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A DIVISION OF PLAIN LANGUAGE MEDIA

# DIAGNOSTIC TESTING & Emerging Technologies

New Trends, Applications, and IVD Industry Analysis

February 2018

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## Venture Capital Investment in Diagnostic Companies Strong in 2017

Venture capital investments in health care innovation reached an all time high in 2017, including in diagnostics/tools (Dx/Tools) companies, according to Silicon Valley Banks' preliminary *2018 Healthcare Investments and Exits Report*. Investment was strong in Dx/Tools companies, particularly in companies using artificial intelligence, informatics, and liquid biopsy technologies.

"As Dx/Tools companies integrate computational methods such as artificial intelligence, we see tech investors, many new to health care, starting to invest in these deals," writes lead author of the report Jonathan Norris, managing director at Silicon Valley Bank.

In total, U.S. health care venture fundraising reached a record $9.1 billion, a 26 percent increase over 2016. The previous record was $7.5 billion raised in 2015. Dx/Tools fundraising increased 40 percent, reaching $2.8 billion in 2017. However, 60 percent of this total—or $1.6 billion—came from investments in liquid biopsy companies Guardant Health (Redwood City, Calif.) and GRAIL (Menlo, Park, Calif.), an Illumina spin off.

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## Gene Expression Panels Less Cost-Effective in Real-World Settings

Gene expression profile tests may be less cost effective in real-world, clinical settings than previously thought, according to a study published Jan. 8 in the *Journal of Clinical Oncology*.

Oncotype DX (Genomic Health; Redwood City, Calif.) is the most commonly used, commercially available gene expression profile test and helps predict breast cancer recurrence. Under ideal, research protocols, the test was determined cost effective by current standards. However, this new study questions the test's cost effectiveness when used in community practice.

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Venture Capital Investment in Diagnostic Companies Strong in 2017, *from page 1*

## AI, Liquid Biopsy Led Dx/Tools Investments

- In total, 19 Dx Test companies received more than $2 billion in investment.
- Large investments were also made in the DX Analytics space with 16 companies receiving a combined $749 million, including 23andMe (Mountain View, Calif.), WuXiNextCode (Cambridge, Mass.), Color (South San Francisco, Calif.), and AccuraGen (Menlo Park, Calif.).
- The Dx/Tools subset that Silicon Bank calls R&D Tools, defined as research equipment and services for biopharma and academia, closed 42 deals valued at $981 million in 2017, up 50 percent since 2016. These investments benefited the analytics platform company Human Longevity (San Diego, Calif.) and liquid biopsy tools makers Quanterix (Lexington, Mass.) and RareCyte (Seattle, Wash.).
- Liquid biopsy investment "exploded" with $1.8 billion (85 percent of the total raised) in Guardant Health, GRAIL, and Human Longevity.

## Early-Stage Investments Are Smaller

In contrast to previous years, series A investments were made in early-stage Dx companies. Overall, the Dx/Tools sector saw an increase in the number of series A investments (73 in 2017 versus 55 in 2016). However, the value of investments fell slightly from $516 million 2016 to %500 million in 2017. This caused the median round size to also drop from $5.3 million in 2016 to $4.7 million in 2017.

- The R&D Tools subset had four series A investments at $25 million or more. Norris attributes this interest in R&D Tools companies to the lack of regulatory and reimbursement hurdles facing other Dx/Tools subsectors.
- However, the majority of deals valued at $10 million or more were companies using artificial intelligence, like PathAI (Cambridge, Mass.) and M2Gen (Tampa, Fla.).

## Dx/Tools Companies Lacking Exits in 2017

Dx/Tools had no big mergers and acquisitions in 2017 and only one initial public offering. Given the strength of investments in Dx/Tools, Norris does anticipate big exits in the sector in the next few years. This, he says, will be driven by the emergence of tech giants, who have been making investments in the Dx/Tools sector, as potential acquirers.

"We anticipate that tech-focused investors will continue to apply their software expertise in Dx Analytics deals that leverage artificial intelligence," explains Norris. "While tech corporate venture participation has increased, these investors focus on a small set of deals most compatible with their own technologies."

