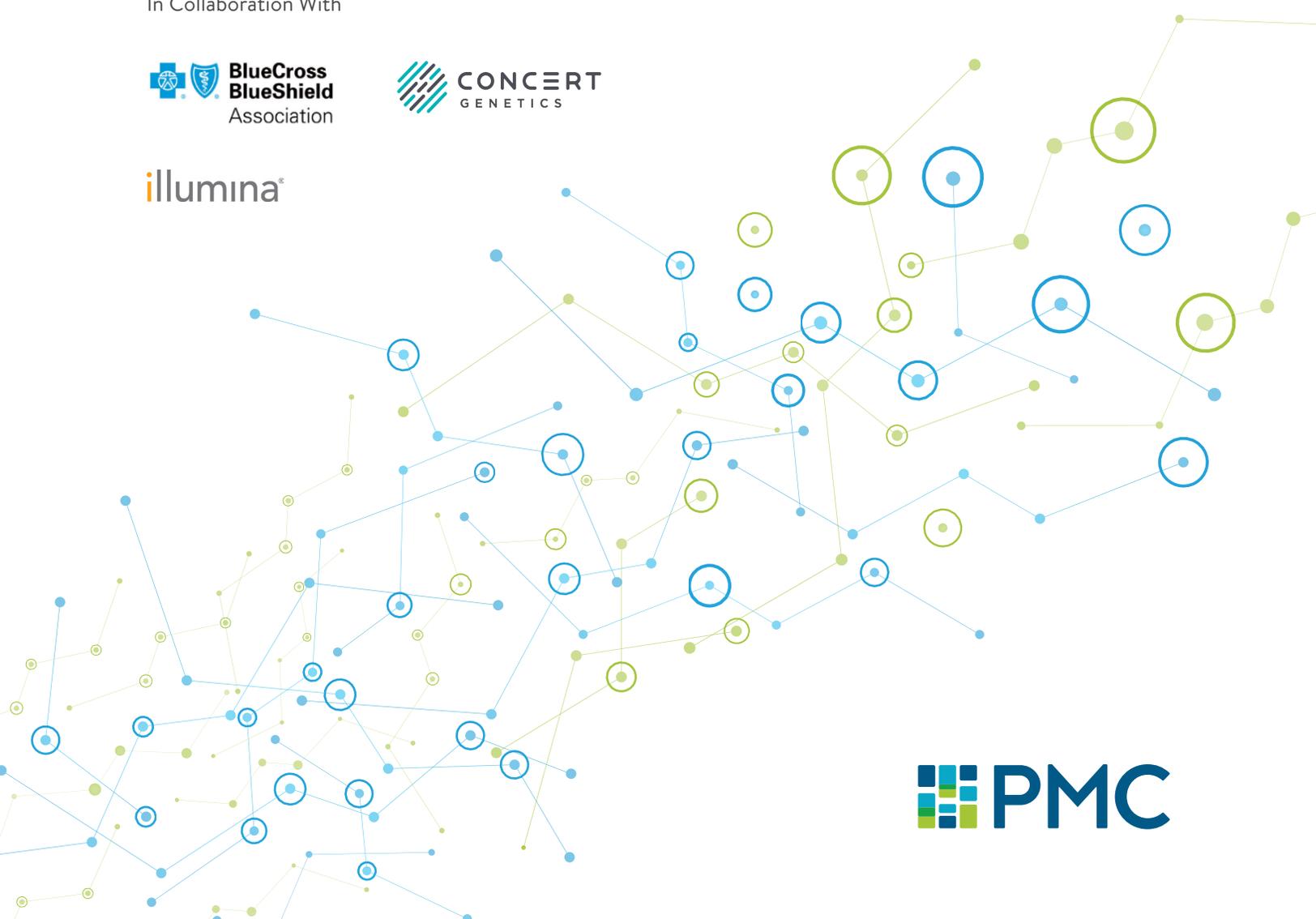

UNDERSTANDING GENOMIC TESTING UTILIZATION AND COVERAGE IN THE US

JUNE 2020

In Collaboration With



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UNDERSTANDING GENOMIC TESTING UTILIZATION AND COVERAGE IN THE US

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4 Illumina

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INTRODUCTION

Personalized medicine rests on the assumption that genomic testing, among other types of diagnostics, can inform medical management decisions, yielding clinical value for patients and economic value for health systems. By efficiently detecting a range of variants in different genes that may contribute to disease development or influence a patient's response to treatments, the logic underpinning the field suggests that genomic testing technologies may inform tailored prevention and/or treatment strategies. However, genomic testing technologies — defined herein as sequencing-based tests that analyze multiple genes or data at the level of the exome or genome — are relatively new. Payers should therefore adopt modernized policies and procedures in order to facilitate widespread access to medically appropriate genomic testing and prompt health care providers (HCPs) to utilize genomic tests in clinical practice.

Critically evaluating patterns related to the clinical use of genomic testing can uncover utilization gaps and inform strategies to address those gaps. For example, a lack of payer coverage of genomic testing may negatively impact utilization because HCPs may be reluctant to order tests that would increase direct costs for their patients. Additionally, non-coverage policies may bolster perceptions about genomic testing as a fledgling technology with limited clinical and economic utility.

Conversely, where there is favorable payer coverage indicating medically necessary genomic testing, identification of inconsistent or under-utilization may indicate HCP education gaps or other barriers to access. Examining the relationship between payer coverage and utilization can aid the efforts of HCPs and policymakers to understand and overcome barriers associated with integrating and delivering genomic medicine to all patients who can benefit.

In that context, this collaborative project examines genomic testing utilization and payer coverage patterns in three clinical areas: noninvasive prenatal testing (NIPT) in prenatal screening, whole exome sequencing (WES) in patients with rare and undiagnosed genetic diseases, and comprehensive genomic profiling (CGP) of tumors in patients with advanced cancer. Multiple robust, aggregated data sources are used for different analyses: census data, payer claims data, plan membership data, and test/policy catalogs. Key findings are shared on the following page and discussed in more detail in this document.

