

PERSONALIZED MEDICINE IN BRIEF

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Developments in Brief

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The emergence of COVID-19 underlines the need for diagnostic tools that can help target the most intensive medical interventions to those who need them most.

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During the first educational briefing hosted by the Congressional Personalized Medicine Caucus, lawmakers and other thought leaders cultivate additional support for personalized medicine by explaining its benefits to policymakers and the public.

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In a development that may lead to greater clarity and encourage additional investment in personalized medicine diagnostics if it prompts collaborative progress with participation from the many impacted stakeholders, FDA publishes a table outlining drug-gene associations the agency believes are well-established.

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To better account for personalized medicine's benefits, the Institute for Clinical and Economic Review (ICER) alters the methodology underpinning its influential assessments of the value of therapies. The changes improve the outlook for personalized treatments whose integration into health systems has been slowed by perceptions that their list prices are artificially inflated.

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In a move that will help facilitate the efficient advancement of a promising class of personalized treatments, FDA finalizes a series of guidance documents establishing a clearer regulatory framework for gene therapies.

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CMS clarifies its coverage policy for a group of diagnostic tests underpinning many personalized health care strategies by issuing a revised national coverage determination for next-generation sequencing in oncology.

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PRESIDENT'S BRIEF

Personalized Medicine in the Aftermath of COVID-19

by Edward Abrahams, PMC President



Over the course of the last month, leaders from the Personalized Medicine Coalition have been considering how the emergence of the SARS-CoV-2 virus has reshaped our lives in a matter of weeks.

In the United States, many, including PMC Board Secretary Michael Pellini, M.D., Managing Partner, Section 32, a venture capital firm, have argued that we missed an opportunity to employ diagnostic testing early on to detect and contain the pathogen.

In an opinion piece published on March 29 in *The Timmerman Report* titled “Knowledge is Power: Don’t Give Up on Diagnostic Tests for COVID-19,” Pellini



In an opinion piece in *The Timmerman Report* titled “Knowledge is Power: Don’t Give Up on Diagnostic Tests for COVID-19,” PMC Board Secretary Michael Pellini, M.D., Managing Partner, Section 32, a venture capital firm, who is pictured here at *The 15th Annual Personalized Medicine Conference at Harvard Medical School*, calls for a national testing program that would help the United States combat COVID-19 by targeting the most intensive medical interventions and deploying resources to those who need them most — something that personalized medicine has long promised to do.

laments the fact that following “a decade of breathtaking progress” in science and technology, citizens in every corner of the country have been forced into virtual exile to avoid this new virus. In Pellini’s estimation, we must demand that our government employ all available testing technologies to help target treatments to those patients who most need them and focus prevention strategies on at-risk geographic areas without shutting down the economy of the country. Our failure to do so thus far, he writes, “borders on malpractice at the national level,” though he notes that industry has stepped up to meet the need since the outbreak of the virus.

Former Food and Drug Administration commissioner Scott Gottlieb, M.D., and Lauren Silvis, a Senior Vice President at Tempus, a “data-driven precision medicine” company, echo the need for an evidence-based approach in an op-ed for *The Wall Street Journal* on March 29 titled “The Road Back to Normal: More, Better Testing.” Gottlieb and Silvis call on Congressional leaders to fund a “sentinel surveillance system” that “allows cases to be identified and tracked in real time without overburdening providers with data entry and case reports.”

These lessons learned from the emergence of COVID-19 will undoubtedly shape discussions about the future of health care in America and around the world for years to come. As demonstrated in the following pages, PMC is well-positioned to influence those discussions, believing that personalized medicine can and will play an increasingly important role.

The overwhelming influx of patients who may be infected with the new virus reminds us of the need for diagnostic tools that can help target the most intensive medical interventions to those who need them most. As PMC Senior Vice President for Public Policy Cynthia A. Bens explains on pp. 4–5, policymakers in the U.S. are increasingly recognizing that personalized medicine gives us the ability to do that.

Congressional lawmakers, Bens notes, have formed a bipartisan, bicameral Personalized Medicine Caucus that is committed to advancing the field. And officials at FDA and the Centers for Medicare and Medicaid Services have taken steps to ensure that safe and effective products and services underpinning personalized medicine are available as quickly as possible.

To bolster PMC's educational efforts, the Coalition will soon convene an Education Council that will shape messages disseminated to decision-makers in the public and private sectors, beginning with those outlined in the forthcoming *Personalized Medicine Report: Opportunity, Challenges, and the Future* (see p. 8). The report, written by Daryl Pritchard, Ph.D., Senior Vice President, Science Policy, and overseen by an advisory committee of experts in the field, will describe the rapid pace of scientific progress in personalized medicine and highlight the ongoing challenges it faces in regulation, reimbursement, and clinical adoption. As Pritchard explains on pp. 6–7, PMC has also developed *A Research Program Studying the Clinical*

and Economic Utility of Personalized Medicine in Multiple Disease States, which will encourage payers and providers to adopt supportive policies and practices by underlining the clinical and economic benefits of the field.