## 2018 Predictions

Overall, Norris expects a slight pullback in health innovation-related investment in 2018, predicting that fundraising will "be strong," but will decline

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***Diagnostic Testing and Emerging Technologies*** (ISSN 2330-5177) is published by G2 Intelligence, Plain Language Media, LLLP, 15 Shaw Street, New London, CT, 06320.
**Phone:** 1-888-729-2315
**Fax:** 1-855-649-1623
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to below $7 billion in 2018. In line with this, Dx/Tool investments will also decline. However, the decline may appear dramatic, as the 2017 numbers were substantially boosted by large investment in just a few deals, namely GRAIL. Despite the anticipated decline in the value of investment, Norris, expects the number of Dx/Tool deals to remain "steady" in 2018.

*Takeaway: the Dx/Tools sector saw strong venture capital investment in 2017, driven in large part by huge interest in artificial intelligence-based analytics and liquid biopsy technology.*

## Basket Study Shows Early Efficacy Targeting Cancer Only On Alterations

Early results from an ongoing "basket study" show that targeted therapies may be effective strictly based on the tumor's molecular profile, and not primary tumor type, according to a rapid communication published Jan. 10 in the *Journal of Clinical Oncology*. The ongoing MyPathway study is testing off-label use of four approved targeted therapies in multiple tumor types.

> *"Molecular alterations in these genes and pathways also occur in a variety of nonindicated tumor types."*
>
> — John D. Hainsworth

Molecular profiling is becoming the standard of care to guide the selection of targeted therapies for the treatment of patients with lung, breast, and colon cancers based upon molecular alterations in human epidermal growth factor receptor-2 (HER2), epidermal growth factor receptor (EGFR), v-raf murine sarcoma viral oncogene homolog B1 (BRAF) genes, and the Hedgehog pathway.

"Molecular alterations in these genes and pathways also occur in a variety of nonindicated tumor types," write the authors led by John D. Hainsworth, from the Sarah Cannon Research Institute in Nashville, Tenn. "The low incidence of the targeted molecular alterations in these tumor types (usually less than 5 percent) has made it difficult to recruit sufficient numbers of patients into traditional drug development studies, although activity has been documented in anecdotal reports."

The MyPathway study, supported by Roche/Genentech, is a nonrandomized, phase IIa multiple basket study that is evaluating the efficacy of four treatments targeting molecular alterations in HER2 (pertuzumab plus trastuzumab), BRAF (vemurafenib), Hedgehog pathway (vismodegib), or EGFR (erlotinib) in patients with tumor types outside of current labeling for these treatments. Eligible patients were required to have previous genomic profiling demonstrating one of the target alterations at a CLIA-approved laboratory.

Between April 1, 2014, and Nov. 1, 2016, 251 patients with 35 different tumor types received study treatment at 38 different centers, but analysis only included the 230 who had reached the first efficacy evaluation. Participants had completed a median of 2.5 prior systemic treatment regimens. Identified tumor molecular alterations included HER2 (66 percent), BRAF (21 percent), Hedgehog (9 percent), and EGFR (4 percent).

Nearly one-quarter of patients (23 percent) had objective treatment responses (complete, n = 4; partial, n = 48). All four targeted treatments produced

meaningful responses in 14 different tumor types. Four tumor-pathway cohorts enrolled at least 12 patients and had protocol-mandated efficacy review: HER2 amplified/overexpressing in colorectal cancer (objective response in 14 of 37), HER2 amplified/overexpressing non-small cell lung cancer (NSCLC; objective response in two of 16), HER2-mutated NSCLC (n = 14), and BRAF V600E-mutated NSCLC (objective response in six of 14). The study was closed to further accrual of BRAF non-V600 mutations because of the low response rate (one of 23 patients with diverse tumor types).

"To date, most basket trials have reported mixed results, which may be due to the pathways being targeted, the methods of molecular testing, or the therapeutic agents being tested," writes Hainsworth and colleagues. "The design of MyPathway maximizes the chance of success by using CLIA-approved molecular testing readily available in the clinic and by selecting FDA-approved targeted agents backed by more than a decade of translational science and clinical experience."

*Takeaway: Early results from an ongoing basket trial show that targeting treatment strictly based on molecular alterations and not tissue of origin is a promising strategy.*

## Study Shows Progress Towards a Blood-Based, Multi-Cancer Screen

A blood-based screening test capable of detecting multiple forms of early cancer just took one step closer to becoming a reality. A study published Jan. 18 in *Science* highlights the use of the blood test in a large study of both early-stage cancer patients and seemingly healthy controls.

