Genetic testing: Opportunities to unlock value in precision medicine

Winning diagnostics companies will integrate advanced analysis of genomic data with other data sets and electronic medical records, as well as effective reimbursement strategies.

Queenie Cheong, Sastry Chilukuri, David Quigley, and Jonathan Usuka

With a growing repository of personalized data at the molecular level, molecular-diagnostics companies are uniquely positioned to unlock value. The global market for personalized medicine has grown rapidly since the inception of the Precision Medicine Initiative, announced by Barack Obama during his 2015 State of the Union address. Market research estimated the 2016 global market at $44 billion in revenues. And these revenues are forecast to more than triple, to $140 billion, by 2026.[1]

The cost-efficiency of sequencing, a major driver of precision medicine, is improving. Thanks to a number of technological, scientific, and frontline operational advances, the cost of deciphering the entire human genome has dropped by an order of magnitude, from $10,000 in 2011 to about $1,000 today.[2] Other drivers of precision medicine include more accurate sequencing, a growing number of targeted therapies, and the recognition (especially in oncology and rheumatic illnesses) that diseases are heterogeneous.

Next-generation sequencing (NGS), which is replacing the Sanger method, has become a revolutionary and mature technology widely adopted in academic research and clinical practice. NGS refers to a group of non-Sanger high-throughput sequencing technologies that make it possible to sequence millions of DNA strands in parallel. Despite the advent and rapid growth of whole-genome sequencing (WGS), we expect multigene NGS to remain the largest segment of the market over the next five years. WGS should catch up in the next ten years, a development mainly attributed to reimbursement policies.[3]

Diagnostic-test-service providers create value in both tangible and intangible forms. Revenues from pharmaceutical companies, consumers, or payers are clearly tangible, while the potential value of additional insights from collected data is intangible. In this era of bioinformatics, the wealth of data that diagnostic tests generate has become a new option value, like oil-exploration leases, to power the value and strategy of businesses.

Take 23andMe as an example: using genotyping chips, the company offers tests for the genetic blueprint of its customers' ancestry and health or trait markers. So far, it has gathered data from more than two million customers,[4] who have the choice of allowing their data to be used for biomedical research. In addition to receiving tangible revenues from selling such genetic tests, 23andMe struck a $60 million deal in 2015 ($10 million up front and $50 million in milestone payments) to give Genentech access to these data.[5] Since then, 23andMe has launched a drug-discovery arm and continued to develop partnerships to give pharmaceutical companies (including Pfizer) access to its data. That illustrates how companies can create value strategically by aggregating genetic information.

F. Hoffmann-La Roche's recent acquisition of Flatiron Health and Foundation Medicine represents another potential step—this one toward accelerating the progress of precision medicine in oncology. Flatiron Health offers customers its OncologyCloud platform infrastructure, which comprises electronic-medical-record (EMR) work-flow software, longitudinal clinical data, claims billing, and analytics capabilities for two million active cancer patients with all types of tumors.[6]

The Clinico-Genomic Database, codeveloped by Flatiron Health and Foundation Medicine, links the genomic data of 120,000 cancer patients to their longitudinal EMR data.[7] This provides unprecedented opportunities not only to validate current approaches toward targeted therapy, such as those targeting the anaplastic-lymphoma-kinase (ALK)[8] and epidermal-growth-factor-receptor (EGFR)[9] mutations, but also to expedite the development of novel targeted therapies. As this example shows, the value of data, when used in a way consistent with data-privacy regulations, comes

from its quantity, its quality (for example, data fitness for a specific use case), and its accuracy.

In the United States, the revenues of genetic-testing service providers, which perform tests that healthcare providers use to make diagnoses and guide treatments, come primarily from reimbursements by public and private payers.

Three major market trends

Broad industry surveys and expert interviews point to three major trends that will affect the market for genetic testing:

1. Data integration and analytics to realize the value of data have become increasingly important for the healthcare-delivery value chain.

