G2 INTELLIGENCE

Diagnostic Testing & Technology Report

Competitive Intelligence & Analysis for an Expanding Global Market

Issue 12-12/December 2012

CONTENTS

www.G2Intelligence.com

Labs See Companion Diagnostics as Driver of Future Business Growth

The majority of laboratories believe companion diagnostic (CDx) testing volumes will increase and drive growth in lab business over the next few years, according to survey results released publicly for the first time by Ventana Medical Systems (Tucson, Ariz.; a Roche company) during G2's 30th annual Lab Institute, held in Arlington, Va., Oct. 10-12.

Ventana surveyed more than 100 laboratories and included personnel from different functional areas including the C-suite, lab managers, pathology managers, and histology managers. The survey found that more than 90 percent of respondents believe that CDx testing volume will increase in the next three years. Half of labs reported that CDx utilization has already helped grow their lab's business, while three-quarters believe that that increased utilization will be responsible for growth in their lab's overall business in the coming three years.

"At Ventana we believe that companion diagnostics are critical to what we believe is the industry's future for both pharma as well as diagnostics," says Mara Aspinall, president of Ventana, in her keynote address at Lab Institute. "We are proud to have 188 collaboration projects with 38 partners, and Roche and Genentech are among them, but the vast majority is outside."

For more on the future role of diagnostics in the transition to personalized health care and more on how Aspinall views the current state of diagnostics, please see *Inside the Diagnostics Industry* on page 5.

CMS Decision to Reimburse Molecular Tests Via Clinical Lab Fee Schedule Viewed Positively by Labs

Much to the pleasure of many in the clinical laboratory community, the Centers for Medicare and Medicaid Services (CMS) announced on Nov. 1 that new molecular pathology test codes will be reimbursed via the clinical laboratory fee schedule (CLFS). As was also anticipated, a gap-filling methodology will be used to determine pricing for 2013. While no real negative impact on molecular diagnostic test development is expected, the rule's true impact won't be known until pricing is finalized.

"While this was largely expected, we believe this will be viewed as a positive given the more onerous cost-based method of determining reimbursement

Continued on p. 2

▲ **CMS Decision to Reimburse Molecular Tests,** *from page 1*

for the physician fee schedule," wrote Amanda Murphy, an analyst from William Blair & Co., in a research note following the announcement.

Believing that most molecular pathology tests do not require physician interpretation, CMS said it would pay for 101 new molecular tests codes under the CLFS. But CMS is also creating a new HCPCS code, G0452, for molecular pathology procedures that require physician interpretation and report beyond the reporting of laboratory results. This one code will be reimbursed on the physician fee schedule and will replace current CPT code 83912-26.

"We can check one box off now," says Rina Wolf, vice president commercialization strategies at the consulting firm XIFIN. "But until we know how pricing will be done we can't be sure [what the impact will be]."

To set pricing for 2013 CMS will use the gap-fill procedure, which allows each Medicare carrier to determine local reimbursement rates. Experts say carriers may determine pricing using charges for the test with routine discounts; resources required to perform the test; payment amounts determined by other payers; and charges, payment amounts, and resources utilized for comparable tests.

"Gap-fill is typically used when there is no existing comparable test available, and this is somewhat the case with molecular codes since the current practice of utilizing stacking codes has made it virtually impossible to compare, as each lab varies greatly in the use of the codes," says Donna Beasley, vice president of laboratory sales and marketing, McKesson. "With this extreme inconsistency in the number of codes billed, a cross-walk method to price the molecular tests isn't feasible."

For 2014 prices CMS will use the 2013 median carrier amount to set the national limitation amount.

"The biggest concern is that it is looking unlikely that we will actually have prices for [Jan. 1]," warns Wolf. "It is a huge job, and it is a complex process. This could also impact commercial payers, who typically purchase the fee schedules from CMS on an annual basis. If there are no CMS prices, or there is variance from contractor to contractor, these schedules may have zeroes in place of prices."

CMS also announced that it would not recognize multianalyte assays with algorithmic analyses as valid Medicare codes for the coming year and cut the technical component of surgical pathology code 88305 by 52 percent; the global payment reduction for this code is about 33 percent.