In brief, we believe, as Gregory Downing, D.O., Ph.D., formerly a government official at the U.S. Department of Health and Human Services, contends on pp. 10–11, that “there has never been a better time to be an innovator in health care.” As Downing also notes, our continued success will depend on “broad coalitions of stakeholders” working together “to achieve the common good” in the interest of patients.

All of this underlines the increased importance of *The 16th Annual Personalized Medicine Conference at Harvard Medical School*, scheduled for November 18–19, where we will convene more than 500 of the world's leading clinicians, industry executives, investors, patient advocates, payers, policy experts, and researchers to explore the issues facing the field in what we hope will be the aftermath of the COVID-19 crisis as well as the 2020 elections in the U.S.



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Policymakers Improve Outlook for Personalized Medicine in US With Attention to Educational, Regulatory, Reimbursement Priorities



by Cynthia A. Bens, PMC Senior Vice President, Public Policy

In recent months, policymakers in the U.S. have advanced a series of educational, regulatory, and reimbursement initiatives designed to improve the outlook for personalized medicine. In addition to encouraging continued investments in the field, these initiatives underline the progress proponents for personalized medicine have made in informing decision-makers about personalized medicine's significance for patients and health systems.

Some members of Congress are now standing four-square behind personalized medicine. On the morning of February 26, for example, *Politico Pro* published an interview with Rep. Eric Swalwell (D-CA), who serves as co-chair of the newly formed Congressional Personalized Medicine Caucus alongside Rep. Tom Emmer (R-MN) and Sens. Tim Scott (R-SC) and Kyrsten Sinema (D-AZ). The interview is titled "Swalwell's Plan to Slash Health

Care Costs With Precision Medicine." Citing contentions also expressed in the Personalized Medicine Coalition's *Personalized Medicine Report: Opportunity, Challenges, and the Future*, Swalwell touted the benefits of curative personalized treatments and avoiding the "costly trial-and-error process." At the caucus' first briefing, which PMC co-hosted with the caucus co-chairs during the afternoon of the same day, Emmer echoed those sentiments.

Emmer also encouraged policymakers to help "define the regulatory process to ensure that innovation isn't stalled." On this front, officials at the Food and Drug Administration continue to make progress under the direction of newly confirmed Commissioner Stephen M. Hahn, M.D.

In a series of recently released final guidance documents about gene therapies, for example, FDA outlined a clearer



The Congressional Personalized Medicine Caucus' first briefing featured remarks from the following panelists from the private sector (listed from left to right in the order in which they appear): Peter Halliburton, caregiver to son, Carter; Keith Stewart, M.B., Ch.B., Director, Center for Individualized Medicine, Mayo Clinic; Lance Baldo, M.D., Chief Medical Officer, Adaptive Biotechnologies; Lauren Silvis, Senior Vice President, External Affairs, Tempus; Cynthia A. Bens, Senior Vice President, Public Policy, Personalized Medicine Coalition.

“With policymakers embracing key priorities in the critical areas of education, regulation, and reimbursement, an incrementally improved outlook for personalized medicine is coming into focus.”

regulatory framework that promises to help facilitate the efficient commercialization of this evolving class of personalized treatments. As PMC noted in its comment letter about draft versions of the guidance documents, these publications will “establish regulatory approaches suitable for an era in which biopharmaceutical companies are increasingly developing therapies that can treat disease in just a few doses by permanently changing the genes in patients’ own cells.”

Federal officials are also making progress at the Centers for Medicare and Medicaid Services, where strict statutory requirements about the levels of evidence needed to begin covering new tests and treatments can sometimes make it challenging for the agency to cover the cutting-edge products and services underpinning personalized health care strategies. In response to feedback provided by PMC and other proponents for personalized medicine, CMS has made some strides in clarifying its coverage policy for next-generation sequencing (NGS) in cancer care. In addition to reimbursing for NGS-based testing of tumor cells to guide genetically targeted treatment options, the agency’s revised coverage policy institutes national coverage of FDA-approved or -cleared NGS-based testing for genetic variants present in all of a patient’s cells that may make patients more susceptible to developing breast and ovarian cancers in the future. The policy also allows regional Medicare Administrative Contractors to cover non-FDA-approved tests for these and other preventive purposes at their discretion. The policy does not, however, cover re-testing, which can be important in managing some cancer diagnoses.

“CMS recognizes that innovation is happening quickly and evidence is moving fast, and the agency wanted to ensure that patients have ready access to this diagnostic test when appropriate,” the agency said in a statement.



