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Multiplex, Point-of-Care Test for STIs Could Offer Public Health Benefits

Point-of-care (POC) testing that could simultaneously identify multiple sexually transmitted infections (STIs) could be a valuable addition to sexual health clinics, according to a U.K. study published Sept. 10 in *BMJ Open*. Such a test, if commercially available, would benefit patients, cut transmission of STIs, and reduce unnecessary antibiotic prescribing.

In addition to the personal, long-term reproductive-health consequences for patients, STIs pose a public health concern and antibiotic stewardship headaches. In symptomatic patients, empirical antimicrobial therapy is usually guided by results of immediate microscopy of genital discharge, but this approach is known to have low sensitivity—missing up to half of Neisseria gonorrhoeae (NG) and Trichomonas vaginalis (TV) infections in women—and having poor specificity for predicting Chlamydia trachomatis (CT) or Mycoplasma genitalium (MG).

Currently, routine diagnosis requires laboratory-based nucleic acid amplification tests (NAATs), which can take up to two weeks for return of results. In the United Kingdom most genitourinary medicine services do not routinely conduct NAATs for MG or TV.

However, emerging POC tests enable testing for multiple STIs, which could address antibiotic stewardship challenges and improve patient and public health outcomes. Presumably, POC tests would require fewer clinic visits, reducing the number of patients lost to follow-up

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One-Fourth of Myriad's Variants of Unknown Significance Reclassified Over 10 Years

Variant reclassification following hereditary cancer genetic testing is common, according to a study published by Myriad Genetics (Salt Lake City) Sept. 25 in the *Journal of the American Medical Association*. Over a 10-year period, one-fourth of all reported variants of uncertain significance were reclassified, including downgrading of 91 percent to benign or likely benign and upgrading of nine percent to pathogenic or likely pathogenic.

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and saving patients time, money, and anxiety. Diagnosing at STIs at the initial clinic visit would improve STI management.

The U.K.-based researchers built a model to assess costs, benefits, and cost-effectiveness of three testing strategies using microscopy plus hypothetical NAAT POCTs that deliver results in 30 minutes for a dual chlamydia and gonorrhea test, a triple test that also includes M. genitalium, and a quadruple test which also includes trichomoniasis, compared current practice of using microscopy plus a laboratory NAAT for chlamydia and gonorrhea.

The model used a hypothetical cohort of just under 1 million people with symptoms of a lower genitourinary tract infection attending English genitourinary medicine service. The model considered costs (e.g., staff time, diagnostic kit, drugs and other consumables) and reimbursement to genitourinary services associated with diagnosing and managing STIs, but did not include long-term complications associated with STI infection (e.g., infertility) other than pelvic inflammatory disease. The model also assumed that treatment was started on the day of diagnosis. Sample average costs included $17.22 for a CT-NG NAAT laboratory diagnostic test, $31.37 for a POC CT-NG test, $37.91 for a POC CT-NG-MG test, and $44.44 for a POC CT-NG-MG-TV test.

The researchers found that the current standard of care was the cheapest strategy when considering the costs to genitourinary services, with all three POC strategies adding additional expenses—a 5 percent increase for the dual POC test, a 10.4 percent increase for the triplex POC test, and 10.8 percent increase for the quadruplex POC test. However, when looking at payment by results, the tariff-based reimbursement), the standard of care became the most expensive and the quadruplex POC test became the least expensive.

Specifically, the quadruplex POCT was the most cost-effective relative to the other strategies, using tariff costing, saving an estimated $34.6 million (mostly in averted clinic visits). The quadruplex POC test also generated the most other benefits, including 240,467 fewer clinic visits, 808 fewer STI transmissions, and 235,135 averted inappropriate antibiotic treatments, compared with the standard of care.

"POC pathways generated some cost-savings, primarily because patients had fewer return visits. However, these did not outweigh the higher cost of the POC tests compared with laboratory-based NAATs when estimating total pathway costs," write the authors led by Susie Huntington, Ph.D., from Aquarius Population Health in the United Kingdom. "Cost implications are driven by the cost of POC tests and would vary somewhat in different geographical areas due to differences in the subgroup mix and the prevalence of the four STIs."