"88305 represents about 5 percent of Medicare volume and 20 percent of Medicare lab spending," explains Murphy, but "88305 does not represent a big financial risk to labs." However, the cuts will have a significant impact on the bottom line of pathology groups. The reduction provides further evidence that CMS continues to focus on utilization trends for heavily employed codes, which perhaps could ultimately curb the ongoing physician insourcing trends, noted Murphy.

Illumina Launches First Apps in Its BaseSpace Cloud

Illumina (San Diego) has launched the first 10 apps in its BaseSpace Apps store in conjunction with the American Society of Human Genetics conference (San Francisco; Nov. 6-10). The apps, created by third-party developers, are part of the company's strategy to create a cloud-based ecosystem that will foster greater ease of DNA data management while more rapidly improving genomic understanding.

"The rapid adoption of BaseSpace coupled with BaseSpace Apps will help us achieve our goal to create an ecosystem where users of Illumina next-generation sequencers can easily access a broad range of genome analysis tools from the world's leading bioinformatics vendors," said Alex Dickinson, Illumina's senior vice president of cloud genomics, in a statement when BaseSpace launched in July. "By providing an open application programming interface and collaborative environment, we can encourage more rapid proliferation of the tools that will enable scientists to analyze, understand, and make use of massive amounts of genetic data."

As part of its BaseSpace genomic cloud computing platform, Illumina is offering a freemium strategy in which Illumina users can get free storage of 1 terabyte of DNA data and free DNA processing from its machines along with what will ultimately be an Apple-inspired store full of apps to purchase to aid genomic analysis.

BaseSpace will help researchers and clinicians overcome some of the challenges associated with employment of next-generation sequencing technology, including the need for dedicated infrastructure for data storage and in-house bioinformatics expertise or heavy software investment. BaseSpace provides an end-to-end solution allowing real-time uploads of sequencing data, secure storage, and one-click access to bioinformatics apps, including visualization and graphical genome browsing, annotation and filtering, gene expression analysis, as well as data-sharing options.

"By providing an open application programming interface and collaborative environment, we can encourage more rapid proliferation of the tools that will enable scientists to analyze, understand, and make use of massive amounts of genetic data."
—Alex Dickinson

"We combined the power of the cloud with increased price performance," Dickinson tells *DTTR*. "The generation of data from sequencing can be overwhelming, but it is not generated at an overwhelming rate. The data can be uploaded while it is still running on the instrument using the bandwidth of a home Internet connection—the same bandwidth needed to stream an HD movie. Within a couple minutes after the run, the data is already loaded to the cloud without a delay."

The launch of the cloud platform represents a strategic shift for Illumina from an instrument manufacturer to offering computational support, which has been fostered by the rapid decline in the cost of cloud services (Amazon Web Services offers pricing of 1 cent per gigabyte per month, or roughly $10 a year to store an entire genome) coupled with the rapid increased power of next-generation sequencing instruments.

Among the initial app developers are DNASTAR (Madison, Wis.) launching a de novo bacterial genome assembly application; Golden Helix (Bozeman, Mont.) with its GenomeBrowse genomic visualization and annotation platform for both DNA and RNA sequence data; and Partek (St. Louis) with Partek Flow, a single tool for both primary and secondary analysis with interactive visualization. Revenue is shared 30-70 between Illumina and the developers with the developers setting the app price.

Dickinson says that there has been "good uptake" in the BaseSpace app developers' portal and he expects two to three additional apps to be launched each week with currently 100 established developers signed up already. In the first quarter of 2013 Dickinson says the system will be opened to individual academic developers.

By simplifying the entire sequencing process, including processing, storage, and analysis, Illumina is hoping its BaseSpace platform will hasten sequencing adoption by hospitals and clinicians eager to apply genomics to patient care. Additionally, BaseSpace will change the paradigm of research by fostering greater collaboration between researchers and a shift in focus toward data mining in large sets of thousands or hundreds of thousands of genomes, Dickinson says.

Boehringer Focuses on Clinical Oncology Biomarker Testing

Boehringer Ingelheim Pharmaceuticals (Ridgefield, Conn., and Germany) is establishing its new franchise in the field of oncology therapeutics, presenting a total of 13 abstracts at the recent European Society for Medical Oncology Congress (Vienna, Austria; Sept. 28-Oct. 2).

