGS. Stewardship programs strive to advance healthcare delivery, high-value care, and efficient operations. Although early programs focused primarily on analytical systems, test performance represents only one component of the testing process (*2*). As healthcare systems evolve to become more nuanced and complex, interdisciplinary collaboration among laboratory medicine professionals, genetic counselors, clinicians, and administrators is essential to ensuring patients have access to testing that informs high-quality, individualized care (*2*,*3*). Leveraging a team-based approach to stewardship allows healthcare leaders and subject-matter experts to evaluate medical advancements, establish clinical utility, assess operational feasibility, and perform cost analyses to protect patients from financial harm.

In this article, we describe a collaborative initiative that brought together leaders in prenatal genetic counseling, maternal-fetal medicine, and laboratory medicine to develop a clinical algorithm for optimizing use of molecular diagnostics for prenatal testing at our institution.

Establishing an ordering algorithm for fWGS

To address the diagnostic needs of their patients, professionals in the division of maternal-fetal medicine at Johns Hopkins University strongly advocated for an examination of access to molecular diagnostics in prenatal care, specifically for investigating fetal anomalies detected by ultrasound.

Prior to this initiative, testing followed a tiered approach that was largely reflective of guidelines set forth by the American College of Obstetricians and Gynecologists (ACOG) and the Society for Maternal-Fetal Medicine (SMFM) (*4*). When fetal anomalies were identified via ultrasound, patients were counseled on the potential for an underlying genetic etiology and relevant testing options. If an invasive procedure was elected, a chromosomal microarray was typically recommended as the first-line diagnostic analysis.

Indications for fWGS

1. Previous pregnancy with anomaly. If performed, genetic testing did not identify the cause.
2. Pregnancy termination likely to be pursued if clinical suspicion is confirmed.
3. Chromosomal microarray expected to have low diagnostic yield (i.e., strong suspicion of single gene disorder) and rapid results required to change trajectory of care.

All cases require approval by a prenatal genetic counselor.

Box 1. Indications for direct fWGS ordering

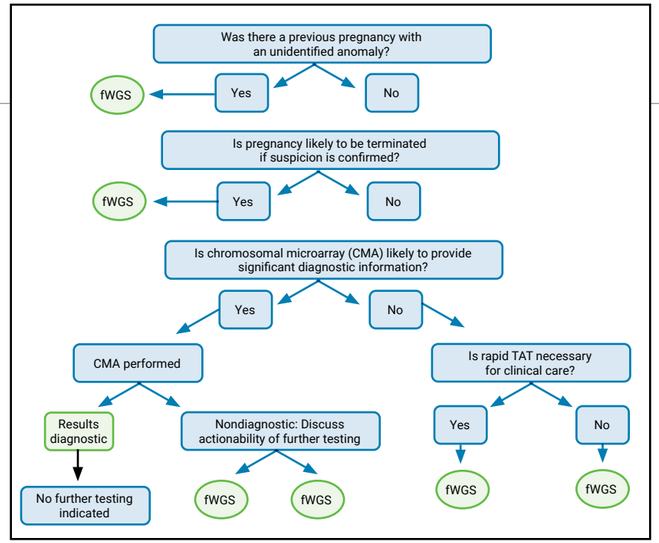

Figure 1. Institutional ordering algorithm for fWGS

If the microarray results were nonexplanatory for the ultrasound findings, fWES would be offered to patients who wanted to pursue additional testing. Although the use of fWES for prenatal sequencing goes beyond the scope of ACOG and SMFM guidelines, the additive value in select cases is supported by a 2022 position statement published by the International Society for Prenatal Diagnostics (ISPD) (*5*). Nevertheless, there were instances when this tiered-testing paradigm fell short, highlighting a clinical need for access to fWGS.

To evaluate this need, the university established a working group comprised of prenatal genetic counselors and leaders from maternal-fetal medicine and laboratory medicine. They performed a needs assessment to define the current state of testing and highlight where it was inconclusive or precluded timely clinical intervention. The working group brought a wealth of knowledge and diverse experiences to the review of specific cases, leading to a clear determination of which patients would benefit most from fWGS (Box 1).

Their work culminated in the establishment of an ordering algorithm — a framework that relies on clinical judgment while ensuring that early implementation of fWGS remains focused and appropriate (Figure 1). The team also conducted a financial review to ensure the new framework did not strain health-system resources and to help clinicians advise patients regarding the potential financial burdens of testing.

Building on initial success

After the working group completed its proposal, the institution's laboratory formulary committee reviewed and approved the new ordering algorithm and financial analysis. The algorithm was used as a key tool to define the clinical utility of fWGS, estimate projected test volumes, and perform cost assessments. The team enlisted the engagement and support of the institution's prenatal genetic counseling team to ensure patients received appropriate guidance and felt empowered to make informed decisions.

This initiative sparked further collaboration between the maternal-fetal medicine department and the laboratory formulary committee at Johns Hopkins. In subsequent projects, we evaluated diagnostics for fetal methylation disorders and fragile X syndrome. More recently, we established a mechanism to perform fetal blood typing in order to prepare whole-blood products for neonates who require emergency cardiac surgery at delivery.

Although each new project requires a slightly different approach, we follow the same core process to ensure smooth integration: cultivating consensus among the treating team while examining clinical utility, analytical validity, regulatory compliance, and operational feasibility. In each instance, a concurrent financial review is also performed to ensure we remain responsible stewards.

As we build on these promising initial experiences, we remain committed to working in interdisciplinary teams. Such collaboration is key to promoting robust and transparent billing practices and implementing systematic improvements for integrating novel and clinically impactful genetic tests into clinical practice.

View the references online at myadlm.org/cln.

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BY RACHEL NOTESTINE, MS, CGC

Scam alert: Lessons learned from an analysis of genetic testing fraud cases

Healthcare professionals' knowledge of genetics and available testing options is expanding rapidly, leading to more informed diagnoses, better care management, and targeted therapies. In spite of this, the complexities of genetic risk assessment and test selection, coupled with the abundance of tests on the market, also have made genetic testing a common tool for healthcare fraud.

Fraud, waste, and abuse (FWA) are a spectrum of behaviors that result in unnecessary costs. Examples include duplicate ordering or billing, billing for services not rendered or performed, and "unbundling" claims to bill for each test separately instead of billing for the relevant panel. In particular, fraud involves intentional deception for personal or financial gain and often includes criminal activity. A behavior could be deemed fraud, waste, or abuse depending on the intent and context.

The costs of fraudulent activity in the healthcare sector are wide-ranging. Financially, fraud alone is estimated to comprise 3%–10% of the national healthcare expenditure (NHE) in the United States — potentially 1 out of every 10 dollars (*1*). The majority of NHE is funded by the federal government, which means taxpayer money is forfeited. Fraudulent claims cause monetary strain for public and private insurance companies (payors). In turn, measures to address fraud, such as prior authorizations, audits, and fraud prevention programs, may add to the administrative burden and systemic complexities in healthcare. People may experience unexpected bills for goods or services they never received, or pay increased premiums as payors balance their budgets. Fraud can cause future harm if a medically necessary claim is denied because the insurance company thinks it has previously been provided through a false claim.