Lawmakers underlined their expanding commitment to educational, regulatory, and reimbursement issues in personalized medicine during the first educational briefing hosted by the co-chairs of the newly formed Congressional Personalized Medicine Caucus, which took place on February 26. Rep. Eric Swalwell (D-CA), left, said American families are “counting on us to make [reimbursement policies] right.” Rep. Tom Emmer (R-MN) called on policymakers to “define the regulatory process to ensure that innovation isn’t stalled.”

Of course, the policy landscape for personalized medicine is not without its challenges. Constituents’ continued demands for legislation that will reduce the prices they pay for prescription drugs could prompt legislators to adopt sweeping measures that unintentionally eliminate the incentives for developing high-value personalized treatments that address the root causes of diseases. And until policymakers define a clear oversight framework for diagnostic tests in collaboration with industry leaders, many investors hesitate to commercialize tests that would otherwise help make personalized medicine possible by identifying which patients will respond favorably to certain treatments.

Still, with policymakers embracing key priorities in the critical areas of education, regulation, and reimbursement, an incrementally improved outlook for the field is coming into focus.

With Focus on Evidence Development, Personalized Medicine is on Course Toward Increased Clinical Integration



by Daryl Pritchard, PMC Senior Vice President, Science Policy

Research and innovation in personalized medicine are extensive and expanding. However, despite a steady increase in the number of high-value molecular diagnostics and targeted, cell-based, and gene therapies, the health system has been slow to integrate personalized medicine into clinical practice. Lincoln Nadauld, M.D., Ph.D., Chief, Precision Health, Intermountain Healthcare, told *The Salt Lake Tribune* in July that he “has grown tired of young



Lincoln Nadauld, M.D., Ph.D., Chief, Precision Health, Intermountain Healthcare, who is pictured here at *The 15th Annual Personalized Medicine Conference at Harvard Medical School*, says he is “tired of young patients showing up in our centers with advanced diseases, when we probably could have known about it and prevented it with personalized medicine.” In light of this and similar sentiments circulating among health care professionals, many decision-makers are doubling down on their efforts to accelerate the pace at which personalized medicine is integrated into clinical work streams.

patients showing up in our centers with advanced diseases, when we probably could have known about it and prevented it with personalized medicine.”

Motivated by this and similar sentiments circulating among many health care leaders, decision-makers in the public and private sectors are committed to several priorities that will help bring personalized medicine closer to the forefront of patient care. Although their enthusiasm for the field will not usher in an era of widespread clinical adoption immediately, their support is already having a positive impact for personalized medicine and patients on multiple fronts.

We are beginning to gain a better understanding, for example, of the current landscape of personalized medicine integration and the extent to which reimbursement and operational challenges are slowing the pace of clinical implementation in the U.S.

The Personalized Medicine Coalition commissioned a study to examine various perspectives and practices in order to capture a holistic picture of the clinical adoption of personalized medicine strategies and technologies at a representative sample of health care delivery institutions across the country. The survey informed the calculation of a quantitative framework that assesses progress toward personalized medicine integration at the institutional level, with consideration of multiple clinical areas. Institutions were assigned scores between one (minimal personalized medicine integration) and five (expansive and systematic integration).

The survey found that although U.S. health care organizations are widely distributed in terms of integration across clinical areas, most are at level two or level three. While level four and level five institutions stand out as pioneers in personalized medicine and are still not

“Despite evidence development challenges and significant clinical implementation barriers, the rapid pace of scientific progress, along with an increased recognition of personalized medicine’s value proposition, suggest that we are on a course toward expanded clinical adoption.”

common, the dearth of level one institutions suggests that personalized medicine is penetrating health care delivery throughout the broader system and is starting to become more widely practiced. The study will help inform efforts to address the most critical outstanding integration challenges. A team of researchers at Health Advances will join PMC in publishing a report on the findings later this year.

To translate our enhanced understanding of human heterogeneity into clinical applications that are useful to patients and society and to advance their clinical adoption, personalized medicine’s leaders must continue to collaborate with policymakers to ensure the efficient advancement of novel diagnostics and targeted treatments.

Here, too, we are making progress.

In *Personalized Medicine at FDA: The Scope & Significance of Progress in 2019*, PMC classified 11 of the 44 new therapeutic molecular entities approved by the U.S. Food and Drug Administration in 2019 — and one new gene therapy — as personalized treatments. The report also highlighted seven newly approved or cleared diagnostics that will expand the frontiers of personalized medicine. The newly approved therapies bring the count of available personalized medicines to more than 230, while each of the diagnostics represents an important breakthrough for a field that is now supported by tens of thousands of tests developed by diagnostic companies and clinical laboratories. The field shows no signs of slowing down. An analysis conducted by L.E.K. Consulting and published by PMC in October, for example, showed that 55 percent of clinical trials for cancer treatments conducted in 2018 involved the use of biomarkers, compared to just 15 percent in 2000.

