NATIONAL ACADEMIES Sciences Engineering Medicine

Board on Health Sciences Policy

Views & Voices: Reporting Genetics and Genomics

Roundtable on Genomics and Precision Health

Genomics Roundtable Hybrid Workshop
12:30 – 2:30 PM ET June 22, 2022

Register Here:
https://www.eventbrite.com/e/views-voices-reporting-genetics-and-genomics-tickets-342858106827

Roundtable on GENOMICS and PRECISION HEALTH

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AGENDA

NATIONAL ACADEMIES Sciences Engineering Medicine

Board on Health Sciences Policy

Views & Voices: Reporting Genetics and Genomics Roundtable on Genomics and Precision Health

Public Webinar: June 22, 2022

CLICK HERE TO REGISTER

WEDNESDAY, JUNE 22, 2022 12:30 – 2:30 PM ET

Moderator: Jacquelyn Taylor, Columbia University School of Nursing and Karen Weck, University of North Carolina

Purpose

- To examine how the public views and consumes news related to genomics and precision health and how reporters cover topics in these fields.
- To explore management of the crisis of credibility in genomics and precision health by reporters.

12:30–12:35 PM ET

Welcoming Remarks
Michelle Penny, *Roundtable Co-Chair*

12:35–12:40 PM

Introduction to the Session and Charge to the Participants
Nikoletta Sidiropoulos
Medical Director of Genomic Medicine
Associate Professor of Pathology and Laboratory Medicine
Department of Pathology and Laboratory Medicine
University of Vermont Health Network
Larner College of Medicine at the University of Vermont

12:40–1:00 PM

Level Setting Talk
Rick Weiss
Director
AAAS SciLine

1:00–1:30 PM

Opening Remarks from Speakers
Jennifer Abbasi
Associate Managing News Editor
JAMA

Alex Knapp
Senior Editor, Health & Science
Forbes

Tina Hesman Saey
Senior Writer, Molecular Biology
Science News

Turna Ray
Managing Editor
Precision Oncology News
GenomeWeb

Sarah Zhang
Staff Writer
The Atlantic

1:30–2:25 PM — **Panel Discussion**

2:25–2:30 PM — **Reflections on the Discussion**
Nikoletta Sidiropoulos
Medical Director of Genomic Medicine
Associate Professor of Pathology and Laboratory Medicine
Department of Pathology and Laboratory Medicine
University of Vermont Health Network
Larner College of Medicine at the University of Vermont

2:30 PM — **Adjourn**

GENOMICS ROUNDTABLE INFORMATION

NATIONAL ACADEMIES Sciences Engineering Medicine

Roundtable on GENOMICS and PRECISION HEALTH

The sequencing of the human genome is rapidly opening new doors to research and progress in biology, medicine, and health care. At the same time, these developments have produced a diversity of new issues to be addressed.

The National Academies of Sciences, Engineering, and Medicine has convened a Roundtable on Genomics and Precision Health (previously the Roundtable on Translating Genomic-Based Research for Health) that brings together leaders from academia, industry, government, foundations and associations, and representatives of patient and consumer interests who have a mutual concern and interest in addressing the issues surrounding the translation of genome-based research for use in maintaining and improving health. The mission of the Roundtable is to advance the field of genomics and improve the translation of research findings to health care, education, and policy. The Roundtable will discuss the translation process, identify challenges at various points in the process, and discuss approaches to address those challenges.

The field of genomics and its translation involves many disciplines, and takes place within different economic, social, and cultural contexts, necessitating a need for increased communication and understanding across these fields. As a convening mechanism for interested parties from diverse perspectives to meet and discuss complex issues of mutual concern in a neutral setting, the Roundtable: fosters dialogue across sectors and institutions; illuminates issues, but does not necessarily resolve them; and fosters collaboration among stakeholders.

To achieve its objectives, the Roundtable conducts structured discussions, workshops, and symposia. Workshop summaries will be published and collaborative efforts among members are encouraged (e.g., journal articles). Specific issues and agenda topics are determined by the Roundtable membership, and span a broad range of issues relevant to the translation process.

Issues may include the integration and coordination of genomic information into health care and public health including encompassing standards for genetic screening and testing, improving information technology for use in clinical decision making, ensuring access while protecting privacy, and using genomic information to reduce health disparities. The patient and family perspective on the use of genomic information for translation includes social and behavioral issues for target populations. There are evolving requirements for the health professional community, and the need to be able to understand and responsibly apply genomics to medicine and public health.