SUMMARY OF FINDINGS

- Medically appropriate genomic testing is inconsistently utilized across U.S. states.
- Payer genomic testing coverage policies vary considerably between states and are inconsistent. However, coverage of many genomic tests has been growing over time.
- Favorable coverage policies do not always correlate with higher utilization rates across states.
- Inconsistent coverage and reimbursement policies remain barriers to genomic testing access, but do not entirely explain inconsistent utilization. Other access barriers need to be addressed.

METHODOLOGY

This project examines trends and potential barriers to genomic testing access and utilization across the U.S. to help inform strategies to address gaps. Four aggregated data sources were used to understand payer genomic testing coverage policies, as well as clinical utilization for three clinical areas over a three-year period.

Utilization Data

The genomic testing utilization analyses included in this report use a proprietary database from Concert Genetics. The database includes test catalog data, claims data, health plan membership data, and U.S. census data. National volume estimates from Concert Genetics are based on data from a sample of 40 million commercially insured lives, extrapolated to a nationally representative estimate for current utilization for that state. Claims data are enriched with a machine learning algorithm trained to match complex, multi-CPT (current procedural terminology) code claims to the ordered tests. Genomic testing claims of U.S. members insured by national and regional commercial health plans are included, from which common patterns and reimbursement trends are examined. Details about the methodology used for these analyses are located in the Appendix.

Coverage Policy Data

The coverage policy analyses included in this report use a proprietary database from Concert Genetics containing standardized, publicly available U.S. commercial medical and reimbursement policies. To calculate coverage by state, weighted by the market share of each plan in the state, plan membership data were used (Kaiser Family Foundation's *Insurance Market Competitiveness Tables* at www.kff.org). Coverage policy scores are based on medical and reimbursement policy data points for included clinical areas of genomic testing (NIPT, WES, CGP). A policy scoring rubric is applied to give a state coverage score between 0 (low coverage policy) and 10 (high coverage policy). Details about the methodology and policy scoring rubric used for these analyses are located in the Appendix.

SUMMARY OF METHODOLOGY



Four Aggregated Data Sources

- Test and policy catalogs
- U.S. census data
- Payer claims data
- Plan membership data



Three Clinical Areas

- NIPT in prenatal screening
- WES in rare and undiagnosed genetic disease
- CGP in advanced cancer



Two Genomic Testing Access Points

- Payer policy and coverage
- Clinical utilization



Two to Three Year Period

- Utilization data from Jan. 1, 2017, to Dec. 31, 2019 (annualized)
- Policy coverage data from Jan. 1, 2018, to Dec. 31, 2019

FINDINGS IN DEPTH

- ◉ **Medically appropriate genomic testing is inconsistently utilized across U.S. states.**

Utilization can be viewed geographically across the U.S. using heat maps that show areas with lower estimated utilization (lighter shades) and higher estimated utilization (darker shades) using 2019 utilization data for NIPT (blue), WES (green), and CGP (teal) (Figure 1A/B/C). Please note differences in scales (all per million members).

While utilization was low based on tests per million members across states, relative utilization rates varied widely between states. Utilization rates for genomic tests in each of the clinical areas (NIPT, WES, CGP) were often inconsistent within and across states. This finding is based on estimates from quarterly utilization rates per million members extrapolated to a population estimate for that state.

FIGURE 1: Genomic Testing Utilization Heat Maps

A. NIPT (2019)

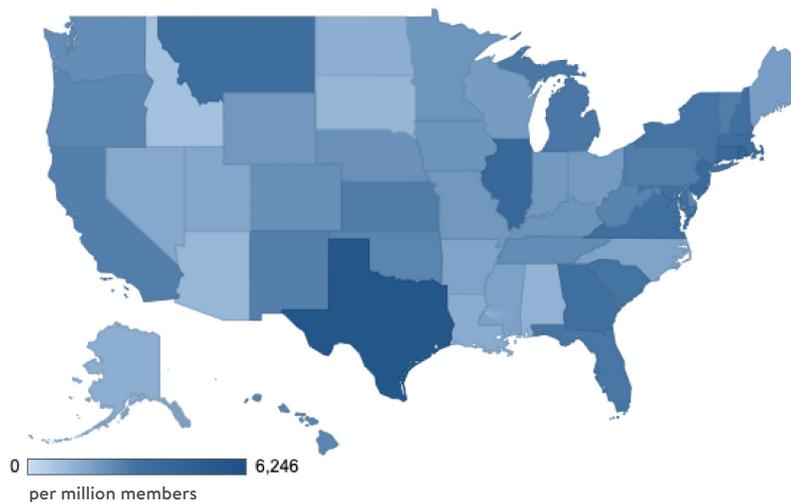
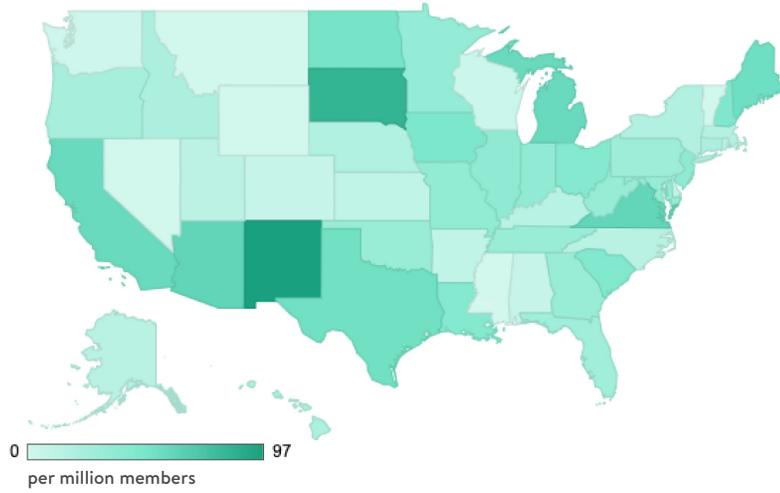