While there are no triplex or quadruplex POC STI tests currently on the market, there is at least one multiplex STI POC assay in development.

Takeaway: A multiplex, POC test for STI may offer patient-level and public health benefits, despite the potential increase in cost.

DTET

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AI May Cut 'Wrong Blood in Tube' Errors

Machine learning-based multianalyte delta checks may be effective at identifying 'wrong blood in tube' (WBIT) errors, according to a proof-of-concept study published in the *American Journal of Clinical Pathology*. The authors say that these technology-enabled multianalyte delta check will be more effective at identifying errors and improving patient safety than traditional single analyte delta checks.

Because laboratories usually manage the analytic phase of testing with internal quality control measures, the pre- and postanalytic phases may be the most vulnerable to errors, experts say. These preanalytic errors can include improper specimen collection and transport, or WBIT mislabeling errors. WBIT errors can negatively impact clinical care diagnostic or treatment decisions are based on test results corresponding to the wrong patient.

"Although only a very small proportion of specimens are presumably affected by WBIT errors, WBIT errors in aggregate may not be rare due to high test volume," , writes coauthor Matthew Rosenbaum, M.D., from Massachusetts General Hospital in Boston. "For example, even if only one in 1,000 (0.1 percent) specimens were impacted by a WBIT error, a hospital testing a million specimens per year might report 1,000 sets of erroneous results every year."

Given the impossibility of eliminating all human error, processes to reliably detect WBIT errors before result reporting could impactful. So-called delta checks consider the absolute change in a test result for the same patient, but traditionally, they have only evaluated a single analyte. Multivariate machine learning-based model can distinguish physiologic changes from those indicating WBIT errors.

Rosenbaum and his colleague Jason Baron, M.D., simulated WBIT errors within sets of routine inpatient chemistry test results to develop, train, and evaluate five machine learning-based WBIT detection algorithms. Using data extracted from relevant inpatient laboratory tests results stored in the hospital's laboratory information system, the researchers linked and aligned the results from each patient collection to the results from the most recent prior collection for the same patient admission for 11 commonly tested analytes (calcium, magnesium, plasma blood urea nitrogen [BUN], plasma creatinine, plasma glucose, phosphorous, anion gap, plasma chloride, plasma potassium, plasma bicarbonate, and plasma sodium).

The model was trained to identify WBIT errors based upon absolute change in test result, absolute velocity of change, and the actual values of prior test results (not the change between results). The training data consisted of 10,799 patient collections from 2,369 patient admissions, while the test data consisted of 9,839 patient collections from 2,486 patient admissions.

BUN and creatinine were the most powerful individual analytes in identifying WBIT errors, both having area under the curve (AUC) values of 0.84. At a sensitivity of 80% BUN and creatinine, were only 66 percent and 74 percent specific, respectively. Velocity of change was less powerful than absolute difference across all analytes best-performing WBIT detection algorithm.

The best performing multivariate model, a support vector machine including the absolute change and current values for each analyte as predictors, had an AUC of 0.97 and a specificity of 96 percent at 80 percent sensitivity. However, at 80 percent sensitivity, this best performing multivariate delta check achieved a positive predictive value (PPV) of only 52 percent.

"Delta check models will only be useful in clinical practice if they can achieve a sufficient PPV to avoid 'alarm fatigue'," write the authors. "Because WBIT errors are presumed to be quite infrequent, these differences in accuracy translate into very important differences in PPV."

Takeaway: Machine-learning-based algorithms may be able to improve the performance of delta checks by incorporating multiple common analytes in the hopes of identifying WBIT errors and improving patient safety.

Liquid Biopsies Enable Pediatric Brain Cancer Monitoring

Liquid biopsies may enable physicians to monitor treatment effectiveness for children with brain cancer, enabling detection of progression earlier than MRI imaging, according to a small study published Oct. 15 in *Clinical Cancer Research*. The authors say this is the first evidence of the feasibility and clinical utility of ctDNA for longitudinal surveillance in pediatric brain cancers.