Of increasing importance is the need to identify the economic implications of using genome-based research for health. Such issues include incentives, cost-effectiveness, and sustainability.

Issues related to the developing science base are also important in the translation process. Such issues could include studies of gene-environment interactions, as well as the implications of genomics for complex disorders such as addiction, mental illness, and chronic diseases.

Roundtable sponsors include federal agencies, pharmaceutical companies, medical and scientific associations, foundations, and patient/public representatives. For more information about the Roundtable on Genomics and Precision Health, please visit our website at nationalacademies.org/GenomicsRT or contact Sarah Beachy at 202-334-2217, or by e-mail at sbeachy@nas.edu.

500 Fifth Street, NW, Washington, DC 20001
Phone 202.334.2217 E-mail sbeachy@nas.edu nationalacademies.org/GenomicsRT

Roundtable on Genomics and Precision Health Membership

W. Gregory Feero, M.D., Ph.D. (Co-Chair) *JAMA*
Michelle Penny, Ph.D. (Co-Chair)

Naomi Aronson, Ph.D.
BlueCross/BlueShield Association

Aris Baras, M.D., M.B.A.
Regeneron Pharmaceuticals

Vence Bonham, Jr., J.D.
National Human Genome Research Institute

Bernice Coleman, Ph.D., ACNP-BC, FAHA, FAAN,
American Academy of Nursing

Robert B. Darnell, M.D. Ph.D.
The Rockefeller University / NY Genome Center

Geoffrey Ginsburg, M.D., Ph.D.
Global Genomic Medicine Collaborative (G2MC)

Jennifer Goldsack, MChem, M.A., M.B.A.,
Digital Medicine Society (DiMe)

Eric Gustafson, Ph.D.,
Merck & Co.

Jill Hagenkord, M.D. FCAP
Optum Genomics

Cassie Hajek, M.D.
Helix

Richard Hodes, M.D.
National Institute on Aging

Geoff Hollett, Ph.D.
American Medical Association

Mira Irons, M.D.
College of Physicians of Philadelphia

Praduman Jain, M.S.
Vibrent Health

Sekar Kathiresan, M.D.
Massachusetts General Hospital

Alisha Keehn, M.P.A.
Health Resources and Services Administration

Muin Khoury, M.D., Ph.D.
Centers for Disease Control and Prevention

Charles Lee, Ph.D., FACMG
The Jackson Laboratory for Genomic Medicine

Christa Lese Martin, Ph.D., FACMG
Geisinger

Mona Miller, M.P.P.
American Society of Human Genetics

Adele Mitchell, Ph.D.
Biogen

Jennifer Moser, Ph.D.
U.S. Department of Veterans Affairs

Maximilian Muenke, M.D., FACMG
American College of Medical Genetics and Genomics

Kathryn Phillips, Ph.D.
University of California, San Francisco

Victoria M. Pratt, Ph.D., FACMG
Association for Molecular Pathology

Murray Ross, Ph.D.
Kaiser Foundation Health Plan, Inc.

Wendy Rubinstein, M.D., Ph.D.
Food and Drug Administration

Nadeem Sarwar, Ph.D.
Eisai Inc.

Sheri Schully, Ph.D.
All of Us Research Program, NIH

Nonniekaye Shelburne, C.R.N.P., M.S., A.O.C.N.,
National Cancer Institute

Geetha Senthil, Ph.D.
National Institute of Mental Health

Nikoletta Sidiropoulos, M.D.
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Katherine Johansen Taber, Ph.D.
Myriad Women's Health

Ryan Taft, Ph.D.,
Illumina

Jacquelyn Taylor, Ph.D.
Columbia University

Sharon Terry, M.A.
Genetic Alliance

Joyce Tung, Ph.D.
23andMe, Inc.

Jameson Voss, M.D.
U.S. Air Force

Karen Weck, M.D.
College of American Pathologists

Catherine A. Wicklund, M.S., C.G.C.
National Society of Genetic Counselors

Huntington F. Willard, Ph.D.
Genome Medical, Inc.