The company is taking a personalized approach to developing targeted therapies like afatinib for non-small cell lung cancer (NSCLC), including incorporating a diagnostic test to confirm epidermal growth factor receptor (EGFR) mutation status. Ahead of regulatory submissions the company has already launched an unbranded educational campaign stressing the importance of biomarker testing in advanced NSCLC, targeting multidisciplinary health professionals.

Among the data presented at the ESMO Congress were results on afatinib from the pivotal phase III trial, LUX-Lung 3, which demonstrated a significant progression-free survival advantage of 11.1 months compared to standard chemotherapy treatment and quality of life improvement among NSCLC patients with an EGFR mutation receiving first-line treatment. Afatinib is an investigational oral, once-daily irreversible ErbB Family Blocker that inhibits EGFR (or ErbB1), human epidermal receptor 2 (HER2 or ErbB2), and ErbB4.

Although there have been general improvements in the utilization of EGFR testing, the current average time to identify EGFR mutation status is five days, as was observed in LUX-lung 3, says Boehringer spokesperson Susan Holz. She tells *DTTR* that the company believes there is an opportunity to expedite the identification of EGFR mutations "so that testing becomes part of the diagnosis process and the results are available more immediately—similar to the progress that has been made in breast cancer."

To that end Boehringer is partnering with Qiagen (Venlo, the Netherlands) to develop a real-time polymerase chain reaction assay companion diagnostic. In the company's release of third-quarter financial results in the beginning of November, Qiagen reiterated that it expects to submit in 2012 its therascreen EGFR assay as a companion diagnostic for use with Boehringer Ingelheim's investigational medicine afatinib for regulatory approval.

In addition to its partnership with Qiagen, Boehringer has created the new disease awareness program, called Let's Test. The campaign aims to educate health care professionals about the critical role of automatic, or "reflex," biomarker testing in determining a patient's specific type of advanced NSCLC to help match each patient with the most appropriate and available targeted therapy as early as possible.

G2 INTELLIGENCE
Inside the Diagnostics Industry

Preparing for Diagnostics 4.0: We're Almost in the Golden Age

Mara Aspinall, president of Ventana Medical Systems

Despite long-standing reimbursement and regulatory challenges, many industry insiders, including Mara Aspinall, president of Ventana Medical Systems (Tucson, Ariz.; a Roche company), are hopeful that with the advent of personalized medicine, the era of diagnostics has arrived.

"We have seen the ups and downs of industry, but I believe we are heading into the golden age of diagnostics, what I'll call diagnostics 4.0," Aspinall said during a keynote address at G2 Intelligence's Lab Institute (Arlington, Va.; Oct. 10-12), in which she outlined how the diagnostics industry has arrived at the threshold of personalized medicine and what the industry needs to do to ensure diagnostics become the standard of personalized care.

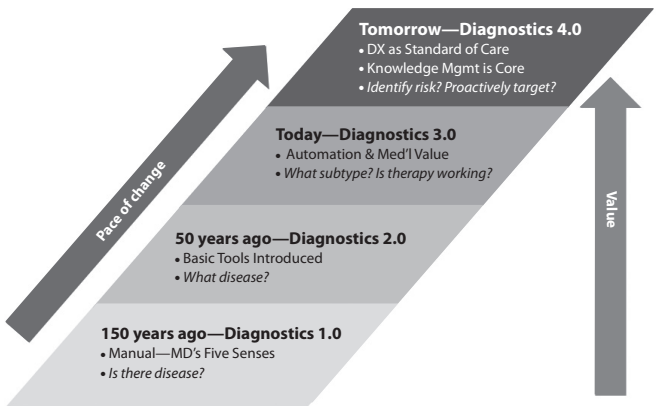
Diagnostics 4.0 is achieved, Aspinall says, when physicians have full confidence in diagnostics, payers understand the economic benefits of testing, and patients are comfortable with treatment decisions made on the basis of the physician's exam and relevant test results. Then, diagnostics become the standard of care, Aspinall says. In the 4.0 vision, diagnostics are not about one test at the beginning of a patient's treatment, but repeated diagnostics to screen and to monitor throughout the full course of disease. At its core, Aspinall says, "The 4.0 questions answered are, what is the patient's risk of advanced disease? Which root causes of disease can we proactively target?"