Federal and state governments, as well as various coalitions, have implemented legislation and task forces to help with the identification, prevention, and prosecution of healthcare fraud. Legislation such as the Federal Civil False Claims Act (FCA), the Anti-Kickback Statute, the Physician Self-Referral Law (Stark Law), and the Criminal Health Care Fraud Statute serves as the primary mechanism for federal prosecution. Federal organizations, including the Department of Justice and the Office of the Inspector General, have highlighted genetic testing specifically as a common area of fraudulent activity. Perhaps most famously, in 2019's Operation Double Helix, federal law enforcement charged 35 individuals responsible for over $2.1 billion in losses through submission of fraudulent cancer genetic testing (*2*).

Given the high prevalence and costly nature of genetic testing fraud, we set out to better understand it in order to inform preventive strategies. We did this by performing a qualitative analysis of 42 court cases involving genetic testing fraud published between 2019 and 2023 through a retrospective review of a legal database and public sources (*3*).

Themes and common characteristics of genetic testing fraud

Six primary themes emerged from our analysis:

1. **Submission of medically unnecessary claims:** The majority of cases reported that genetic testing claims were medically unnecessary. In many cases, testing was completely unrelated to patients' true medical histories or diagnoses.
2. **Payment for signed orders:** In 90% of cases, healthcare providers received kickbacks or bribes to sign orders for genetic testing, often for patients they never met. These payments were disguised as processing and handling fees for testing, research incentives, investment opportunities, and meals and happy hours.
3. **Minimal or no patient contact:** In 71% of cases, providers had minimal or no contact with the patients for whom they ordered genetic tests. Intermediaries such as "telemarketing" companies often identified lists of beneficiaries, arranged logistics of sample collection, secured signed genetic test orders, and submitted for reimbursement.
4. **Inappropriate billing practices:** More than half of the analyzed cases revealed improper billing practices, including charging for services not rendered and "upcoding," in which a less accurate or inaccurate procedural code is selected to maximize reimbursement.
5. **Fraud concealment:** Perpetrators employed various strategies, including wire fraud and money laundering, to hide their profits. Sham contracts masked illegal payments as legitimate marketing services for laboratories or research initiatives for providers.
6. **Inappropriate documentation:** Nearly half of the cases involved fraudulent documentation, such as falsifying patient records, misrepresenting diagnoses, or fabricating signatures. Fraudulent documentation supported false claims and legitimized medically unnecessary testing so claims would be reimbursed.

We also reviewed characteristics of claims submitted fraudulently to identify categories of genetic testing claims that could be prioritized in fraud identification and management policies (Figure 1, online).

Cases involving telehealth, targeting Medicare beneficiaries, and utilizing cancer genetic testing were three of the most common categories of fraud we identified. These are illustrated by a striking case that involved a doctor who "received approximately $30 in exchange for each doctor's order he signed authorizing [durable medical equipment (DME)] and cancer genetic test orders that were not legitimately prescribed, not needed, or not used — totaling more than $466,000 in kickbacks. The Medicare beneficiaries for whom [doctor] prescribed DME and cancer genetic testing were targeted by telemarketing campaigns and at health fairs and were induced to submit to the cancer genetic testing and to receive the DME regardless of medical necessity" (*4*).

Another of the court cases we analyzed that illustrates a number of the themes above involved a nurse practitioner who, in 2020, "ordered more cancer genetic tests for Medicare beneficiaries than any other provider in the nation, including oncologists and geneticists. She then billed Medicare as though she were conducting complex office visits with these patients, and routinely billed more than 24 hours of 'office visits' in a single day" (*5*).

The role of genetics experts

As the majority of cases reported medically unnecessary testing, integrating genetics experts like genetic counselors and medical geneticists into the ordering and billing process is essential to combatting genetic testing FWA. Because of the complexity of genetics and genetic testing, high levels of training are needed to perform risk assessments and select the best test options. Similarly, genetics experts informed about FWA are the perfect reviewers (or whistleblowers) to recognize when a genetic test does not quite make sense with a patient's given medical history.

Importantly, integration of genetics expertise must be balanced with accessibility. Increased access to genetics providers at the ordering or claim review stages may help prevent and uncover fraudulent activity. Efforts that may increase access include genetic counseling licensure and recognition by Medicare. Laboratory stewardship and insurance claim review programs also aim to ensure best testing practices and limit waste for medically necessary testing.

Other steps we can take to prevent FWA

Although our findings focused on genetic testing fraud, which is intentional, medically unnecessary testing, inaccurate billing, and inappropriate documentation practices can occur unintentionally as well. Either way, if you witness suspicious activity, report it to 1-800-HHS-TIPS or oig.hhs.gov/fraud/hotline. Additionally, certain key takeaways can be used to examine and modify practices within our own organizations that may fall on the waste and abuse end of the spectrum (Figure 2, online).

Fraud trends can inform policy and anti-fraud technology, including data analytics or artificial intelligence, which in turn can supplement genetics expertise and traditional methods of audits or prior authorization. Broad public education initiatives, as well as targeted education for populations like Medicare beneficiaries, laboratory stewardship programs, and payors, may also help prevent and identify FWA.

Conclusion

FWA using genetic testing causes significant harm to individuals, laboratories, payors, and the healthcare system overall. Continuing to research trends can aid policies and education in reducing FWA while supporting the genuine needs of patients. Through laboratory stewardship and individual accountability, we can better safeguard patients and the genetics field by identifying and reporting fraud, raising awareness of FWA, and reflecting on personal and institutional practices with the goal of optimizing our healthcare resources.

View the references and figures online at myadlm.org/cln.

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Regulatory Roundup

FDA approves companion diagnostic for lung cancer

Thermo Fisher recently announced Food and Drug Administration (FDA) approval of its Oncomine Dx Express Test for use as a companion diagnostic (CDx) for Dizal's Zegfrovy (sunvozertinib) and in tumor profiling.

The approval brings rapid next-generation sequencing (NGS) results in as little as 24 hours to decentralized settings closer to where patients receive care, which aids in timely decision making, Thermo Fisher said.

Approved to run on the Ion Torrent Genexus Integrated Sequencer, the Oncomine Dx Express Test identifies patients with non-small cell lung cancer (NSCLC) who harbor *EGFR* exon 20 insertion mutations. The test also is approved for profiling solid tumors and detects mutations with evidence of clinical and potential clinical significance in 46 genes.

The Ion Torrent Genexus Integrated Sequencer automates the NGS workflow from sample preparation to data analysis and reporting. It is designed to make NGS accessible to more laboratories, including those that are smaller and lack NGS expertise. The sequencer also enables labs to generate timely CDx results and tumor profiling reports to expedite insights and access to precision oncology.

Zegfrovy, developed by Dizal, received FDA accelerated approval following its breakthrough therapy designation and priority review for treatment of NSCLC patients with *EGFR* exon 20 insertion mutations. With the approval of the Oncomine Dx Express Test as a companion diagnostic for this therapy, clinicians can now identify eligible patients quickly — and support earlier intervention and expanding access to targeted therapy, Thermo Fisher said.

NEXT-GENERATION SEQUENCING SYSTEM GETS CE CERTIFICATION

Fulgent Genetics has received CE certification under the European Union's In Vitro Diagnostic Regulation 2017/746 (IVDR) for its germline next-generation sequencing system.

The system includes FulgentExome and Fulgent Pipeline Manager (PLM). FulgentExome is a phenotype-driven system designed for clinical analysis to identify germline variants to aid diagnosis of suspected genetic conditions. FulgentExome examines coding region and splice junctions for more than 4,600 genes and reports variants of plausible clinical relevance. Within the FulgentExome system, Fulgent PLM software analyzes genetic information from sequencing data.