Sarah Wordsworth, Ph.D.
University of Oxford

Shannon Zenk, Ph.D.
Natioanl Institutes of Nursing Research

Project Staff
Sarah H. Beachy, Ph.D., *Roundtable Director*
Kathryn Asalone, Ph.D., *Associate Program Officer*
Meredith Hackmann, *Associate Program Officer*
Samantha Schumm, Ph.D., *Associate Program Officer*
Lydia Teferra, *Research Assistant*

VISION	**Realizing the full potential of health for all through genomics and precision health.**
MISSION	**We bring together diverse voices to encourage innovation and actions that foster the wide adoption of and equitable access to the benefits of genomics and precision health.**

As a group of committed stakeholders, we believe in…

- Creating an inclusive and optimistic environment for discussion
- Learning from successes and missteps in the field
- Demanding reproducible evidence-based science
- Sharing trustworthy information
- Embracing interdisciplinary strategies
- Optimizing data privacy and security
- Advancing health equity in all that we do

The Roundtable focuses its energy and resources on these priorities:

DRIVE **INNOVATION** IN GENOMICS AND PRECISION HEALTH	Identify the competing barriers and facilitators of innovation for genomics-based diagnostics, risk assessment tools, and therapies. Leverage opportunities to learn from and promote innovative approaches that can accelerate commercialization and integration to drive impact of genomics on precision health.
SPUR THE **ADOPTION** OF GENOMICS-BASED TOOLS AND PRECISION HEALTH APPROACHES	Cultivate evidence-based practices across the health care and public health systems for adopting genomics and precision health. Draw attention to gaps in adoption and their root causes and highlight potential solutions.
ACHIEVE **EQUITY** IN GENOMICS AND PRECISION HEALTH	Foster action related to underrepresentation and inequities in genomic research, workforce, and access to genomic services by people who need them. Look internally to improve the processes and practices the Roundtable employs to achieve its mission.
SHAPE THE **POLICY DIALOGUE** ABOUT GENOMICS AND PRECISION HEALTH	Accelerate the dissemination of actionable knowledge to shape practice and increase public awareness. Inform and influence how decisions are made.

DEFINITIONS

Precision Health | Inclusive of precision medicine, precision health is a broader, proactive and people-focused approach to health, relying on individual-focused care and everyday decision-making to better predict, prevent, and treat disease.

Genetics | Study of heredity, genes, and genetic variation.

Genomics | Study of the genome by using DNA sequencing and other technologies to understand gene structure, function, and regulation.

WORSKHOP INFORMATION

NATIONAL ACADEMIES Sciences Engineering Medicine

Board on Health Sciences Policy

Views & Voices: Reporting Genetics and Genomics

Roundtable on Genomics and Precision Health
June 22, 2022

Speaker Biographies

Jennifer Abbasi is a health and science journalist and the associate managing news editor at JAMA, the *Journal of the American Medical Association.* Before joining JAMA's Chicago-based news team in 2016, she was a freelance writer for national magazines including *Discover*, *Health, Popular Science and Scientific American.* Prior to that, she held staff editor positions at *Science Illustrated* magazine, *Parenting* magazine and *aMagazine: Inside Asian America*. She is a member of the National Association of Science Writers, the Association of Health Care Journalists and the Asian American Journalists Association.

Alex Knapp, J.D. is a senior editor at *Forbes* covering healthcare, science, and cutting edge technology. He received his B.S. in Biochemistry from Worcester Polytechnic Institute and his J.D. from University of Kansas School of Law.

Turna Ray has been a journalist for 17 years. In 2006, she joined the online news publication *GenomeWeb*, where she reports on the evolving role of genomics within the healthcare system, with a particular focus on how this is upending norms in medicine and introducing regulatory, legal, and ethical challenges. She is the founding editor of *GenomeWeb*'s *Precision Oncology News* sister site, which focuses on how cancer care is changing amid advances in genomics and other technologies. She is responsible for the editorial vision of the publication and manages its day-to-day editorial operations.