Policymakers that manage access to novel personalized medicine technologies have a different perspective, however, and often make decisions based on different evidentiary standards. Persistent questions about the

clinical and economic utility of some advanced diagnostic tests are still giving pause to discerning payers and providers, who are responsible for ensuring that patients have access to high-value medical interventions.

To address these utility concerns and thereby help facilitate an increased clinical uptake of personalized medicine, PMC plans to summarize the evidence demonstrating the importance of personalized medicine in a new edition of its *Personalized Medicine Report: Opportunity, Challenges and the Future* for publication later this year. The Coalition is also seeking partners to support an even more robust *Research Program Studying the Clinical and Economic Utility of Personalized Medicine in Multiple Disease States*.

Meanwhile, efforts to build the evidence that demonstrates the value of personalized medicine have made some headway in affecting access policies. In addition to the Centers for Medicare and Medicaid’s recent national coverage determination for genomic sequencing in cancer care, many public and private payers favor coverage and reimbursement for genomic tests used for a number of purposes, including for cancer tumor testing, noninvasive prenatal testing, and for patients with rare or undiagnosed diseases. To gain a better understanding of how payer coverage policies affect the utilization of genomic testing, PMC is working with Illumina and other partners on a study titled *The Utilization of Genomic Testing in the US: A Landscape Analysis*. This analysis will provide further insight into genomic testing implementation trends and barriers.

Despite evidence development challenges and significant clinical implementation barriers, the rapid pace of scientific progress, along with an increased recognition of personalized medicine’s value proposition, suggest that we are on a course toward expanded clinical adoption.

Patients hope for no less.

As COVID-19 Spotlights Health Care Issues, Advocates Push Education on Personalized Medicine



by Christopher J. Wells, PMC Vice President, Public Affairs

As the emergence of COVID-19 grips the global psyche, policymakers and citizens will increasingly turn to thought leaders in health and medicine for answers about how to equip our health systems to respond to medical challenges in a new era.

Proponents for personalized medicine are ready.

Having inspired the launch of a Congressional Personalized Medicine Caucus through earlier advocacy on Capitol Hill, most of the field's advocates are focused on preparing commentaries and reports explaining how personalized medicine offers a solution to today's health care challenges. To support these efforts in the coming months, the Personalized Medicine Coalition will virtually convene an Education Council for the first time to review and inform a campaign educating decision-makers in the private and public sectors about the significance of personalized medicine in the context of global needs in health care.

A revised edition of PMC's *Personalized Medicine Report: Opportunity, Challenges, and the Future* will form the backbone of the campaign. To be developed by Daryl Pritchard, Ph.D., Senior Vice President, Science Policy, in consultation with the members of the Education Council,

the report will summarize the evidence suggesting that by targeting more effective prevention and treatment strategies to those who will benefit, personalized medicine can make patients healthier and help us direct finite health care resources to those who need them most. It will also inform the development of a fact sheet and slide deck on the basics of personalized medicine.

PMC will encourage its network of leaders from every sector of the health care ecosystem to share the report and the supporting materials with their Congressional representatives and decision-makers in the private sector as appropriate.

The Coalition has also included a proposal to develop an online *Library of Personalized Medicine* that will serve as a clearinghouse for the available resources in personalized medicine as part of its sponsorship prospectus outlining *A Research Program Studying the Clinical and Economic Utility of Personalized Medicine in Multiple Disease States*.

Those with an interest in participating on the Education Council to help shape the messages articulated in the campaign are encouraged to be in touch with PMC staff.

“As the emergence of COVID-19 grips the global psyche, policymakers and citizens will increasingly turn to thought leaders in health and medicine for answers about how to equip our health systems to respond to medical challenges in a new era.

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“By covering the science, policy and business of this emerging paradigm, *Personalized Medicine* assists our understanding of where the field is heading, and should be essential reading for anyone with an interest in the subject.”

Edward Abrahams, *Personalized Medicine Coalition, USA*

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Delivering on the Promise of Personalized Medicine

Remarks made during *Get the Medications Right: Innovations in Team-Based Care*, co-hosted by the Bipartisan Policy Center and the GTMRx Institute

by Gregory Downing, D.O., Ph.D., Founder, Innovation Horizons LLC



The following remarks were prepared by Gregory Downing, D.O., Ph.D., Founder, Innovation Horizons LLC, for Get the Medications Right: Innovations in Team-Based Care, a briefing co-hosted by the Bipartisan Policy Center and the GTMRx Institute. The remarks have been lightly edited for clarity.