The blood test, called CancerSEEK, simultaneously evaluates levels of eight common cancer-associated proteins and the presence of mutations on 16 cancer genes from cell-free DNA circulating in the blood. Unlike other liquid biopsy technologies, the test also relies on artificial intelligence to find patterns in the protein and genetic results to pinpoint the tissue of origin. The cancers that the test screens for—ovarian, liver, stomach, pancreas, esophageal, colorectal, lung, and breast—account for more than 60 percent of cancer deaths in the United States. Five of the cancers covered by the test—ovarian, liver, stomach, pancreas, and esophageal—currently have no screening test.

Despite the hype and large investments in commercial companies like GRAIL (spun out of Illumina with $1.2 billion in venture funding) and Freenome, which raised $65 million in early-stage venture funding, neither pan-cancer test hopeful has published data on their test. However, PapGene and Personal Genome Diagnostics, both spun out of laboratories at Johns Hopkins University, have published data on their liquid tests, including this study in Science, and are hopeful they can turn their technology into testing realities.

Among the eight cancer types evaluated, the median sensitivity of CancerSEEK was 70 percent, but the sensitivities ranged from 98 percent for ovarian cancers to 33 percent in breast cancers. For the five cancer types with

> *"Our study lays the conceptual and practical foundation for a single, multi-analyte blood test for cancers of many types."*
>
> — Joshua Cohen

no current screening test available, the sensitivities ranged from 69 percent for esophageal cancer to 98 percent for ovarian cancer.

The specificity of CancerSEEK was greater than 99 percent, with only seven of 812 healthy controls testing positive.

"New blood tests for cancer must have very high specificity; otherwise, too many healthy individuals will receive positive test results, leading to unnecessary follow-up procedures and anxiety," write the authors led by Joshua Cohen, from the Johns Hopkins School of Medicine in Baltimore, Md.

Lastly, machine learning was used to predict the underlying cancer type in patients with positive CancerSEEK tests. CancerSEEK was able to narrow the cancer to a small number of anatomic sites in a median of 83 percent of the patients and pinpoint the cancer to a single organ in a median of 63 percent of these patients. The accuracy of the prediction varied with tumor type and was highest for colorectal cancers and lowest for lung cancers.

"Our study lays the conceptual and practical foundation for a single, multi-analyte blood test for cancers of many types," writes Cohen and colleagues, who say they anticipate commercializing the test for under $500. "To actually establish the clinical utility of CancerSEEK and to demonstrate that it can save lives, prospective studies of all incident cancer types in a large population will be required."

*Takeaway: A new study highlights that a multi-cancer, blood-based screening test may become a clinical reality.*

## Penicillin Skin Testing Can Delabel Misidentified Allergic Patients

In an era of growing concerns over antibiotic stewardship, there is renewed interest in delabeling misidentified penicillin allergies as part of quality improvement efforts. Most patients who report being allergic to penicillin actually test negatively, according to a presentation at the American College of Allergy, Asthma and Immunology meeting (Oct. 26-30, 2017; Boston; Mass.). The study also showed that penicillin skin testing (PST) is feasible in real-world outpatient allergy practice.

The researchers obtained a penicillin allergy history from new and existing patients of an outpatient allergy practice. All qualifying patients were offered PST, followed by an amoxicillin challenge with 30-minute observation if PST was negative.

Nearly 16 percent of all patients seen (119 of 755) reported a penicillin allergy. Forty-eight patients completed a PST, with 85.4 percent testing negative. In the remaining 65 patients reporting penicillin allergies, but not undergoing PST, 20 were on interfering medications, seven reported a delayed reaction, five reported anxiety or needle fear, five experienced time constraints, five had a recent reaction, four had a recent positive PST, and eight were scheduled for future PST or challenge. An additional 11 were not tested for other reasons.

"Our analysis provides a real world representation of the feasibility of PST and illustrates that quality improvement projects aimed at PST can improve its utilization," wrote S. Shahzad Mustafa, from University of Rochester in New York, in the conference abstract.