FulgentExome may be used as an inclusion test for clinical trials and may help ensure eligibility for reimbursement pathways for public health programs under IVDR, the company said.

COLORECTAL CANCER RESIDUAL DISEASE TEST GETS MEDICARE COVERAGE

Exact Sciences' Oncodetect molecular residual disease (MRD) test has received Medicare coverage through the Centers for Medicare & Medicaid Services Molecular Diagnostic

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Services Program for serial use in patients with stage II, III, and resectable stage IV colorectal cancer (CRC) in adjuvant and recurrence monitoring settings over a 5-year period.

The Oncodetect test tracks up to 200 circulating tumor DNA variants and can identify signs of cancer recurrence up to 2 years earlier than imaging alone, according to Exact Sciences.

The company said the Oncodetect test is supported by robust clinical validation studies. These include Beta-CORRECT, which confirmed the test's prognostic power across stages II–IV CRC, and Alpha-CORRECT, one of the longest-followed MRD cohorts for CRC recurrence.

The test's integration with the ExactNexus technology platform enables seamless ordering alongside other Exact Sciences Precision Oncology solutions, the company said.

DIASORIN ANNOUNCES FDA CLEARANCE FOR BLOOD CULTURE PANEL AND POC SUBMISSION

Diasorin has earned 510(k) Food and Drug Administration (FDA) clearance for the Liaison Plex Gram-Positive Blood Culture Assay, a syndromic blood culture panel for the microbiological diagnosis of bloodstream infections on the Liaison Plex platform.

The company also has submitted an FDA 510(k) premarket notification and CLIA waiver application for its Liaison NES, a next-generation molecular point-of-care testing platform.

The Liaison Plex Gram-Positive Blood Culture Assay detects 17 targets — including 13 gram-positive bacteria and four relevant resistance gene targets — in under 2 hours. Targets include *Bacillus subtilis* and the gene *mec*C, providing clinicians with the ability to make rapid and targeted treatment decisions.

The submission covers the Liaison NES Flu A/B, RSV, and COVID-19 panel, designed to simultaneously detect and differentiate between four of the most common and clinically significant respiratory pathogens: influenza A, influenza B, respiratory syncytial virus, and SARS-CoV-2.

LEX SUBMITS APPLICATIONS FOR FAST POINT-OF-CARE MOLECULAR DIAGNOSTICS PLATFORM

LEX Diagnostics has submitted dual applications to the Food and Drug Administration seeking 510(k) clearance and CLIA waived status for its VELO system, an ultra-fast point-of-care molecular diagnostics platform.

The platform is designed to deliver highly sensitive PCR results for key respiratory pathogens directly from a swab sample in 6 to 10 minutes.

The LEX system supports multiplex testing for key respiratory pathogens, including influenza A, influenza B, and COVID-19. It is engineered to integrate easily into clinical workflows across primary care settings, urgent care clinics, pharmacies, physician office laboratories, and decentralized acute settings. The system's proprietary cartridge-based design eliminates the need for external liquid handling, promoting ease of use and reliability.

LEX recently completed clinical studies in the United States with the VELO system and the influenza/COVID assay during the 2024-2025 respiratory season.

EGFR MUTATION TEST GETS EU CERTIFICATION

The Biocartis Idylla *EGFR* Mutation Test has received the EU Technical Documentation Assessment and Quality Management System certificate under the European Union In Vitro Diagnostic Regulation.

The companion diagnostic (CDx) detects *EGFR* exon 19 deletions and the L858R mutation, key biomarkers that guide targeted therapies for patients with non-small cell lung cancer (NSCLC). Designed for use on the Idylla Platform, the test qualitatively detects 44 mutations across exons 18, 19, 20, and 21 of the *EGFR* gene — all within a single cartridge. Among these, exon 19 deletions and L858R mutations are validated as CDx targets, for which the test has 99.2% sensitivity and 99.0% specificity, respectively. The remaining mutations have been analytically validated, Biocartis said.

Utilizing formalin-fixed, paraffin-embedded tissue samples, the test is fully automated from sample to result, delivering fast results in under 3 hours, streamlining laboratory workflows, and empowering oncologists to provide timely treatment decisions for their patients, the company said.

Industry Playbook

Rapid sepsis test slashes mortality in company-funded study

Cytovale recently announced that a large study of its rapid, early IntelliSep sepsis test shows that the rapid host response diagnostic cleared by the Food and Drug Administration reduced the relative rate of sepsis mortality by 39% (Healthcare 2025; doi: 10.3390/healthcare13111273).

It also shows that the test shortened hospital length of stay and enabled more efficient resource allocation in the emergency department, the company said.

The study followed more than 12,000 patients over 1 year at Our Lady of the Lake Regional Medical Center, a 900-bed in-patient acute care facility and Level 1 trauma center in Baton Rouge, Louisiana.

The research reveals unchanged nonsepsis mortality and validates the impact of IntelliSep on targeted triage. Results show a 0.76 day decrease in average hospital length of stay for sepsis patients, with strong implications for improved throughput and cost reduction, as well as a 40% decrease in blood culture usage in low-risk patients and an 8% increase in high-risk cases, the company noted.

COLLABORATION FOCUSES ON COMPANION DIAGNOSTICS FOR RARE BLOOD CANCERS

A new global collaboration between Qiagen and Incyte aims to develop a novel diagnostic panel to support Incyte's portfolio of investigational therapies for patients with myeloproliferative neoplasms (MPNs), the companies recently announced.

MPNs, a group of rare blood cancers comprising about 40% of hematological malignancies, involve chronic accumulation of different mature blood cell types in blood. Incyte's monoclonal antibody INCA033989, now under development in myelofibrosis and essential thrombocythemia, targets mutant calreticulin, a protein that helps drive this overproduction of blood cells.

Under the agreement, Qiagen will develop a multimodal panel using next-generation sequencing (NGS) technology for detecting clinically relevant gene alterations in hematological malignancies. This panel will serve as a companion diagnostic for INCA033989.

The panel validation will occur via NGS technology and the Illumina NextSeq 550Dx platform as part of Qiagen's partnership with Illumina to leverage its NGS diagnostic platforms for patient testing. Qiagen will support regulatory submission processes and market access activities across the United States, European Union, and Asia-Pacific regions.

DEAL ADVANCES HIGH VOLUME TESTING AND TECHNOLOGY

Waters Corporation and BD recently announced a definitive agreement to combine BD's Biosciences & Diagnostic Solutions business with Waters.

The deal joins their complementary technologies to serve high-volume testing in regulated end-markets including liquid chromatography, mass spectrometry, flow cytometry, and diagnostic solutions, Waters and BD said. The deal will lead to new ways to separate large molecules and drive growth in biologics and novel modalities with next-generation consumables, they added.

The transaction allows Waters to systematize instrument replacement,

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service plan attachment, e-commerce adoption, and new product launches while delivering cost synergies involving manufacturing, supply chain, selling, general, and administrative expenses. Additionally, Waters can maintain its commitment to both research and development and commercial investments, the companies said.

The deal provided an immediate opportunity to apply the company's expertise to realizing the full potential of its flow cytometry and specialty diagnostics portfolios, Waters officials said.

BD said the deal enhances their company's strategic focus as a leading medical technology company.

COLLABORATION TO ADVANCE SALIVA-BASED CANCER TESTS

The University of California, Los Angeles (UCLA) School of Dentistry recently announced a 3-year sponsored research agreement with South Korean semiconductor firm Dongwoon Anatech to develop a noninvasive, saliva-based technology for early detection of oral cancer and other diseases.