Good morning. I'm honored to be with you here today for this important gathering. My acknowledgements to the Bipartisan Policy Center and the leadership of GTMRx for their taking up this cause.

I firmly believe that there's never been a better time to be an innovator in health care. And that's why we're here today.

I am an optimist and I believe we live in unparalleled times for research and development in the interest of the public good. This is even true for the future of preventive medicine.

I'd like to begin with a story.

So, let me tell you about Molly.

Molly is a 46-year-old school teacher whose life was changed two years ago after a fainting spell in her classroom. "Syncope of unknown etiology" is what physicians would call it for an indeterminant diagnosis.

She had no significant medical illnesses in her background but her family history included the sudden death of her father when he was 45 years old. She also had two cousins with unexplained "heart attacks" at a young age. Upon arrival to a local hospital she was diagnosed with a near fatal heart rhythm disorder that leads to heart failure.

Later, at a referral center, a cardiologist determined that she had an electrical conduction defect that affected the rhythm of her heart, related to what is known as a calcium channel abnormality. This is frequently an inherited genetic defect. Her laboratory studies included a test known as a whole genome sequence that provided her health care team with the identity of the several inherited

mutations, or changes in her DNA, that were likely responsible for the heart arrhythmia (and quite possibly the early deaths of her relatives).

The clinical challenge was that there are many types of mutations that can cause the problem, and different mutations respond better to certain anti-arrhythmic drugs, like flecainide (a class C1 anti-arrhythmic). Other patients using the same medications can become worse and potentially have a fatal drug-induced event. And, the science that correlates the mutations with the type of arrhythmia is still evolving; so this unknown represented a big dilemma for those responsible for Molly's care.

However, using the genetic information, her cardiologist, internist, and pharmacist were able to work together to develop a personalized treatment plan to guide the prevention of further arrhythmias.

As the science continues to unfold the evidence in determining the significance of each of the mutations, alerts are still sent to her health care team through her electronic medical record, enabling her medications to be changed based on the evolving information. Her health care team monitors her EKG remotely, tracks her digital prescription medication history, observes for any patient-reported side effects through a smart phone app, and updates her providers as the scientific evidence evolves to guide changes in her treatment plan — almost at a moment's notice.

Today, Molly is back in the classroom with the confidence that her care team has the most up-to-date information at their fingertips to guide her care decisions in near real-time. Molly's health care team provides the virtual guidance system needed for her care.

This is personalized medicine.

The right treatment for the right patient at the right time.

How did we get here?

“I am an optimist and I believe we live in unparalleled times for research and development in the interest of the public good.”

In many domains of disease management today, laboratory information is being used to guide the identification of unique features of disease and conditions, as well as the selection of therapies.

From oncology to many immune disorders, targeted molecular therapies are increasingly being customized to provide the best options based on a biological feature of disease, known as a biomarker. The majority of new chemical entities approved by the U.S. Food and Drug Administration last year featured labeling language related to a test result. So, the future is here.

The “scientific framework” for personalized medicine is accelerating quickly, with many new targets, therapies, and patient management choices. The big question is, how do we engage this promise into our current practice of health care?

I'd like to mention a few of the milestones that have gotten us to the point of this combination of diagnostic test and medical treatment selection. As you will see, public policy played a big role and there is likely a lesson to be learned here for our goals ahead.

Therapeutic monitoring started in the 1970s using laboratory tests to measure blood levels and metabolism of drugs with a narrow therapeutic index or a high likelihood of toxicity, such as digoxin, a potent but toxic heart medication, and antibiotics that have kidney toxicity. All clinicians learned to guide clinical practice and decision-making through the use of this information.

In the 1980s, the use of “viral load” as a biomarker for drug activity and surrogate endpoint for monitoring of response to antiviral therapies in patients with HIV emerged. Viral load and immune markers revolutionized drug discovery and clinical care in that era.

The 1990s saw the advent of pharmacogenomics in the laboratory testing of drug metabolism enzymes and common testing to identify individuals with variations in the breakdown of drugs — many associated with serious side effects.

Warfarin, the commonly used blood thinner, is among the most notable of these, and hospitals and clinics set up laboratories for coagulation lab monitoring of bleeding measures and testing of warfarin's drug metabolizing enzymes known as cytochrome p450. The result of abnormal metabolism led to a wide range of biological activity and potentially hemorrhage and stroke. Pharmacogenomics helped identify those at risk and guided dosing — or enabled clinicians to choose another drug.

1998 was a watershed period for the molecular therapy era. Herceptin, a drug developed by Genentech, was the first to be developed in concert with a genetic defect in the HER2neu gene in women with triple negative breast cancer. This opened the door for combination diagnostic and therapy strategies in drug development and cancer treatment, which now is nearly the mainstay of cancer therapy.