FIGURE 1 (continued): Genomic Testing Utilization Heat Maps

B. WES (2019)



C. CGP (2019)

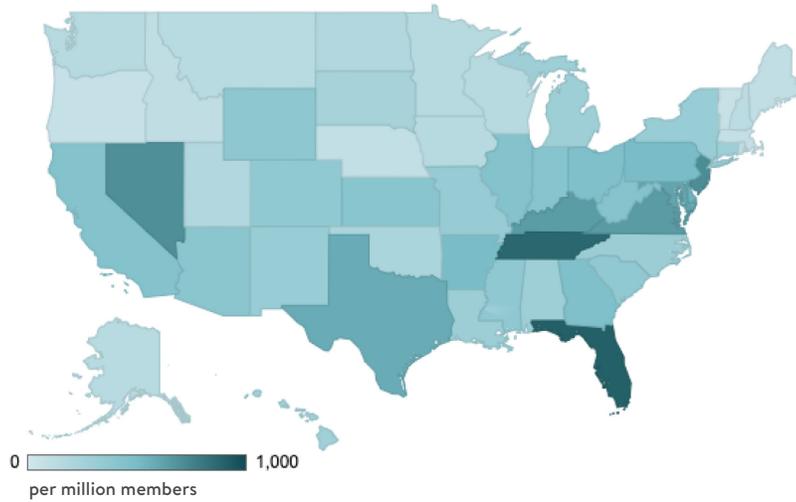
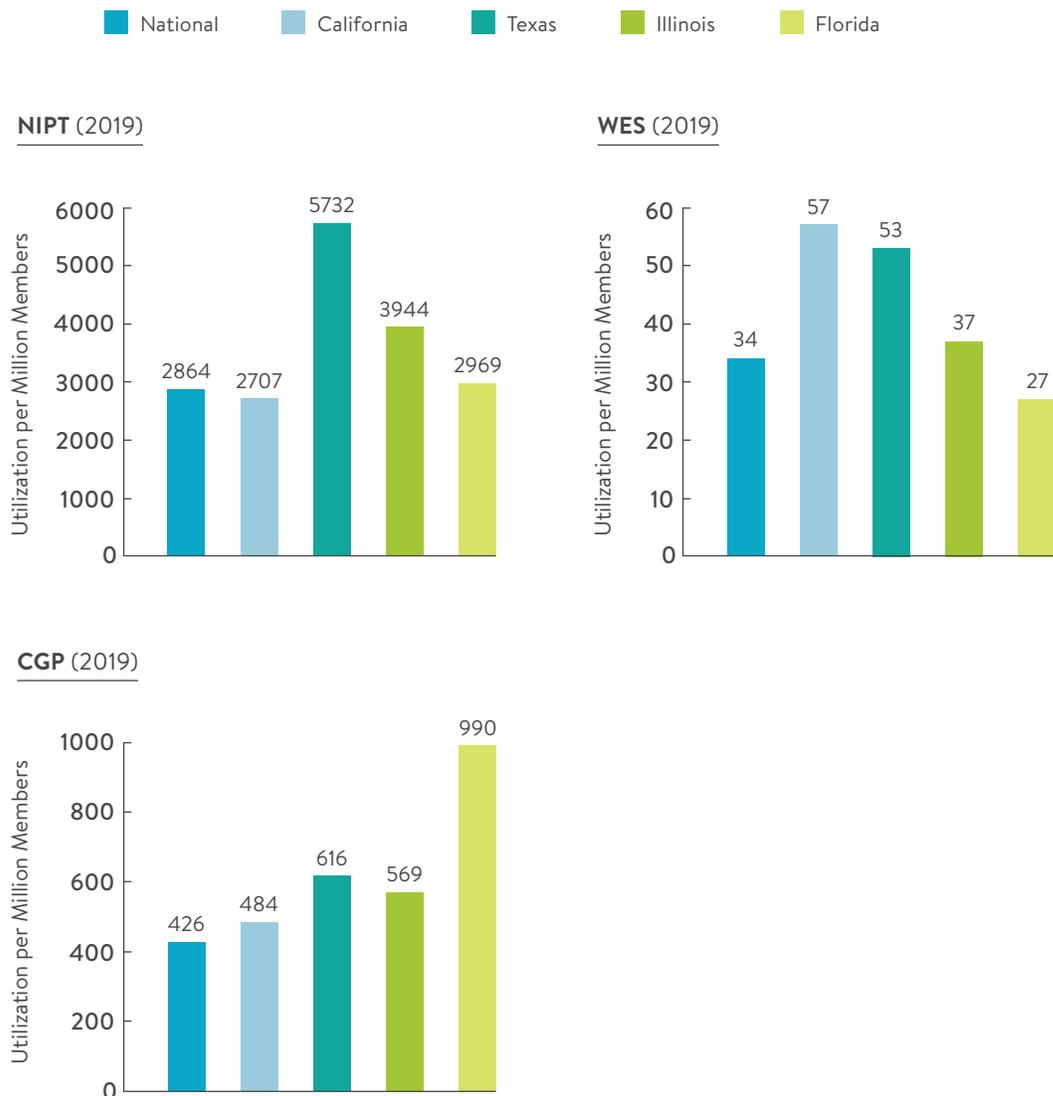


Figure 2 shows average estimated utilization rates from 2019 (annualized) for NIPT, WES, and CGP nationally, and for four states that illustrate inconsistency in utilization: California, Texas, Illinois, and Florida. These states were chosen because each has an estimated total commercial population greater than seven million. Please note scale differences (all per million members).

When looking at 2019 annualized data, NIPT utilization per million members was between 36% and 72% higher in Texas than in the other three states. For WES, California showed more than twice the utilization per million members than seen in Florida and Illinois (71% higher and 65% higher, respectively). CGP utilization per million members was between 47% and 69% higher in Florida than in the other three states.