The agreement centers UCLA's Electric Field-Induced Research and Measurement (EFIRM) liquid biopsy platform, which isolates and analyzes biomarker signals directly from body fluids like saliva without complex sample preparation. Prior studies demonstrated EFIRM's ability to spot tumor-specific mutations, especially for nonsmall cell lung cancer, with high sensitivity and specificity, UCLA said.

The deal involves research that will begin with optimization of various protocols for Dongwoon Anatech's saliva-based glucose monitoring system, DpSaLife, in patients with and without diabetes, using clinical samples from hospitals in both the United States and South Korea. Later phases will focus on the development and clinical validation of EFIRM I, a fully automated diagnostic device designed to detect salivary biomarkers for cancers such as lung, gastric, and oral cancer.

PARTNERSHIP TO BUILD COMPREHENSIVE RHEUMATOID ARTHRITIS CLINICO-GENOMIC DATASET

Scipher Medicine and Savant Bio have announced an expanded strategic partnership to build an advanced rheumatoid arthritis (RA) clinico-genomic dataset.

The collaboration aims to transform real-world data from the electronic health records of patients tested with Scipher's clinically validated molecular signature test, PrismRA, which predicts nonresponse to tumor necrosis factor inhibitor therapies.

The partnership will rely on Savant's platform, which uses large language models paired with domain-specific quality controls to extract structured variables from free-text clinical documentation, such as physician notes and pathology reports. A variety of information can be linked to claims, labs, and prescribing data for longitudinal analysis. These data will then be converted into structured, analysis-ready formats.

Linking Scipher's validated genomic insights with structured patient journeys will enable the creation of a foundation for the next generation of real-world evidence and enable faster studies, richer evidence, and more targeted therapies for RA, Savant officials said.

PARTNERSHIP FOCUSES ON HOME COLON CANCER RNA SCREENING TEST

Viome Life Sciences and Scripps Research have established a strategic partnership to develop and clinically validate an RNA test for detecting precancerous colon polyps, the companies recently announced.

The partnership involves an observational study that will analyze RNA data from 1,000 healthy patients who get routine colonoscopies at Scripps Health. Relying on Viome's RNA sequencing and artificial intelligence platform and Scripps Research's clinical and translational expertise, the study aims to train Viome's platform to detect molecular signs of polyp development well before cancer symptoms emerge.

The research involves collecting Viome stool and saliva samples prior to colonoscopies, as well as Viome's comparative analysis of gene expression profiles and use of its platform to train predictive models to identify early biomarkers. The study also will evaluate sensitivity and specificity.

Index to Advertisers

Ask The Expert

How to implement a paperless remote sign-out process for electrophoresis

By Xiaochun Susan Zhang, MD, PhD, DABCC, DABMLI, FADLM

What is a paperless remote sign-out process for serum protein electrophoresis (SPE) and immunofixation electrophoresis (IFE)?

a: Making sure pathologists verify that these tests are completed through a sign-out system ensures clinical accuracy and allows qualified professional billing.

A paperless remote process digitizes the workflow, enabling electronic processing of all information, including protein fraction values (e.g., albumin, alpha-1, alpha-2, beta-1, beta-2, gamma), monoclonal (M) protein quantification, text-based interpretation comments, and the pathologist's digital signature. This allows pathologists to review and finalize cases remotely, eliminating the need for them to be physically present in the laboratory as well as the need for printed records.

Why should labs adopt this process?

A paperless process improves efficiency by eliminating the need to access the full paper trail associated with a patient's historical results, which technologists must spend substantial time retrieving, updating, and maintaining. By instead using a database that is integrated into the vendor's electrophoresis software, labs can maintain a digital archive of patients' results, preserving complete histories that support future research and artificial intelligence applications.

Paperless systems also reduce transcription errors by removing the need to do manual data entry. In labs where technologists, residents, or clinical chemists perform preliminary interpretations and pathologists complete final sign-out, this process facilitates collaboration through a shared digital environment.

How does the process work?

First, patient demographics, serum total protein levels, and test orders are downloaded from the laboratory information system (LIS) to the electrophoresis software, either directly or via middleware. The software controls the SPE instruments that perform the tests. Technologists analyze electrophoretograms, marking protein fractions and M protein peaks, and the software calculates their concentrations using peak-area percentages and total protein values.

If SPE results are abnormal, IFE or immunotyping is performed. IFE gel images are scanned and digitally linked to corresponding SPE results. Interpretive comments are added in the software or LIS, noting the presence or absence of M protein, its isotype, migration region, and comparisons to prior results for patients with existing histories. All results are then transmitted from the electrophoresis software to the LIS, where pathologists verify, digitally sign, and release them to the patient's electronic medical record.

How can I implement this process?

Implementation requires collaboration among stakeholders. Laboratory IT specialists configure LIS interfaces and test setups. The vendor's IT team installs electrophoresis software on local instruments and institutional servers. The server team works with the vendor and lab IT professionals to manage software installation and updates, and to secure remote access for pathologists. A medical or technical director oversees the project, ensuring it remains compliant with clinical and regulatory standards. Pathologists and technologists also contribute sign-out and operational insights.

A critical step is to standardize interpretative comments. Using a structured reporting format with consistent verbiage enables the creation of drop-down lists of standard comments in the electrophoresis software or mnemonic codes in the LIS, forming the basis for digital sign-out. Another key step is coding M proteins by isotype in the electrophoresis software and mapping them to standardized LIS entries for reporting.

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ADLM CLINICAL LAB EXPO PRODUCT SHOWCASE: HIGHLIGHTS OF THE INNOVATIONS THAT EXHIBITORS DISPLAYED AT ADLM 2025.

A1c by Sebia

Sebia's fully automated, high-capacity HbA1c testing with the CAPILLARYS 3 system delivers high-resolution, accurate results with hemoglobin variant detection. Designed for simplicity and reliability, it supports multi-assay consolidation, making it the ideal solution for efficient, high-quality diabetes diagnosing and monitoring.

Mass Spect Gold

For over 35 years, Golden West Companies has been a trusted partner to laboratories, research institutes and IVD manufacturers. Mass Spect Gold products are premium, non-synthetic, human matrices. They are prime candidates in the preparation of quality control materials and as a blank diluent for a wide range of analytes.

VACUETTE® Blood Collection Tubes

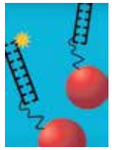
VACUETTE® Blood Collection Tubes manufactured by Greiner Bio-One are designed for the collection, transport and processing of blood in the clinical laboratory. Originally developed in the 1980s as a safe alternative to glass blood tubes, VACUETTE® tubes are made of highly transparent, virtually unbreakable PET plastic. They are available in a range of sizes.

VACUETTE® EVOPROTECT SAFETY Blood Collection Set

The VACUETTE® EVOPROTECT SAFETY Blood Collection Set from Greiner Bio-One is a winged needle with semi-automatic safety mechanism designed for one-handed, in-vein activation and improved protection from the risk of needlestick injuries. EVOPROTECT is available in several configurations of needle gauge, tubing length and attachment for flexibility in blood collection and infusion.