Evolution of Diagnostics—From 1.0 Toward 4.0

Diagnostics has evolved over the last 150 years from 1.0, a manual practice—"art without science that depended upon the doctor's five senses," Aspinall suggests, to a more sophisticated practice with automated, algorithm-based tests that resolve questions like, "What is the subtype of disease? What therapies will work? Is therapy working?"

This transition is enabled by the dramatic growth in the ability to classify disease into therapy-relevant categories. In 1891, the first international classification of disease (ICD) had just 14 categories; by 1975 this had increased to 1,000. But today, ICD-10 has 16,000 different classifications of disease.

The Evolution of Diagnostics: Climbing the Value Chain



Source: Mara Aspinall

"I get tired of hearing that diagnostics is not considered a core piece of the health care system. Too often it is the overlooked piece," says Aspinall. "We need to look back historically to see that diagnostics is the absolutely critical bridge to effective treatment."

Insulin predated diagnostic test strips just as antibiotics predated microbial testing. But only with the invention of the diagnostic panel could infectious diseases be effectively targeted and cured patient by patient, Aspinall illustrates.

Similarly, the introduction of the first urine diagnostic tests strip allows those with diabetes to more accurately treat the disease and live a normal life.

"The most current example that really tells the story of diagnostics is in AIDS," says Aspinall. "Anti-retroviral therapy was available for several years before we had viral load testing and genotyping. For AIDS patients anti-retroviral therapy only increased their life expectancy by two to five years. After viral load and genotyping enabled the customization and titration of drug dosing, we are talking about close to normal life span—it's all about the diagnostic."

In the transition to diagnostics 4.0 and personalized care, it is widely believed that companion diagnostics will make cancer more treatable.

"We clearly have radiation and chemotherapy as established treatments. Are they working? Yes. Is it good enough? No," emphasizes Aspinall. "Overall survival rates for cancer are 56 percent. But with companion diagnostics we can make many cancers that are today not treatable, treatable."

With lingering regulatory, reimbursement, and adoption challenges, why does Aspinall believe we are entering the golden age? She points to both the challenges faced by the pharmaceutical industry, as well as positive drivers within the diagnostics industry.

Pharmaceutical's Challenge

"We can see the power shifting from pharmaceuticals to diagnostics," says Aspinall. "Generics now have 80 percent market share of all prescriptions, and there is no reason to believe that will abate. New drug approvals have slowed, payers and providers are pushing back on cost, and more pharma and biotech spending is focused on understanding the disease pathway in order to target the drug more effectively. The challenge cannot be hoped away—a new strategy is needed and is emerging."

Quantifying the Value of Diagnostics

- $160 billion of drug spend is ineffective
- $15 billion saved by companion diagnostics
- $604 million in annual savings if CRC patients are given a KRAS test before treatment
- 17,000 strokes prevented annually if warfarin was properly dosed using a genetic test

Source: Mara Aspinall; The Case for Personalized Medicine*, 3rd Edition; Dx Insights; NIHS Study on Warfarin*

Personalized medicine will be the "new normal" both clinically and in pharmaceutical development. Thirty percent of pharmaceutical companies are requiring that all compounds go forward in development with biomarkers, Aspinall says, with each of the top 10 pharmaceutical companies having a drug with a biomarker in the label.

"They are focused on this, and I expect this list to double every year," Aspinall predicts. "It has created a companion diagnostic growth rate five times the growth rate of the rest of the [diagnostic] industry."

Given the financial constraints of the health care system, society is recognizing that the system cannot afford to offer a $100,000 treatment that is not effective simply because a patient was not diagnosed as accurately as possible.

