

Delivering on the Value Proposition of Precision Medicine: The View From Healthcare Payers

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Tremendous enthusiasm, investment, and hope surround the proposed transformation of healthcare through genomics-based precision medicine. In theory, as we learn more about how individual differences in genes, environment, and lifestyle impact responses to specific therapies, healthcare systems will be able to target the right treatment to the right patient, improve individual health outcomes, and reduce waste. By extension, through more efficient resource use, precision medicine should yield population health benefits at lower costs.

To deliver on this value proposition, precision medicine innovations must be readily accessible to patients and clinicians. Because genetic tests and genetically targeted therapies will only be widely utilized if payers opt to cover them, collaboration among payers, scientists, and clinicians is essential for accelerating uptake and value creation. Conversely, if scientists and clinicians are not sensitive to the payer perspective, delays and substantial waste of resources will likely result. Although the long-term value proposition of precision medicine for payers may seem clear, escalating costs, lack of evidence, and mediocre quality of evidence can be considerable barriers to adoption.

The cost liability of genetic testing is difficult for payers to predict. With more than 65,000 genetic testing products available and an estimated 10 new products added each day, genetic and molecular testing is now the fastest-growing segment of the laboratory market in the United States.¹ Although spending on genetic tests currently accounts for only 10% of health insurers' total laboratory costs, increased utilization is driving these costs upward at an annual rate of 15% to 20%.¹ Total costs for genetic testing are projected to reach \$15 to \$25 billion by 2021, up from \$5 billion in 2010.²

Genetically targeted therapies pose an even greater cost risk for payers. Often classified as specialty medications, these therapies promise benefits not available from conventional drugs and have no available substitutes, thus complicating payers' abilities to gauge their value, estimate potential demand, and establish a basis for price negotiations. Because manufacturers price drugs based on expected sales volume, the targeted use

ABSTRACT

A long-held assumption and expectation has been that genomics-based precision medicine will provide clinicians with the tools and therapies they need to consistently deliver the right treatment to the right patient while simultaneously reducing waste and yielding cost savings for health systems. The pace of discovery within the field of precision medicine has been remarkable, yet optimal uptake of new genetic tests and genetically targeted therapies will occur only if payers recognize their value and opt to cover them. Coverage decisions require clear evidence of clinical effectiveness and utility and an understanding of how adoption will impact healthcare costs and utilization within a payer's network. Research in precision medicine has often not considered the payer's perspective, and despite demonstrations of clinical effectiveness for many promising precision medicine innovations, coverage determinations have been deferred because relevant findings that payers can use to make informed decisions are lacking. Collaboration among payers, scientists, and clinicians is essential for accelerating uptake and value creation. By pairing clinical outcomes with claims and cost data and collaboratively conducting well-designed pragmatic clinical or observational studies, all stakeholders can learn from more meaningful and relevant outcomes. In turn, there will be a collective understanding of how precision medicine innovations impact the health of populations and care delivery within healthcare systems.

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TAKEAWAY POINTS

- ▶ Clinical research trials assessing genomics-based precision medicine innovations often do not measure outcomes that would allow payers to properly assess their utility and value.
- ▶ Promising innovations have failed to translate into clinical practice, as they have lacked demonstration of real-world effectiveness and favorable economic end points.
- ▶ Innovative collaborations among scientists, clinicians, and payers can potentially accelerate the adoption of precision medicine tools and therapies.
- ▶ Such collaborations could include pairing clinical outcomes with payer cost and utilization data or implementing pragmatic clinical trials that provide opportunities to study precision medicine innovations within the context of the healthcare system.

of drugs can lead to considerably higher prices on a per patient basis. Overall, spending on specialty medications is growing by more than 15% each year and is expected to account for half (\$235 billion) of total annual pharmacy spending by 2018.³ Many targeted therapies also require genetic testing to determine suitability and dosage intensity, obligating payers to cover tests for all patients presenting with a specific condition and possibly spending substantial sums to screen out those who would not benefit from the drug.