Tina Hesman Saey, Ph.D. is a senior writer in molecular biology for *Science News*. She is a geneticist-turned-science writer who covers all things microscopic and a few too big to be viewed under a microscope. She is an honors graduate of the University of Nebraska-Lincoln where she did research on tobacco plants and ethanol-producing bacteria. She spent a year as a Fulbright scholar at the Georg-August University in Göttingen, Germany, studying microbiology and traveling. Her work on how yeast turn on and off one gene earned her a Ph.D. in molecular genetics at Washington University in St. Louis. Tina then rounded out her degree collection with a master's in science journalism from Boston University. She interned at the *Dallas Morning News* and *Science News* before returning to St. Louis to cover biotechnology, genetics and medical science for the *St. Louis Post-Dispatch*. After a seven year stint as a newspaper reporter, she returned to *Science News*. Her work has been honored by the Endocrine Society, the Genetics Society of America, the National Academies of Sciences, Engineering, and Medicine and by journalism organizations.

Rick Weiss is the director of SciLine, a philanthropically funded free service for journalists and scientists, with a mission of making it easier for reporters to include validated scientific information in their stories. Rick founded SciLine in 2017 at the nonprofit American Association for the Advancement of Science in response to changes in the journalism landscape that saw a loss of specialty science reporters from many local newsrooms and a need to help local and general assignment reporters integrate more research-backed evidence into their reporting. He has more than three decades of experience in journalism and media affairs, including 15 years as a science reporter at *The Washington Post*, where he wrote more than 1,000 news and feature articles about the economic, societal, and ethical implications of advances in science and technology. He has led science and technology strategic communications operations in the public, private, and nonprofit sectors, including within the White House and the Department of Defense. Rick earned a bachelor's degree in biology from Cornell University and a master's degree in journalism from the University of California, Berkeley.

Sarah Zhang is a staff writer at *The Atlantic*, where she covers science and health. In 2021, she was a Livingston Award finalist for her reporting on Down syndrome. Before joining *The Atlantic*, she was a staff writer at *Wired*, and her writing has also appeared in *The New York Times*, *Nature*, and *Discover*, among other publications. Zhang is the recipient of an American Association for the Advancement of Science Kavli Science Journalism Award. She studied neurobiology and graduated from Harvard University.

NATIONAL ACADEMIES Sciences Engineering Medicine

Board on Health Sciences Policy
Roundtable on Genomics and Precision Health

Meeting of the Roundtable on Genomics and Precision Health

Views & Voices

June 22, 2022

SPEAKER GUIDANCE: CONTEXT AND QUESTIONS

The Genomics Roundtable adopted a new strategic plan in 2020 for 2021-2025. One of the new working groups, the Shaping the Dialogue Group, seeks to accelerate the dissemination of actionable knowledge to shape practice and increase public awareness and to inform and influence how decisions are made. The goal of this session is to have an open dialogue with reporters on the perceived credibility of science within genomics and precision health. Thank you for joining us for this session!

Questions to frame level-setting speaker's initial statements:

1. What is challenging about covering genomics and precision health in your work?
2. Looking back, how has communications and reporting on genomic science changed since the completion of the Human Genome Project in 2003?
3. Is there a "crisis of credibility" - of the perceived credibility of science and scientists with the public- within genomics and genetics? Why or why not?
4. What have you learned from scientific reporting regarding COVID-19 that may be relevant to reporting advances in genomic science? (e.g. vaccine misinformation; changing public health policies and guidance as new information is collected and analyzed)

Key questions for all speakers to address:

1. Is there a "crisis of credibility" - of the perceived credibility of science and scientists with the public - within genomics and genetics? Why or why not?
2. How do you view your role in communicating genomic advances with the public?
3. What would help you overcome some of the challenges of covering genomics and precision health in your work?
4. How do you select the stories that you report on? How do you determine the relevant issues in the field of genomics and precision health?
5. How do you identify credible versus non-credible sources for your research and reporting?
6. As a convener of experts who can bring attention to issues in the field, how can the Roundtable help you and other reporters?

BACKGROUND MATERIALS

Links to Additional Resources

Views & Voices: Reporting on Genomics and Precision Health

- Americans' Trust in Scientists, Other Groups Declines, Pew Research Center
- Abbasi, J. 2021. Researchers Tie Severe Immunosuppression to Chronic COVID-19 and Virus Variants. *JAMA*: 325(20):2033-2035. doi:10.1001/jama.2021.7212
- Abbasi, J. 2020. COVID-19 and mRNA Vaccines–First Large Test for a New Approach. *JAMA*: 324(12):1125-1127. doi:10.1001/jama.2020.16866
- Special report: Genetic testing goes mainstream, ScienceNews
- We finally have a fully complete human genome, ScienceNews
- The first human genetic blueprint just turned 20. What's next? ScienceNews
- DNA databases are too white, so genetics doesn't help everyone. How do we fix that? ScienceNews
- Genetic diversity data offers medical benefits, ScienceNews
- When They Warn of Rare Disorders, These Prenatal Tests are Usually Wrong, NYT
- Genetic Non-Invasive Prenatal Screening Tests May Have False Results: FDA Safety Communication, FDA
- Matching drugs to DNA is 'new era of medicine', BBC