About the same time, from 1996 to 2005, a vast public-private partnership was undertaken to develop a map of the human genome that would guide scientific discovery. The development of a public database spawned an unprecedented period of scientific and technological discovery that is geared toward understanding individual biological differences in the origins of diseases and conditions in humans. The doors of biomedical research had been blown open to new understandings of disease and discovery of new treatments. Maintaining the genomic information in the public domain turned out to be a critical part of the success. (Later this was borne out by the U.S. Supreme Court decision in 2013, *Association of Molecular Pathology v. Myriad Genetics*).

In the early 2000s, public investments brought us disease maps, relatively low-cost, high-fidelity genome sequencing technology, and the earliest clinical guidelines for the appropriate use of genomic testing. FDA issued guidelines for labeling of drugs where genetic test information could inform patient prescribing use, dosage, and side effects.

Soon thereafter, there was a dramatic commercial ramp up of diagnostic genetics.

Innovative drug development programs led to targeted genetic disease therapies in rare diseases. Kalydeco, which emerged in 2012, was a breakthrough for some forms of cystic fibrosis, correcting the chloride channel mutation.

In 2014, FDA issued a companion therapeutic/diagnostic guidance, which has guided the pharmaceutical, device, and laboratory industry on parameters where genetic tests should be used in prescribing.

Congress has played a major role in shaping the roadmap for personalized medicine by advancing policies to address patient protections, regulatory oversight of insurance and laboratory industries, research funding, and much more.

Some examples of the government's work include:

- *The Genetic Information Non-Discrimination Act of 2008*;
- Regulating clinical genomic testing authorities (e.g., CLIA);
- The expansion of genetic testing coverage, to include expanded access and national coverage decisions for genome sequencing in certain cancers; and
- *The 21st Century Cures Act*.

So, public policy has charted the guideposts to personalized medicine. And, by and large, I think that federal agencies have done a good job of laying down the rules and regulations to make personalized medicine safe and accessible to those who need it.

So, where are we today with concerns about delivering on the promise of personalized medicine?

There are important challenges and shortcomings with clinical implementation and adoption of the concept of individualization of medical decision-making. Going forward, I would argue that it cannot simply be the role of government to be the pacesetters for change. To create the culture change needed, we need new incentives and broad coalitions of stakeholders to achieve the common good.

Why?

Pharmaceutical development has vastly changed in 20 years, and many of the new FDA drug approvals involve a companion diagnostic test. Health care professionals are not well trained in the practice of testing to augment decision-making about medications. They cannot interpret complicated genomic testing results. They don't know how to communicate interpretations of these tests to patients.

I'll give you an example.

In recent years, antiviral therapy for Hepatitis C has been shown to be curative for a large number of patients. But it has been shown that without the proper team care and coordination, treatment failures occur, dosing is incomplete, and an expensive therapy provides no value. A study at Geisinger Medical Center a few years ago showed that without a structured care pathway to coordinate the

specialist, the testing, and medication administration, cure rates dropped from 95 percent to around 60 percent.

Yet, providers, clinics, and health systems have struggled with systematic adoption even when clear clinical guidelines exist. Some studies show that only 40 percent of patients with newly diagnosed lung cancer have genetic studies on the tumor biopsy, despite the knowledge that treatment success is clearly related to the selection of the right molecularly targeted drugs. These are missed opportunities that cost lives.

Although improving, there are confusing insurance coverage policies for genetic testing. Prior authorizations for laboratory testing are complicated and time consuming, adding anxiety and delaying access to care.

Electronic health records systems and the lack of effective clinical decision support through them has been a big challenge, and the overwhelming amount of information in lab reports burdens providers.

What the patient needs is an integrated guidance system for the management of medical needs.

The information burden that laboratory testing and treatment selection provides is overwhelming without a system to support it. We need tools to curate the information and support provider decision-making.

We need innovation to establish coordinated care teams of health care professionals — primary care providers, pharmacists, pathologists, psychologists, geneticists, care support teams, and even new roles will emerge for addressing clinical adoption. Other barriers remain in the areas of:

- Clinical evidence development;
- Guideline development and integration into digital health tools; and
- Interpretative requirements of test results.

We lack incentives to redesign care delivery pathways and services to encourage personalized medicine practices (such as anticoagulation and pharmacogenomics clinics, uses of telehealth for genetic counseling, etc.)

What are the most important domains of work?

Information infrastructure that will make test results and treatment guidelines easily understandable and actionable is an important one. I believe that modular tool environments supported through the interoperability of data will take on greater importance than electronic health records in the future to support personalized medicine. If we can't have the data follow the patient, we will not succeed in the delivery of our promise.

Care coordination and innovative team management approaches, including patient engagement and education, advanced patient portals, and software applications, are also critical.

