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CLN Clinical Laboratory News

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[Assays for acquired thrombocytopenia] include but are not limited to those for platelet number and function, a peripheral blood smear, and immature platelet fraction.
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Federal Insider

ADLM urges funding for key pediatric and diagnostic initiatives in federal budget

The Association for Diagnostics & Laboratory Medicine (ADLM, formerly AACC) has requested federal funding for two important healthcare initiatives in the federal government's fiscal year 2026 budget. ADLM is seeking $10 million for the Centers for Disease Control and Prevention (CDC) to enhance pediatric reference intervals (PRIs), well-known by clinical laboratories as essential for accurate pediatric diagnoses.

Many current PRIs are inadequate, potentially leading to misdiagnoses in children, according to ADLM. Enhanced CDC resources to develop and update PRIs would enable clinicians to deliver age-specific, individualized treatments for all patients. "Many of the existing PRIs fall short," ADLM wrote in a letter to lawmakers. "They frequently miss capturing the full spectrum of biological changes in children as they grow, leading to potential misdiagnoses or misguided treatment protocols. Investing in this area means prioritizing an accurate, evidence-based approach to pediatric healthcare."

ADLM also is requesting $7.2 million for CDC's clinical laboratory test standardization work. Assay standardization and harmonization can prevent discrepancies between test results that should be equivalent, ensuring that clinicians can interpret patient results consistently, regardless of location or instrumentation. In the letter, ADLM emphasized that bipartisan support reflects the importance of this work.

ADLM URGES CMS TO FIX LAB FEE CUTS

The Association for Diagnostics & Laboratory Medicine (ADLM, formerly AACC) wrote to the Centers for Medicare and Medicaid Services (CMS) to express strong concerns over proposed cuts to Medicare payments for clinical laboratory tests. The letter to CMS Administrator Chiquita Brooks-LaSure underscored the potential negative impacts on patient access and laboratory operations of further cuts to reimbursement.

Congress has acted to delay implementation of the CMS cuts — for now. Lawmakers passed a short-term Continuing Resolution to keep the government funded through December 20 that included a 1-year delay in the cuts. This marks the sixth consecutive year that Congress has postponed Protecting Access to Medicare Act (PAMA) cuts.

CMS's proposed rule would have reduced payments by 15% starting January 1, 2025, as part of ongoing adjustments mandated by PAMA. ADLM argues that the current data collection process, which heavily weights the pricing from large commercial laboratories, does not accurately represent the broader laboratory field, including hospital laboratories, academic medical centers, and others.

ADLM has supported the Saving Access to Laboratory Services Act (SALSA) to ensure a fair data collection process and stabilize payment rates. ADLM is calling for collaboration with CMS and legislators to implement these reforms, emphasizing the critical role of laboratories in healthcare delivery.

LAB DATA EXCHANGE IN FOCUS IN PROPOSED RULE FROM OFFICE OF THE NATIONAL COORDINATOR

The Association for Diagnostics & Laboratory Medicine (ADLM, formerly AACC) recently submitted comments on the proposed rule on healthcare information interoperability from the Office of the National Coordinator (ONC), emphasizing that interoperability is vital for improving patient care, reducing costs, and enhancing public health through laboratory medicine.

ADLM supports the integration of the United States Core Data for Interoperability (USCDI) Version 4 but is advocating for ONC to add more data elements to improve laboratory data exchange. These include device and test kit identifiers to help healthcare providers and public health officials to trace specific test kits and devices; specimen collection date/time for interpreting time-sensitive tests and tracking clinical progression; and test performed date/time to enhance quality management and monitoring for potential device defects. ADLM also underscored the need for robust but clear guidelines around information blocking.

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Bench Matters

What sources of glucose should be used for an oral glucose tolerance test?

William E. Winter, MD

If a patient presents with clinical signs of diabetes mellitus (DM), such as polyuria, polydipsia, or unintended weight loss, the diagnosis of DM is confirmed once hyperglycemia or a diabetic crisis (e.g., diabetic ketoacidosis or hyperglycemic hyperosmolar state) is confirmed. In symptomatic patients, hyperglycemia is defined as a random plasma glucose (PG) of ≥200 mg/dL, a fasting PG of ≥126 mg/dL, a 2-hour PG during a 75-g oral glucose tolerance test (OGTT) of ≥200 mg/dL, or a hemoglobin A1c level of ≥6.5%.

In asymptomatic patients, DM is diagnosed when hyperglycemia is confirmed using two different tests on the same day or on two different days. The criteria for defining hyperglycemia are the same as for symptomatic patients, except that random PG levels are not used for asymptomatic individuals.

In individuals who are not pregnant, the OGTT is performed after an overnight fast. A fasting plasma glucose (FPG) sample is obtained, followed by ingestion of 75 grams of glucose in ≥300 mL of water over no more than 5 minutes. Two hours after beginning the glucose challenge, the 2-hour PG sample is collected. Children receive 1.75 grams of glucose per kilogram, up to a maximum of 75 grams.

During the test, participants should not smoke, eat, or engage in physical activity. Morning medications should be withheld until the test is completed. The patient should be in stable health, as recent illness, stress, hospitalization, or surgery may cause falsely abnormal results. The OGTT is rarely used to screen for type 2 DM unless the patient has a hemoglobinopathy or shortened red blood cell survival. Most commonly, screening for type 2 DM is performed using hemoglobin A1c.

If DM is diagnosed in the first trimester of pregnancy, it is considered preexisting DM (typically type 2 DM). The diagnosis of DM in the second or third trimesters [gestational diabetes mellitus (GDM)] is approached in several ways. Screening for GDM is recommended between 24 and 28 weeks of gestation. Traditionally, a 1-hour PG is measured following a 50-gram oral glucose challenge. If the 1-hour PG is ≥130 mg/dL or ≥140 mg/dL, depending on the physician's choice, a 100-gram, 3-hour, four-point OGTT is performed. For the 50-gram screening test, the patient need not be fasting.

For the 3-hour OGTT, GDM is diagnosed if any two of the following Carpenter-Coustan cut points are met or exceeded: fasting, 95 mg/dL; 1-hour, 180 mg/dL;

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2-hour, 155 mg/dL; or 3-hour, 140 mg/dL. Alternatively (with no 50-gram screening test), a 75-gram, 2-hour, three-point OGTT can be performed, with GDM diagnosed if any one of the following thresholds are met or exceeded: fasting 92 mg/dL, 1-hour 180 mg/dL, or 2-hour 153 mg/dL. Hemoglobin A1c is not used to screen for GDM.

CHALLENGES WITH REPRODUCIBILITY AND STANDARDIZATION

Classifying patients as normoglycemic, prediabetic, or hyperglycemic using the OGTT has significant variability (*1-5*). Given this, it is critical for laboratorians conducting OGTTs to standardize the procedure.

One ongoing debate surrounds the type of sugar that should be used in the test. The only acceptable form of glucose for an OGTT is glucose diluted in water, with a maximum concentration of ~0.33 g/mL. Various commercial glucose beverages, often called "glucolas," are available in 50 g, 75 g, and 100 g serving sizes.

Unfortunately, many patients, particularly pregnant patients, find glucola beverages nauseating. Consequently, some researchers have explored alternative glucose sources, such as jellybeans or licorice. However, the sugar composition (e.g., glucose, fructose, sucrose, or lactose) and sizes of candies vary widely, making reproducibility unacceptable. One small study showed that jellybeans had lower sensitivity than traditional glucose challenges (*6*). Similarly, in older studies, jellybeans also proved less sensitive (*7*). In two separate studies with 20 pregnant women each, Racusin et al. found that licorice was an acceptable alternative to glucola in GDM testing (*8*, *9*). However, more data is needed before nonglucola sugar sources can be justified.

Patients' experience with glucolas can be improved by chilling the beverage, diluting it, or sipping it slowly over 5 minutes.