VACUETTE® Urine STB Tube

VACUETTE® Urine STB tubes from Greiner Bio-One are designed to stabilize urinalysis samples at room temperature for up to 72 hours. They contain a preservative made of ethylparaben, chlorhexidine and sodium propionate to limit bacterial and yeast growth, stabilizing key parameters for dipstick tests, clinical chemistry and sediment analysis. Evacuated for optimal urine-to-preservative ratio, Urine STB tubes are available in multiple draw volumes.



xMAP® Technology

xMAP® Technology is a bead-based multiplexing platform that enables rapid detection of up to 500 analytes, including proteins or nucleic acids, from a small sample volume. The technology's sensitivity makes it ideal for complex serological applications. Luminex's Partners have developed > 100 FDA 510(k)-cleared assays using xMAP Technology. Visit us.diasorin.com/en/luminex-ltg/xmap-technology to learn more!

The LIAISON PLEX® System

The LIAISON PLEX® System is Diasorin's next-generation, sample-to-answer platform for syndromic molecular testing. Its proprietary Flex® Software allows users to select and pay only for clinically relevant targets they need, with the option to release unprocessed targets on demand. This unique capability to customize results empowers clinicians to follow their diagnostic stewardship guidelines, while saving on operational budget.

LIAISON® MeMed BV®

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CLN Clinical Laboratory News

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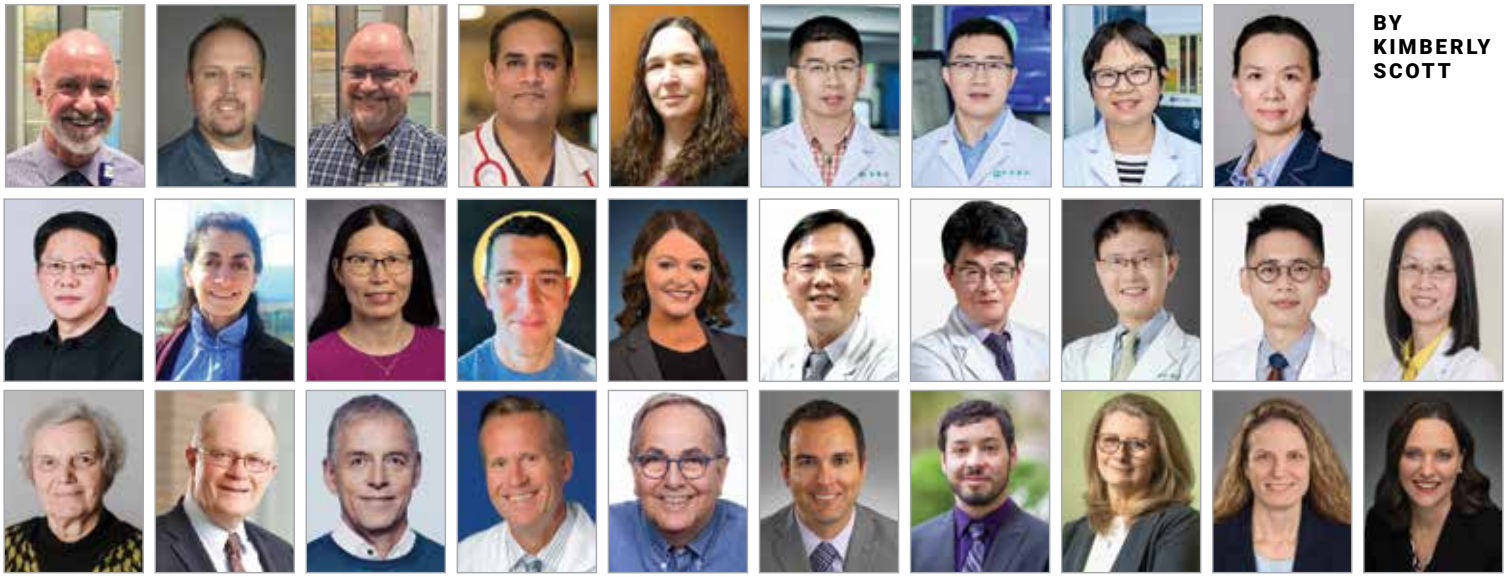
SLASHING COSTS

$395 million

The amount that a new warfarin monitoring test could save annually worldwide

PAGE 2

UNIVANTS 2025 awardees demonstrate power of collaboration



BY KIMBERLY SCOTT

From eradicating *H. pylori* to improving how warfarin is monitored, clinical laboratories across the globe are leading interdisciplinary teams to improve patient outcomes and save lives.

This year, six initiatives have received awards of achievement or distinction from the UNIVANTS Healthcare of Excellence awards program, a joint initiative of Abbott, the Association for Diagnostics & Laboratory Medicine (formerly AACC), Healthcare Information and Management Systems Society, Modern Healthcare, and other healthcare organizations. UNIVANTS recognizes healthcare teams that utilize avant-garde problem-solving and novel application of laboratory data to achieve better outcomes for patients, clinicians, payors, and health systems. The six award-winning initiatives are highlighted below.

REPLACING CONVENTIONAL WARFARIN MONITORING

Up to 80 million people worldwide take oral anticoagulant medications — primarily warfarin — to treat thromboembolic disorders such as atrial fibrillation (AF), pulmonary embolism, and deep-vein thrombosis (the latter two are known as venous thromboembolism, or VTE). Because warfarin can dangerously interact with other drugs and foods, causing highly variable anticoagulation that could lead to both thromboembolism and bleeding, conventional warfarin management can be difficult. Patients taking warfarin are typically monitored by prothrombin time-international normalized ratio (PT-INR), a test that gauges how long it takes blood to clot.

In addition, many clinical guidelines now prefer newer direct oral anticoagulants (DOACs), which do not require regular blood monitoring, over warfarin for AF and VTE patients. According to large clinical trials, DOACs like dabigatran, apixaban, and rivaroxaban are safer than warfarin in nonvalvular AF and VTE, although warfarin remains safer and more effective for high-risk patients such as those with mechanical heart valves, rheumatic heart disease, and antiphospholipid antibody syndrome. Moreover, due to its low cost, warfarin is often still the global treatment of choice for AF and VTE.

A cross-disciplinary team at Landspitali National University Hospital of Iceland has developed a new warfarin monitoring test that optimizes affordability, safety, and effectiveness, outperforming PT-INR–monitored warfarin and in some cases even the more expensive DOACs.

Warfarin, which is known as a vitamin K agonist (VKA) anticoagulant, inhibits the formation of four vitamin K-dependent coagulation factors (F): II, VII, IX, and X. Conventional PT-INR monitors FII, FVII, and FX and is highly influenced by FVII, which has the shortest half-life of the four factors. The antithrombotic effect of VKAs is mainly generated by safely reducing FII and FX.

The new test, called the Fiix-test (Fiix-PT), is sensitive only to reductions in FII and FX and is intended to stabilize anticoagulation variability, according to Pall Onundarson, MD, professor emeritus of hematology and laboratory medicine at the Landspitali National University Hospital of Iceland.

"There is much less anticoagulation variability with the Fiix test," he explained. "Fewer tests are needed and there is reduced need for dose adjustments." According to Onundarson, there is a 40% to 56% lower chance of thromboembolism without an increase in major bleeding compared to traditional PT-INR–monitored warfarin treatment.

The benefit was initially shown in a blinded, randomized controlled trial published in the journal *The Lancet Haematology* in 2015, and a pre-post study published in *Blood* in 2021 confirmed this finding. Another study, published in May 2025 in *Blood VTH*, also suggests the Fiix test can improve warfarin management. Further, it provides evidence that Fiix-warfarin could be more effective than DOAC drugs for patients with AF.

With a 34% decrease in annual monitoring tests and a 33% increase in the median interval between dose changes (from 60 days to 90 days), resource utilization is significantly reduced, Onundarson said. He estimates that these findings could translate to a savings of $395 million annually worldwide.