Pediatric diffuse midline glioma (DMG) are highly malignant tumors with poor clinical outcomes, particularly for the estimated 70 percent of patients that harbor the histone 3 p.K27M (H3K27M) mutation.

Currently, imaging and clinical-based disease monitoring are the standard of care. Complete surgical resection of DMG is not possible and while biopsy at presentation can be feasible, rebiopsy at the time of tumor progression is rare due to risks, sensitive anatomic location, costs, and clinical regulations.

"The inability to accurately assess disease response and treatment-related molecular changes confer significant challenges, particularly for emerging biologically targeted strategies such as immunotherapy," write the authors led by Eshini Panditharatna, from Children's National Health System in Washington, D.C.

Researchers assessed the clinical utility of H3K27M in ctDNA of 48 newly diagnosed patients with DMG to evaluate the feasibility of tumor genomic profiling of biopsies and treated patients. Mutations were assessed using droplet digital polymerase chain reaction (ddPCR) in 110 specimens (30 cerebrospinal fluid [CSF], 79 plasma, and one cyst fluid sample). Blood was collected from for ctDNA analysis at the time of initial diagnosis, as well as with each MRI. ddPCR was chosen as it has high sensitivity and can enable detection and quantification of rare mutations.

The researchers found that both CSF and plasma are suitable sources for detection of ctDNA, although CSF was more enriched. H3K27M mutations were identified in 88 percent of DMG patients, a level comparable to detection with traditional biopsy. Additionally, multiplexing was feasible enabling detection of H3K27M and additional driver mutations.

"There is an urgent need for the development of ctDNA assays for clinical applications in pediatric central nervous system [cancer] patients"

— Javad Nazarian, Ph.D.

The authors note that mutations were identified in 80 percent of known pretreatment biopsies. They speculate that the four patients in whom a known mutation was not detected could be because of the "high blood brain barrier integrity" and the resulting lack of ctDNA in plasma samples. However, in two of these patients with initially undetectable H3K27M mutations, longitudinal samples subsequently had a detectable histone mutation.

A significant decrease in H3K27M plasma ctDNA was detected and agreed with MRI assessment of tumor volume in response to radiotherapy in 10 of 12 of patients.

Additionally, ctDNA analysis was conducted for nine patients enrolled in a clinical trial for precision therapy. Researchers found a decrease in plasma ctDNA from biopsy through early cycles of precision therapy and a subsequent increase in plasma ctDNA with disease progression.

"There is an urgent need for the development of ctDNA assays for clinical applications in pediatric central nervous system [cancer] patients," writes senior author Javad Nazarian, Ph.D., from George Washington University in Washington, D.C. "Tumor-associated ctDNA can be quantified using ddPCR, which will allow for a rapid and more sensitive method for surveying tumor mutations. This represents a key advance particularly for tumors with limited tissue acquisition, or prohibitive sampling at multiple time points."

Takeaway: This is the first evidence for the utility of monitoring pediatric brain cancer mutations and tumor progression using ctDNA found in plasma and CSF. This marks and advance in the ability to use liquid biopsies for assessing tumors that may be unable to biopsied.

Similar Driver Mutations Seen Across Metastasized Cancer

Driver mutations that are responsible for cancer growth are similar among metastases in a single patient, according to a study published Sept. 7 in *Science*. Thus, the authors say, a single biopsy is likely representative and able to capture most of the functionally important mutations in metastases and provide critical information for therapeutic decision-making.

Most studies assessing genetic variability within cancer have focused mainly on primary tumors. While research has identified hundreds of driver genes, relatively few mutations are thought to be important in the development of an individual's cancers. Many mutations—even in driver genes—may not be functionally important. Understanding the extent of driver gene heterogeneity is critical to the success of personalized medicine.