MEDICO-LEGAL IMPLICATIONS AND SOLUTIONS

Using unvalidated sources of glucose for screening presents significant medico-legal risks. If candy is used and a false-negative result occurs, delaying the diagnosis of GDM, it would be difficult to defend the use of candy as an appropriate diagnostic tool. The risk of missing a diagnosis necessitates validated and reliable glucose sources for testing.

Some patients express concerns about dyes and artificial flavors in glucola beverages. To address these concerns, dye- and flavor-free options such as Fresh Test are available (thefreshtest.com). However, before using more expensive alternatives, patients' experience with standard glucolas beverages can be improved by chilling the beverage, diluting it, or sipping it slowly over 5 minutes—the maximum time allowed for consuming the glucose beverage.

In conclusion, glucose-containing beverages (such as glucola or Fresh Test) are the only suitable glucose challenges for an OGTT. Although the OGTT is far from perfect, it remains a standard diagnostic tool requiring careful preanalytical performance.

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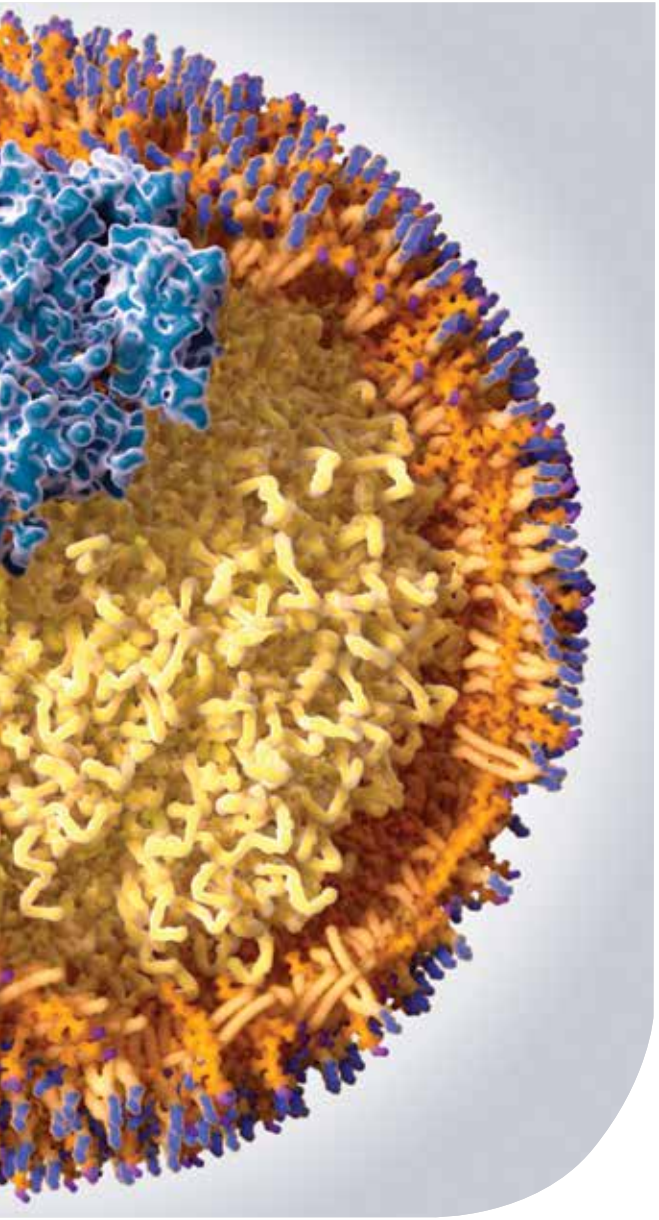
The Sample



Quantitative clinical chemistry proteomics deployed for lipid panel

A recent study proves the feasibility of high-throughput liquid chromatography-tandem mass spectrometry (LC-MS/MS) applications in a large clinical trial on cardiac risk called ODYSSEY OUTCOMES (J Appl Lab Med 2024; doi: 10.1093/jalm/jfae092).

The current lipid panel — including low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, total cholesterol, and triglycerides — lacks the molecular definition to address the residual risk of major adverse cardiovascular events. Apolipoproteins, the functional proteins of lipid metabolism, are potential candidates to fulfill this unmet clinical need. They are molecularly defined and can be measured directly with LC-MS/MS.

To evaluate the clinical performance and effectiveness of a multiplex apolipoprotein (Apo) panel in the context of precision diagnostics, researchers used quantitative clinical chemistry proteomics (qCCP) to measure ODYSSEY OUTCOMES trial patients who had recent acute coronary syndrome. This study is the first qCCP trial at this scale performed in a diagnostic clinical chemistry laboratory to meet test process requirements and predefined analytical performance criteria for clinical medical tests.

The researchers measured serum apolipoproteins from 23,376 samples with a laboratory-developed multiplex apolipoprotein A (Apo A) test on four Agilent LC-MS/MS systems. They designed a fit-for-purpose process with tailored additions that enhanced the accredited laboratory infrastructure and the total testing process. Quality assurance was organized in three steps: system suitability testing, internal quality control evaluation with adjusted Westgard rules to fit a multiplex test, and interpeptide agreement analysis. Data were semiautomatically evaluated with a custom R script.

The researchers performed LC-MS/MS analyses with the following between-run coefficients of variation: for Apo-A, 6.2%; Apo A-I, 2.3%; Apo A-II, 2.1%; Apo A-IV, 2.9%; Apo B, 1.9%; Apo C-I, 3.3%; Apo C-II, 3.3%; Apo C-III, 2.7%; and Apo E, 3.3%. The average interpeptide agreement Pearson r was 0.981.

These results bring the field a step closer to cardiovascular precision diagnostics, according to researchers. They add that having both a routine general clinical chemistry laboratory and research laboratory facilities within the same department was essential for the study's successful execution.

STUDY MAKES CASE FOR UNIVERSAL GENETIC TESTING IN NEW BREAST CANCER PATIENTS

Universal genetic testing identifies actionable germline pathogenic breast cancer variants in more than 1 in 5 diagnosed patients, a recent study found (JAMA Open 2024; doi:10.1001/jamanetworkopen.2024.31427).

About 5–10% of breast cancers are associated with an inherited germline pathogenic or likely pathogenic variant (GPV) in a breast cancer susceptibility gene, a situation that could affect therapy recommendations. However, traditional genetic testing criteria miss a meaningful proportion of these cases.

In a cross-sectional study, researchers aimed to evaluate the prevalence and pathological

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association of GPVs in two groups of breast cancer susceptibility genes (BCSGs) in an ethnically diverse cohort of women with newly diagnosed breast cancer.

The researchers offered genetic counseling to eligible participants with a first diagnosis of invasive breast cancer, including a panel with *BRCA1*, *BRCA2*, and *PALB2* (*B1B2P2*), and an optional secondary panel of 14 additional BCSGs. Eligibility criteria included being 18 years of age or older and having a diagnosis of a first primary invasive breast cancer not more than 6 months before the time of referral to the study.

Of 1,017 referred patients, the researchers found 805 eligible patients. Of these, 90.6% consented to testing. Almost two-thirds were of European ancestry. The researchers found 54 GPVs in 53 patients (7.3%), including 39 patients (5.3%) with *B1B2P2*. They also found 15 patients (2.1%) with six of the 14 secondary panel *BCSGs (ATM*, *BARD1*, *BRIP1*, *CHEK2*, *RAD51D*, and *STK11*). On multivariable analysis, clinical factors independently associated with B1B2P2-positive status were being younger than 40 (odds ratio [OR], 6.83; 95% CI, 2.22–20.90), triple-negative breast cancer (OR, 3.19; 95% CI, 1.20–8.43), high-grade disease (OR, 1.68; 95% CI, 1.05–2.70), and family history of ovarian cancer (OR, 9.75; 95% CI, 2.65–35.85). Of 39 *B1B2P2*-positive patients, 13 (33.3%) were eligible for poly (adenosine diphosphate-ribose) polymerase (PARP) inhibitors.