Medical News & Perspectives

Getting Pharmacogenomics Into the Clinic

Jennifer Abbasi

What if there were a way to know if a depressed patient would respond to an antidepressant—before it was prescribed? Or to predict a bleeding event from an antiplatelet therapy? In recent years, advances in genetic testing have made such drug-response predictions possible for patients with certain gene variants. But physician adoption is moving slowly, say experts in the growing field of pharmacogenomics.

"While we've made tremendous rapid advances in terms of basic science and technological advances, and [while] clinical outcomes [are] there for some gene-drug pairs, clinical implementation unfortunately has been lagging behind," said Edith A. Nutescu, PharmD, MS CTS, associate professor and director of the Center for Pharmacoepidemiology and Pharmacoeconomic Research at the University of Illinois at Chicago College of Pharmacy.

In the results of a nationwide survey by the American Medical Association and Medco released in 2012, only 13% of more than 10 000 responding physicians had ordered a pharmacogenomic test in the previous 6 months, although almost all of them—98%—agreed that drug responses may be influenced by genetic variations.

Genotype-guided prescribing—also referred to as pharmacogenetics, or PGx—is expected to become routine as genetic profiling becomes more commonplace.

"[I]t is likely that a time will come in the near future where patients will start to demand the use of such information during care—that they will ask of their physician, 'Have you considered my genomics?' before accepting a prescription," said Peter H. O'Donnell, MD, associate director for clinical implementation at the University of Chicago's Center for Personalized Therapeutics.

In the meantime, major efforts are under way to prove that pharmacogenomic tests have clinical utility and to make it easier for physicians to choose these tests and interpret and act on the results, translating them into better outcomes for their patients.

How Does Pharmacogenomics Work?

"Genetic variability affects essentially every single gene in the human genome and sometimes it's going to affect genes whose proteins are critical for drug response," said Mary V. Relling, PharmD, chair of the pharmaceutical sciences department at St Jude Children's Research Hospital.

Most so-called pharmacogenes encode drug-metabolizing enzymes, and each individual's genotype for a particular gene can be categorized into 1 of 5 phenotypes that describe the enzyme's activity—ultrarapid metabolizer, rapid metabolizer, normal metabolizer, intermediate metabolizer, and poor metabolizer—Nutescu explained.

Other genes encode the enzymes that are the site of action where drugs exert their effects; patients with variations in these genes may be more sensitive or resistant to certain drugs than normal.

Knowing this information can help clinicians choose the right medication or dose for a patient.

A patient who has a genetic variant associated with slow metabolism of the drug thinner warfarin, for example, might experience major bleeding on a standard dose. In contrast, a patient with a variant associated with fast warfarin metabolism might not get any benefit from the standard dose, putting them at greater risk of a major stroke or thromboembolism.

"Warfarin is consistently among the top 10 medications that leads to hospitalizations due to adverse events," Nutescu said. "Drugs that are more prone to side effects, complications, hospitalizations, [and] resource use, clearly should be on the radar."

By screening for variants in the 2 genes that influence warfarin metabolism and sensitivity, *CYP2C9* and *VKORC1*, respectively, a physician can adjust the dose to optimize treatment and prevent an adverse event.

"The goal is to avoid trial and error, to make patients safer, and to increase the chance for effectiveness when they start a medication," O'Donnell said.

Advocates of pharmacogenomics say the field is an emerging resource for improving patient safety. Since 2012, more than 1 million adverse drug events have been reported each year to the US Food and Drug Administration (FDA), "many of which might be preventable using PGx testing," Geoffrey S. Ginsburg, MD, PhD, director of the Center for Applied Genomics and Precision Medicine at Duke University Medical Center, said in an email.

