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Genetic Test Availability And Spending: Where Are We Now? Where Are We Going?

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ABSTRACT Genetic testing and spending on that testing have grown rapidly since the mapping of the human genome in 2003. However, it is not widely known how many tests there are, how they are used, and how they are paid for. Little evidence from large data sets about their use has emerged. We shed light on the issue of genetic testing by providing an overview of the testing landscape. We examined test availability and spending for the full spectrum of genetic tests, using unique data sources on test availability and commercial payer spending for privately insured populations, focusing particularly on tests measuring multiple genes in the period 2014–17. We found that there were approximately 75,000 genetic tests on the market, with about ten new tests entering the market daily. Prenatal tests accounted for the highest percentage of spending on genetic tests, and spending on hereditary cancer tests accounted for the second-highest. Our results provide insights for those interested in assessing genetic testing markets, test usage, and health policy implications, including current debates over the most appropriate regulatory and payer coverage mechanisms.

The human genome was mapped only fifteen years ago, but since then the adoption of genetic testing has skyrocketed. Much of this trend is explained by the critical role genetic testing plays in precision medicine (an approach to disease treatment and prevention that seeks to maximize effectiveness by taking into account individual variability in genes, environment, and lifestyle)¹ as well as by advances in next-generation sequencing methods and concurrent reductions in sequencing costs.

Despite the increased interest in genetic testing, little empirical evidence exists on test availability and spending that reflects the genetic testing landscape across the various types of genetic tests and that uses recent information from large data sets from commercial payers in the United States. Previous studies have focused on the use of specific tests, such as *BRCA1/2*

testing for breast cancer risk,^{2–4} or spending on tests by a single payer (either public or commercial).^{5,6} Prior studies have also relied on data that are now four to six years old.^{2,5}

Our objective was to provide an overview of the genetic testing landscape by examining test availability and spending for the full spectrum of genetic tests. We used unique data on genetic test availability and commercial payer claims that are the most comprehensive and recent available. Although health policy researchers typically use public data sets for analyses intended for the academic or peer-reviewed literature, they less commonly collaborate with companies to use proprietary data sets. Our use of proprietary data enabled us to provide current insights into the rapidly evolving field of precision medicine and to conduct analyses that would otherwise have been infeasible.

We focused particularly on the growth in the

number of and spending for tests evaluating multiple genes simultaneously. Genetic testing has evolved from single-gene tests toward more complex tests that measure multiple genes. Genetic tests vary by what is being analyzed (single genes, multiple genes, exomes, or an entire genome), and the techniques used (for example, microarrays or sequencing). Whereas a single-gene test is an assay of a single gene for a single indication, a panel tests multiple genes for a common indication. Whole exome sequencing assays the entire exome (the coding regions of the genome), and whole genome sequencing evaluates the entire genome (both coding and noncoding regions). The term *whole genome analysis* refers to testing the entire genome by a broad set of methods, including sequencing, microarray, and karyotype, and thus includes whole genome sequencing. Noninvasive prenatal testing is a specific type of panel test based on circulating cell-free DNA.

Our results provide insights into genetic testing markets, test usage, and related health policies. The data we used identify available tests and what commercial payers spend on them and thus provide valuable information for policy debates on the most appropriate steps in coverage and regulation. Our results fill a critical gap in the existing literature and can serve as a baseline assessment for investigators and policy makers who are interested in examining the growth of the industry over time.

Study Data And Methods

DATA We used data from two sources, the test catalog database and the genetic testing claims database maintained by Concert Genetics, a health information technology company focused on the clinical genetics testing market. Concert Genetics maintained all raw data for the two sources and assembled extracts of aggregate data using Amazon Redshift and internal tools developed in Python. The test catalog database contains information taken from public websites, curated and standardized using tools developed by Concert Genetics and organized using a taxonomy developed and owned by the company. All tests are tracked using a standard identification code, known as the Genetic Testing Unit or GTU, also developed and owned by the company. Tests were categorized by clinical domain and type (scope of analytes assayed by the test). The domains were prenatal tests, hereditary cancer tests, oncology diagnostics and treatment, biochemical tests, pharmacogenetic tests, hematology (noncancer) tests, human leucocyte antigen (HLA) typing, neurological tests, gastroenterological tests, tests for identity and foren-