Universal genetic testing identifies actionable germline pathogenic breast cancer variants in more than 1 in 5 diagnosed patients.

The researchers wrote that evidence from this and other studies allows them to offer mainstream, oncology-led genetic testing to all new invasive breast cancer patients under age 50, those with TNBC and/or bilateral breast cancer, and those potentially eligible for PARP inhibitors.

MOTHERS' HCV INFECTIONS LINKED TO NICU STAY

Maternal hepatitis C virus (HCV) infection is associated with a twofold increase in the odds of neonatal intensive care unit (NICU) admission and a nearly threefold increase in the odds of birth weight below the 5th percentile (Obstet Gynecol 2024; DOI: 10.1097/AOG.0000000000005703).

The researchers evaluated the risk of adverse maternal and neonatal outcomes associated with pregnancies complicated by HCV in a secondary analysis of a multicenter prospective cohort study of HCV infections in pregnancy.

The researchers screened participants for HCV infections with serum antibody tests. At enrollment, they prospectively matched each participant with a positive result with up to two individuals with negative HCV results, by gestational age. Maternal outcomes included gestational diabetes, abruption, preeclampsia or gestational hypertension, cholestasis, and preterm delivery. Neonatal outcomes included jaundice, NICU admission, small-for-gestational-age (SGA) birth weight, and neonatal infection. Infections were either sepsis or pneumonia. The researchers adjusted models for maternal age, body mass index, injection drug use, and maternal comorbidities.

The researchers prospectively matched 249 pregnant women in the case group with 486 individuals in the control group. The groups had significant demographic differences, including race, socioeconomic markers, education, insurance status, and drug and tobacco use, but the frequencies of gestational diabetes, preeclampsia, and abruption in the mother were similar in both groups. Preterm birth was also similar between the two groups.

However, neonates born to case-group mothers were more likely to be admitted to the NICU, with 45.1% of case-group babies going there, compared with 19% in the control group. Case-group babies also were more likely to have SGA birth weights below the 5th percentile, with 6.1% of case-group babies in this category, versus 3.1% in the control group. The researchers saw no increased odds of jaundice or neonatal infection.

Predicting RISK for preeclampsia

The American College of Obstetricians and Gynecologists recently responded to the Food and Drug Administration's marketing authorization of an sFlt-1:PlGF ratio test. This test could make it easier to determine which pregnant patients will not go on to develop preeclampsia — and to focus resources on those who will.

BY GRACE BROWNE

Preeclampsia is a serious hypertensive disorder in pregnancy that affects an estimated 3.4% of pregnant individuals in the United States. It's one of the leading causes of maternal and neonatal morbidity and mortality — the cause of about 14% of deaths in pregnant patients and between 10% and 25% of perinatal deaths. Although the underlying cause is still poorly understood, it's thought to potentially arise because of the placenta not developing properly. Left untreated, the patient can die.

Despite the danger of the condition, determining who is at risk of developing a severe form of preeclampsia has historically proven tricky. The traditional method involves testing a patient for high blood pressure, checking urine protein levels, and looking for neurological problems or signs of kidney dysfunction. "That paradigm has existed for the last hundred years," said Ananth Karumanchi, MD, professor of medicine at Cedars-Sinai Medical Center. "The problem is that those are fairly nonspecific." Headaches could be explained away by migraine disorder; high blood pressure could be from kidney disease.

The broadness of the clinical criteria means that some cases may be classified as preeclampsia unnecessarily. "It is clear that we need additional methods of prevention, monitoring, and treatment for patients experiencing serious hypertensive disorders like preeclampsia," said Christopher Zahn, MD, chief of clinical practice and health equity and quality at the American College of Obstetricians and Gynecologists (ACOG).

Now, guidelines on how to use a new blood test that aims to help streamline the clinical decision-making process have been published by the organization; in June 2024, ACOG released a new clinical practice update on sFlt-1:PlGF ratio testing for preeclampsia.

According to clinical research outside of ACOG's guidance, 9 times out of 10, the test can correctly determine which pregnant individuals hospitalized for hypertensive disorders are at risk for progression to a severe form of preeclampsia. A positive result may indicate that severe preeclampsia could develop within the next 2 weeks, and that those patients need to be monitored closely in case their babies need to be delivered early. Those who test negative can be expectantly managed, which means the pregnancy can be prolonged safely and the baby delivered at a later point in pregnancy when the complications related to prematurity are lower. Altogether, this means that use of the test could enable hospitals to better prioritize treatment for those most in need.

However, some laboratory medicine experts still harbor doubts about the clinical utility of sFlt-1:PlGF ratio testing, and challenges remain that must be overcome before the test can be widely implemented across the U.S.

IS IT REALLY READY FOR PRIME TIME?

The biomarker assay works by measuring the ratio of two placental proteins in maternal serum: soluble fms-like tyrosine kinase-1 (sFlt-1) and placental growth factor (PlGF). This is based on the idea that, when placentation is abnormal, levels of sFlt-1 and PlGF are altered.

In 2023, Thermo Fisher Scientific became the first company to receive Food and Drug Administration (FDA) marketing approval for the test in the U.S. ACOG's new guidelines recommend the use of the ratio be limited only to patients who meet the inclusion criteria that were described in the PRAECIS trial; that is, the test should not be used in asymptomatic, nonhospitalized individuals at less than 23 weeks or more than 35 weeks of gestation and in postpartum individuals. The PRAECIS clinical trial, for which Karumanchi was a co-author, included more than 1,000 pregnant women who were between 23 and 35 weeks along at 18 U.S. medical centers from 2019 to 2021. The aim was to identify and validate a sFlt-1:PlGF ratio that could be used to stratify the short-term risk of developing preeclampsia with severe features in pregnant individuals with hypertension who were hospitalized in late pregnancy.

Not everyone is convinced of the efficacy and utility of the test, however. For Ann Gronowski, PhD, a professor of pathology and immunology, and obstetrics and gynecology at Washington University School of Medicine in St. Louis, the test doesn't have the positive predictive value — the measure of how often someone

Although additional methods are needed for diagnosing and treating severe preeclampsia, not everyone is convinced of the efficacy of the sFlt-1:PlGF ratio.

who tests positive for disease actually has disease — that it needs to be useful. "There's insufficient data to recommend management strategies after a positive or negative," she said. "So why do we do a test where it's not going to change our management?"

Indeed, Zahn said that the organization recommends that "the sFlT-1:PlGF ratio alone should not replace current clinical criteria for diagnosing or excluding a diagnosis of preeclampsia with severe features." Instead, it should serve as a complementary risk-stratification test that will add to the diagnostic work-up.

For other lab professionals, Gronowski urges her peers to exercise caution. "I certainly hope that other laboratorians have the same reservations, because I feel like it is our job to think critically about test utility." What Gronowski would like to see are studies that investigate how the use of the test affects outcomes. She admits that in certain populations, it could turn out to be really high-performing. "Then the proof will be in the pudding," she said. "In my personal opinion, I don't think this is ready for prime time, but I would be delighted if I'm proven wrong."

"I would use caution and think about, for this population, what do we need? What is the ideal test? What kind of positive predictive value do we need? And I would argue that I don't think this test is delivering the positive predictive value that we need for the population in which its use is currently recommended," she said.

Also, there is still no effective treatment for preeclampsia other than delivering the baby. However, Karumanchi said that this test may help to develop therapeutics down the line by enabling clinical trials to focus on patients at the greatest risk for adverse outcomes. Gronowski agreed that it perhaps "could be used to stratify patients when we're going to test treatments for preeclampsia."

EXPANDING THE TEST'S USAGE

The need for the test — and better therapeutic interventions — is reinforced by the fact that rates of preterm birth are on the rise in the U.S. Preterm birth can have long-term negative developmental effects for the baby, and experts believe preeclampsia is one of many factors contributing to its uptick. Driven by a rise in obesity, the incidence of preeclampsia almost doubled in the U.S. from 2007 to 2019. Even more concerning is the fact that preeclampsia disproportionately affects Black pregnant patients and is the top cause of maternal mortality among Black people, who are three times more likely to die from pregnancy-related causes than White people.