To better understand the potential heterogeneity of metastases, researchers comprehensively analyzed sequencing data (single nucleotide variants and small insertions and deletions) from 115 samples derived from 76 untreated metastases in 20 patients with eight types of cancer (breast, colorectal, endometrial, gastric, lung, melanoma, pancreatic, and prostate cancers). Each patient had at least two distinct treatment-naïve metastases. Researchers

characterized variants into putative driver and passengers mutations based on the Cancer Genome Atlas consensus list of 299 putative driver genes. They also developed a mathematical model to determine the evolutionary mechanisms of intermetastatic driver mutation heterogeneity.

The researchers identified a median of 4.5 mutated driver genes per patient. Within individual patients, a large majority of driver gene mutations were common to all metastases, suggesting that the original founding clone of the primary tumor most likely seeds all detectable metastases. Further analysis revealed that the driver gene mutations that were not shared by all metastases were unlikely to have functional consequences.

"Because therapy selection and treatment success of previously untreated patients increasingly depends on the identification of genetic alterations, it will be critical to extend this analysis to larger cohorts and more cancer types in order to investigate whether minimal driver gene mutation heterogeneity is a general phenomenon of advanced disease," write the authors led by Johannes Reiter, from Stanford University in Palo Alto, Calif.

Takeaway: Driver mutations of cancer metastases may be similar across sites in individual patients, suggesting that a single biopsy may be adequate to make targeted therapeutic decisions.

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Evidence Suggests Need for Expanded HCV Testing, Particularly Coupled With Opioid Screening in Young People

Current hepatitis C virus (HCV) screening strategies may not be adequate in the face of the opioid epidemic. Previous screening guidelines have focused on reaching the estimated 2.7 million persons with chronic HCV infection in the United States, the vast majority of whom were born from 1945 to 1965. Given the high prevalence in this population, both the Centers for Disease Control (CDC) and the United States Preventive Services Task Force recommend one-time testing for all persons in this birth cohort, as well as patients with known risk factors, like injection drug use.

However, new data shows that the incidence of acute infection with HCV has increased nearly three-fold between 2010 and 2015 due to increases in injection drug use as part of the opioid epidemic. It is estimated that the rate of new infections may be as high as 40,000 new infections per year, with the largest increases occurring in younger people.

To combat the rising incidence of infection, and because of the availability of new, effective treatments, there has been renewed interest in re-examining HCV testing strategies. Several new studies verify that HCV testing is often overlooked in younger, at-risk people and that universal testing of all adults may be cost-effective.

Model Shows Universal HCV Testing is Cost-Effective

Universal screening may be more cost-effective than either birth cohort screening or no screening at all, according to a study published Sept. 8 in *Clinical Gastroenterology and Hepatology.*

"The incidence of hepatitis C among younger drug-injecting patients is skyrocketing so we have a blip in HCV cases that's no longer isolated to the baby boomer cohort," said Mark Eckman, M.D., the lead author of the modeling study, in a statement.

> *"With adoption of a policy of universal adult testing, all clinical care settings should initiate HCV testing programs."*
>
> — Mark Eckman, M.D.

Eckman and colleagues estimated the cost effectiveness of universal, one-time screening for HCV infection in all adults over the age of 18 years living in the United States and to determine the prevalence of HCV antibody above which HCV testing (followed by treatment of infected patients with guideline-recommended therapy) is cost-effective. The model assumed prevalence of chronic HCV antibody positivity among adults born between 1945 and 1965 is 2.6 percent and in the non-birth cohort of 0.29 percent. Additionally, the model assumed a third generation enzyme-linked immunosorbent assay (EIA) with a sensitivity of 94 percent and a specificity of 97 percent, and a cost screening of $40.03 (HCV antibody EIA test plus level one office visit).

The researchers found that universal screening followed by guideline-based treatment of all those with chronic HCV infection has an incremental cost effectiveness ratio of $11,378 dollars per quality-adjusted life years (QALY) gained, compared with birth cohort screening alone. Not screening is more expensive and less effective than both of the screening strategies.

Universal one-time screening of the general adult U.S. population at a prevalence of HCV antibody greater than 0.07 percent cost less $50,000/QALY, the generally accepted threshold for cost-effectiveness, compared with a strategy of no screening. Compared with one-time, birth cohort screening, universal, one-time screening and treatment cost $11,378/QALY gained.