2. Payers are facing increasing pressure on costs and looking for new opportunities to control them.

3. The US reimbursement landscape, which drives the profitability of most diagnostics players, is gradually evolving.

1. Data integration and analytics

Thanks to recent technological advances, digital healthcare-data and -analytics capabilities are proliferating. These include (but aren't limited to) data at the individual level, as well as capabilities that link genetic data with other health indicators, such as medical records and even nonmedical information. Moreover, the general computing trend toward artificial intelligence could potentially make these broader but linked data sets even more valuable.

The healthcare data landscape has shifted and expanded as a result of the increased pace of adoption of EMR by office-based physicians, the tracking of patients' lifestyles, and the large-scale collection of genomic data at different levels. Many stakeholders—for example, eMERGE, IGNITE, and Vanderbilt PREDICT[10]—have started to use genomic data linked to EMR for personalized medicine. That is creating an unprecedented opportunity to integrate data sources and generate deeper insights through advanced analytics.

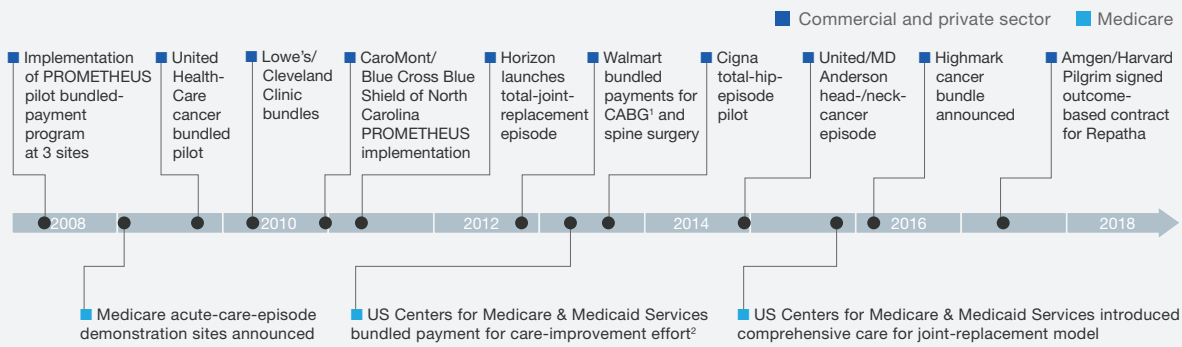
Meanwhile, data-privacy laws are becoming stricter. Stakeholders must therefore ensure that their processes collect, retain, and share data in accordance with all applicable privacy laws and regulations. These include the Health Insurance Portability and Accountability Act (HIPAA) in the United States and the General Data Protection Regulation (GDPR) in Europe.

2. Increasing cost pressures

There are two major reasons for the increasing cost pressures on payers. First, healthcare costs are growing faster than insurance premiums, at a compound annual growth rate of 5 percent[11] and 3 percent,[12] respectively, from 2013 to 2016. Second, innovative tests are proliferating: in 2018, more than 30 Current Procedural Terminology (CPT) codes[13] (the majority focused on oncology genetics testing) were added for reimbursement filings in the United States.[14] Payers therefore use genetic tests in an increasingly sophisticated way and hope that these tests and precision medicine will enable potentially curative or preventative therapies that improve the management of costs.

As cost pressures increase, payers are also gradually shifting from fee-for-service to outcome- and episode-based payment models (Exhibit 1). Outcome-based contracting is a payment-arrangement model between manufacturers and payers: manufacturers commit themselves to give payers rebates based on the performance of therapies in real-world situations. Episode-based payments, also known as bundled payments, base reimbursements to healthcare providers on clinical episodes of care, regardless of the services provided, including a broad range of diagnostic tests, disease-management techniques, and therapies.

Exhibit 1 In the United States, outcome- and episode-based payments will probably promote interest in (and the reimbursement of) genetic tests.



[1]Coronary-artery bypass graft surgery.
[2]1,137 sites of care as of Jan 2018.