In addition to the pressures to develop companion diagnostics emanating from the pharmaceutical industry, there are positive growth drivers in the diagnostics industry, including:

- **New technologies**—Some of the trends in technology include utilization of new sample types, multifactorial testing, digital pathology, circulating tumor cells, immune profiling, mobile technology, and next-generation DNA sequencing.
- **Test expansion**—Diagnostics will provide accurate information for screening, managing, diagnosing, and monitoring across the entire spectrum of care.
- **Emerging markets**—Increased spending in emerging health care systems in Asia and Latin America includes adoption of diagnostics early in their investment cycle with fundamentally different and more aggressive uptake there compared to the U.S. market, Aspinall says.

Looking Ahead

To ensure that diagnostics 4.0 is realized as the new standard of care the industry needs to address the need for new and more impactful data, Aspinall says. A more aggressive approach to generating data can reshape the industry's efforts in rectifying regulatory, reimbursement, and publishing challenges.

Aspinall says cross-industry initiatives are imperative to addressing lingering reimbursement issues.

"We have all heard over and over again that diagnostics are 2 percent of the health care spend and account for 60 percent of the decisions. Ten years ago when we first heard it that seemed very powerful. We've also heard many times that drugs only have a 50 percent efficacy and that's why we need personalized medicine. But now, we've said it too often, and it doesn't seem to have changed enough," says Aspinall.

Aspinall says the road forward calls for not only embracing the new tests and technologies, but also for publishing more on them, partnering across the industry, and advocating for the role of diagnostics.

"Too often the folks outside of this industry do not understand the power of diagnostics," says Aspinall. "We need to come together as an industry and be business model-agnostic and technology-agnostic to educate on a broad basis about our products. I do believe the rising tides will raise all ships."

Educating stakeholders requires publishing, she argues.

"If you look at the key publications across the health care industry, diagnostics remains less than 10 percent," cautions Aspinall. "Are there fewer submissions—probably. Are the diagnostic submissions different from traditional pharma ones—almost certainly. Does diagnostics development, without classic double-blind clinical trials, make them more difficult to evaluate—definitely. . . . Only with more aggressive peer-reviewed publishing can we make new strides in influencing the use of diagnostics."

Aspinall says cross-industry initiatives are imperative to addressing lingering reimbursement issues.

"We need to combine data across products, across companies, even if they are competitive, to put together that data and go to these payers together to say this is the power of diagnostics," Aspinall stresses. "We need to approach payers collectively so they are looking at the savings and treatment costs at the same time as they are looking at the increase in cost [with diagnostics]. We need to bring more data forward, as an industry, than we have ever done."

RPS Launching POC Pink Eye Test, Continues Work on Robust Pipeline in Eye Care

Pink eye is rarely diagnosed or treated appropriately with the majority of clinicians prescribing ultimately ineffective antibiotics for patients that have virally caused conjunctivitis. Furthermore, most clinicians fail to swab these patients with pink eye for pathogen confirmation. Sarasota, Fla.-based Rapid Pathogen Screening (RPS) has developed and is poised to launch commercially a rapid, point-of-care (POC) test to improve diagnosis of pink eye.

The test, AdenoPlus, uses a small tear sample to diagnose the Adenoviral form of conjunctivitis in the doctor's office. Robert Sambursky, M.D., co-founder and RPS CEO, tells *DTTR* that the platform's direct sampling enhances both sensitivity and ease of use. AdenoPlus has 90 percent sensitivity and 96 percent specificity and is reimbursable using an established CPT code. The test lists for $13.50 and is reimbursed for $17 by a wide range of third-party insurers and Medicare, Sambursky says.

While the rapid (10-minute) test has already received regulatory approval (CE marking in April 2011, 510(k) clearance in May 2011, and Clinical Laboratory Improvement Amendments waiver in April 2012) the company has just begun commercialization efforts in earnest. In mid-October RPS signed a U.S. licensing and distribution agreement with FSC Pediatrics (Charlotte, N.C.) granting FSC an exclusive cobranding license and nonexclusive distribution rights to pediatric primary care practitioners across the United States. But RPS maintains commercial rights to the U.S. urgent care and nonpediatric primary care markets.

In late July RPS also signed a licensing agreement granting NicOx (France) full exclusive rights outside the United States and exclusive rights to commercialize the test to eye care professionals in the United States. In addition to the AdenoPlus test, the agreement also covers two other tests currently in development—one for ocular herpes and the second for a combined Adenoviral-allergic conjunctivitis detection test. Under the agreement, NicOx will pay license and option fees to RPS, as well as royalties and additional milestone payments. NicOx will also pay for half of the development costs for the two other ocular diagnostics in development.