Most important, to make coverage decisions, payers need clear evidence of effectiveness: that a test detects what it is designed to detect (analytic validity); correlates with the presence, absence, or risk of a specific disease (clinical validity); and improves patients' clinical outcomes, such as mortality, morbidity, and quality of life, through better clinical decision making compared with current tests or no test at all (clinical utility). In combination, these standards allow payers to assess the clinical value of a test, or the likelihood that it will direct an effective targeted therapy to those patients who will benefit. Additional cost information is also needed for payers to make informed decisions about reimbursement. Lack of evidence about the net benefit of a test and/or treatment, in terms of both clinical and cost outcomes, is often the key factor in payers' decisions to not provide coverage.³

In general, payers will cover a genetic test if it is clearly indicated for a patient and the results legitimately inform treatment decisions. This determination often depends on whether a treatment is available and can readily be used for a condition. Most payers cover tests for tumor components that are the target of a specific drug or tests that are developed as companion diagnostics to optimize drug therapy.⁴ Because linking a test to a drug response requires a clinical trial, these tests usually have stronger levels of evidence clearly tied to increased therapeutic effectiveness. Inclusion of pharmacogenomic information in FDA-approved drug product labeling is a common theme among more broadly covered pharmacogenomics tests.³ However, multigene panel testing is not yet widely covered. Although these tests can include multiple pharmacogenes with high levels of evidence and/or identify hereditary syndromes for which a specific therapy is indicated, they also often include low- to moderate-risk genes without well-established management guidelines.¹ Payers

perceive considerable risk in covering these broader tests without a clear line of sight into how they will be used clinically.

Genotype-guided dosing for targeted therapies is an area in which the payer community typically requires robust evidence of both clinical and cost-effectiveness to endorse coverage. For example, the discovery of a genetic influence on warfarin sensitivity suggested that genotype-guided dosing could expedite dose optimization and reduce adverse events,

which would be a welcome advance for a drug that is notoriously difficult to manage clinically. However, clinical trials to date have involved too-narrow populations, offered inconclusive evidence of clinical utility, or not measured the cost outcomes that are of most interest to payers.⁵ As a result, CMS and private payers have so far deferred coverage determinations. Better evidence has been provided in the case of genotype-guided clopidogrel prescribing, in which meta-analyses and findings from a large pragmatic clinical trial have demonstrated that patients who are intermediate and poor clopidogrel metabolizers are at increased risk of adverse cardiovascular events while taking clopidogrel versus alternative therapy after percutaneous coronary intervention.⁶ Cost models have provided further evidence of economic value, and thus CYP2C19 genotyping for clopidogrel is currently covered by some private payers.⁷

Clearly, to increase the likelihood that precision medicine innovations will be both covered by payers and used appropriately in clinical practice, scientists and clinicians must provide better information about their comparative benefits, risks, and costs. However, for many reasons, they are poorly equipped to do this on their own or at an optimal pace. Collaboration with payers offers a unique opportunity to more rapidly develop the information required for evidence-based decision making. By linking genomic and clinical information with claims and cost data at the population level, conclusions can be drawn about the clinical and cost-effectiveness of genetic tests and targeted therapies in the domains and patient populations that are most important to payers. In fact, well-designed real-world observational studies or pragmatic clinical trials conducted in collaboration with payers could strengthen the evidence base for precision medicine by including head-to-head comparisons with the current standard of care, clinically meaningful outcomes and economic end points, and larger, more diverse patient populations that can be tracked over time.

Large projects, such as Vanderbilt University Medical Center's PREDICT program, the US Department of Veterans Affairs' Million Veterans Program, the collaboration partnering Renown Health and the Desert Research Institute with 23andMe, and Geisinger's MyCode Community Health Initiative with the Regeneron Genetics

Center, are now working to combine various sources of health, population, genetic, medication, and environmental data to support precision medicine innovations. For the most part, however, large payers have been reluctant to enter this space, as the incentives are better aligned for them to consume published evidence rather than to develop it.

At University of Pittsburgh Medical Center (UPMC), an integrated delivery and financing system in Pittsburgh, Pennsylvania, efforts are under way to demonstrate the value of genomic information for many of the health plan members enrolled in the University of Pittsburgh's patient registry, Pitt+Me, and its linked precision medicine biobank. Specifically, we are developing processes to share and store data; implement clinical pathways around genomic tests and therapies, such as pharmacogenomics; deliver results at points of care; and support adoption of precision medicine within sustainable reimbursement models. UPMC is also a partner in other initiatives, such as the National Institutes of Health's All of Us research program, which is designed to combine biological, lifestyle, healthcare, and environmental data on 1 million Americans.

Most people would agree that precision medicine is the future of healthcare. But the path can be direct or circuitous. Rather than continue to waste our precious resources or wait decades for important developments to be diffused, we propose to accelerate value creation by opening lines of communication with payers and strengthening collaboration for evidence generation. ■

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