"With adoption of a policy of universal adult testing, all clinical care settings should initiate HCV testing programs," writes Eckman and colleagues from University of Cincinnati Medical Center in Ohio. "However, realizing that resources are scarce, data regarding the cost effectiveness threshold can guide local policy decisions by directing testing services to settings where they generate sufficient benefit for the cost."

Universal Screening in Real-World Settings

Despite several years of birth cohort screening, it is presumed many infected individuals outside of this age range remain undiagnosed, but exact estimates are lacking. Several studies presented at IDWeek 2018 (San Francisco; Oct. 3-7) showed results of universal screening in real-world emergency department settings. Vanderbilt University Medical Center initiated a screening program in the emergency department. Adult patients who underwent clinically necessary phlebotomy

were offered HCV screening. Samples were initially tested for HCV antibodies, but if positive, reflexed for HCV RNA testing.

From April 2017 through March 2018, 11,637 screening tests were performed. Of these, 8.7 percent were HCV antibody positive and 4.2 percent were RNA positive. The authors note, 81 of 1,008 HCV antibody positive samples could not undergo RNA testing due to insufficient sample volume.

While people born between 1945 and 1965 did have the highest percent of HCV antibody-positive results (11.9 percent) and HCV RNA-positive results (4.9 percent), there were a notable number of people outside of the birth cohort that were antibody or RNA positive (7.2 percent and 3.9 percent, respectively). Overall, the majority of HCV RNA positive cases (63.5 percent) were born outside of the birth cohort. Additionally, only 31.6 percent of HCV RNA-positive cases had a known history of intravenous drug use. More than one-third of HCV RNA-positive cases (36.7 percent) were both outside of the birth cohort and without a known intravenous drug use history.

"Universal screening identified many infections that would have been missed using age cohort and risk factors alone," write the authors led by Cody A. Chastain, M.D., from Vanderbilt University in Nashville, Tenn. "Emergency department HCV screening may be a useful method to augment guideline-based testing and intervene among populations not consistently screened."

Testing Not Happening in Younger, Opioid Users

Teens and young adults who have injected drugs are at high risk for HCV, but most aren't tested, according to another study presented at IDWeek 2018 (San Francisco; Oct. 3-7). Further, the study authors suggest that while current guidelines recommend testing in with known injected drug use, health care providers may not be comfortable screening adolescents and young adults for opioid use disorder, thus underestimating who is at risk for HCV infection.

The researchers retrospectively identified 13- to 21-year-olds who had a least one outpatient visit at any of 98 participating U.S. Federally Qualified Health Centers from 2012 to 2017. Using electronic medical record data to evaluate the frequency of HCV testing and predictors of HCV screening.

Over the study period, 269,287 youth meeting inclusion criteria were identified (54.7 percent female; 37.6 percent White, 33.5 percent Hispanic, 17.6 percent Black). The mean age at first HCV screening was 18.5 years.

Over the study period, 2.5 percent of teens and young adults were tested for HCV and of these 2.2 percent had reactive HCV testing. Confirmatory RNA testing was conducted in 76.5 percent of patients with positive screening tests, with 55.6 percent of these having detectable RNA.

Only 35 percent (325 of 933) of patients with diagnosed opioid use disorder and 8.9 percent of patients with any diagnosed drug use were tested for HCV. Further, only 10.6 percent of individuals tested for HCV also were tested for HIV.

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Older age (19-21 versus 13-15 years old at study end), Black race, and a diagnosis code for substance use disorder (amphetamine, opioids, cocaine, or cannabis) were independently associated with receiving HCV testing.

"Screening for opioid use disorder and other drug use, and then testing for hepatitis C in those at high risk, can help us do a better job of eliminating this serious infection, especially now that very effective hepatitis C medications are approved for teenagers," said lead author Rachel Epstein, M.D., from Boston Medical Center in Massachusetts, in a statement. "Even when drug use is identified, there's a belief that youth are less likely to test positive for HCV, which isn't necessarily the case as we show in our study. Clearly, this is an overlooked group that is at high risk."