sics, tests of disease risk, cardiological tests, and tests for pediatric and rare diseases. The types were single-gene tests, multiple-gene tests, multi-analyte assays with algorithmic analyses (these tests involve the analysis of various materials, the results of which are used to assign a numeric value to, for instance, the activity of a given disease or a patient's risk of a particular disease), noninvasive prenatal tests (NIPTs), whole exome sequencing, and whole genome analysis (this includes tests conducted using sequencing, microarrays, and karyotype), and miscellaneous *Current Procedural Terminology* (CPT) codes.

We used data for the period 2014–17 from the test catalog database, which tracks existing and new tests marketed by Clinical Laboratory Improvement Amendments (CLIA)-certified laboratories, as long as the tests are marketed by the laboratories externally (for example, the database excludes hospital labs that conduct only in-house testing). The unit of analysis is a test product, which is an orderable test unit defined by a unique lab catalog code, a unique combination of an analyte or analytes (for example, mutations) and a technique or techniques (such as sequencing), or both. Tracked tests include tests used in the diagnosis or monitoring of germline or somatic (for example, cancer) genetic diseases and tests for DNA, RNA, and protein-based measures. Data in the test catalog database are updated weekly, using tools designed to monitor and collect test listings from online laboratory catalogs. Test data are managed by a curation team (consisting of a PhD molecular biologist, a genetic counselor, and data scientists) and standardized using Human Genome Organisation (HUGO) Gene Nomenclature Committee terms, aligned with external disease taxonomies (Online Mendelian Inheritance in Man, Disease Ontology). All tests are assigned to clinically relevant categories of similar tests, which are then organized into the higher-order structure of domains (for example, prenatal testing). Test listings are validated in one of the following three ways: through a community curation process, whereby users can report errors in test curation; through the hospitals using the catalog data for their test orders; and through the identification of laboratories and tests in insurance claims. Errors in catalog data (including missing tests, obsolete tests, and inaccurate test information) are reported at a rate of two errors per 10,000 tests viewed by users.

The genetic testing claims database includes 1.7 million commercial payer claims for genetic tests submitted during the three-year period from January 2014 to December 2016. It contains information about nearly forty million

covered lives from all fifty states and twenty-eight health plans and includes ages and states of residence with a similar distribution of ages and states as privately insured individuals, excluding Medicare Advantage (online appendix exhibit A1).⁷ We identified relevant claims using the Healthcare Common Procedure Coding System (HCPCS) codes based on CPT codes (appendix exhibit A2).⁷

ANALYSIS We analyzed data from the test catalog database to observe trends in genetic test products available in the period March 2014–August 2017 from 257 actively monitored laboratories. We analyzed data from the genetic testing claims database for the period January 2014–December 2016 to examine commercial payers' spending on genetic tests. We defined *spending* as the allowed amount on the claim, which includes both the amount the health plan paid and the amount paid by the patient as copayment or coinsurance. To evaluate the amount of spending associated with particular categories of tests, we matched each claim to both a test domain and a test type, using the HCPCS codes. We were able to match 87 percent of total spending to clinical domains. Unmatched claims included claims with miscellaneous codes, those with codes that were not analyte specific, and those that were not domain specific. The accuracy of the matching algorithms was independently validated using medical record data: Domain was correctly matched 94 percent of the time, and type was correctly matched 100 percent of the time. For matching claims to type of test, we present the miscellaneous codes as one type so that all claims are represented in the analysis.