FIGURE 2: Average Estimated Utilization Rates – National and Across Four States



This shows inconsistent utilization of genomic tests considered to be medically appropriate (based on payer coverage policies) across these states. The same genomic test was estimated to be used at variable rates in different states. In general, estimated utilization rates increased or remained stable over time.

There are likely many reasons for the inconsistent utilization (and possible under-utilization) of genomic testing as health care systems adjust to take full advantage of new technologies. One potential factor could be reduced access if there is inadequate health insurance coverage of genomic tests. Thus, we set out to examine the genomic testing coverage policy environment.

WES EXAMPLE – Inconsistent Utilization Suggests Under-Utilization?

This analysis does not account for the underlying epidemiology of the relevant disease states or for population demographics, such as age. Despite this, the demonstrated inconsistent utilization may suggest under-utilization of medically appropriate genomic testing.

Using WES as an example, utilization observed in claims data can be compared to an estimation of the population size of members eligible for WES, as shown below:

- **N≈3,945,875** annual U.S. births (based on 2016 data).¹
- **1–3%** of pediatric patients with clinical indication for WES (e.g., multiple congenital anomalies, moderate to severe intellectual disability, significant developmental delay, early-onset epilepsy). The epidemiology of patients with suspected genetic diseases is not well characterized. The range shown here is conservative based on published epidemiology of genetic disease.^{2,3,4}
- **56%** of the U.S. population estimated to have commercial insurance.⁵
- **68%** of commercially insured includes coverage for WES (see “Policy Analysis” methodology in Appendix).

Given this, we would expect between ~15,000–45,000 eligible patients nationally per year presenting with clinical indications for WES testing and who have coverage for WES under their insurance. (Note: this does not include the total prevalent population with undiagnosed diseases, which would include new patients over several years.)

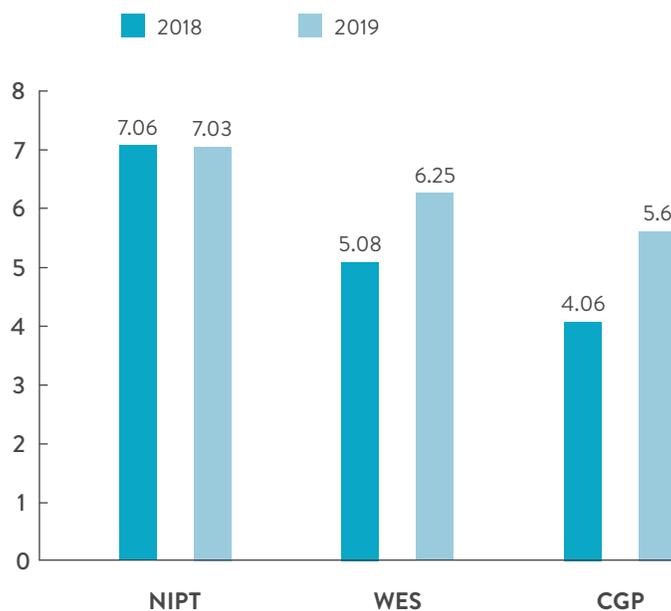
Based on 2019 estimated national utilization rates for WES from the analysis performed, this extrapolates to ~5,600 WES tests estimated utilized nationally. This is much lower than the rough estimate of ~15,000–45,000 patients eligible for WES nationally using the above assumptions. Additionally, the birth incidence of individuals with rare and undiagnosed genetic disease is not documented to vary geographically. One would not expect per capita utilization of WES to vary from state to state, yet that was found from the analysis performed. This suggests under-utilization of medically appropriate genomic testing with WES.

- **Payer genomic testing coverage policies vary considerably between states and are inconsistent. However, coverage of many genomic tests has been growing over time.**

Payer coverage policies for genomic testing varied widely between states and clinical areas. Average coverage levels were not consistently high across or between states for any clinical areas examined, determined using commercial medical plan data (Figure 3).

NIPT had the highest average policy scores, indicating relatively consistent coverage across the U.S. Average policy scores for WES and CGP were lower, indicating less consistent coverage across the U.S. in these areas; however, average payer coverage levels increased from 2018 to 2019. Although the average policy score increased most for CGP (estimated increase of 37.9%), more policy data were available to score in 2019 so this change may be overestimated.

FIGURE 3: Average Genomic Testing Coverage Policy Scores by Disease Area



Some new 2019 policies were also more restrictive. Overall, while coverage levels remained relatively low for WES and CGP, higher NIPT coverage levels and increasing average coverage levels for WES and CGP indicate a coverage policy environment for genomic testing that is trending upward.

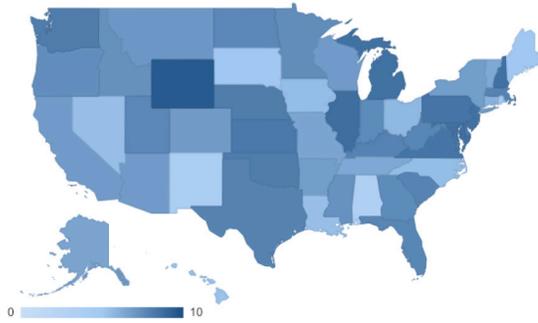
Coverage policies can also be viewed geographically across the U.S. over time using heat maps (Figure 4). The maps show areas with lower coverage policy scores (lighter shades) and higher coverage policy scores (darker shades) using 2018 and 2019 policy coverage data for NIPT (blue), WES (green), and CGP (teal) [See Table 1 in the Appendix for the policy coverage scoring rubric that corresponds to color shading scale (0–10)].

Some states had relatively low coverage policy scores, while others had moderate to high policy scores depending on the clinical area. Payer policy coverage of one genomic test was not necessarily predictive of coverage of other tests in other clinical areas. Some states (e.g., Michigan) had high policy scores for one test (e.g., WES) and lower scores for others (e.g., CGP). This shows that payers consider regional coverage policies differently between clinical areas of genomic testing.