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Physicians and payers struggle to differentiate among proliferating innovative tests, so clinical studies are needed to demonstrate (for reimbursement purposes) the cost-effectiveness of extensive genetic testing. This approach will promote the adoption and reimbursement of genetic tests that have well-established clinical utility and analytical validation.

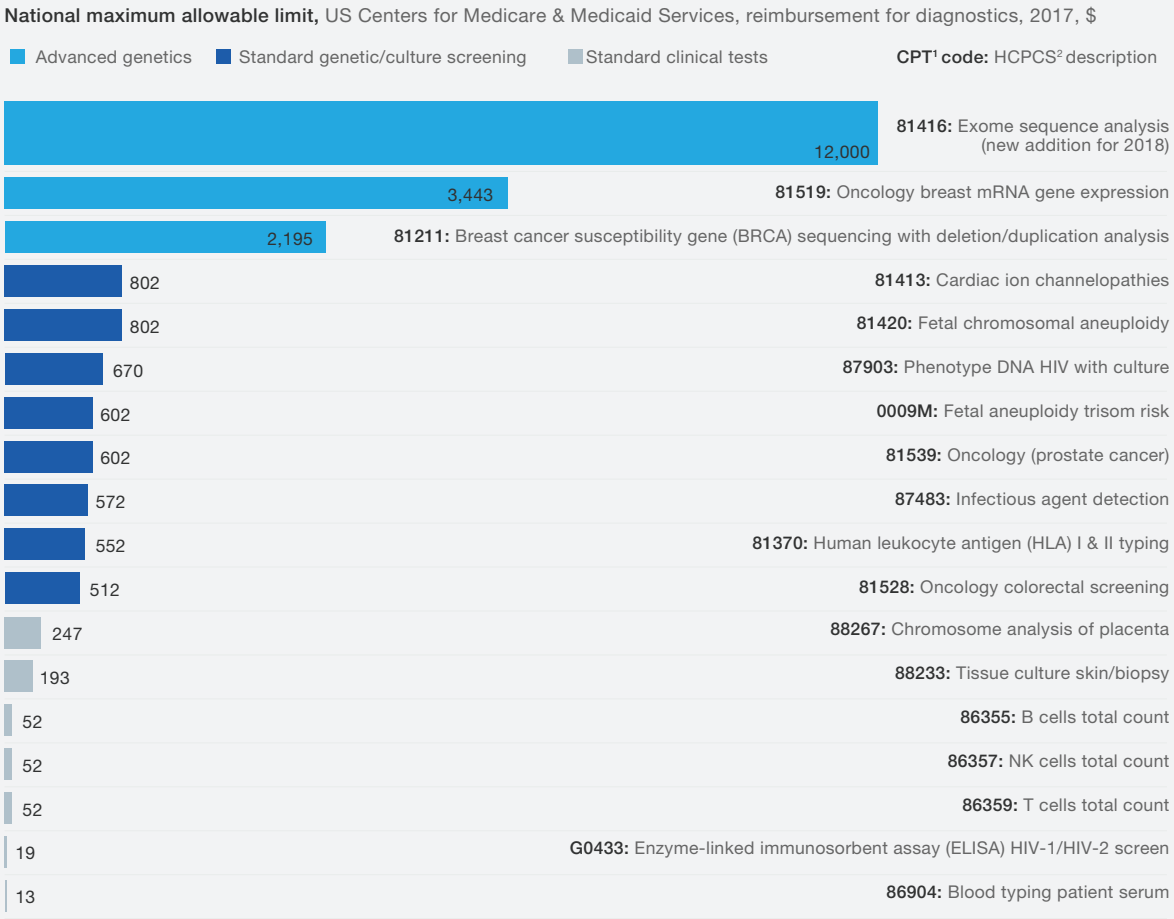
3. The evolving US reimbursement landscape

The Protecting Access to Medicare Act (PAMA) regulations decreased Medicare (public payer) reimbursement levels by pegging them to payments to private insurers. PAMA, which requires labs to report the amounts private insurers pay for laboratory tests, was signed into law in 2014.[15] Medicare used these private-payer rates to update (effective January 1, 2018) the Clinical Laboratory Fee Schedule for laboratory tests. The US Centers for Medicare & Medicaid (CMS) reduced initial payments for clinical lab tests by some 5 to 10 percent. However, the impact may vary dramatically among tests, especially the new molecular-diagnostics ones.