Pharmacogenomics may also help inject more science into the art of prescribing. Mark A. Frye, MD, professor and chair of the department of psychiatry and psychology at the Mayo Clinic, believes the technology has the potential to transform antidepressant treatment for major depressive disorder, multiple anxiety disorders, and some chronic pain conditions.

Up to a third of patients with major depression do not fully respond to antidepressant treatment, Frye said, and many experience serious adverse effects. In a recent article on psychiatric pharmacogenomics published in *Mayo Clinic Proceedings*, Frye and coauthors wrote that "[i]t is increasingly recognized that genetic variation may contribute to this differential risk to benefit ratio."

Frye added that clinical research is needed to better understand what level of value genetic testing adds for patients seeking treatment for depression. "Value added can mean many things—getting better faster, complete remission of symptoms, less side effect burden, better quality of life, [and] less hospital cost are only a few examples," he said.

Building a Case

According to a 2015 *Nature* review article that Relling coauthored, drugs currently known to be affected by "actionable" inherited pharmacogenes represent around 7% of FDA-approved medications and 18% of US outpatient prescriptions. In addition to antidepressants and blood thinners, these drugs include, antivirals, chemotherapy agents, immunosuppressants, pain relievers, and statins, among others, making the field of pharmacogenomics relevant for precision medicine in a variety of medical specialties.

"It is my view that someday—probably not far in the future—we will look back on the idea of treating all patients who have the same 'disease' with the same drug as a simply archaic practice," O'Donnell said in an email.

Despite the promise of pharmacogenomics, physician uptake has been slowed by a lack of implementation guidance and clinical and outcomes data.

The FDA has included pharmacogenomic information on the labels of more than 150 medications. But some of these do not translate the genetic test results into specific prescribing actions, Relling said.

To help advise physicians, the international, nonprofit Clinical Pharmacogenetics Implementation Consortium (CPIC) has written guidelines for gene-drug pairs that the group believes have sufficient evidence from randomized controlled trials and other clinical studies to influence prescribing.

The CPIC—a joint project between the National Institutes of Health's Pharmacogenomics Research Network and the online Stanford-hosted Pharmacogenetics Knowledge Base (PharmGKB)—has identified more than 300 gene-drug pairs of interest. Relling, who coleads CPIC, said that about half of those will have actionable prescribing based on genetics. So far, the group, which focuses on inherited genomic variations, has released clinical practice guidelines for 13 genes affecting the response to more than 30 drugs.

A handful of clinical research institutions in the United States have begun implementing pharmacogenomics testing. "These demonstration projects are creating a path for more widespread implementation and a toolbox for the broader community to use," Ginsburg said.

In 2010, Vanderbilt University launched blood panel-based preemptive pharmacogenetic testing to screen patients for a group of actionable genetic variants based on the likelihood of needing the information in the future. A study of Vanderbilt's current testing panel found that 91% of almost 10 000 genotyped patients had at least 1 of 14 variants associated with 5 gene-drug interactions.

Nevertheless, Muin J. Khoury, MD, PhD, director of the Office of Public Health Genomics (OPHG) at the Centers for Disease Control and Prevention, said that for most gene-drug pairs, more outcomes data are needed to justify routine testing outside of a research setting.

His office has identified a handful of non–cancer-related pharmacogenomic tests that have enough synthesized evidence to support routine clinical implementation. These include tests for gene variants associated with the HIV drug abacavir, the epilepsy drug carbamazepine, and the cystic fibrosis drug ivacaftor, for example.

However, for most pharmacogenomic tests, clinical utility—the balance of benefits and harms in practice—hasn't been sufficiently established yet, Khoury said. As an example, pharmacogenomic tests for gene variants associated with warfarin responsiveness fell among those OPHG concluded did not have enough evidence to support routine use in clinical practice.

Although some experts in the field say OPHG's standards for evidence are too high, a push is under way to develop more outcomes evidence to support broader pharmacogenomic testing.

"Within the pharmacogenetics community we're really trying to focus on… build[ing] the evidence for that last step that proves the clinical value of doing these things," said Julie A. Johnson, PharmD, dean and distinguished professor at the College of Pharmacy at the University of Florida.

Johnson leads a project in the NIH-funded Implementing Genomics in Practice (IGNITE) network. Out of 6 IGNITE projects—all based in academic medical centers—3 are focused on pharmacogenomics implementation. Johnson's team is tracking implementation metrics, such as test adoption rate and drug therapy changes initiated after test results, as well as clinical outcomes.