Takeaway: New evidence suggests that birth cohort-based HCV screening might not be adequate to capture rising rates of infection associated with the opioid epidemic.

One-Fourth of Myriad's Variants of Unknown Significance Reclassified Over 10 Years, *from page 1*

"The implications of this study are three-pronged," said senior study author Theodora Ross, M.D., Ph.D., in a statement. "Physicians need to be aware of how rapidly knowledge about gene variants is advancing and that reclassifications are common. Labs need to review gene variant information on a regular basis and alert physicians to changes. Finally, patients and their family members need to be made aware of reclassifications by their physicians so they can make well-informed choices."

Researchers retrospectively analyzed results of individuals (95.6 percent women) who had genetic testing (initial single-syndrome test, pan-cancer panel, or both) conducted at Myriad Genetics from 2006 through 2016. Variants were classified as benign, likely benign, variants of uncertain significance (VUS), likely pathogenic, or pathogenic. An automated system analyzed new evidence from published literature and methods specific to the testing laboratory daily. When variant reclassification was appropriate, the testing laboratory sent an amended report indicating the new classification to the clinician. Additionally, a retrospective chart review was conducted for a subset of patients (n = 8,427) seen at the University of Texas Southwestern Medical Center (UTSW).

Over the study period, there were 44,777 unique variants detected and observed a total of 6.22 million times. In the UTSW subset, 3,158 unique variants were detected a total of 187,033 times. Overall, 5.4 percent (n = 90,052) of all test reports were positive (with at least one pathogenic or likely pathogenic variant) and 5.8 percent (n = 96,684) were negative (no pathogenic or likely pathogenic variant), but with one or more VUS. In the UTSW subset, 9,493 initial test reports were issued over the study period, of which 6.9 percent (n = 658) had a positive test result and 9.4 percent (n = 897) had a negative test result with at least one VUS.

Of the 1.67 million initial tests, 59,955 reports were amended over the study period due to variant reclassification, with 6.4 percent of 44,777 unique variants reclassified. Reclassification (upgrades or downgrades) to a different clinical category was rare among unique variants initially classified as pathogenic/likely pathogenic (61 of 9,112) or benign/likely benign (15 of 8,995).

Of the 26,670 unique VUS that were initially detected (seen 184,327 times), 7.7 percent were reclassified—with the vast majority (91.2 percent) downgraded to less severe classifications and 8.7 percent upgraded to more severe classifications. (either pathogenic or likely pathogenic variants). This yielded reclassification of 24.9 percent (46,890 of 184,327) of all reported VUS.

In the UTSW subset, 9.1% (287 of 3,158) of unique variants were reclassified, including 11 VUS that were upgraded to pathogenic or likely pathogenic. No known interim cancers were diagnosed in the patients prior to reclassification. However, in three cases, upgrades of VUS enabled patients to qualify for new treatments.

"The number of individuals with variants of uncertain significance will likely continue to rise nationally as (1) genetic awareness increases leading to more individuals being tested, (2) disease gene panel adoption rises, (3) the number of genes included in testing increases, and (4) the cost of genetic testing decreases," write the authors led by Jacqueline Mersch, from University of Texas Southwestern Medical Center in Dallas. "As such, the absolute number of individuals with variants of uncertain significance that are later upgraded to pathogenic will continue to rise."

The median time to the amended report due to variant reclassification was 1.10 years overall, and 1.06 years in the UTSW subset.

"Collectively, this highlights the continued importance of an efficient and accurate reclassification program to ensure up-to-date clinical management to reduce hereditary cancer risk," warn the authors.

Takeaway: Reclassification of VUS is common and laboratories need to ensure they have a system in place to re-evaluate new evidence and to report updated findings to clinicians and patients.

New Studies ID Strategies to Address Overuse of Laboratory Testing

The cost and quality of care are the focus of improvement initiatives happening at health systems across the country. Like imaging and other procedures, the necessity of laboratory testing, too, is being examined. Two recently published studies highlight how resident training and electronic medical record (EMR) order prioritization can impact potential overuse of laboratory testing.