In addition to the upcoming infectious ocular tests and a test for dry eye measuring MMP-9 levels that is expected to receive U.S. regulatory approval next year, RPS received a U.S. Department of Homeland Security award to adapt the POC platform for detection of a biological attack or pandemic event. The rapid assay will differentiate a viral from bacterial infection using blood from a fingerstick, as well as distinguish viral exposure from chemical warfare.

EHRs Having Mixed Effect on Testing, Clinical Care

There is mixed evidence on whether health information technology, including automatic clinical reminders in electronic health records (EHRs), is living up to the promise of improving adherence to recommended screening guidelines and bettering patient care. Recently published studies show benefit for diabetes care but no improvements in cancer screenings with the use of automated reminders.

Cancer Screening

An electronic medical record-based clinical reminder system had little impact in improving colorectal cancer (CRC) screening rates in the Veterans Affairs (VA) system, according to a large study published online Oct. 8 in the *Journal of Clinical Oncology*.

The Oncology Watch (OncWatch) clinical reminder system was implemented at eight hospitals within Veterans Integrated Service Network 7 to improve CRC screening rates. The researchers analyzed administrative data for veterans at average risk, aged 50 to 64 years for the years 2006 and 2007, prior to the 2008 system implementation, as well as 2009 and 2010 following implementation. For comparison, 121 hospitals without the program were used as controls.

"Use of a commercially available certified EHR was associated with improved drug treatment intensification, monitoring, and physiologic control among patients with diabetes, with greater improvements among patients with worse control and less testing in patients already meeting guideline-recommended glycemic and lipid targets."
—Mary Reed, Dr.P.H.

The adherence rates were 37.6 percent, 31.6 percent, 34.4 percent, and 33.2 percent at the intervention sites, respectively, and 31 percent, 30.3 percent, 32.3 percent, and 30.9 percent at the control sites. The intervention was associated with a significant 2.2 percentage-point decrease in likelihood of colonoscopy adherence among those eligible for screening and a 5.6 percentage-point decrease in likelihood of screening among the adherent. But total colonoscopies for all indicators increased 3.6 per 100 veterans.

"This absence of favorable impact may have been caused by an unintentional shift of limited VA colonoscopy capacity from average-risk screening to higher-risk screening and to CRC surveillance, or by physician fatigue resulting from the large number of clinical reminders implemented in the VA," conclude the authors, led by John Bian, Ph.D., from the William Jennings Bryan Dorn VA Medical Center in Columbia, S.C.

But in a study of EHRs in ambulatory care practices in a community-based setting, published online Oct. 3 in the *Journal of General Internal Medicine*, researchers found that both breast cancer screening and CRC screening were improved. In the study of 466 physicians and 74,618 patients in Hudson Valley, N.Y., both breast cancer screening and CRC screening were significantly higher among physicians utilizing EHRs compared to paper records (76.1 percent versus 73 percent, respectively for breast cancer screening, and 49.6 percent versus 45.8 percent for CRC screening).

Diabetes Care

In the same study of New York ambulatory patient care practice, rates of hemoglobin A1c (HbA1c) testing were significantly higher among EHR-using physicians (87.7 percent) versus paper record physicians (81.1 percent). Rates of low-density lipoprotein (LDL) testing and nephropathy screening were also higher among physicians using EHRs compared to those using paper, but not significantly so, possibly because of limited statistical power for those measures the authors suggest.

The evidence for improved diabetes care seems consistent. Implementation of an EHR system in a large integrated health system was associated with even greater improvements in clinical care including appropriate test utilization and better intermediate outcomes for outpatients with diabetes, according to a study published Oct. 2 in the *Annals of Internal Medicine*.