*Takeaway: Verifying patient-reported penicillin allergies with PST is feasible in routine care and can improve antibiotic stewardship.*

## Testing Guidelines at a Glance

### New Guidance on the Use of Lab Testing to Monitor Pain Management Patients

The American Association of Clinical Chemistry released the practice guideline, "Using Clinical Laboratory Tests to Monitor Drug Therapy in Pain Management Patients," in the January issue of the *Journal of Applied Laboratory Medicine*. The committee says that while urine drug testing is regarded as the standard for adherence monitoring of patients taking controlled substances to manage chronic pain, test results are read and interpreted by distinctly different sets of individuals, including laboratory scientists and clinicians. The comprehensive guideline encompasses test use (laboratory and point-of-care [POC]) and results reporting and is based on both evidence-based recommendations and consensus-based expert opinion.

The guideline addresses tests for relevant over-the-counter medications, prescribed and nonprescribed drugs, and illicit substances in pain management patients. Some of the more than 30 recommendations include:

- The three main tiers of testing (routine monitoring, testing of high-risk patients, and clinically needed testing) and classes of drugs to be tested should be based on risk, with more frequent laboratory testing recommended for patients with a personal or family history of substance abuse, mental illness, evidence of aberrant behavior, or other high-risk characteristics.
- Urine is the preferred specimen type for pain management drug testing, as the evidence supporting alternative matrices (e.g., saliva, blood, plasma, serum, or hair) is currently insufficient for monitoring patient compliance.
- Qualitative definitive tests should be used over immunoassays because they are more effective with superior sensitivity and specificity.
- POC (oral and urine) qualitative presumptive immunoassays offer similar performance characteristics to laboratory-based immunoassays for some can detect some over-the-counter medications, prescribed and nonprescribed drugs, and illicit substances in pain management patients, but POC tests must be performed exactly according to the manufacturer's instructions.
- Qualitative immunoassay drug testing before prescribing controlled substances can identify some illicit drug use and decrease adverse outcomes.
- Random urine testing is recommended to assess compliance, although there is not clarity around the ideal frequency.
- Definitive testing should be used to follow-up any unexpected results for any immunoassay (laboratory-based or POC).
- Quantitative definitive urine testing is not more useful than qualitative definitive urine testing for detecting outcomes in pain management. Quantitative definitive urine testing should not be used to evaluate dosage or adherence to prescribed dosage regimens. However, qualitative results may be useful in complex cases to determine the use of multiple opioids, confirm spiked samples, and/or rule out other sources of exposure.
- At a minimum specimen validity testing should include pH, temperature, creatinine, and oxidant testing on all urine drug tests for pain management patients, even not all forms of adulteration can be detected.

# Internet-Based Testing for STIs Increase Uptake

Providing internet-based testing for sexually transmitted infections (e-STI testing) could increase the number of people being tested for syphilis, HIV, chlamydia, and gonorrhoea, including among high-risk groups, according to a study published Dec. 27, 2017 in *PLOS Medicine*. e-STI testing doubled testing uptake compared to testing uptake among participants randomized to testing at usual care health clinics.

The World Health Organization says that increasing testing, diagnosis, and treatment of STIs and reducing time to treatment is a global priority to reduce the prevalence of STIs and their downstream consequences. In the United Kingdom, like in the United States, STI testing levels remains sub-optimal.

Interventions, like e-STI, that increase access, particularly among high-risk and hard-to-reach groups, are of high interest to maximize the public health benefits of STI testing, while offering patient benefits such as increasing convenience and removing embarrassment associated with face-to-face STI services. e-STI testing typically enables users to order a test kit from a website or app, collect their own samples, mail test samples to a laboratory, and receive results electronically.

In the U.K.-based study, 2,072 sexually active young people (aged 16 to 30 years of age residing in two London boroughs), with stated willingness to take an STI test, were randomized to receive a text message. The text message provided either the website for eSTI or the location of a local STI health clinic. Randomization balanced gender (male, female, transgender), age (16 to 19 years, 20 to 24 years, and 25 to 30 years), number of sexual partners in last 12 months, and sexual orientation. If participants reported using another health service outside of the study providers during the study period, STI testing, diagnosis, and treatment data was collected.