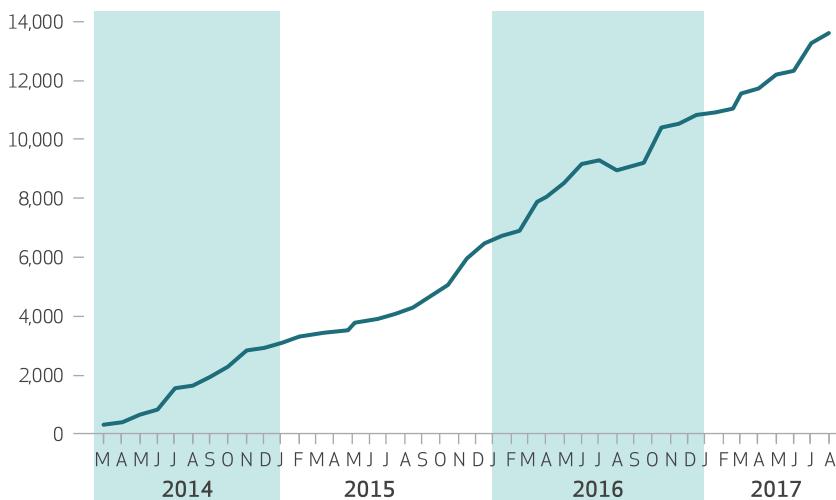
We identified multiple-gene tests in claims as a billed incident of care submitted with either a panel HCPCS code or more than one single-gene HCPCS code within a single claim.

LIMITATIONS Our study had several limitations. First, its scope was limited to examining test availability and spending. We were unable to examine patient-level test usage, the amounts billed for testing, or the rate of insurer denials. We also did not attempt to infer the indication for testing (using diagnosis codes); therefore, we were unable to examine tests' clinical application.

Second, we used the best available data, but they had limitations in turn. The test catalog data do not include information on in-house tests that are not marketed externally. The claims data reflect paid commercial preferred provider organization plans covering forty million member lives but do not include other types of plans or public insurers. Ninety-three percent of the money spent in the claims analyzed in this study was accounted for by laboratories within the test catalog database. Our results thus are underestimates of total spending—particularly for conditions more common in the elderly, such as cancer. We did not analyze denied claims or detect tests ordered for the study population but not billed to insurance. Because tests that measure multiple genes are often not specifically coded using panel codes, we created a category that combined tests with specific HCPCS panel codes and those with multiple single-gene codes in the same claim. This approach is frequently used by labs such as PreventionGenetics, Mayo Clinic, and GeneDx.^{8–10} However, we could not verify that tests with multiple single-gene codes in a single claim were indeed the equivalent of a panel test. Panel tests may also have been coded as miscellaneous tests rather than as specific panel tests.

EXHIBIT 1

Cumulative number of new genetic tests on the market, by month, March 2014–August 2017



SOURCE Authors' analysis of data from the Concert Genetics test catalog database.

Study Results

As of August 1, 2017, there were approximately 75,000 genetic tests on the market, representing approximately 10,000 unique test types. Eighty-six percent of the genetic tests were single-gene tests. The remaining tests were panel tests, including 9,311 multi-analyte assays with algorithmic analyses, 85 noninvasive prenatal tests, 122 whole exome sequencing tests, and 873 whole genome analysis tests (which included whole genome sequencing tests).

There has been rapid growth in the number of new tests entering the market, with about ten new tests appearing daily. Nearly 14,000 tests have come on the market since March 2014 (exhibit 1). Of these, about two or three per

day are panel tests. Two new NIPTs and two new exome tests enter the market each month.

Analyses of the genetic testing claims database by clinical domain showed that prenatal tests (NIPTs and carrier screening) accounted for the highest percentage of spending in 2014–16, ranging from 33 percent to 43 percent, followed by hereditary cancer tests at approximately 30 percent (exhibit 2). All other categories of testing accounted for much smaller fractions of overall spending. For example, spending on oncology diagnostics and treatment was only about 10 percent of spending, and spending on pharmacogenetic testing was less than 5 percent.