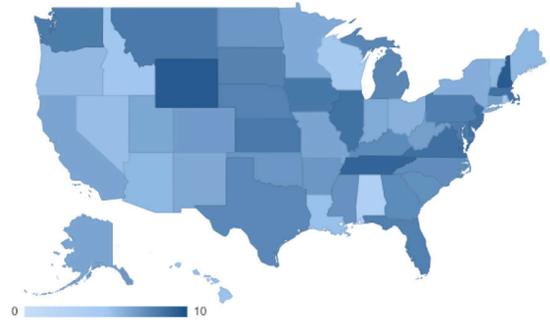
Genomic testing coverage policy scores increased between 2018 and 2019 in some states but decreased in others, in all of the clinical areas examined. This indicates inconsistent policies that may be hard for HCPs to track and navigate.

FIGURE 4: Genomic Testing Policy Coverage Heat Maps

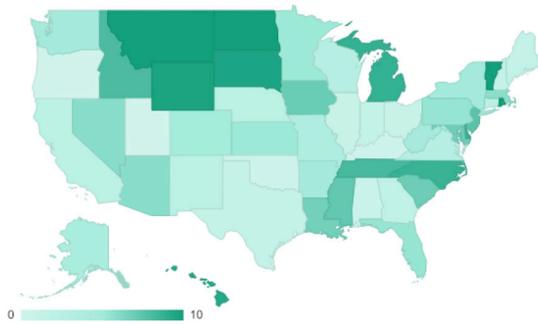
NIPT (2018)



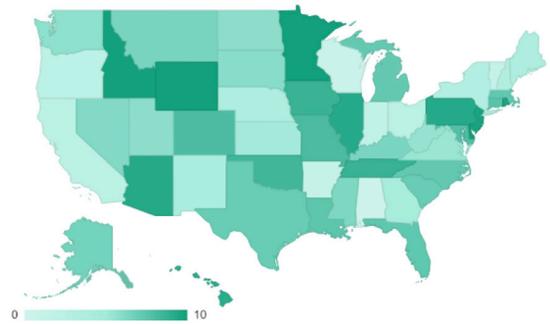
NIPT (2019)



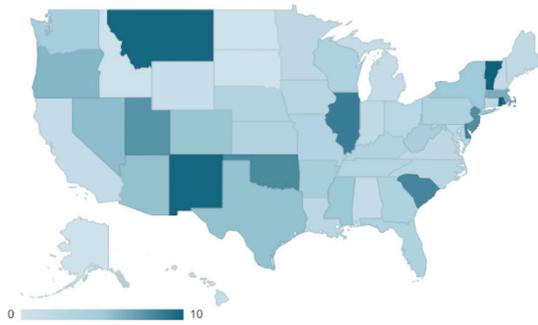
WES (2018)



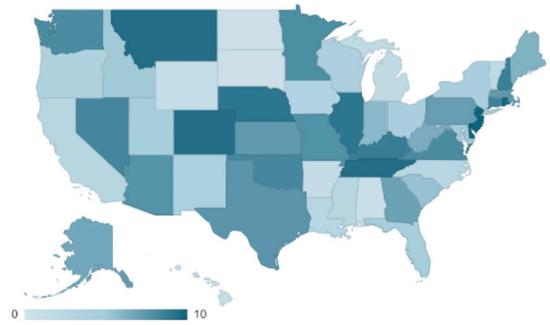
WES (2019)



CGP (2018)



CGP (2019)



See Table 1 in the Appendix for the policy coverage scoring rubric that corresponds to color shading scale (0 - 10).

- **Favorable coverage policies do not always correlate with higher utilization rates across states.**
- **Inconsistent coverage and reimbursement policies remain barriers to genomic testing access, but do not entirely explain inconsistent utilization. Other access barriers need to be addressed.**

Genomic testing estimated utilization related to coverage data can be viewed geographically across the U.S. using two-factor heat maps (Figure 5). These maps show states with lower to higher coverage policy scores (color shade gradient) for NIPT (blue), WES (green), and CGP (teal) using 2019 policy coverage data. These maps also show lower to higher utilization levels using 2019 utilization data (pattern gradient).

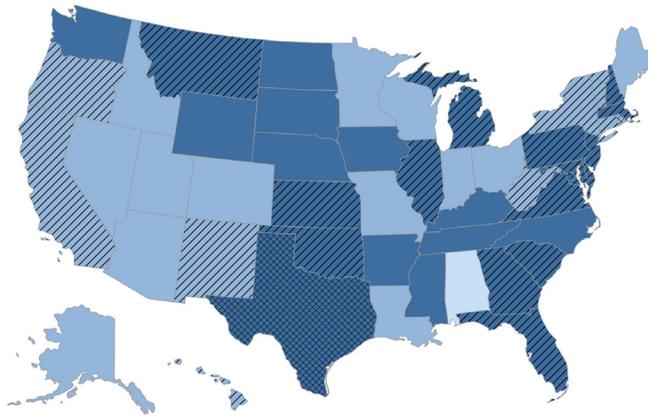
Estimated utilization as related to coverage was variable and inconsistent across states and clinical areas. Coverage levels did not always correlate with utilization levels. In some cases (e.g., Texas, Illinois, New Jersey) high coverage policy scores aligned with high utilization levels in all clinical areas, while some states with low coverage policy scores in all clinical areas also had low utilization rates (e.g., Oregon and Maine).

However, several states showed low utilization despite high coverage policy scores in some clinical areas (e.g., Washington for NIPT and CGP; Colorado for WES). Others showed high utilization despite lower coverage levels in some clinical areas (e.g., New York and Connecticut for NIPT; California and Ohio for CGP and WES).

Comparison of utilization rates to coverage policies in states with similar policy scores highlights this inconsistency and suggests regional disparities in access to genomic testing (see Table 1).