The e-STI program, SH:24, offers free postal self-sampling test kits for chlamydia, gonorrhoea, HIV, and syphilis. All test kits contained a lancet and collection tube to obtain a blood sample for serological testing for syphilis and HIV, as well as either a vaginal swab (women) or urine collection (men) for chlamydia and gonorrhea. For men who have sex with men (MSM), test kits also contained swabs to take pharyngeal and rectal samples. The tests kits included pictorial brochures with instruc-

## FDA Weighs Self-Sampling for Pap Testing

In early January a U.S. Food and Drug Administration (FDA) expert panel met to address the feasibility, benefits and risks of self-collection cervical sampling for cervical cancer screening by Pap testing. Speakers were split on whether the benefits of self-sampling, primarily increasing access to testing particularly among underserved populations, outweighed the risks posed by accuracy concerns and uncertain standards for follow-up on abnormal results.

The U.S. Centers for Disease Control and Prevention presented data showing that screening levels have remained stable since 2000 (about 80 percent) and that certain populations remain underscreened (e.g., women with lower educations, underinsured, and those from certain ethnicities and geographical regions).

The panel seemed to agree that any self-collection devices for Pap testing must be held to the same standards necessary for current clinic-performed Pap testing. Yet, there was not agreement on the design of studies to assess the performance of self-selection against current standards of care. Other unresolved issues included whether laboratories should report these results directly to patients and how those with abnormal results could be linked to follow-up care.

Shyam Kalavar, a scientific reviewer with the FDA's Office of In Vitro Diagnostics and Radiological Health, told Medscape that although the meeting was focused on self-collection for liquid-based Pap testing, it could lay the groundwork for how the agency might approach other self-collection devices for cervical cancer screening.

tions for sample collection and a Youtube blood sample collection video on SH:24 website. After 2 weeks, non-returners were sent reminders via text and resent test kits, if required. Chlamydia, gonorrhoea, and syphilis results were returned by text message, while positive HIV results were returned by phone. Confirmatory testing and treatment were provided at local clinics.

The researchers found that at 6 weeks, significantly more participants in the intervention group completed an STI test compared to the control group (50 percent versus 26.6 percent). However, there were no significant differences in the number diagnosed nor the time to treatment.

"The long-term public health benefits of e-STI services will depend on testing, diagnosis, and treatment rates when implemented. These outcomes should be subject to ongoing monitoring and evaluation," write the authors led by Emma Wilson, from the London School of Hygiene & Tropical Medicine in the United Kingdom. The authors add in a statement that, "going forward we advise joint commissioning of these different modalities of care to ensure that users are able to move easily from one to another according to their health care needs, allowing continuity of care."

*Takeaway: e-STI may increase testing uptake, including upon high-risk populations.*

## Older Adults Undertested, Underdiagnosed with the Flu

Hospitals around the nation are seeing high volumes of patients with the flu this season. A new study, published online Jan. 17 in the *Journal of the American Geriatrics Society*, shows that older adults hospitalized with fever or respiratory symptoms during influenza seasons are less likely to have a provider-ordered flu test, compared to younger patients.

"Further strategies are needed to increase clinician understanding of the challenges in clinically identifying influenza in older adults, as well as the limitations of diagnostic tests, to better diagnose and treat cases of influenza in this vulnerable population," write the authors led by Lauren Hartman, M.D., from Vanderbilt University in Nashville, Tenn.

Older adults are disproportionately hospitalized for the flu and existing evidence shows that early diagnosis and treatment improves outcomes. The U.S. Centers for Disease Control and Preventions says that a total of 8,990 laboratory-confirmed influenza-associated hospitalizations were reported between Oct. 1, 2017, and Jan. 13, 2018. The overall hospitalization rate was 31.5 per 100,000 people. The highest rate of hospitalization is among adults 65 years and over (136.5 per 100,000), followed by adults aged 50 to 64 years (33.2 per 100,000) and then children aged 0 to 4 years (22.8 per 100,000).

Vanderbilt University researchers assessed influenza testing among 1,422 adults hospitalized with acute respiratory illness or nonlocalizing fever at four hospitals (one academic and three community facilities) in Tennessee between November 2006 and April 2012. They prospectively performed reverse-transcriptase polymerase chain reaction (RT-PCR) influenza

testing for all patients, even if the patients' providers had not ordered it. The researchers then compared demographic and clinical characteristics of patients whose providers had ordered testing with those of patients for whom laboratory-based diagnostic tests had not been ordered.