In this study the researchers analyzed data from 169,711 patients with diabetes mellitus before and after implementation of a commercially available outpatient EHR system across 17 medical centers throughout Kaiser Permanente Northern California. The researchers found that use of an EHR was associated with improved clinical care, specifically a significant increased likelihood of one-year retesting for HbA1c and LDL-C levels among all patients. The most dramatic change in retesting was among patients with the worst disease control (HbA1c of 9 percent or greater or LDL-C of 3.4 mmol/L or more). There was also significant decrease in 90-day retesting among patients with HbA1c level less than 7 percent or LDL-C levels less than 2.6 mmol/L. The EHR was also associated with improved patient outcomes, namely a statistically significant reduction in HbA1c and LDL-C levels, with the largest reductions among patients with the worst control.

The authors, led by Mary Reed, Dr.P.H., from Kaiser Permanente's Division of Research in Oakland, Calif., concluded that, "Use of a commercially available certified EHR was associated with improved drug treatment intensification, monitoring, and physiologic control among patients with diabetes, with greater improvements among patients with worse control and less testing in patients already meeting guideline-recommended glycemic and lipid targets."

European C. Diff Testing Guidelines Not Followed, Study Finds

Despite believing that Clostridium difficile infections (C. difficile) are on the rise, European clinicians are not following European testing guidelines, according to results of a multinational survey presented at the international ID Week 2012 conference (San Diego; Oct. 17-21).

Researchers surveyed 868 clinicians (81 percent hospital physicians including microbiologists and infectious diseases specialists and 19 percent general practitioners) in five European countries with 33 questions. The survey was commissioned by Astellas Pharma Europe (United Kingdom).

"These data reveal a difference between what is requested by clinicians and the tests performed by laboratories. . . . It's concerning to see that there appears to be confusion about which C. diff tests are actually being used."
—Mark Wilcox, M.D.

The European Society of Clinical Microbiology and Infectious Diseases guidelines recommend a two-step testing approach for the diagnosis of C. difficile, but just 22 percent of surveyed health care professionals understood that laboratories use this two-test diagnostic algorithm to detect both the presence of C. difficile and the presence of toxins.

Overall stool culture and EIA toxin A+B+ were the most frequently requested diagnostic tests—64 percent and 44 percent, respectively. But microbiologists predominantly used EIA toxin A+B+ tests (75 percent) followed by stool culture (42 percent), GDH antigen testing (30 percent), and real-time PCR (28 percent).

"These data reveal a difference between what is requested by clinicians and the tests performed by laboratories," write the authors, led by Mark Wilcox, M.D., from the University of Leeds (United Kingdom). "It's concerning to see that there appears to be confusion about which C. diff tests are actually being used."

Test requests also varied geographically with the highest number of requests for stool cultures in Spain and France (70 percent to 80 percent) and the lowest number of requests

in the United Kingdom (50 percent). The highest number of requests for EIA toxin A+B+ were in France (more than 65 percent) with the lowest number in Spain (30 percent).

"The findings suggest that the recommended CDI diagnostic tests may not be being conducted systematically across Europe. This could lead to underdiagnosis or misdiagnosis, ultimately meaning that patients may not receive optimum care," said Wilcox. "The net effect of this nonstandardized approach to testing could also mean that the true incidence of CDI across Europe is underestimated."

The authors say that education is required with clinicians and laboratories needing to "engage to optimize" how and when C. difficile testing is performed.

Pathogenic Oral Bacteria Tied to Increased Risk of Pancreatic Cancer; Higher Levels of Common Oral Microbiota Reduce Risk

There is a twofold increase in the risk for pancreatic cancer among individuals who have high levels of antibodies to the oral pathogen Porphyromonas gingivalis (P. gingivalis) compared to individuals with lower levels, according to a study published online Sept. 18 in *Gut*. There is currently no biomarker with sufficient sensitivity and specificity for population-level screening for pancreatic cancer, so efforts aimed at prevention of risk factors may improve the notoriously dismal survival rates for pancreatic cancer.

The researchers measured antibodies to oral bacteria in blood samples from 405 pancreatic cancer cases (prediagnosis) and 416 matched controls participating in the European Prospective Investigation into Cancer and Nutrition study. Mean follow-up time was five years (and up to 10 years) for cases from the time of blood draw to diagnosis date, thus minimizing the likelihood that changes in immune response could have occurred after pancreatic cancer development.