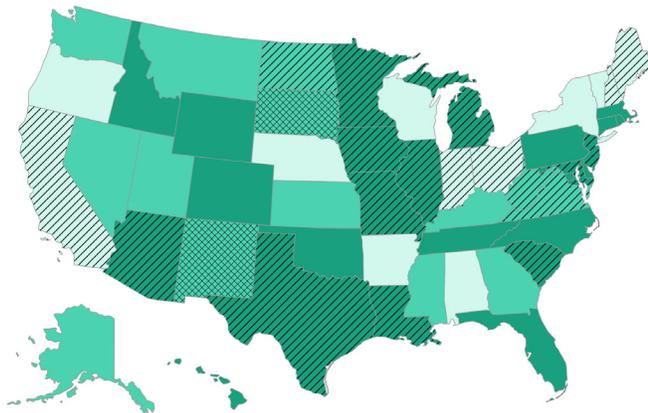
FIGURE 5: Genomic Testing Utilization/Policy Coverage Heat Maps

NIPT (2019)



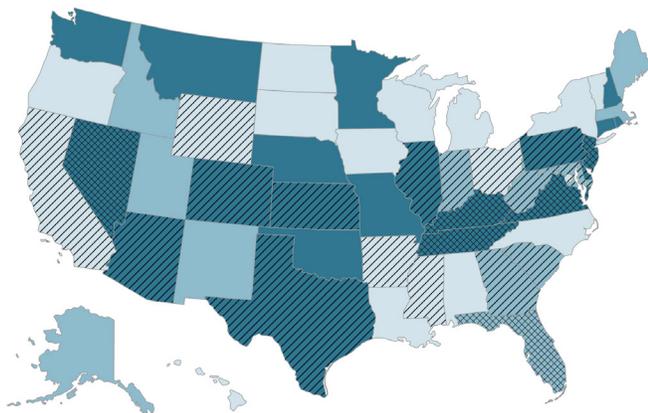
- Low Policy
- Med Policy
- High Policy
- Low Utilization
- Med Utilization
- High Utilization

WES (2019)



- Low Policy
- Med Policy
- High Policy
- Low Utilization
- Med Utilization
- High Utilization

CGP (2019)



- Low Policy
- Med Policy
- High Policy
- Low Utilization
- Med Utilization
- High Utilization

TABLE 1: Inconsistent Estimated Utilization in States with Similar Coverage Policies**Compare** – Virginia vs. Washington State

State/Genomic Test (Clinical Area)	Coverage Policy Score	Estimated Utilization (per million members)
Virginia/NIPT	8.59	3,221
Washington/NIPT	8.13	2,324
Virginia/WES	5.33	60
Washington/WES	5.75	3
Virginia/CGP	7.97	647
Washington/CGP	7.97	159

Some states expanded coverage of genomic testing, but in many cases, this did not correlate with increased utilization. For example, Rhode Island, Vermont, and New Mexico all received a higher coverage policy score for WES in 2019 compared to 2018. However, this did not correlate with an increase in utilization.

Coverage levels vary widely between states and are inconsistent across clinical areas, in some cases changing year to year. This suggests a coverage policy landscape that may be confusing for HCPs. If coverage policies are not clear or are difficult to navigate, HCPs' abilities to utilize genomic testing would likely be lower. However, it is likely that coverage policy issues do not entirely explain inconsistent utilization. This is because favorable policies do not always correlate with higher estimated utilization rates, observed in many cases and clinical contexts.

Many challenges still need to be addressed. Other barriers, such as a lack of awareness and education about genomics and testing technologies, socioeconomic disparities, and inadequate system processes and practices related to genomic testing, may also be stifling clinical adoption. In the Discussion, we consider several additional barriers to genomic testing utilization and discuss areas for future analysis.

LIMITATIONS

We note potential limitations of these analyses. The data analyzed did not include epidemiologic endpoints for the clinical areas relevant to each included genomic test, such as total number of pregnancies, individuals with rare/undiagnosed genetic disease, or cancer cases per state. Data were also limited to individuals with commercial health insurance coverage, excluding those with publicly funded federal or state-based coverage (e.g., Medicare, Medicaid). Medicaid covers a significant portion of U.S. births, so future work could include these health plans. Genomic testing utilization rates were not a direct measurement. They were based on estimates from quarterly utilization rates per million members, extrapolated to a nationally sized estimate for that state. Utilization data for 2019 were only available for Q1–3 2019, so these rates were annualized. Lastly, medical policy coverage data were limited to publicly available data, which themselves were highly variable and at times unclear. Details of plans customized to a particular employer for their employees, which could exclude certain genomic tests, would not necessarily be available publicly.

DISCUSSION

This analysis allowed unique, proprietary, and shared datasets to be evaluated within carefully constructed analytic frameworks to examine patterns of genomic testing across the U.S. health system. This revealed key insights about genomic testing utilization and access, but also raised new questions about overcoming barriers and pointed to opportunities for future work.

- **Medically appropriate genomic testing is inconsistently utilized across U.S. states.**

There are likely many reasons for inconsistent and variable utilization, related to a health care system that is evolving to appropriately account for novel genomic testing technologies. In the case of WES, the utilization data suggest under-utilization. Our analyses examined the impact of reimbursement by determining the relative utilization rates between regions with more or less favorable coverage policies. However, this alone does not explain inconsistent utilization and other barriers need to be explored.

- **Payer genomic testing utilization and payer coverage policies vary considerably and are inconsistent. However, coverage of many genomic tests has been growing over time.**

Heat maps provided a state-by-state comparison of medically appropriate genomic testing utilization and payer coverage policies within the three clinical areas studied. Both utilization and payer coverage of genomic testing vary widely between states. By comparing payer coverage to estimated utilization rates, we can evaluate the impact of coverage on use. Further evaluation of those states with extremely variable utilization can help inform efforts to increase access to and utilization of medically appropriate genomic testing.

While some states had relatively low coverage policy scores for genomic testing, others had moderate to high policy scores in different clinical areas. NIPT coverage policies had the highest average policy score, while CGP coverage policies had the largest average increase in policy score between 2018 to 2019. This suggests that payer policies may be becoming more favorable for genomic testing. However, even with favorable genomic testing coverage in some states, payer policies vary widely between states and clinical areas. Policies can also be inconsistently applied and subject to change over time. Inconsistency and lack of clarity in coverage policies continue to present barriers to utilization, as HCPs may not be aware of genomic testing coverage availability in specific regions and/or contexts.