Last year, she presented data from University of Florida's IGNITE project at the annual American Heart Association (AHA) meeting showing that genotype-guided clopidogrel therapy reduced cardiovascular events after angioplasty and stent placement. Among patients with a loss-of-

function genotype that leads to reduced clopidogrel effectiveness after these procedures, those who switched to a different antiplatelet therapy after the procedure had a reduced risk of major adverse cardiovascular events compared with patients who continued taking clopidogrel.

Data on a approximately 4500 patients from a larger multicenter trial that includes the University of Florida cohort will be presented at this year's AHA meeting in November. "If those data turn out the way our data turned out in the cohort at University of Florida, that has a potential… to be the kind of evidence that might be needed for more people to embrace that approach," Johnson said.

Barriers to Entry

Additional challenges stand in the way of pharmacogenomics implementation. Physicians say they need tools to help them understand and use the tests.

"Just because you make the test available, it doesn't mean that your providers are able to interpret the test results and are able to integrate it at the bedside," Nutescu said.

O'Donnell added, "Decision-support—in other words, guidance about how to use genomic information—is needed for prescribers who will be increasingly encountering pharmacogenomic results for their patients, because most clinicians in practice have not been formally trained in genomics."

To that end, the IGNITE website offers a toolbox of resources for health systems and clinicians, such as example clinical decision support alerts for electronic health record (EHR) systems and test result decision tables.

The CPIC is currently updating the existing guidelines to provide more computational tables and data that can be directly uploaded into EHR systems to facilitate implementation of genetic testing. Relling was part of a CPIC group that recently published standardized pharmacogenomics terms in *Genetics and Medicine* that can be interpreted exactly the same way across all EHR systems.

Pharmacogenomics leaders say that a lack of reimbursement for genetic tests is another huge challenge that cannot be underestimated. The Centers for Medicare & Medicaid Services does not cover panel-based testing, which Johnson said is often the most cost-effective and logical approach to pharmacogenetics-guided treatment.

"Even though the cost of genetic tests is coming down all the time, somebody has to bite the bullet and pay for that test, and we just don't have a health care system that's geared toward doing that at this point," Relling said. Johnson believes that clearing up reimbursement issues would be one of the fastest ways to get doctors to embrace pharmacogenomic testing.

Some say the change can't come soon enough. "PGx is the leading edge of genomic medicine," Ginsburg said. "Providers who are not at least thinking about how to incorporate PGx into their practices might find themselves behind the curve in the next 3 to 5 years as the evidence accumulates and practice guidelines adopt this area [of] genetics in the clinic." ■

Note: The print version excludes source references. Please go online to jama.com.

The JAMA Forum

Time to Hit the Pause Button on Medicare's Payment Demonstration Projects?

Gail Wilensky, PhD

After a slow start in 2011, the Center for Medicare & Medicaid Innovation (CMMI) at the Centers of Medicare & Medicaid Services (CMS) seems to have gone into overdrive. As part of the Department of Health and Human Services' pledge to move the majority of Medicare payments away from undifferentiated fee-for-service payments to some type of value-based care, CMMI has been sponsoring a wide variety of models. These include models that feature fee-for-service payments with incentives added, bundled or episode-based payments, and population-based payments.

Some of ongoing or scheduled demonstration models featuring fee-for-service with incentives are the patient-centered medical home model, the Comprehensive Primary Care initiative, and the Comprehensive Primary Care Plus initiatives (which I discussed in a recent *JAMA* Forum). Some episode-based payment models are procedure-based models, such as the voluntary Bundled Payment for Improvement Initiative (BPCI), and the mandatory Comprehensive Joint Replacement (CJR) program, which applies to all Medicare patients receiving a joint replacement in areas where the pilot project. A mandatory cardiovascular program, which will cover all services that occur with 90 days of the hospital discharge for patients who experience acute myocardial infarction and coronary artery bypass graft surgery (discussed in a recent JAMA Forum), is scheduled to begin in 2017. Other episode-based payment models feature condition-based episode payments, such as the Oncology Care Model, which began in July 2016, and the Medicare Diabetes Prevention Program, which has not yet started.

Gail Wilensky, PhD

Finally, there are a variety of population-based models. These include the Medicare Shared Savings Program—the original