The sFlT-1:PlGF ratio could potentially help with all of this, but despite having FDA approval for over a year, the test is still not as widely used as it could be, Karumanchi said. This may be because the instrument that the FDA-approved test runs on is not available in all hospitals. The assay is designed to run on Thermo Fisher's Brahms Kryptor Compact Plus clinical analyzer; however, many labs do not possess this technology as of yet. In Karumanchi's hospital, where they do have this platform, they can turn around the test results in an hour. However, some hospitals are sending the test to a reference lab, which takes as long as 48 hours to get a result. "It might still be useful in many of the cases, but if a patient was really sick, 48 hours is too late," he said.

It's worth noting that sFlT-1:PlGF ratio testing is already widely used in the U.K. and Europe, and has been for many years. Karumanchi said that the U.S. should look across the Atlantic to see how the use of the test has evolved in the past decade or so.

Sofia Cerdeira, MD, PhD, an academic clinical lecturer in women's health at the University of Oxford who researches preeclampsia, has seen firsthand how the test is being used in the U.K. and Europe. She thinks the test is a "game-changer" for preeclampsia, though she does echo others' words of caution that it is important that clinical decisions aren't based on the test alone. Rather, the test's results should be incorporated with the rest of the patient's clinical signs and symptoms.

But in her opinion, it's the negative predictive value — the likelihood that a person who has a negative test result does not have preeclampsia — that is where the real benefit lies. "For the first time, we have a biomarker that can help you to tell who is not going to develop the disease with a negative predictive value of 99.3%." That means you can reassure that patient in the next week with over 99% accuracy they are not going to develop the condition. "We have witnessed an exponential adoption of this test in maternity centers and most of our clinicians are now familiar with its use."

Grace Browne is a freelance journalist who lives in London. She currently has a fellowship funded by the International Center for Journalists through the Health Innovation call.

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Bringing PERSO

Validated, risk-based equations allow clinicians to fine-tune their approach to chronic kidney disease, and ensure patients get the right care at the right time. Clinical laboratories can usher in this new era.

NALIZED medicine to patients with CKD

BY HEBA ELGUBTAN, BHSC, AND NAVDEEP TANGRI, MD, PHD, FRCPC

More than 1 in 3 U.S. adults (approximately 86 million people) are at risk for developing chronic kidney disease (CKD), and more than 1 in 7 (37 milllion) already have it (*1*). Yet many of these individuals have no idea they have the condition. Often dubbed a "silent killer" due to a lack of physical symptoms until later stages, CKD can lurk undetected — and thus untreated — for years. In fact, roughly one-third of patients with severe CKD aren't aware that anything is wrong.

Fortunately, we have the tools to change that. Clinical guidelines now recommend using validated, lab-based equations that predict kidney-failure risk as an essential part of CKD management. While most patients with CKD have early-to-mid stages (G1–G3), a minority will progress to kidney failure. Having a way to assess each patient's risk of disease progression enables clinicians to make better treatment decisions and engage in informed discussions with patients and their families.

As the developers of the kidney-failure risk equation (KFRE) (*2*,*3*), a highly accurate, lab-based equation for predicting kidney-failure risk in patients with CKD stages G3-G5, we make the case in this article for taking an individualized approach to risk assessment when evaluating and managing patients with CKD.

This strategy, which builds on the current CKD risk-staging system (heatmap) to provide more personalized information, was recently emphasized in the 2024 guidelines from KDIGO (Kidney Disease: Improving Global Outcomes). What's more, the integration of risk equations into labs' automated reporting systems has the potential to usher in a new era in CKD management, with laboratory professionals leading the way toward more precise clinical decision support.

DIAGNOSIS AND DEFINITION OF CKD

Currently, the diagnosis of CKD is based on estimated glomerular filtration rate (eGFR) using markers such as serum creatinine and the presence of albumin in the urine (*4*). Both serum creatinine and the urine albumin-to-creatinine ratio are required to diagnose, stage, and prognosticate CKD (*4*).

Current guidelines from the National Kidney Foundation's Kidney Outcomes Quality Initiative (KDOQI) recommend using the race-free Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI-2021) equation (*5*) to calculate eGFR (*6*). (The previous use of a race multiplier — which required inputting whether a patient was African-American — in eGFR equations came under scrutiny for its lack of recognition that race is a social construct rather than a biological one, prompting the recent development of a race-free equation.)

When it comes to using eGFR to help define CKD, most nephrologists rely on clinical practice guidelines from the global nonprofit organization KDIGO,

Figure 1. CKD Heatmap: Prognosis of CKD by GFR and albuminuria category. Adapted from KDIGO 2012: Clinical Practice Guidelines for the Evaluation and Management of CKD (*8*)
Notes: Green: low risk; yellow: moderately increased risk; orange: high risk; red: very high risk.

			Albuminuria (mg/g)		
			A1 <30	**A2** 30 - 300	**A3** >300
Estimated Glomerular Filtration Rate (eGFR) (ml/min/1.73 m²)			Normally to mildly increased	Moderately increased	Severely increased
G1	≥ 90	Normal or high			
G2	60 - 89	Mildly decreased			
G3a	45 - 59	Mildly to moderately decreased			
G3b	30 - 44	Moderately to severely decreased			
G4	15 - 29	Severly decreased			
G5	< 15	Kidney failure			

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which formally defines CKD as the presence of abnormalities of kidney structure or function and a reported eGFR <60 mL/min/1.73m^2 for 3 months or more, irrespective of cause (*7*). Abnormality in kidney function can be determined by the presence of albuminuria, which is defined as an albumin-to-creatinine ratio (ACR) in urine of ≥30mg/g (≥3 mg/mmol)(*7*).

Using eGFR and albuminuria values, the KDIGO guidelines classify CKD into five eGFR-based stages (G1-G5) and three albuminuria-based stages (A1-A3) (*8*).

Risk for adverse clinical outcomes (kidney failure, all-cause mortality, cardiovascular events, and acute kidney injury) can then be visualized as a grid of colored squares across the two axis variables (eGFR and albuminaria), forming a heatmap. Green squares indicate low risk; yellow and orange show intermediate and high risk, respectively; and red reflects very high risk (Figure 1) (*8*). The diagonal distribution of risk reflects the equal importance of both low eGFR and high levels of albuminuria in increasing a person's likelihood for disease progression.

INDIVIDUALIZED RISK PREDICTION AND THE KIDNEY-FAILURE RISK EQUATION

While the heatmap is a useful tool, it's important to remember that the squares reflect only relative risk. In other words, patients in red, orange, or yellow squares of the heatmap have higher risks of kidney failure on average than those in green squares, but there is still considerable variability in the risk of CKD progression within each color group. Two patients in the same square can have up to a 40-fold difference in their 5-year risk of kidney failure, with Patient A having a 1-2% risk and Patient B having a risk up to 80% (*7*).

This is where individualized risk assessment can make a difference. Accurate, validated risk equations address this variability by providing a more nuanced risk assessment for each patient.

One such equation is the KFRE, a predictive model used in outpatient clinical settings to assess the 2- and 5-year risk of kidney failure in patients with stages G3-G5 CKD. The KFRE is the most widely used prediction model in clinical practice for patients with kidney disease (*2,3*).

We developed this equation in 2011 and subsequently validated it in 2016 in more than 30 countries and 700,000 individuals (*9*). Since then, the KFRE has been proven accurate across diverse populations and validated in more than 50 countries.

The probability of kidney failure in the next five years for patients with CKD Stages G3-G5 can be calculated using one of two KFREs (*2,3*): the 4-variable or 8-variable KFRE model. The 4-variable model uses age, sex, eGFR, and urine ACR to calculate kidney failure risk (*2,3*), while an 8-variable model includes additional laboratory values of serum albumin, bicarbonate, calcium, and phosphorus (*2,3*).