- **Favorable coverage policies do not always correlate with higher utilization rates across states.**

Favorable coverage policies do not always correlate with higher utilization rates. This was observed in many cases for all clinical areas and was not state-specific. Some states expanded coverage of medically appropriate genomic testing, but in many cases, this did not correlate with increased utilization. There are many potential coverage policy-related contributing factors that can contribute to inconsistent utilization: opaque payer policies, capped payer agreements with hospitals (particularly for WES), or HCPs with policy coverage awareness gaps. However, genomic testing utilization in all clinical areas is relatively low despite favorable coverage policies in many cases.

- **Inconsistent coverage and reimbursement policies remain barriers to medically appropriate genomic testing access, but do not entirely explain inconsistent utilization. Other access barriers need to be addressed.**

Payer coverage policy variability denotes an inconsistent coverage landscape with considerable complexity, posing challenges for HCPs to provide genomic testing access. However, there is an increasing awareness of the clinical utility of medically appropriate genomic testing within the payer and HCP communities. This correlates with indications from this analysis that the genomic testing coverage environment is becoming more favorable. Inconsistent utilization rates of medically appropriate genomic testing cannot entirely be explained by coverage limitations. Other barriers need to be evaluated and addressed to take advantage of opportunities for the continued expansion of genomic testing in clinical practice.

Barriers and Challenges

Ensuring appropriate coverage and reimbursement policies is one of several key challenges to providing access to medically appropriate genomic testing. We reviewed the literature and conducted a series of interviews⁶ to identify other barriers that HCPs encounter as they adapt to new requirements, practices, and policies associated with access to genomic testing. The associated obstacles are summarized below.

- **Coverage and reimbursement policy**
 - Lack of clarity and consistency of payer coverage policies within and between states and across clinical areas
 - Insufficient evidence or awareness of the value of genomic testing amongst coverage and reimbursement policy decision-makers
 - Complex administrative policies and prior authorization requirements
- **Socioeconomic determinants of health**
 - Distance to genomic medicine specialists, including limited access to genetic counseling services that accompany the testing process⁷
 - Cultural and community factors that drive down utilization of genomic tests, including known racial and ethnic health disparities across the health care system^{8,9}
 - Economic factors that prohibit adoption of technology, including community hospitals and health clinics with limited budgets struggling to afford state-of-the-art technologies and services
 - Concerns about data security and privacy
- **Awareness/knowledge of personalized medicine amongst stakeholders across the health care system**
 - Lack of health care workforce awareness and education about genomics and how to navigate testing for patients¹⁰
 - Lack of payer, HCP, and policymaker understanding of the clinical utility of genomic testing for patients¹¹
 - Lack of patient awareness/education about genomics and the value of genomic testing to their health and their families' health¹²

Opportunities for Improvement

Genomic testing to diagnose disease, or to detect predictive and prognostic biomarkers that help guide prevention and treatment strategies, brings great value to patients and the health care system. Over the last 20 years, a steadily growing number of genetic biomarkers that contribute to disease have been discovered. New targeted therapies being developed to improve outcomes for responder patients add to this value proposition. However, utilization rates for medically appropriate NIPT, WES, and CGP genomic testing are inconsistent and variable – even when favorable coverage policies exist. The full value of genomic testing cannot be realized unless utilization increases.

To improve utilization rates, proponents of personalized medicine must continue to develop and disseminate evidence supporting the clinical and economic utility of genomic testing. While payer coverage is a key factor in providing access to NIPT, WES, and CGP, inconsistent utilization cannot completely be explained by coverage gaps. Increasing utilization will require a better understanding of the clinical and economic value of genomic testing that is equitably and easily accessed. This includes addressing socioeconomic determinants of health, as well as increasing genomics awareness and education for stakeholders across the health care system.

To effectively inform efforts to address gaps, it will also be important to evaluate the impact of each factor on genomic testing utilization. What would be the impact of clear and consistent payer coverage on utilization? What roles do proximity to genomic testing facilities and genetic counselors play? Will a concentrated effort to address racial and ethnic disparities increase utilization in some communities? Do health care systems with strong genomics education and clinical decision support tools utilize more genomic testing? Seeking answers to these questions will allow us to better understand and address inconsistent utilization. This provides the opportunity to see increased use of genomic testing and to better reap the clinical and economic benefits that come with it.