"By using prediagnostic bloods, we were able to minimize reverse causation and examine the association with antibodies many years prior to diagnosis of cancer," write the authors, led by Dominique Michaud, Sc.D., from Brown University in Providence, R.I. "We had detailed data on smoking history and other known risk factors of pancreatic cancer and conducted multivariate analyses to rule out potential confounding by these factors."

Individuals with high levels of antibodies against P. gingivalis ATTC 53978 (greater than 200 ng/ml) had a twofold higher risk of pancreatic cancer than individuals with lower levels (200 ng/ml or less) of these antibodies. On the other hand, increased levels of antibodies against commensal or nonpathogenic oral bacteria might reduce the risk of pancreatic cancer. In cluster analysis, those with overall higher levels of antibodies for commensal or nonpathogenic oral bacteria had a 45 percent lower risk of pancreatic cancer than a cluster with overall lower levels of commensal antibodies (OR 0.55; 95 percent CI 0.36 to 0.83).

"High levels of antibodies to P. gingivalis ATCC 53978 may be the best antibody marker for high bacterial load and aggressive periodontal disease, which is in agreement with the third National Health and Nutrition Examination Survey data, and thus may explain why it was the only suspected periodontal pathogen associated with an elevated risk of pancreatic cancer," conclude the authors.

G2 Insider

Computer Algorithm Aids in Rapidly Identifying Patients at Risk of Surgical Site Infections . . . A hybrid, human-adjudicated electronic surveillance model for detection of surgical site infections (SSI) may make the workload for human infection preventionist reviewers more manageable, according to a report commissioned by the Agency for Healthcare Research and Quality.

The intent of the study was to develop techniques to improve the identification and surveillance of likely cases of SSI using data derived from electronic medical records, laboratory test results, and patient demographics for four common procedures—hernia repair, coronary artery bypass grafts, and hip and knee arthroplasty. The researchers were led by co-principal investigator Lucy A. Savitz, Ph.D., from Intermountain Healthcare (Salt Lake City), which implemented a similar scheme early on in the adoption of electronic health records.

The report, "Improving the Measurement of Surgical Site Infection (SSI) Risk Stratification and Outcome Detection," focuses on the development and testing of a computer-assisted algorithm able to flag the charts of patients most likely to have an SSI, thereby improving the efficiency (time spent to find a positive case) of human reviewers and creating significant resource savings. Electronic-only approaches have typically had poor specificity. But by combining the benefits of manual surveillance (adaptability to situational awareness) and of an automated system (rapidity), the researchers set out to build a two-tiered system utilizing an algorithm with high negative predictive value that favored sensitivity over specificity. Human adjudication improved the specificity of the SSI surveillance system.

The authors say that if charts are reviewed in roughly 20 minutes and the fraction of SSI among procedures is roughly 1 percent, then 33 hours of review could be anticipated for every SSI found. If electronic tools could effectively remove 80 percent of charts, then only 6.6 hours would be spent for every SSI found. The authors recommend that algorithms are validated at each health system in which they will be introduced, "in a manner akin to the quality assurance policies regarding new laboratory equipment." G2

Company References

Agency for Healthcare Research and Quality
301-427-1364

Astellas Pharma Europe
+44 203 379 8000

Boehringer Ingelheim Pharmaceuticals
+49-6132-77 0

Centers for Medicare and Medicaid Services
877-267-2323

DNASTAR 608-258-7420

Golden Helix 406-585-8137

Illumina 858-202-4500

Parktek 314-884-6174

Rapid Pathogen Screening
941-556-1850

Ventana Medical Systems
520-887-2155

 Diagnostic Testing & Technology Report (ISSN 1531-3786) is published by G2 Intelligence, 1 Phoenix Mill Lane, Fl. 3, Peterborough, NH 03458-1467. Tel: 800-401-5937. Fax: 603-924-4034. Web site: www.G2Intelligence.com.

Kimberly Scott, Managing Editor, kscott@G2Intelligence.com; Lori Solomon, Editor; Heather Lancey, Designer; Beth Butler, Marketing Director; Dan Houder, COO and Publisher

Receiving duplicate issues? Have a billing question? Need to have your renewal dates coordinated? We'd be glad to help you. Call customer service at 800-401-5937.