Because the performance of the two models is similar in most healthcare settings, the simpler 4-variable model is preferred for broad implementation (*10*).

In 2021, the United Kingdom's National Institute for Health and Care Excellence (NICE) updated its guidelines to incorporate the KFRE in their referral criteria for

Clinical laboratories can drive meaningful change by automating reporting of the KFRE.

patients with CKD (*11*). These guidelines outline key thresholds to guide clinical decisions based on the patient's calculated risk score (*11*). NICE recommends that adults with CKD be referred to a nephrologist if their 5-year kidney failure risk is greater than 5%, as measured using the 4-variable KFRE (*11*).

These thresholds also are used in clinical practice guidelines and pathways in Canada and several other health jurisdictions.

UPDATED KDIGO CKD CLINICAL PRACTICE GUIDELINES

KDIGO's 2024 guidelines strongly emphasize taking a personalized approach to CKD management that includes estimating risk using a validated prediction equation like the KFRE for all patients with CKD Stages G3–G5 (1A Recommendation) (*7*).

In addition, the guidelines endorse a risk-based approach to care and clinical decision-making that complements the eGFR-based strategy and favors:

- Transitioning patients to nephrology from primary care at kidney failure risks of 3–5% vs. eGFRs of 30-60
- Moving to interdisciplinary CKD care at 2-year risks of 10%, and
- Planning for hemodialysis access when 2-year risks exceed 40% (*7*).

The KDIGO guidelines represent a paradigm shift in CKD care. Rather than basing clinical decisions solely on eGFR values, clinicians can use a patient's individual risk of progression to guide their approach around nephrology care or kidney replacement therapy (dialysis or transplant). KDIGO strongly recommends that laboratory services providers, primary care providers, and electronic health records manufacturers integrate validated risk equations like the KFRE to facilitate risk-based care for patients (*7*).

AUTOMATED REPORTING BY CLINICAL LABORATORIES

We believe that clinical laboratories can and should automatically report KFRE scores for patients with eGFR values of ≤60 mL/min/1.73m^2 and available albuminuria data. There are many benefits to doing this, including:

Overcoming EMR Challenges. Automated reporting of the KFRE by clinical laboratories serves as a potential solution to some of the challenges associated with varying electronic medical record (EMR) systems and software. For example, the KFRE is built into the base version of the EPIC Electronic Health Record (EHR) (*12*), but the equation is not accessible to all EPIC users, since some may be using older versions of the software.

Providing Clear Prognostic Information to Primary Care Providers. Primary care providers, who manage the majority of patients with CKD, are unlikely to keep pace with the latest clinical practice guidelines in every therapeutic area (*13*). Automated reporting would do this work for them. Tools like the KFRE display show the risk of CKD progression for all patients with CKD, irrespective of their care provider. This would eliminate extra steps towards manual calculation, since prediction models and their inputs/outputs often reside in a separate screen or view.

Offering a Leadership Role for Clinical Laboratories. Clinical laboratories already play a pivotal role in CKD care, given that the disease's diagnosis, prognosis, and complications are largely defined using lab criteria. Laboratory professionals routinely optimize CKD care by reporting eGFR and standardizing serum creatinine and urine albumin measurements. In addition, as recently as 2021, they took the lead in updating the eGFR equations to incorporate race-free methods (*5*). Now, clinical

laboratories have another opportunity to drive meaningful change by automating reporting of the KFRE, reinforcing their role as integral partners in CKD care delivery.

FUTURE CONSIDERATIONS

Although the KFRE has a wide evidence base and is strongly recommended for use in patients with CKD Stages G3-G5, the guidelines acknowledge the need for validated equations to identify patients in earlier stages of disease who are at risk for progression.

We and others have developed models that enable early intervention, including models that incorporate biomarkers (*14*), clinical and laboratory data (*15*), as well as those that rely solely on data collected in routine lab settings (*16*) (Table 1). As evidence builds for their use, labs can also consider offering these models to patients and providers, further supporting personalized care at all stages of CKD.

Although research is ongoing, it's clear that both CKD patients and practitioners can benefit from better understanding individual risk of disease progression. Automated reporting of risk will usher in a new era in CKD management, where implementation will be aligned with evidence, and the clinical laboratory will play a key part in getting us there.

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Table 1. Summary of externally validated risk-prediction models for predicting kidney failure by CKD stage. Adapted from KDIGO 2024: Clinical Practice Guidelines for the Evaluation and Management of CKD (7). BP, blood pressure; CBC, complete blood count; CKD, chronic kidney disease; CKD-PC, Chronic Kidney Disease Prognosis Consortium; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; HbA1c, hemoglobin A1c (glycated hemoglobin); KFRE, Kidney Failure Risk Equation; KIM-1, kidney injury molecule 1; TNFR1, tumor necrosis factor receptor 1; TNFR2, tumor necrosis factor receptor 2; UACR, urine albumin-to-creatinine ratio

CKD Stage	Model Name	Model Inputs	Model Outcome	Discrimination Accuracy (AUC)
G1 G2	Klinrisk (*16*)	20 variables derived from CBC, chemistry panel, and urine	2- and 5-year probability of a 40% decline in eGFR	0.84 – 0.88
G3a G3b	CKD-PC Progression (*15*)	16 variables — demography eGFR, UACR, CVD risk factors, medications, other lab values	2- to 3-year probability of ≥ 40% decline in eGFR or kidney failure	0.74 – 0.77
	KidneyIntelx (*14*)	3 proprietary biomarkers — TNFR1 TNFR2, KIM-1 + eGFR, UACR, HbA1c, and BP	5-year probability of kidney failure, or ≥ 40% decline in eGFR in patients with type II diabetes mellitus	0.77
G3a G3b G4 G5	KFRE (*2*)	Age, Sex, eGFR, UACR (4-varaible model) + albumin, bicarbonate, calcium, and phosphate (8-variable model)	2- and 5-year probability of kidney failure for a patient with CKD stage G3-G5	0.88 – 0.91

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Secondary data from EHR improves celiac disease care

By Deborah Levenson

Clinical laboratories can leverage secondary data — information collected for clinical care but useful for other purposes — to improve healthcare for a variety of patient populations.

The electronic health record (EHR) is full of these real-world data, and in recent years has become more accessible through data warehouses and related tools. "These data can be useful for understanding population health and the impact of laboratory testing at the population level," said Lee F. Schroeder, MD, PhD, associate director in the division of clinical pathology at the University of Michigan.

"For example, the data can be used to evaluate how labs affect the cascade of care and demonstrate different diagnostic strategies' impact on outcomes that are important to health systems, like identifying patients that would truly benefit from referrals, and in the process, reducing scheduling delays for specialty care," Schroeder said. "Laboratory data can also be leveraged to understand gaps in health services delivery in different patient groups."

Schroeder gave one of two presentations that demonstrated the usefulness of secondary data from EHRs at the Association for Diagnostics & Laboratory Medicine (ADLM, formerly AACC) July 2024 Data Science Summit. The event, held after ADLM's annual meeting, showcased labs' use of data to improve patient care, a strategy that is becoming ever more common and important in medicine.

Schroeder's presentation showed how a celiac disease testing algorithm helped reduce unnecessary biopsies by improving how physicians ordered tests early in the diagnostic process. The second talk demonstrated how linking geospatial tools to EHR data can find inequities in kidney health screening among people with diabetes.

Improving the value of referrals for biopsy

As is the case in most specialties, gastroenterology patients often are subject to scheduling delays and many wait months for appointments. "Any change in the diagnostic process that could reduce low-value referrals could greatly benefit patient care," Schroeder said.

In an interview, Schroeder explained how he used about 10 years' worth of EHR data to study a University of Michigan celiac disease testing algorithm designed to identify the subset of tests that make the most sense for each patient, thus optimizing sensitivity and specificity.