The researchers found that over the study period, providers requested tests for just over one-fourth of patients (28 percent). Of those patients with tests ordered, patients who were younger were significantly more likely to have provider-ordered testing were younger than untested patients (average age, 58 years for tested patients versus 66 years for untested patients). Part of this difference was explained that tested patients were more likely to have flu-like symptoms (e.g. fever, cough, and/or sore throat), which decreased with age.

RT-PCR testing identified flu in 10 percent of patients (n=136), but of those patients with confirmed flu, 43 percent did not have test orders placed by their providers. Patients receiving care in the academic hospital were more likely to have provider-ordered influenza tests (41 percent versus 20 percent in community hospitals). The 450 provider-ordered tests were primarily for antigen detection (97.0 percent), 7.3 percent were for viral culture, and 8.5 percent were for RT-PCR.

"The challenge of influenza diagnosis in hospitalized older adults is to not only identify cases clinically, but select an appropriate sensitive diagnostic test such as RT-PCR," write Hartman and colleagues.

*Takeaway: Older, hospitalized patients are undertested and underdiagnosed with the flu. Furthermore, when testing is ordered it is most often not sensitive diagnostic tests, like RT-PCR.*

## Routine, PreoOp Testing Costlier for Medicare Than Previously Thought

The traditional 30-day window prior to the date of surgery does not always capture routine preoperative medical testing that occurs when surgery is first contemplated. When considering Medicare patients whose surgery occurs more than 30 days after initially contemplated, routine preoperative medical testing is more prevalent and more costly than previously reported, according to a study published Jan. 18 in *JAMA Ophthalmology*. This study was limited to cataract surgery, but the findings likely applicable for other ambulatory procedures, the authors say.

"Prior studies on routine preoperative testing, which usually highlight the testing that occurs during a 30-day preoperative window, have not accounted for the extended preoperative testing period that begins when the decision is first made to operate," write the authors led by Catherine Chen, M.D., from University of California, San Francisco. "There are likely to be more patients undergoing routine preoperative testing before low-risk surgical procedures similar to cataract surgery than previously recognized, despite the existence of guidelines recommending against such interventions."

The researchers assessed preoperative care in a sample of 440,857 Medicare beneficiaries (mean age, 7.1 years) who underwent ambulatory cataract

*"As a cost-cutting measure, routine preoperative medical testing should be avoided in patients with cataracts throughout the interval between ocular biometry and cataract surgery."*

— Catherine Chen, M.D.

surgery in 2011. Ocular biometry, a diagnostic test to determine the required power of the intraocular lens to be implanted during cataract surgery, was the procedure-specific indicator to mark the extended preoperative testing period. The testing rates in the interval between ocular biometry and cataract surgery and compared to testing rates in the 6 months preceding biometry.

Identified laboratory tests that are commonly performed for preoperative workup in older patients, included chemistry panels, complete blood counts, coagulation panels, and urinalysis. (Other included non-laboratory tests included electrocardiography, echocardiography, cardiac stress test, chest radiograph, and pulmonary function tests.)

The researchers found that 96.1 percent of patients had an ocular biometry claim before index surgery. In 6.3 percent the biometry claim was on the day of surgery, 25.4 percent had the biometry claim more than 30 days before surgery, and 5.1 percent had the biometry claim more than 90 days before surgery.

More than 1 million tests were performed during the extended preoperative interval between biometry and surgery. Routine preoperative testing rates were higher during the time interval between biometry and surgery (1.7 tests/patient/month) versus the baseline time period (1.1 tests/patient/month) or in the months following cataract surgery (1.1 tests/patient/month). Preoperative testing peaked both in the 30 days after biometry (1.7 tests/patient/month) or the 30 days before surgery (1.8 tests/patient/month).

For patients with the longest preoperative window—patients who had surgery either 6 months or 9 months after biometry—an increase in testing was seen both in the month immediately after biometry (2.4 and 2.6 tests/patient/month, respectively) and another increase during the month before surgery (2.2 and 2.3 tests/patient/month, respectively) compared with the baseline rate of testing (1.3 tests/patient/month in both cohorts).

Extrapolating the findings for the total Medicare population undergoing cataract surgery in 2011, the total number of routine preoperative tests that were performed during the extended preoperative interval between biometry and surgery cost approximately $45.4 million annually.