"In addition, with Fiix monitoring of warfarin, markedly fewer patients suffer strokes, systemic embolic events, heart attacks, and other life-threatening complications," which results in fewer hospitalizations, less disability, and even reduced deaths, he explained.

Replacing conventional warfarin monitoring

40%-56%: Decrease in thromboembolic events for patients taking warfarin monitored with Fiix-PT versus warfarin monitored with conventional PT-INR.

33%: Decrease in the variability of the anticoagulant effect when warfarin is monitored with Fiix-PT.

$2,000: Potential savings per AF patient per year if Fiix-PT monitoring enables some to take warfarin instead of DOACs.

"The savings from the reduced number of monitoring tests are considerable," Onundarson said. "However, savings from reduced hospitalizations for acute and chronic care would be considerably more if the test would become generally applied in patients needing warfarin."

If the improved clinical outcomes with Fiix monitoring lead some patients to be switched from DOACs to warfarin, even more cost savings can be achieved, resulting in about $2,000 per AF patient per year, according to his group's calculations.

The Fiix initiative, which was recognized with honors of distinction by UNIVANTS, is highly scalable, but will require the strong involvement of a test manufacturer and possibly a patient advocacy initiative, Onundarson said.

IMPROVING SYPHILIS SCREENING STRATEGIES

Syphilis remains a significant global public health concern, with millions of new cases reported annually. In China, between 2014 and 2019, the rate of syphilis rose from 30.93 cases per 100,000 to 38.37 per 100,000, a 4.41% annual growth rate. The proportions of latent and tertiary syphilis also increased, underscoring the urgent need for accurate and early diagnosis to mitigate transmission and improve patient outcomes.

Traditional stepwise syphilis testing involves an initial screening with a nontreponemal test such as rapid plasma reagin (RPR) followed by a confirmatory treponemal test like treponema pallidum particle agglutination (TPPA). However, this "one test at a time" method often leads to missed diagnoses, misdiagnoses, and patient loss to follow-up, resulting in delayed treatment, according to Jing Peng, deputy chief technologist of laboratory medicine at Tongji Hospital in Wuhan, China. Such inefficiencies increase the risk for transmission and progression, placing additional burden on the healthcare system.

In 2009, Tongji Hospital launched a new protocol, the "Innovative Reflex Simultaneous Testing Strategy," to replace stepwise testing. It includes:

- Simultaneous RPR and TPPA testing after a chemiluminescence immunoassay (CLIA)-reactive test result
- A new follow-up protocol for isolated CLIA-reactive results (CLIA+TPPA-RPR), and
- New diagnostic thresholds (CLIA signal-to-cutoff values) tailored for children to achieve a 95% positive predictive value.

Compared with traditional syphilis testing, the new initiative streamlines the testing process and reduces diagnostic turnaround time, according to Peng. The approach enables clinicians to manage syphilis patients comprehensively and accurately, facilitating early diagnosis and treatment. In addition, it minimizes the risk of missed diagnoses and misdiagnoses, thereby alleviating patient anxiety and financial burdens.

As a result of the new testing protocol, among patients with isolated CLIA-reactive results, 14.9% were diagnosed with syphilis during follow-up. The initiative also resulted in a 67% reduction in the number of visits required for diagnosis, resulting in an average cost savings of 113.7 renminbi (RMB) per patient. This equates to about $16. The savings are attributable to reduced transportation fees and minimized work loss from multiple appointments. The strategy also prevented progression to late-stage syphilis, which brings additional treatment costs ranging from RMB 2,100–4,300 ($293–$599) per person.

"Early diagnosis avoids more expensive late-stage treatment, which can range from RMB 7,700–9,800 [$1,073–$1,366] per visit," Peng said.

The strategy is highly scalable, Peng said, noting that it demonstrates high adaptability, allowing for straightforward implementation in comparable institutions and clinical centers. The assays involved — CLIA, TPPA, and RPR — are readily accessible, and the accompanying algorithms are user-friendly and easy to execute. Two hospitals in Hubein Province have successfully implemented the initiative, and 24 more medical institutions across four provinces have been influenced by academic exchange and demonstration efforts, Peng said.

The initiative, which was recognized with honors of distinction by UNIVANTS, also resulted in an overall increase in testing at the hospital. Between 2008 and 2024, excluding the pandemic years (2020-2022), total testing volume surged from 41,374 to 283,804.

"The consistent upward trend suggests that the strategy has had a definite impact on syphilis testing rates," Peng said. "The specific reasons can be attributed to a combination of factors, including improved access, enhanced clinical protocols, public health initiatives as well as our care initiative."

Improving syphilis screening strategies

67%: Reduction in the number of visits required for diagnosis, resulting in an average cost savings of RMB 113.7 per outpatient.

14.9%: Percentage of patients who initially screened negative for syphilis who were ultimately diagnosed with the disease through enhanced screening.

RMB 2,100 to RMB 4,300: Healthcare cost savings per patient based on mitigation of disease progression to late-stage syphilis.

ENHANCING SURVIVAL OF HCC TRANSPLANT PATIENTS

Hepatocellular carcinoma (HCC) is the sixth most common cancer worldwide. Liver transplantation currently offers the best prognosis for HCC patients, with a 5-year survival rate exceeding 70% globally using the University of California San Francisco (UCSF) criteria — standard guidelines for determining who qualifies for transplantation.

The problem is that many patients are excluded as transplant candidates due to locally advanced tumors. For these patients, the focus is usually on palliative care. The 3-year survival rate for them without transplantation is 20%–30%.

In 2020, a team from the transplant center at Chang Gung Memorial Hospital in Kaohsiung, Taiwan, developed a new approach to identify more transplant-eligible patients. In addition to using UCSF criteria, the center integrated alpha-fetoprotein (AFP) levels and positron emission tomography (PET) results to create a predictive model for post-transplant recurrence.

Before transplant, the team applied transarterial radioembolization (TARE, Yttrium-90) or proton therapy — two forms of radiation — to patients with locally advanced HCC to reduce the size or extent of their liver tumors (downstage them). After transplant, they used lenvatinib for adjuvant treatment in high-risk recipients.

Among 43 patients treated with these therapies, 24 were successfully downstaged and subsequently received liver transplants. Compared to historical data, these 24 patients demonstrated a decreased recurrence rate (8.3% at 3 years versus 35.2% prior to the initiative) and improved overall survival (85.9% at 3 years versus 69.3%).

"For patients with locally advanced HCC, who were previously considered incurable and ineligible for liver transplantation, we have successfully performed transplants on seven such patients, with only one patient experiencing disease recurrence at median follow-up of 20 months," said Chih-Che Lin, vice superintendent at the hospital. "Our strategy has given previously ineligible patients a chance for a cure, leading to enhanced survival rates and elevating the reputation of our medical team."

Since the hospital implemented the initiative, its use of AFP and PET for screening high-risk liver cancer patients has increased, as has the annual utilization of proton therapy and Y90 treatments. Patients treated with proton therapy increased from 56 patients in 2019 to 141 in 2023. Those treated with Y90 rose from 10 in 2019 to 20 in 2024.

According to Lin, the project — which was recognized with honors of distinction by UNIVANTS — has the potential to be adopted as a national policy, significantly enhancing longevity and reducing mortality rates. Although liver transplant costs $114,404 per patient, the initiative can reduce the amount of money spent on palliative treatments. There are also positive cost effects for the economy overall, Lin noted.