Analyses of the genetic testing claims database by test type showed that the highest percentage of spending was for multiple-gene tests, defined as tests submitted with a specific panel code or with more than one single-gene code within the same claim (exhibit 3). The growth in the percentage of spending on NIPTs is particularly notable, as that became the second-largest category

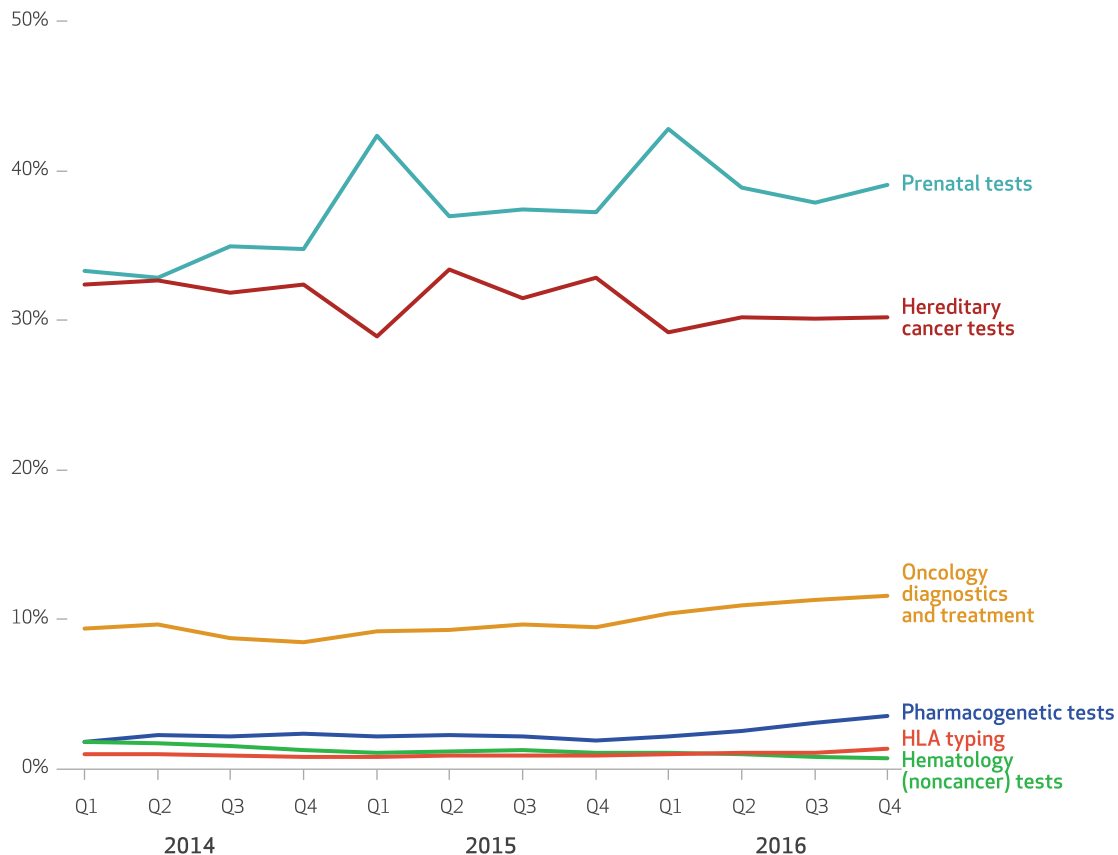
of spending. Spending on single-gene tests declined over the study period.

Discussion

We found that there were a large number of available genetic tests and a rapid growth in the number of tests, particularly those measuring multiple genes. We also found large growth in spending on genetic tests, with the highest levels of spending for prenatal tests, hereditary cancer tests, and tests coded in claims as measuring multiple genes. It is noteworthy that the highest levels of spending were on prenatal tests (carrier screening and NIPTs). Factors contributing to the growth of NIPTs include that these tests meet a clinical need by being an alternative to prenatal screening methods that incur a risk of miscarriage (such as amniocentesis) and that private payers have moved quickly to cover NIPTs for high-risk women.¹¹