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APPENDIX

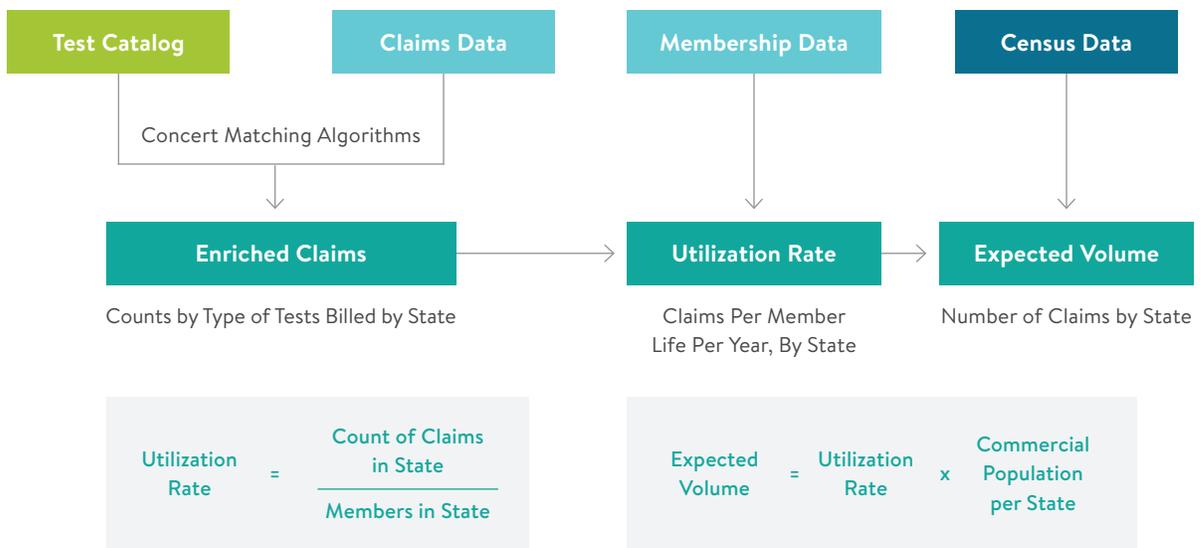
Claims Analysis

Diagnostic testing catalog data included regularly updated detailed testing attributes (e.g., genes, test methodologies, pricing), providing a historical snapshot of over 200,000 unique testing products. The database grouped tests by clinical uses (e.g., domains, categories), enabling comparability across laboratories and testing categories.

Health plan claims were matched with specific tests (or testing category) using a proprietary machine learning algorithm trained to match complex multi-CPT code claims and cross-referenced with geographic information (e.g., state-level Census data). The Claims Analysis Methodology is shown in Figure 1 below, resulting in a utilization rate by state, as well as an expected volume of claims within that state.

Estimated NIPT volumes were based on all claims in the Concert Genetics database matching at the category level to NIPT and extrapolated to state and national estimates. Estimated CGP volumes were based on the number of claims matching to CGP. Estimated WES volumes were based on the calculated number of claims matching to WES.

FIGURE 1: Claims Analysis Methodology



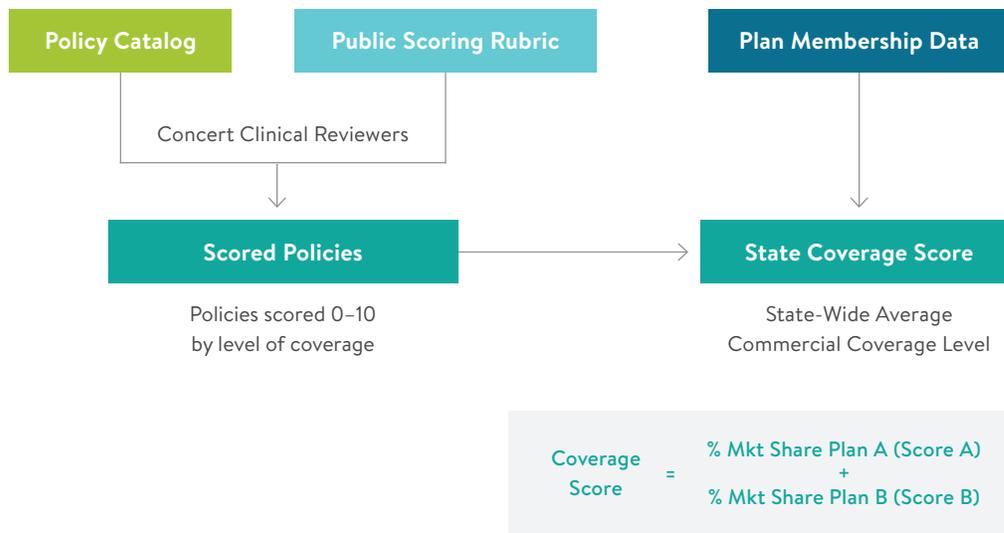
NOTE: Most panels are billed with multi-CPT code claims. Claims are counted in which at least one code was paid. Claims are matched to tests based on the billed claim (assuming billed signature most accurately reflects the test). Member count is calculated as average members per month over the period represented. Expected volume is calculated using state-level population data.

Policy Analysis

The commercial policy analysis methodology is shown in Figure 2 below. Notably, more policies were available to score in 2019 than in 2018.

Each health plan policy was normalized (weighted) to the market share it represents. Taking this together, the policy scoring rubric (see Table 1 below) is applied to give a state coverage score between 0 (low coverage policy) and 10 (high coverage policy).

FIGURE 2: Policy Analysis Methodology



NOTE: All policies were curated from publicly available policy documents for commercial lines of business. In the small minority of cases where a specific policy was not identified, it was scored as a 5, given that it would then fall under the plan’s general medical necessity policy. Membership data for each state was taken from the Kaiser Family Foundation’s *Insurance Market Competitiveness Tables*.

TABLE 1: Medical Policy Coverage Scoring Rubric

Genomic Test	Coverage Policy Score	Scope of Coverage in Policy	Score
NIPT (non-invasive prenatal testing)	None	Plan does not cover NIPT at all	0
	Partial	Plan covers for high-risk pregnant women only	5
	All	Plan covers for all pregnant women	10
WES (whole exome sequencing)	None	Plan does not cover WES at all	0
	Expanded	Plan covers WES for rare and undiagnosed genetic disease only	10
CGP (comprehensive genomic profiling)	None	Plan does not cover CGP at all	0
	Lung	Plan covers CGP for at least lung cancer	10

ABOUT US

Blue Cross Blue Shield Association

The Blue Cross Blue Shield Association is an association of independent, locally operated Blue Cross and Blue Shield companies.

Concert Genetics

Concert Genetics is a software and managed services company that promotes health by providing the digital infrastructure for reliable and efficient management of genetic testing and precision medicine. Concert maintains a catalog of the U.S. genetic testing market (currently more than 150,000 tests), monitoring and correlating those tests with medical policies and claims data representing millions of covered lives.

Illumina

Illumina is a leading developer, manufacturer, and marketer of genomic sequencing, with integrated systems to access laboratories and clinicians using genomic testing nationwide.

Personalized Medicine Coalition

The Personalized Medicine Coalition is a nonprofit education and advocacy organization representing innovators, scientists, patients, providers, and payers. PMC promotes the understanding and adoption of personalized medicine concepts, services, and products to benefit patients and the health system.



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