"We have provided previously incurable patients with an opportunity for liver transplantation, achieving an estimated 5-year survival rate of over 80%," he said. "Considering Taiwan's per capita GDP of $32,687, each patient has the potential to generate more than $100,000 in economic value for the country."

The initiative is unique, as Chang Gung Memorial is the only hospital in the world that uses this method to identify high-risk patients and successfully reduce their risk by attempting treatment with protons or TARE. Implementation in other facilities would require moderate effort.

DECREASING LENGTH OF STAY IN THE ED

Numerous factors influence how quickly patients who enter emergency departments (EDs) can be safely discharged or admitted to the hospital, including registration, triage, the availability of rooms or providers, test completion, and a review of results to determine next steps. In general, the longer patients stay in the hospital, the more likely they are to have a poor outcome — which is concerning because many EDs struggle with long lengths of stay (LOS).

In February 2023, Banner Health and Laboratory Sciences in Sun City, Arizona, implemented an initiative to reduce LOS in their ED. A multidisciplinary team collaborated to evaluate current practices, analyze performance data, and identify opportunities for improvement. The team consisted of ED clinicians, quality improvement specialists, laboratory and radiology professionals, and hospital administrators

Enhancing survival of HCC transplant patients

26.9%: Reduction in recurrence of HCC in patients who were successfully downstaged and subsequently received liver transplant.

16.6%: Improvement in 3-year survival for patients with locally advanced HCC who received a liver transplant compared to patients who did not receive a transplant.

$500,000: Economic contribution from six patients who were successfully downgraded to enable successful transplantation.

Decreasing patient length of stay in the emergency department

20.2%: Reduction in length of stay for ED patients over 17 months.

70.4%: Improvement in time from patient registration to when patient is seen by a provider.

47%: Reduction in patient wait time from when the provider has completed their disposition until the time of discharge.

and leaders, according to Teri Dahn, Banner's director of quality improvement. The project focused on two large community hospitals, Banner Boswell Medical Center and Banner Del E. Webb Medical Center.

The hospitals implemented a direct-bedding model featuring a coordinated "swarm team" approach. In other words, rather than waiting to get a traditional triage assessment, each patient would receive immediate access to a phlebotomist, nurse, and provider. In cases where direct bedding was not possible, lab leaders helped create phlebotomy-specific areas within triage, allowing teams to get lab services to patients immediately. This approach enables simultaneous clinical assessment and specimen collection, eliminating sequential delays and accelerating the diagnostic process from the moment of patient arrival, Dahn explained.

"By implementing our ED throughput performance improvement project, we enhanced lab turnaround times through strategic measures," said Hites Patel, MD, medical director of emergency services. "Drawing labs directly in the lobby phlebotomy stations and prioritizing the swift placement of orders enabled timely blood draws and expedited specimen transfers to the lab. This seamless workflow significantly reduced delays, ensuring more efficient patient care and improving overall operational efficiency."

As a result of the initiative, patient LOS in the ED decreased by 20.2% over 17 months. Many factors contributed to this. For example, imaging turnaround time decreased 17.5%, from 160 minutes to 132 minutes. The time from patients' registration to when they were seen by a provider also declined 70.4%, from 27 minutes to 8 minutes, and wait time from when providers completed disposition until patient discharge decreased by 47%, from 41.5 minutes to 22 minutes.

During the 17 months, the number of patients who left the ED without being treated also declined by 65%, from 26 to 9. What's more, there was an 82% increase in point-of-care testing (POCT), from 59 to 323 per month.

While the concept of direct bedding is not new, it had not been applied before at Banner's two large community hospitals, Dahn noted.

"It takes collaboration between departments to direct bed patients consistently," she said. "Also, the addition of dedicated phlebotomy areas for use when direct bedding was not possible due to bed availability was unique to our facilities."

The initiative required moderate effort: Some infrastructure changes were required, including the addition of POCT instruments. Dahn noted the approach of integrating mixed methodologies is highly scalable and is already used for most interdepartmental projects.

REVOLUTIONIZING *H. PYLORI* ERADICATION

Helicobacter pylori (*H. pylori*) is an infectious organism that causes dyspepsia, peptic ulcer disease, and gastric cancer. Almost half of the world's population is estimated to be infected, although many people don't have symptoms. In 2017, the World Health Organization listed *H. pylori* as one of 10 antibiotic-resistant pathogens of concern.

To tackle this infection, a multidisciplinary team at University Hospitals Health System in Cleveland in 2019 developed an innovative and cost-effective molecular susceptibility assay to detect resistance-related mutations in *H. pylori*. The test was incorporated into routine anatomic pathology clinical workflows in 2020, and test reports were generated with personalized treatment recommendations based on genetic markers of resistance.

The team developed a pharmacist-led intervention to ensure molecular-guided treatment was utilized, according to Navid Sadri, MD, PhD, chief of the division of genomic and molecular pathology at the health system. The pharmacist directly messaged endoscopists with molecular results that had treatment recommendations. This intervention reduced the use of ineffective regimens and lowered the rate of no treatment. Once providers were fully educated on how to prescribe treatment in line with the recommended regimens based on test reports, this intervention was no longer needed, Sadri explained.

The initiative significantly improved patient outcomes, with a more-than-17% increase in successful eradication compared to previous empirical treatments. It also resulted in a 4.4-fold increase in success with recommended regimens versus unrecommended treatments.

By avoiding ineffective regimens like clarithromycin triple therapy in high-resistance settings, patients experience fewer treatment failures and complications, Sadri said. The initiative also expands treatment options for those without antimicrobial resistance markers, offering more tolerable and convenient alternatives to standard empiric regimens.

Overall, the intervention — which was recognized with honors

of achievement by UNIVANTS — reduced the proportion of treatments that were expected to be ineffective from 15% to 10% and decreased the rate of no treatment from 12% to 5%.

Using tailored therapy based on resistance markers also prevents use of unnecessary antimicrobial agents, according to Leila Hojat, MD, director of antimicrobial stewardship in the health system.

"Even short courses of therapy using the agents included in the available regimens can be associated with adverse effects, alter the microbiome, and increase the risk of acquired resistance both in the patient and the community," she said. "Thus, using molecular susceptibility testing to identify the most optimal treatment regimen first and avoid subsequent courses has a major impact."

In fact, the initiative reduced clarithromycin resistance by 30% over 4 years by minimizing unnecessary macrolide use.

The approach minimizes the need for costly repeat procedures and extended care resulting from failed therapies, Sadri said. By incorporating cost-effective generic medications into treatment protocols, it also reduces costs for payors and insurance plans, while lessening the burden of managing chronic complications of *H. pylori*, such as peptic ulcer disease and gastric cancer, for patients and providers.

"While the long-term costs of these conditions may not be immediately evident to payors, addressing them is a significant public health priority with practical solutions available to improve healthcare quality and safety today," he said.

The initiative has also improved clinician confidence in choice of eradication therapy, according to Linda Cummings, MD, senior attending physician in gastroenterology.

"This initiative has markedly increased our ability to eradicate *H. pylori* with the first course of treatment, reducing the need for multiple rounds of treatment and the frustrations associated with salvage therapy," she said.

This approach could easily be adopted by other institutions, Sadri said. The testing method was developed using existing next-generation sequencing (NGS) equipment to detect key antibiotic-resistance mutations. It can be adapted by institutions without NGS by using PCR technology or utilizing a reference laboratory for testing.