EXHIBIT 2

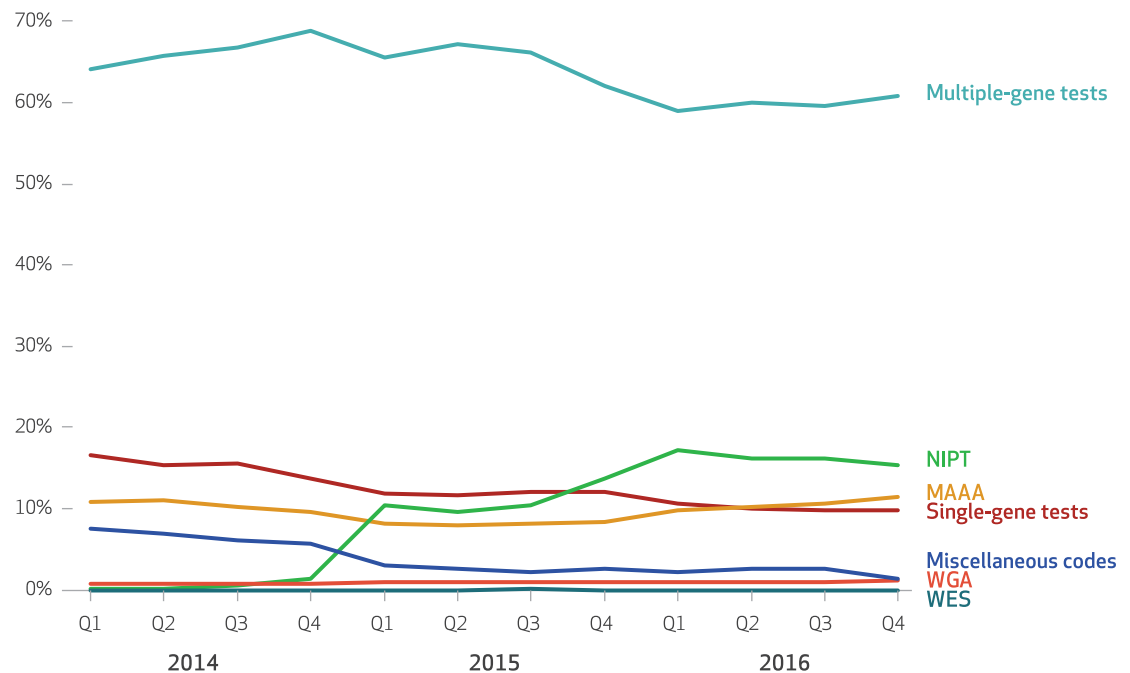
Percentages of spending on genetic testing in six clinical domains, by quarter, 2014–16



SOURCE Authors' analysis of data from the Concert Genetics genetic testing claims database. **NOTES** Claims were curated into domains according to *Current Procedural Terminology* code and billing laboratory. The exhibit shows spending in all domains that accounted for more than 1 percent of spending. Domains are described more fully in the text. HLA is human leucocyte antigen.

EXHIBIT 3

Percentages of spending on types of genetic testing, by quarter, 2014-16



SOURCE Authors' analysis of data from the Concert Genetics genetic testing claims database. **NOTES** MAAA is multi-analyte assays with algorithmic analyses. NIPT is noninvasive prenatal test. WGA is whole genome analysis. WES is whole exome sequencing. "Codes" refers to *Current Procedural Terminology* codes.

Policy Implications

The rapid growth in test availability and spending is a result of the convergence of multiple forces that have implications for relevant health policies.¹²⁻¹⁴ These forces include the clinical need for better tools to predict, diagnose, treat, and monitor disease; increased understanding of the molecular basis of disease; patient demand; industry investment; and regulations that allow the marketing of tests without FDA approval. The combination of unmet clinical needs and increasingly efficient sequencing technologies is a major factor driving the growth of multigene tests specifically. The clinical sequencing market is growing at compound annual growth rate of 28 percent and is forecasted to be \$7.7 billion worldwide by 2020.¹² This growth is fueled by an expanding demand for tests with better performance characteristics and clinical validity in many market segments, such as prenatal screening and monitoring cancer recurrence. At the same time, the production cost of sequencing has dropped dramatically to about \$1,000,¹⁵ informatics and the ability to analyze complex data have improved, new methods such as circulating cell-free DNA techniques have been developed, and databases that facilitate the interpretation of results for clinical use are increasingly available.