The algorithm identifies the patient's immunoglobulin A (IgA) levels and then reflexes to either IgA, immunoglobulin G (IgG), or both; versions of antitissue transglutaminase and antideaminated gliadin antibodies; and possibly antiendomysial antibodies. "What you want to do is identify which tests are going to pay off, and which may lead to unnecessary procedures, and just run those that will benefit each patient," Schroeder said. As celiac screening tests lead directly to referrals for biopsy, it is particularly important to reduce false negatives as well as false positives, he added.

As part of his unpublished study, Schroeder filtered data for first-time celiac screening events using ICD codes from the EHR, labeling each screening event as either appropriate (consistent with the algorithm) or inappropriate and collected biopsy results. He found that when the study started in 2014, the proportion of appropriate orders consistent with the algorithm started out low, less than 10%. After an algorithm name change to make its purpose more obvious, the percentage of appropriate orders increased to about 60% — and was hovering at about 80% at the study's end in 2023.

Schroeder also found that biopsy rate for patients whose clinicians ordered appropriately was 14.9%, versus 18.7% for clinicians who did not order tests consistent with the algorithm.

When Schroeder looked at changes in biopsy rate by physician specialty over the course of the study, he found notable differences among specialty services. The service with the largest volume of ordering was internal medicine, which saw its biopsy rate drop by nearly 30%. Other services increased their biopsy ordering rates. The largest increase was in pediatric emergency medicine, which saw its biopsy rate nearly triple. The emergency medicine and

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hospitalist services each saw gains of about 60%.

Importantly, biopsy positivity rates increased for services that decreased their biopsy ordering rates, thus suggesting higher value referrals. "It also shows that the levers we can control from the laboratory are finding purchase throughout the diagnostic cascade," Schroeder said.

EHRs provide a rich set of observational, secondary data that is less controlled than data in randomized clinical trials, so inferring causality is much more difficult, Schroeder noted. To reduce potential bias in this process, he also used propensity scores to reduce the effect of different patient types receiving various test panels.

"If those at lower risk of disease receive the algorithm while those at greater risk receive other testing strategies, this can cause significant selection bias and confound the study results," he said. "Propensity score matching reduces this bias by selecting a subset of patients so that the two patient populations have a similar likelihood of getting either inappropriate or appropriate testing, thus attempting to mimic a randomized trial." Schroeder also used logistic regression to control for factors such as year and patient demographics. The results were largely unchanged with these controls.

Using geospatial data to increase health equity

Labs, as well as all parts of the healthcare system, increasingly focus on providing equitable access to quality healthcare, with a focus on patient socioeconomic factors. One challenge to determining equitable access is getting data that can help characterize patients' vulnerability. Such data are not always collected comprehensively at the patient level, Schroeder noted.

By looking at census data [...] the pair found that social vulnerability is significantly associated with whether diabetic patients get appropriate kidney tests during encounters with the health system.

To determine nonmedical factors that affect patient health — also called social determinants of health — Schroeder and Vahid Azimi, MD, of Washington University in St. Louis School of Medicine teamed up on a study that used geospatial tools to determine equity in access to testing for kidney health, which is important in diabetes care. The pair conducted geospatial analyses on U.S. Census tracts where patients lived and used that population-level data as a proxy for patient-level features. Azimi presented this research at the ADLM Data Science Summit.

The unpublished study relied on both the census tract data and information from Schroeder and Azimi's respective health systems' EHRs to determine whether social vulnerability affected kidney health testing in people with diabetes.

By looking at census data — including age, sex, employment status, education, housing, and other social factors — the pair found that social vulnerability is significantly associated with whether diabetic patients get appropriate kidney tests during encounters with the health system.

Azimi found that many patients went to the emergency room, likely for something other than a kidney issue, and received a serum creatinine test because it's part of the basic metabolic panel, but they didn't get the urine albumin test. Azimi suggested that these hospital encounters are opportunities to fix the gaps in kidney care for patients with diabetes. Azimi also showed that 80% of those with only a serum creatinine result also had at least one outpatient encounter that provided another opportunity for urine testing.

EHR and geospatial data were just two types of data discussed at the summit. A running theme through many talks was use of artificial intelligence and large language models throughout the pre-analytic, analytic, and post-analytic phases of the diagnostic cascade. These new tools are revealing patterns that may not be obvious to humans, creating new ways to access knowledge — a situation that Schroeder likened to switching to the internet as a means of getting information after decades of looking it up in printed encyclopedias.

Schroeder predicted that data science will be essential for laboratory medicine to enhance patient care and demonstrate the impact of diagnostic strategies on health systems. "That goes beyond analytic accuracy and turnaround times to impacting health outcomes at the population level," he said.

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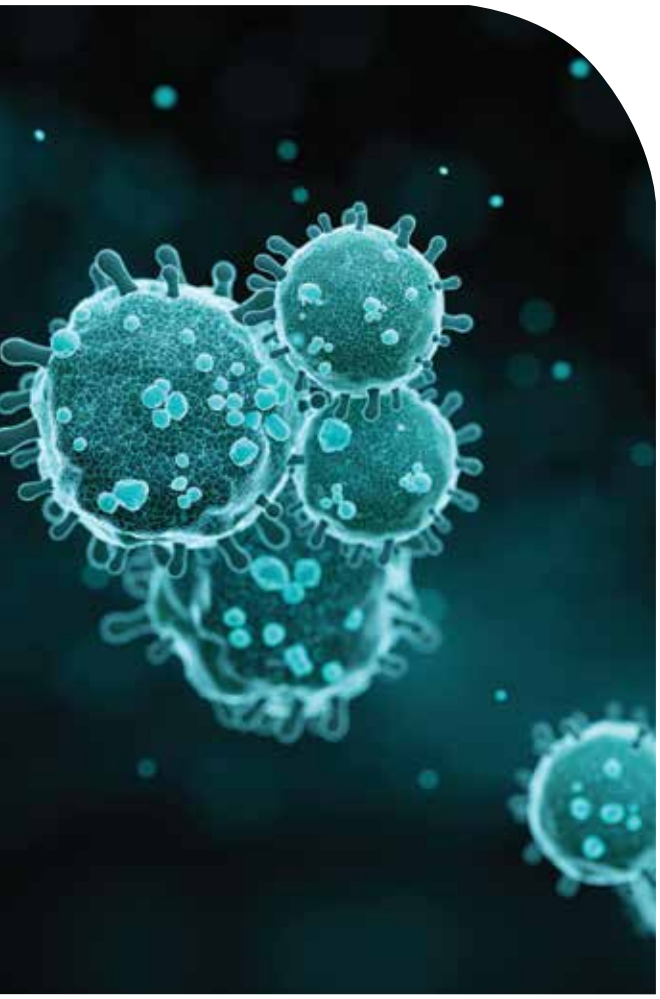
Regulatory Roundup



FDA approves next-generation cancer biomarker test and companion diagnostics

Illumina, Inc., announced Food and Drug Administration (FDA) approval of its in vitro diagnostic (IVD) TruSight Oncology (TSO) Comprehensive test and its two companion diagnostic (CDx) indications.

The company says the test is the first FDA-approved, distributable comprehensive genomic profiling IVD kit with pancancer companion diagnostic claims. The test interrogates over 500 genes to profile a solid tumor, increasing the likelihood of identifying an immuno-oncology biomarker or clinically actionable biomarkers that enable targeted therapy options or clinical trial enrollment.

TSO Comprehensive is approved as a CDx to identify adult and pediatric patients with solid tumors who are positive for neurotrophic tyrosine receptor kinase (*NTRK*) gene fusions that may benefit from treatment with Bayer's VITRAKVI (larotrectinib). The test is also approved to identify adult patients with locally advanced or metastatic rearranged during transfection (RET) fusion-positive non-small-cell lung cancer (NSCLC) that may benefit from treatment with Lilly's Retevmo (selpercatinib).