"Even when taking into account background testing that may occur in this older population, we showed that the cost of testing increased by 37% over a comparable period that occurred 1 year prior to the biometry claim, suggesting that much of the additional testing that occurred in these patients was in anticipation of undergoing low-risk elective surgery," conclude Chen and colleagues. "As a cost-cutting measure, routine preoperative medical testing should be avoided in patients with cataracts throughout the interval between ocular biometry and cataract surgery."

*Takeaway: When accounting for a sizable portion of Medicare patients who undergo cataract surgery more than 30 days after initially consulting a doctor, routine preoperative testing rates are higher than previously estimated. These findings indicate that routine preoperative is common and likely unnecessary among most cataract patients.*

Gene Expression Panels Less Cost-Effective in Real-World Settings, *from page 1*

> *"As with all new technology, it's important to assess real-world implementation to ensure what we're offering patients is useful to them and doesn't add to the societal and patient cost-burden, which is already very high in cancer care."*
>
> — Young Chandler, Dr.P.H.

"As with all new technology, it's important to assess real-world implementation to ensure what we're offering patients is useful to them and doesn't add to the societal and patient cost-burden, which is already very high in cancer care," said the study's lead author, Young Chandler, Dr.P.H., from Georgetown University, in a statement.

Oncotype DX examines the activity of 21 genes in a patient's breast tumor tissue to predict the benefit of chemotherapy based on the risk of cancer recurrence. The test is intended for use in newly diagnosed patients with early-stage (stage I, II or IIIa), estrogen receptor-positive, HER2-negative breast cancer. Patients with test results indicating low-risk can consider skipping chemotherapy, while those with high-risk results are recommended to have chemotherapy. All major, U.S. insurance covers the test, the company says.

Unlike previous studies of Oncotype DX, which were conducted under ideal conditions—all patients received the test, the test's score dictated treatment decisions, and the test had prefect prediction of recurrence—this new research examines who is tested in real-world practice; how many patients at high risk of breast cancer recurrence do not act on treatment recommendations for chemotherapy; conversely, how many patients found to be at lower risk of recurrence chose to get chemotherapy anyway; and the impact of test accuracy on cost effectiveness.

The researchers created a model to compare 25-year incremental costs and quality-adjusted life-years (QALYs) based on community use of Oncotype DX from 2005 to 2012. Results were compared to usual care in the pretesting era (2000 to 2004).

From 2005 to 2012, testing rates among eligible patients in community practice were 24 percent and chemotherapy use rate was 30 percent. In community practice, treatment decisions sometimes ran contrary to test findings—17 to 26 percent of patients with high-recurrence risk scores did not receive chemotherapy as guidelines recommend, and 8 percent of patients with low-risk scores still opted to receive chemotherapy.

The incremental cost-effectiveness ratio of breast cancer management using Oncotype DX testing as observed in community practice versus usual care without testing was $188,125 per QALY ($100,000 per QALY is the usual benchmark for cost effectiveness). The researchers found that under ideal conditions, including perfect test accuracy, the cost-effectiveness ratio was $39,496 per QALY, which is more similar to earlier estimates.

However, cost-effectiveness increased under different scenarios, including lower test costs, higher test accuracy, greater adherence to test-suggested treatment, and consideration of the benefits of testing on quality of life.

- If Oncotype DX costs declined from $3,416 (the current Medicare reimbursement rate, to $2,657, then the incremental cost-effectiveness ratio

*"To truly understand the economics of diagnostic testing, it is important to look for consistency across multiple economic studies."*

— Genomic Health

of community practice versus usual care decreased to $71,250 per QALY.

- Adherence to test-concordant treatment lowered the cost-effectiveness ratio to $85,490 per QALY.
- Factoring in the affects of worry or reassurance as a result of information on recurrence risk, the incremental cost-effectiveness ratio for Oncotype DX testing was $58,431 per QALY.

In response to the study, Genomic Health provided a statement to *HemOnc Today*, which noted limitations of the study's model, including the assumption that Kaiser Permanente patient and testing data was representative of all of community practice. The company added, "Cost-effectiveness analyses are very complex and highly sensitive to the assumptions underlying the economic model. "To truly understand the economics of diagnostic testing, it is important to look for consistency across multiple economic studies."

*Takeaway: New data suggests that gene expression profile testing (Onco Dx, specifically) may be less cost-effective in actual community practice than under the ideal circumstances of research protocols.*