However, it is unclear whether the current

trends in growth and spending are sustainable. There are significant challenges that need to be addressed, and policies and systems must keep pace.¹⁶ The total cost for sequencing technologies is still relatively high (about \$1,000 for a whole genome sequencing test).¹⁵ Some payers are providing coverage and reimbursement for multigene tests, but it remains variable and limited, particularly for large panels that are not targeted to specific conditions (such as whole genome sequencing).¹⁷ There are also concerns that patients may face high out-of-pocket spending for many genetic tests.¹⁸

There also is an ongoing need to determine the clinical utility of genetic tests based on actionable mutations as well as a need for guidance regarding how tests can be implemented in clinical practice. This dual need has been described as a need for both "utility" and "simplicity."¹⁹

Another challenge involves infrastructure. The clinical lab industry is fragmented and likely to evolve in ways that could either facilitate or, conversely, inhibit the growth of genetic testing. There is some evidence that the market is becoming bifurcated, with the less numerous specialized tests performed by labs within organizations, while high-volume centralized labs perform the large-scale tests.²⁰

In addition, regulatory and coverage mecha-

nisms need to evolve to keep pace with the growth and expansion of genetic tests. Traditional means of regulating tests one kit or process at a time may be a poor fit for the current landscape. The rapid influx of tests and the fact that many genetic tests are lab-developed tests that do not require FDA approval create regulatory and coverage policy challenges. It is unclear whether new approaches such as the recent parallel review of the FoundationOne CDx (FICDx), a tumor-sequencing test, by both the FDA as a breakthrough device and the Centers for Medicare and Medicaid Services for Medicare coverage, will increase or decrease access to testing.²¹

As we have stated, evidence suggests that both tests and spending are growing rapidly. Against this backdrop of growth, the variability in coverage for these tests and fragmentation in the testing industry pose challenges for policy. These findings suggest the need to develop better evidence on the number, types, and quality of tests. These data are essential to inform policy. Such evidence can be useful to multiple stakeholders: Patients and providers benefit from knowing what tests are available, payers benefit from the ability to focus on rapidly growing test categories with high current spending and significant predicted future growth, research funders benefit from understanding future trends to support research, test developers benefit from a deeper understanding of market trends for product development, and the government benefits from being able to target key policy development efforts precisely.

One reason for the paucity of evidence on test availability and spending is that the public registries and databases that capture the needed data have limitations. For example, the National Institutes of Health maintains a Genetic Testing Registry, but it is based on voluntary submissions by labs and thus is incomplete. Other issues for public data sets are narrowly defined populations²² and time lags in data availability. Databases that are readily available to researchers are often derived from specific populations such as Medicare beneficiaries and also have a time lag. For example, a study published in 2017 used 2013 Medicare data and thus does not represent current practice.⁵

Another reason why there are few empirical studies is the barriers to data sharing and to academic-industry collaborations. Health care

delivery organizations need to share data on use and spending to more fully understand how often relatively rare tests are used in clinical practice.²³

A related challenge is that better claims and electronic health record coding are necessary to identify the use of and reimbursement for genetic tests, particularly multigene tests, comprehensively and accurately. Although changes have been made in recent years to CPT codes to better identify genetic tests, there remain gaps in the codes and how they are implemented.⁵ Only a limited number of CPT codes have been developed specifically for tests measuring multiple genes. Importantly, even when such codes are available, they are often not used: Fewer than 1 percent of multiple-gene tests are coded in claims data using HCPCS panel codes, although there has been a slow increase in such coding over time. This issue was beyond the scope of our study but remains a fruitful area for future research.

Labs and payers face many challenges in changing their coding practices to use panel codes, including logistical barriers and concerns about lower payments for tests coded as panels (resulting from how panels are defined on fee schedules as well as other factors).²⁴ However, without coding specificity, there will be ongoing difficulties in assessing the use of genetic testing using claims and electronic health records, which can lead researchers, providers, and payers to misinterpret them. For example, because payers may have an incomplete picture of what genetic tests are being used and reimbursed, they may resort to more stringent monitoring such as additional preauthorization and test-ordering requirements that could impose additional burdens on patients and providers. Conversely, a lack of data may result in payers' reimbursing for tests that are later shown to have no clinical value.^{2,5}

Conclusion

Better evidence on the number, types, and quality of genetic tests could be used to inform clinical practice and policy development. This article provides an example of data sharing and industry-academic collaboration to enable analyses that would otherwise have been infeasible and that could help inform the policy community. ■

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