Among therapeutic areas, genetic testing has better recognition for clinical validation and utility in oncology, though many genetic tests for cancers are not approved by the US Food and Drug Administration (FDA) or reimbursed. CMS, however, recently announced that it would begin to reimburse FDA-approved NGS tests for patients with advanced cancers, and a few companies (for example, 23andMe, Foundation Medicine, and Oncomine) have made headway obtaining FDA approval for genetic tests in oncology.[16]

Genetic tests are reimbursed at relatively high rates (Exhibit 2): for example, CPT code 81416 for exome sequencing analysis (added early this year) has a national maximum allowable limit of $12,000. Reimbursements for pharmacogenomics, which assesses the way gene variants affect individual responses to drugs, generally cover the sequencing of multiple genes and vary a good deal, from $100 to $2,000. An interesting example—81408, a CPT code at the higher price end, $2,000—covers 24 genes for various disease conditions (Exhibit 3). Quantitative analysis of private-payer reimbursements from

Exhibit 2 Genetic tests are reimbursed at higher rates.



[1]Current Procedural Terminology (CPT) codes.
[2]Healthcare Common Procedure Coding System.

McKinsey&Company | **Source:** US Centers for Medicare & Medicaid Services

2014 to 2016 indicates that the average level of reimbursement for 81408 has declined, to $1,080 per test, from $1,545. This suggests that higher-priced genetic tests may stabilize at a lower price range.

Genetic testing, along with the current blooming of "omics" technologies, will continue to drive the pace of precision medicine. In this golden age of bioinformatics, the reimbursement landscape is evolving. The winners will gain first-mover advantages by seamlessly integrating existing big genetic or molecular data with electronic medical records—in full accordance with data privacy laws—to validate tests clinically and analytically through real-time advanced analytics.

What does it take for a diagnostics player to lead its competitors in the evolving reimbursement paradigm? The future winners will maximize the data-integration opportunities afforded by

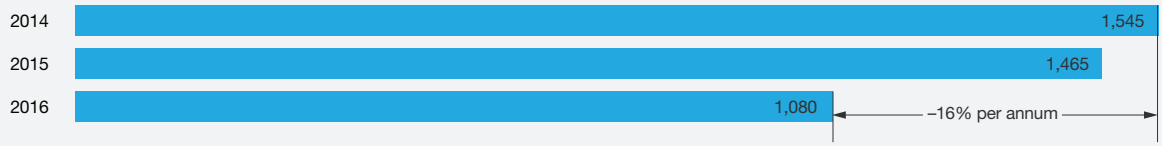
Exhibit 3 Higher-priced genetic tests may stabilize at a lower price range.

Genes included under Current Procedural Terminology (CPT) code 81408

Pathogenic Nonpathogenic

GENE	DISEASE	GENE	DISEASE
ABCA4	Stargardt disease, age-related macular degeneration	ITPR1	Spinocerebellar ataxia
ATM	Ataxia telangiectasia	LAMA2	Congenital muscular dystrophy
CDH23	Usher syndrome, type 1	LRRK2	Parkinson's disease
CEP290	Joubert syndrome	MYH11	Thoracic aortic aneurysms and aortic dissections
COL1A1	Osteogenesis imperfecta, type I	NEB	Nemaline myopathy 2
COL1A2	Osteogenesis imperfecta, type I	NF1	Neurofibromatosis, type 1
COL4A1	Brain small-vessel disease with hemorrhage	PKHD1	Autosomal recessive polycystic kidney disease
COL4A3	Alport syndrome	RYR1	Malignant hyperthermia
COL4A5	Alport syndrome	RYR2	Catecholaminergic polymorphic ventricular tachycardia, arrhythmogenic right ventricular dysplasia
DMD	Duchenne/Becker muscular dystrophy	USH2A	Usher syndrome, type 2
DYSF	Limb-girdle muscular dystrophy	VPS13B	Cohen syndrome
FBN1	Marfan syndrome	VWF	Von Willebrand disease types 1 and 3