We also have outstanding needs for:

- New care delivery pathways for care management;
- Patient/consumer understanding of differences in population variability in response to therapy;
- Ways to assure patient access/avoidance of new health disparities/inequities; and
- Ways to plan health system/care delivery paradigms in anticipation of new therapeutic regimens.

As an example of these last two points, it is highly probable that we will have a genetic approach that can cure sickle cell disease in some patients within three to five years. That would be an amazing scientific advance.

But tell me: What are we doing now to prepare for that possibility? As I look around, I see very little. Shame on us, after all of this public investment, that we cannot have the foresight to capture and claim the benefits of our investments in the lives of people who suffer. Shame on us. We need to own up to our responsibilities by making decisions now to prepare for this avalanche of new gene therapies that science is bringing to the door of the clinic. Or, we will create new inequities in health that will cripple our public trust.

So today, we should ask: “What should personalized medicine look like in 2025?”



Gregory Downing, D.O., Ph.D., who is the Founder of Innovation Horizons LLC, delivered the remarks republished here during a briefing titled *Get the Medications Right: Innovations in Team-Based Care*, which took place at the Bipartisan Policy Center in Washington, DC, on February 6.

Will we look back 10 years from now and say that we did the best we could to optimize the benefits of science for our patients?

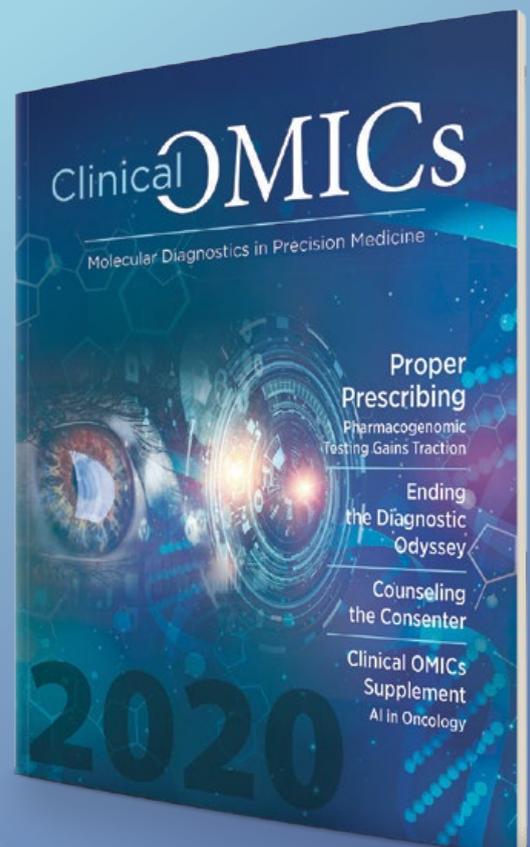
We must be authentic in our work going forward, as it is indeed our responsibility and our time to act to change the future of health care.

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MEDIA BRIEF

From the PMC News Desk

Providing Foundation for Personalized Medicine's Continued Advancement, Congressional Leaders Launch Personalized Medicine Caucus, Host Educational Briefing to Cultivate Additional Support for Field

In collaboration with the Personalized Medicine Coalition, the co-chairs of the newly formed Congressional Personalized Medicine Caucus co-hosted an educational briefing about personalized medicine on February 26 to explain the field's benefits for an audience of policymakers and thought leaders in health care. By cultivating additional support for personalized medicine and uniting a bipartisan group of lawmakers committed to protecting and advancing the field, the bicameral caucus will provide a foundation for personalized medicine's continued development. Another briefing is tentatively scheduled for the month of June.

"The co-chairs should be commended for convening a bipartisan group of lawmakers who are committed to advancing personalized medicine to improve patient care and make our health system more efficient," said PMC President Edward Abrahams.

See *GenomeWeb* (subscription content): "Congressional Caucus Working to Raise Personalized Medicine Awareness Among Legislators"

See *Politico*: "White House Health Week: New Caucus (Not That One)" (February/March 2020)

As Contested Regulatory Landscape Continues to Deter Investment in Personalized Medicine Diagnostics, FDA Publishes Table of Pharmacogenetic Associations to Outline Drug-Gene Associations It Believes are Established Enough to Support Testing

As members of the diagnostic testing community expressed concerns in February about the legality and clinical consequences of the U.S. Food and Drug Administration's efforts to stop the marketing of tests for drug-gene associations that some leaders believe are well-established in medical literature, FDA published a Table of Pharmacogenetic Associations listing the associations the agency believes are backed by "sufficient evidence to support diagnostic testing." The publication of the Table adds yet another wrinkle to the ongoing debate about the most appropriate roles for various governmental agencies in overseeing the development of diagnostics. The contested landscape continues to deter investments in test upon which personalized medicine's advancement partly depends.