NTRK gene fusions are rare and can be challenging to detect. The company says that TSO Comprehensive also interrogates RNA and can identify a broad range of known and novel gene fusion partners across all three *NTRK* gene fusions: *NTRK1*, *NTRK2*, and *NTRK3*. Bayer's Vitrakvi (larotrectinib) is a highly selective TRK inhibitor approved for use in patients with TRK fusion cancer, in accordance with therapeutic labeling.

A separate CE-marked version of TSO Comprehensive already is available in Europe.

COMPANION DIAGNOSTIC FOR SYNOVIAL SARCOMA GETS FDA 510(K) CLEARANCE

Thermo Fisher Scientific announced that its SeCore CDx HLA A Sequencing System has been granted Food and Drug Administration 510(k) clearance for use as a companion diagnostic with Tecelra (afamitresgene autoleucel), Adaptimmune's newly approved T-cell receptor (TCR) therapy for certain adult synovial sarcoma patients.

These patients have unresectable or metastatic synovial sarcoma; have received prior chemotherapy; are HLA-A02:01P, -A02:02P, -A02:03P, or -A02:06P positive; and have tumors that express the MAGE-A4 antigen.

Cancer immunotherapies, including TCR therapies, have become increasingly powerful tools in cancer treatment, particularly for patients with metastatic or unresectable tumors. TCRs interact with specific human leukocyte antigen (HLA) proteins to activate an immune response, making high-resolution HLA typing a critical step in identifying patients most likely to benefit from engineered TCR T-cell therapies like Tecelra.

FDA PROPOSES RECLASSIFICATION OF HEPATITIS B TESTS

The Food and Drug Administration (FDA) has proposed changing antigen, antibody, and nucleic acid-based hepatitis B virus (HBV) assays to a lower-risk classification.

In the September 25 Federal Register, the FDA notes that these tests, currently classified as class III, or high risk, are subject to premarket approval requirements. The FDA proposes changing the devices to class II, or moderate risk, making them eligible for the 510(k) pathway.

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As part of the reclassification, the agency plans to mitigate test risks — false positive and negative results, misinterpretation of results, and failure to correctly operate the devices — by creating special controls for the tests.

The Federal Register notice says the FDA will accept comments on its proposal until November 25.

The panel detects sepsis-causing *Candida* species directly from blood in 3 — 5 hours, without the days-long wait for a positive blood culture

GUARDANT360 CDX LIQUID BIOPSY APPROVED AS COMPANION DIAGNOSTIC IN JAPAN

Guardant Health Japan Corp. recently announced that Japan's Ministry of Health, Labor and Welfare (MHLW) has approved Guardant360 CDx as a companion diagnostic to identify *EGFR* exon 20 insertion mutations in patients with inoperable or recurrent non-small cell lung cancer (NSCLC) for consideration of treatment with amivantamab-vmjw combined with chemotherapy.

This approval makes the Guardant360 CDx comprehensive genomic profiling panel the first blood-based companion diagnostic to be approved in Japan for this purpose. Janssen Pharmaceutical is currently seeking regulatory approval for the use of amivantamab-vmjw in Japan, according to Guardant.

In a retrospective analysis, the Guardant360 test identified *EGFR* exon 20 insertion mutations in 2.4% of East Asian patients with NSCLC, including those from Japan. This approval gives patients in Japan with inoperable or recurrent NSCLC harboring *EGFR* exon 20 insertion mutations a greater opportunity to access targeted treatment options, according to the company.

In March 2022, the agency approved Guardant360 for comprehensive genomic profiling in patients with advanced solid tumors. The test examines 74 cancer-related genes and is approved as a companion diagnostic for multiple cancer drugs approved in Japan.

T2 BIOSYSTEMS RECEIVES FDA CLEARANCE FOR PEDIATRIC CANDIDA PANEL

T2 Biosystems, Inc., has received Food and Drug Administration clearance for its pediatric T2Candida Panel. The panel detects sepsis-causing Candida species directly from blood in 3 - 5 hours, without the days-long wait for a positive blood culture, the company said.

The test runs on the T2Dx Instrument and simultaneously detects five Candida species, including *Candida albicans, Candida tropicalis, Candida parapsilosis, Candida krusei*, and *Candida glabrata*. According to the U.S. Centers for Disease Control and Prevention, these species account for up to 95% of all *Candida* bloodstream infections in the U.S.

T2 Biosystems officials cited studies showing the T2Candida Panel detects *Candida* species significantly faster and with greater sensitivity than blood culture-based diagnostics. They added the test would help clinicians improve outcomes and reduce costs by achieving faster targeted antifungal treatment for their pediatric patients.

FOUNDATION MEDICINE ANNOUNCES ADDITIONAL TISSUE AND LIQUID BIOPSY TEST APPROVALS

Foundation Medicine, Inc., announced Food and Drug Administration (FDA) approval for its FoundationOne CDx and FoundationOne Liquid CDx as companion diagnostics for AstraZeneca's Lynparza (olaparib) in combination with abiraterone and prednisone or prednisolone for the treatment of adult patients with deleterious or suspected deleterious *BRCA*-mutated metastatic castration-resistant prostate cancer (mCRPC).

This FDA decision follows approval of FoundationOne for Lynparza to identify mCRPC patients with homologous recombination repair gene alterations and the approval of FoundationOne Liquid CDx for Lynparza to identify patients with *BRCA1*, *BRCA2*, and/or *ATM* alterations in mCRPC.

Foundation Medicine officials noted the approval helps meet "a critical unmet need for first-line treatment options for patients with *BRCA*-mutated [mCRPC] and this combination therapy is an important advancement." The most recent approval reinforces the importance of testing for genomic mutations at metastatic diagnosis to help guide treatment decisions, they added.

Industry Playbook

Partnership aims to enable molecular diagnostics development

Alveo Technologies, Inc., along with faculty at Johns Hopkins University's School of Public Health, recently announced the launch of an academic arm of its partner program, the Global Virus Network (GVN).

The effort's primary goal is to make available a highly sensitive and easy-to-use platform to institutions and developing countries so they can proactively detect and track illness at the local level.

GVN now includes a research-use-only program focused on enabling innovative research through universities and academic partners. This deeper collaboration with Alveo aims to commercialize tests in countries with significant need, Alveo said.

The GVN and its more than 80 scientific sites, including Johns Hopkins School of Public Health, will help countries develop tests on Alveo's open platform, which GVN said is well-suited for challenging environments, thanks to the devices' ruggedness and portability.

According to Alveo, its device can withstand extreme temperatures, high humidity, shaking, and dropping. Researchers can proactively collect, detect, and track outcomes in Alveo's cloud-based software solution, so test results can be accessed and aggregated from anywhere in the world.

The platform provides precise results comparable to PCR in terms of accuracy and sensitivity without requiring shipment of samples to a lab for processing. Alveo provides on-location results within 30–45 minutes or less.

The platform can upload geotagged results to the cloud, meaning researchers and authorities get near real-time information on a pathogen's spread, regardless of where in the world the test is run, according to Alveo.

COOPERATIVE EFFORT ON NONINVASIVE BLADDER CANCER TEST IN EUROPE

Menarini Diagnostics and Nucleix have announced a long-term commercial agreement for the exclusive distribution of the Bladder EpiCheck test in Europe.

The alliance between the companies aims to accelerate the adoption of the Bladder EpiCheck and transform bladder cancer patients' care in Europe.

The noninvasive CE-marked test detects primary or recurrent bladder and upper tract urinary cancers. The European Association of Urology (EAU) Clinical Guidelines includes Bladder EpiCheck as a urine test that might be used in the initial diagnostic workup of bladder cancer to avoid or implement cystoscopy and in follow-up, to monitor for non-muscle invasive bladder cancer (NMIBC) tumor recurrence, or to replace or postpone cystoscopy. The test is also included in the EAU Clinical Guidelines as an ancillary tool in the diagnosis and monitoring of upper tract urothelial cancer.