Private-payer reimbursement of CPT code 81408, $ dollars



McKinsey&Company | **Source:** American Medical Association; expert interviews; Truven data analysis

electronic medical records. This integration suggests to physicians an appropriate diagnostic-test-ordering opportunity with minimal disruption to the clinical-care work flow, and automates the critical preauthorization step that converts reimbursement opportunities to revenues. These diagnostic companies will also develop a substantial knowledge base of publications that demonstrate medical necessity, recognizing that regulatory approval is only the first step in creating evidence for payers. Finally, and even counterintuitively, the most innovative diagnostics companies will have pragmatic product-development road maps that account for the near-term reality that next-generation DNA sequencing with targeted gene-interpretation panels will continue to have patient impact, creating barriers to reimbursement for more nuanced whole-genome approaches. While the future of personalized medicine belongs to big data from genomics and even proteomics, the present revenue realities in genetic diagnostics are still focused on small gene panels. ■

[1] "Global precision medicine market to reach $141.70 billion by 2026, reports BIS Research," BIS Research, Cision PR Newswire, December 15, 2017, prnewswire.com.

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[8] The anaplastic-lymphoma-kinase (ALK) gene encodes for a protein called ALK receptor tyrosine kinase; genetic alterations in the ALK gene are implicated in cancers including neuroblastoma and lung cancer, "ALK gene," US National Library of Medicine: Genetics Home Reference, ghr.nlm.nih.gov.

[9] The epidermal-growth-factor-receptor (EGFR) gene, which encodes for a cell-surface protein, normally helps the cells grow and divide. EGFR inhibitors that block these growth signals can be used to treat non-small cell lung cancers. "Targeted therapy drugs for non-small cell lung cancer," American Cancer Society, cancer.org.

[10] The eMERGE network, emerge.mc.vanderbilt.edu; Kristin Wiisanen Weitzel et al., "The IGNITE network: A model for genomic medicine implementation and research," *BMC Medical Genomics*, January 5, 2016, bmcmedgenomics.biomedcentral.com; and J.M. Pulley et al., "Operational implementation of prospective genotyping for personalized medicine: The design of the Vanderbilt PREDICT project," *Clinical Pharmacology & Therapeutics*, July 2012, pp. 87–95.

[11] "NHE fact sheet," National Health Expenditures tables, cms.gov.

[12] "Average annual single premium per enrolled employee for employer-based health insurance," Henry J. Kaiser Family Foundation, kff.org.

[13] Current Procedural Terminology (CPT) medical codes are used to report medical, surgical, and diagnostic procedures and services to physicians, health-insurance companies, and accreditation organizations. They are used along with disease-classification codes as part of the electronic-medical-billing process.

[14] "Pathology & laboratory 2018 CPT update effective 1/1/2018," APS Medical Billing, apsmedbill.com.

[15] "PAMA regulations," US Centers for Medicare & Medicaid Services," cms.gov.

[16] "Foundation Medicine gains FDA approval, CMS coverage proposal for NGS cancer profiling test," *GenomeWeb*, November 30, 2017, genomeweb.com; Aaron Smith, "23andMe gets FDA approval for at-home breast cancer risk test," CNN tech, March 6, 2018, money.cnn.com.

Queenie Cheong is an analyst in McKinsey's North American Knowledge Center, **Sastry Chilukuri** is a partner in the New Jersey office, **David Quigley** is a senior partner in the New York office, and **Jonathan Usuka** is a senior expert in the Southern California office.

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