In the absence of a legislative solution, Edward Abrahams, President, Personalized Medicine Coalition, told *STAT News* that he hopes the additional clarity provided in the table "leads to more investment in linking therapies to diagnostics."

See *STAT News* (subscription content): "FDA Names Genes That May Interact With Specific Drugs, Offering Clarity to Genetic Testing Industry" (February 2020)

Demonstrating Importance of Personalized Medicine to Future of Health Care, Report Underlines Benefits of Personalized Medicine Products Advanced by FDA in 2019

In the latest installment of its annual report on the U.S. Food and Drug Administration's activities in personalized medicine, the Personalized Medicine Coalition explains how 12 personalized treatments and seven diagnostics FDA approved or cleared in 2019 will improve patient care and make the health system more efficient by addressing root causes of rare diseases, expanding treatment options for cancer patients, and targeting therapies to responder populations. In classifying 11 of the 44 (25 percent) new therapeutic molecular entities FDA approved last year as personalized medicines, this year's report marks the sixth straight year that personalized medicines have accounted for more than 20 percent of the agency's new drug approvals.

The annual report is designed to raise the profile of personalized medicine and underline its significance to the future of health care.

"*Personalized Medicine at FDA: The Scope & Significance of Progress in 2019* reminds us that personalized medicine offers new hope to patients with devastating diseases as well as opportunities to avoid prescribing therapies that will be unsafe or ineffective for certain populations of patients," said PMC President Edward Abrahams.

See *GenomeWeb* (subscription content): "Even More Personalized Medicines"

See *HealthITAnalytics*: "FDA Approvals Advance Precision Medicine, Genomics Treatments" (February 2020)

Summary of 15th Annual Personalized Medicine Conference at Harvard Medical School Underlines Significance of 'Shared Value' to Future of Personalized Medicine

In a review of *The 15th Annual Personalized Medicine Conference at Harvard Medical School* recently published in *Personalized Medicine*, a peer-reviewed academic journal, Christopher J. Wells, Vice President, Public Affairs, Personalized Medicine Coalition, reports participants' conclusions about the need for cross-sector collaboration to advance the field. Wells considers solutions presented by conference participants in the context of the concept of "shared value," which was defined

by Mark R. Kramer and Marc W. Pfitzer in the *Harvard Business Review* for October of 2016 as the economically and socially desirable result of "policies and practices that contribute to competitive advantage while strengthening the communities in which a company operates." In the concluding section of the review, Wells quotes William S. Dalton, Ph.D., M.D., Founder, Executive Chairman, M2Gen, to summarize why the concept of shared value should drive future progress in health care and personalized medicine.

"There is a need for multiple partners to come together to create resources that will benefit all stakeholders," Dalton said. "This will require not only data-sharing, but also the ability to collaborate and use these data. No one stakeholder can do it by itself."

See *Personalized Medicine*: "A Consensus on Collaboration: Reviewing the 15th Annual Personalized Medicine Conference at Harvard Medical School" (February 2020)

Following Dialogue With Proponents for Personalized Medicine, ICER Alters Value Assessment Methodology to Better Account for Value of Targeted Treatment, Improving Reimbursement Outlook for Field

In an article published in November of 2019 by the *American Journal of Managed Care (AJMC)*, a team of authors including Daryl Pritchard, Ph.D., Senior Vice President, Science Policy, Personalized Medicine Coalition, suggested that because payers may use the Institute for Clinical and Economic Review (ICER)'s conclusions about the value of various therapies to develop coverage decisions that are applicable to all of their beneficiaries, technical shortcomings in the way ICER's framework accounts for personalized medicine "could result in therapies that may be highly effective and cost-effective for one particular group of patients not receiving coverage and reimbursement because they are not cost-effective for everyone."

In a response to the article published in the same issue of *AJMC*, Steven D. Pearson, M.D., M.Sc., President, ICER, confirmed the Institute's commitment to assessing the cost-effectiveness of personalized medicines for different subgroups of patients, but said the Institute's requests for the data necessary to do so often go unfulfilled.

In January, ICER altered the methodology underpinning its value assessments to better account for personalized medicine's benefits.

See *American Journal of Managed Care*: "One Size Does Not Always Fit All in Value Assessment"

See *American Journal of Managed Care*: "Value Assessment and Heterogeneity: Another Side to the Story"

See *ICER*: "ICER Finalizes 2020 Updates to Methods and Public Meeting Procedures for Value Assessment Framework" (November 2019/January 2020)

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MISSION: The Personalized Medicine Coalition (PMC), representing innovators, scientists, patients, providers and payers, promotes the understanding and adoption of personalized medicine concepts, services and products to benefit patients and the health system.