Bladder EpiCheck could detect high-grade disease early and potentially reduce the frequency of cystoscopies, thus potentially reducing the burden of bladder cancer surveillance for patients and health systems, while improving patient outcomes by identifying the patients who will benefit most from intervention, the companies said.

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ADLM (formerly AACC) collected 60 mL of blood from volunteer donors attending the AACC Annual Meeting in Atlanta, GA in order to establish the 99th percentile for cardiac troponin in a healthy population in 2015. In 2021, ADLM collected 60 mL of blood from volunteer donors to investigate the durability of SARS-CoV-2 vaccines and T cell immunity and establish a repository of samples for academic and commercial purposes. In both studies, after collection, the blood was processed on site and transported to the CDC for storage at -80°C. Samples were de-identified and no SARS-CoV-2 test results will be provided. Sets of donor samples are being offered to IVD manufacturers and researchers for clinical assay development, standardization, reference range studies, and any other applications for which the samples might be useful. ADLM has undertaken this activity as part of its mission to further scientific research. THE DONOR SAMPLES ARE PROVIDED "AS IS." ADLM DISCLAIMS ALL WARRANTIES INCLUDING IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE.

DIACARTA CONTRACT FOCUSES ON VEXAS SYNDROME TESTING

DiaCarta recently announced a diagnostic testing service contract with the Department of Veterans Affairs San Francisco Veterans Affairs Health Care System to provide vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic (VEXAS) syndrome testing.

The service includes the QClamp Plex VEXAS test developed at DiaCarta using its XNA technology and validated at its laboratory.

VEXAS syndrome is an autoinflammatory disease characterized by inflammation affecting various tissues and organs, causing bone marrow failure and high risk for clotting. The prevalence is 1 in 4,000. The disease typically occurs in men older than 50, but it is also rarely seen in women. It is distinguished by specific somatic gene mutations in the *UBA1* gene.

Due to its diverse presentations, patients with the disease may be seen by doctors in various clinical specialties but remain undiagnosed or misdiagnosed with relapsing polychondritis, myelodysplastic syndrome, Sweet syndrome, or vasculitis.

DiaCarta officials said that the deal would enable better VEXAS syndrome testing, including improved sensitivity, turnaround time, and cost.

AI-POWERED CARDIOVASCULAR TESTS GET PRELIMINARY PRICING FROM CMS

Cardio Diagnostics Holdings, Inc., has announced that its PrecisionCHD and Epi+Gen CHD tests have received preliminary pricing determinations from the Centers for Medicare & Medicaid Services (CMS).

PrecisionCHD is an artificial intelligence-powered blood test that aids in the diagnosis of coronary heart disease (CHD) by evaluating genetic and epigenetic markers. Epi+Gen CHD assesses the 3-year risk for a CHD event, including heart attacks, using a similar AI-driven, integrated genetic-epigenetic approach.

Preliminary CMS pricing determination marks a key milestone in gaining broad access to Medicare reimbursement.

The determination represents a crucial step toward securing Medicare reimbursement for the blood tests. The company says they can improve risk assessment, diagnosis, management, and monitoring of coronary heart disease (CHD).

If finalized, the decision will allow Medicare contractors to determine pricing for PrecisionCHD and Epi+Gen CHD based on actual cost data from Cardio Diagnostics.

YOURGENE HEALTH AND GENETIX LAUNCH FIRST LOCAL NONINVASIVE PRENATAL TESTING SERVICE IN COLOMBIA

Yourgene Health has installed Colombia's first noninvasive prenatal testing (NIPT) workflow at Genetix.

Genetix has introduced its NipTest, a service that will utilize Yourgene's IONA Nx NIPT Workflow to deliver fast, accurate NIPT results for expectant parents in Colombia.

Using Yourgene's IONA Nx NIPT Workflow offers Genetix a complete CE-marked in vitro diagnostic device to establish its own quality-assured prenatal screening service in-house. The IONA test has been validated on a highly flexible and scalable workflow. It is suitable for low- to high-volume sample throughput and can enable growing clinical labs to meet rising demand.

The NIPT is performed using cell-free placental DNA from maternal blood to screen for trisomy 21 (Down's syndrome), trisomy 18 (Edwards' syndrome), or trisomy 13 (Patau's syndrome). NIPT can also determine the sex of the fetus. The analysis is performed using next-generation sequencing technology, with test results available in 3 days.

Previously, blood samples collected in Colombia were sent to the U.S. for testing. By offering access to its NipTest locally, Genetix will help to ensure expectant parents receive reliable results quickly, while reducing the need for invasive tests and the associated stress and anxiety, according to Yourgene.

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Ask The Expert

Assessing platelet number and function when diagnosing acquired thrombocytopenia

By Olajumoke Oladipo, MD, DABCC, FADLM

How is acquired thrombocytopenia diagnosed?

A: For proper diagnosis, a thorough history and physical examination are needed, in addition to testing with laboratory assays to rule in or rule out the various causes. These assays include but are not limited to those for platelet number and function, a peripheral blood smear, and immature platelet fraction.

What methods are available for measuring platelet number?

Platelets can be counted manually using a microscope with a hemocytometer or in automated hematology analyzers using several methods such as impedance platelet counting, optical light scatter counting, and platelet-specific labels with flow cytometry counting.

The International Council for Standardization in Haematology and International Society for Laboratory Hematology recommend the red blood cell/ratio method for platelet number. With this method, platelets are labeled by fluorescein isothiocyanate-conjugated monoclonal antibodies against two epitopes (CD 41 and CD 61). This is followed by flow cytometry analysis and calculation of the platelet count from the red blood cell/fluorescent platelet ratio.

Most automated systems also measure the mean platelet volume, which is a measure of the average size of platelets. This may be higher in immune thrombocytopenia (ITP) because of the giant (more immature) platelets that may be present in peripheral blood. Other parameters that can be measured as part of the complete blood count include the platelet distribution width, which is a measure of the platelet anisocytosis, and the "plateletcrit," which reflects the volume of circulating platelets in a unit volume of blood.

What methods are available for assessing platelet function?

The most common platelet function tests available for routine use in clinical labs include:

- Platelet adhesion assays, which measure the closure time for platelet plug formation when exposed to an in vitro mimic of endothelial damage due to high shear blood flow.
- Aggregometry-based tests, which assess the ability of platelets to aggregate in the presence of agonists, as well as the response of platelets to antiplatelet therapy.
- Flow cytometry, which involves laser-based detection of labeled platelets.
- Visco-elastic assays, which are global hemostasis tests that assess the rate of clot formation based on agonist effect in the presence of low shear induction.

What should you look for in a peripheral blood smear when diagnosing acquired thrombocytopenia?

Platelet clumping, platelet satellitism, and platelet phagocytosis are just a few of the many abnormalities associated with acquired thrombocytopenia in general.

As for abnormalities associated with particular types of acquired thrombocytopenia, giant platelets can be seen in ITP. Red blood cell schistocytes are seen in microangiopathic hemolytic anemia (e.g., thrombotic thrombocytopenic purpura). Hypersegmented or hyposegmented neutrophils are seen in primary hematologic disorders such as myelodysplasia and myeloproliferative disorders.

How can immature platelet fraction (IPF) be used when diagnosing acquired thrombocytopenia?

Also called reticulated platelets, immature platelets are those that the bone marrow has recently released. They have a high RNA content and are usually larger in size compared to normal platelets. The percent IPF indicates the ratio of immature platelets to the total number of platelets in peripheral blood. It reflects the rate of thrombopoiesis and bone marrow platelet production, and is useful in differentiating between peripheral platelet destruction (associated with ITP and heparin induced thrombocytopenia) and decreased bone marrow production (associated with myelodysplastic syndrome and acute myeloid leukemia).

Olajumoke Oladipo, MD, DABCC, FADLM, is an associate professor of pathology at Pennsylvania State University and medical director of hematology and coagulation at Penn State Hershey Medical Center in Hershey, Pennsylvania.

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