EMR Sequence Impacts Test Ordering

Reprioritizing the sequence of test names in EMR laboratory order search results can reduce the overutilization of more expensive tests, according to a study published Sept. 22 in the American Journal of Clinical Pathology.

A complete blood count (CBC) with leukocyte differential (CBC-DIFF) is frequently ordered in the emergency department, but the DIFF component of

the test often does not impact clinical decision-making. Previous internal analysis at the Cleveland Clinic, showed that CBC-DIFF accounted for up to 98 percent of all CBC orders originating in the emergency department, compared with 53 percent of orders from the inpatient service.

"Performing a slightly more expensive test that will not offer the provider any additional information may appear harmless in the short term but can easily result in a large waste in resources over time," writes lead author Michael Phelan, M.D., from the Cleveland Clinic in Ohio. "With the myriad of reasons for test overutilization, it can be difficult to identify where cost-savings measures can be implemented. The simplest place to start may be to assess the appropriateness of the most commonly ordered tests in the department."

Phelan and colleagues conducted a two-stage performance improvement project and assessed its impact on CBC ordering during pre- and post-intervention periods. The intervention included both an educational component (passive, web-based educational initiative) and a reprioritization of CBC and CBC-DIFF in the EMR orders. (Previously CBC-DIFF was listed first.) The educational component discussed differences between the two tests regarding method, current utilization, and turnaround time, as well as potential alternative tests, including a CBC with absolute granulocyte count and individual component tests (hemoglobin concentration, platelet count).

Orders were identified through the institution's laboratory information system. The pre-intervention period was three months before the educational initiative. The two post-intervention periods included the three months following the educational initiative and then the three months following the changes to the EMR.

The researchers found that there was no difference in the proportion of CBC tests performed after the education intervention. However, there was a significant increase in CBC samples ordered following the EMR intervention, compared to both the education intervention period and the control period.

The authors explain that this saves not just costs, but also time within the laboratory. Reporting additional items (e.g., the differential) increases the likelihood of an abnormal finding (e.g., abnormal ganulocyte scatter using flow cytometry) that will require additional examination (e.g., a peripheral blood smear requiring manual review) by laboratory personnel.

"Our study shows that EMR optimization, in the form of the reprioritization of order entry search menu results to return overused tests at a lower rank when generic queries are used, can help reduce such waste," concludes Phelan.

Resident Training Could Impact Long-Term Ordering

Residents have large variation in laboratory ordering practice, according to a research published Oct. 8 in *JAMA Internal Medicine*.

Researchers from Columbia University analyzed electronic diagnostic test orders placed in the inpatient medical record by 139 internal medicine residents during the academic year 2016-2017. Over the study period the residents ordered 579,935 laboratory tests for 10,707 patients over 13,469 unique patient hospitalizations.

But, there was great variation in ordering practices by resident. The resident who ordered the most laboratory tests (n = 13,604) ordered more than 7 times the tests than the resident who ordered the least (n = 1,870). The resident who ordered the most tests per unique patient hospitalization ordered 41.2 tests per patient versus 9.0 tests per patient for the resident who ordered the least.

There was an association between residents' postgraduate year (PGY) and the total number of laboratory tests ordered, as well as between PGY and the number of laboratory tests per patient. As might be expected, residents in their first PGY residents tended to order more laboratory tests than the residents in their second or third PGY, however, surprisingly, the top three residents by laboratory test ordering volume included individuals from each PGY.

"Even excluding outliers, we observed much more variation in diagnostic test ordering volume than expected given that there were minimal differences in resident schedules among each PGY cohort during the 1-year period," write the authors led by Joshua Geleris, M.D., from Columbia University in New York. "Because residents are 'imprinted' by their training environment, even small reductions in diagnostic test ordering habits during training could translate to years of higher-value care."

Takeaway: Relatively easy solutions, like EMR sequencing of tests and resident training, can potentially curb unnecessary ordering of common laboratory tests.