Revolutionizing H. pylori eradication

30% and 55%: Reduction in rates of inappropriate antibiotic treatment and no antibiotic treatment, respectively.

30%: Reduction in detected clarithromycin resistance over 4 years by minimizing unnecessary macrolide use.

17%: Improvement in eradication success for first-line therapy (from 76% to 93%) through tailored treatment regimens.

Improving testing for CKD in diabetics

53%: Increase in new CKD diagnoses for patients with diabetes and laboratory evidence of CKD in their electronic health record.

7.6%: Increase in use of SGLT2i among people with diabetes and CKD.

32%: Increase in guideline-concordant testing (eGFR and uACR) among people with diabetes.

IMPROVING TESTING FOR CKD IN DIABETICS

Chronic kidney disease (CKD) affects more than 1 in 7 adults in the United States — an estimated 35.5 million people. For Americans with diabetes or high blood pressure, the two most common causes of kidney disease, the risk is even greater. About 1 in 3 people who have diabetes, and 1 in 5 with high blood pressure, also have CKD.

The National Kidney Foundation (NKF) and Sanford Health (Sioux Falls, South Dakota) in 2023 partnered to improve the quality of CKD care among patients with diabetes. An initial data analysis revealed low levels of urine albumin-to-creatinine ratio (uACR) testing, gaps in CKD diagnosis in primary care settings, and limited prescribing of disease-modifying interventions that could slow CKD progression and reduce associated cardiovascular risk, according to Elizabeth Montgomery, national vice president, clinical practice innovation and population health, at NKF.

Albuminuria, which is diagnosed with uACR testing, is often an early indication of kidney disease and may occur before kidney function begins to decline, explained Montgomery, adding that uACR findings are one of the strongest predictors of cardiovascular events and mortality in people with diabetes.

Using NKF recommendations, Sanford developed a system-wide intervention to improve CKD testing and diagnosis and increase the use of sodium-glucose co-transporter-2 inhibitors (SGLT2i). Sanford Health nephrologists helped create the algorithm outlining the care pathway and provided education about CKD.

The intervention included implementing the NKF-recommended

Kidney Profile into the lab and updating relevant electronic health record (EHR) SmartSets to ensure easy access to CKD testing and relevant guideline-directed medical information. It also involved adding CKD testing to the EHR health-maintenance menu, along with embedding other tools and resources.

From the time the program began in 2023 until October 2024, the percentage of people with diabetes receiving guideline-concordant CKD testing, which includes both uACR and estimated glomerular filtration rate (eGFR) tests, rose from 38% of the diabetes population tested to 70%. In addition, the rates of CKD diagnosis among the same patient population with abnormal eGFR and/or uACR values increased from 20% to 73%.

While the rate of SGLT2i utilization among people with diabetes alone remained low, the rate of SGLT2i prescriptions among those with CKD increased from less than 2% to 9.7%. Treatment with SGLT2i is associated with a significant reduction in CKD progression and the rising cardiovascular risk associated with it.

As of October 2024, several thousand new CKD diagnoses were rendered for people with diabetes and laboratory evidence of CKD in their EHR, raising the rate of recognition of CKD from 20% at the program's inception to 73%, said Montgomery.

"Several studies have demonstrated that documentation of CKD in the EHR favorably impacts CKD-related quality of care," she noted. "Guideline-recommended testing for all adults with diabetes will ensure those individuals with proteinuria will be detected early in the course of the disease, offering the opportunity for treatment to reduce albuminuria and its impacts, including cardiovascular disease."

Laboratory intelligence was the foundation of the CKD initiative, said Montgomery. "It identified significant gaps in uACR testing in the institution as well as illuminating that a large population of people with diabetes and laboratory evidence of CKD did not have an accurate diagnosis and appropriate staging of CKD in their health record," she said. "A dramatic increase in uACR testing, coupled with greater awareness of the clinical significance of albuminuria, increased rates of CKD diagnosis."

The initiative, which was recognized with honors of achievement by UNIVANTS, is simple to employ and highly scalable for other institutions, said Montgomery. NFK is currently working with more than 20 other institutions to implement this model. The organization provides guidance on the required data analysis, suggests updates to the lab and EHR systems, and develops tools and resources to support implementation.

"Previously, we had many undiagnosed patients with CKD," she explained. "Identification earlier on in the disease progression helps us to be able to provide the care we need to delay that progression and reduce the associated risk of adverse cardiovascular events. We are very proud of our increase in diagnoses."

MAKING A DIFFERENCE

Each of these initiatives highlights how clinical laboratories are actively involved in multidisciplinary efforts to diagnose and treat health conditions earlier and more effectively, thus potentially reducing mortality.

To learn more about the UNIVANTS of Healthcare Excellence award program, please visit UnivantsHCE.com.

UNIVANTS 2025 teams recognized in this issue

The Fiix project: Reducing anticoagulation variability and adverse patient outcomes through safe and cost-effective factor II and X (Fiix) monitoring in place of conventional PT-INR warfarin monitoring
Landspitali National University Hospital of Iceland
Reykjavik, Iceland

Pall T. Onundarson
Brynja R. Gudmundsdottir
David O. Arnar
Einar S. Bjornsson
Charles W. Francis

Implementation of a comprehensive syphilis screening strategy for cost-effective and timely syphilis management
Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology
Hubei, China

Liming Cheng
Jing Peng
Yong Zhang
Sainan Shu
Huijun Li

Reduced hepatocellular carcinoma recurrence with enhanced 3-year survival for patients post liver transplant
Kaohsiung Chang Gung Memorial Hospital
Kaohsiung, Taiwan

Chih-Che Lin
Jen-Yu Cheng
Hsin-You Ou
Chien-Chin Hsu
Wan-Ting Huang

Improved patient experiences and decreased patient length of stay in the emergency department through a multidisciplinary approach
Banner Health and Laboratory Sciences of Arizona
Sun City, Arizona

Teri Dahn
Brian Thomas
Chris Zufall
Hites Patel
Gordon Weimer

Personalizing *H. pylori* antibiotic therapy for enhanced safety and *H. pylori* eradication
University Hospitals Cleveland
Cleveland, Ohio

Navid Sadri
Linda C. Cummings
Leila S. Hojat
Rachel A. Wells

Enhancing wellness through guideline concordant follow-up and treatment for patients with diabetes and chronic kidney disease
National Kidney Foundation, New York, New York
Sanford Health, Sioux Falls, South Dakota

Christina Lankhorst
Andrew Burgard
Clark Casarella
Rochelle Odenbrett
Elizabeth Montgomery

The Pathway to HCV Elimination: Multidisciplinary Team Effort for Improved Identification, Diagnosis and Treatment of HCV Positive Patients

Musashino Red Cross Hospital

Radiation Reduction: Increased Safety and Improved Length of Stay for Patients with Suspected Mild Traumatic Brain Injury in the Emergency Department

Complejo Hospitalario Universitario Nuestra Señora de Candelaria

TBI Strategies: Expediting Patient Flow and Reducing Length of Stay through Blood Biomarker Guided Management of Patients with Suspected Mild Traumatic Brain Injury

Centre Hospitalier Universitaire of Clermont-Ferrand

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Landspitali National University Hospital of Iceland

Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology

Kaohsiung Chang Gung Memorial Hospital

RECOGNITION OF ACHIEVEMENT

Banner Health and Laboratory Sciences of Arizona

University Hospitals Cleveland

National Kidney Foundation in collaboration with Sanford Health

Abbott

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