2020 NGS Testing Reimbursement Overview

Strategies for Clinical NGS

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BOSTON HEALTHCARE ASSOCIATES

About PierianDx

Leaders in Clinical Genomics

Today

- Full suite of software and services
- Independent CLIA/CAP “dry lab”
- 40+ medical center, cancer center, health system, and reference lab clients
- 200+ yrs of clinical genomics experience

2014

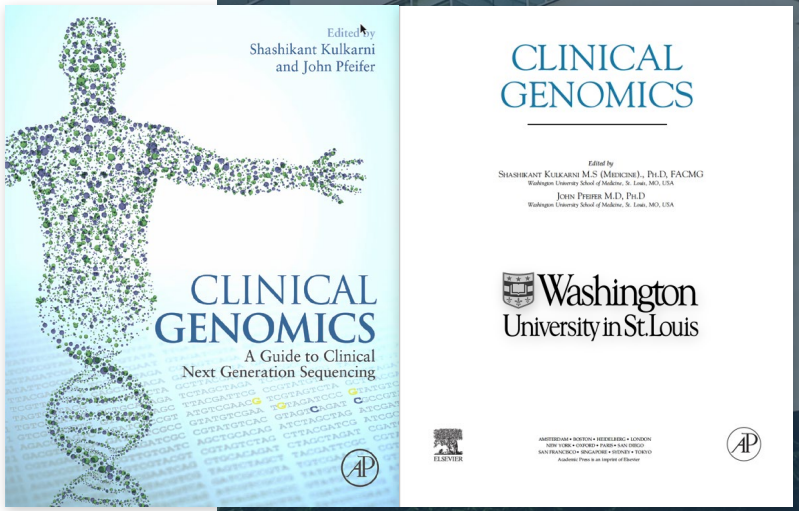
PierianDx established after ~50 labs visit WashU to learn how clinical NGS is operationalized.

2011

WashU among first to validate and clinically report on somatic cancer NGS panels.

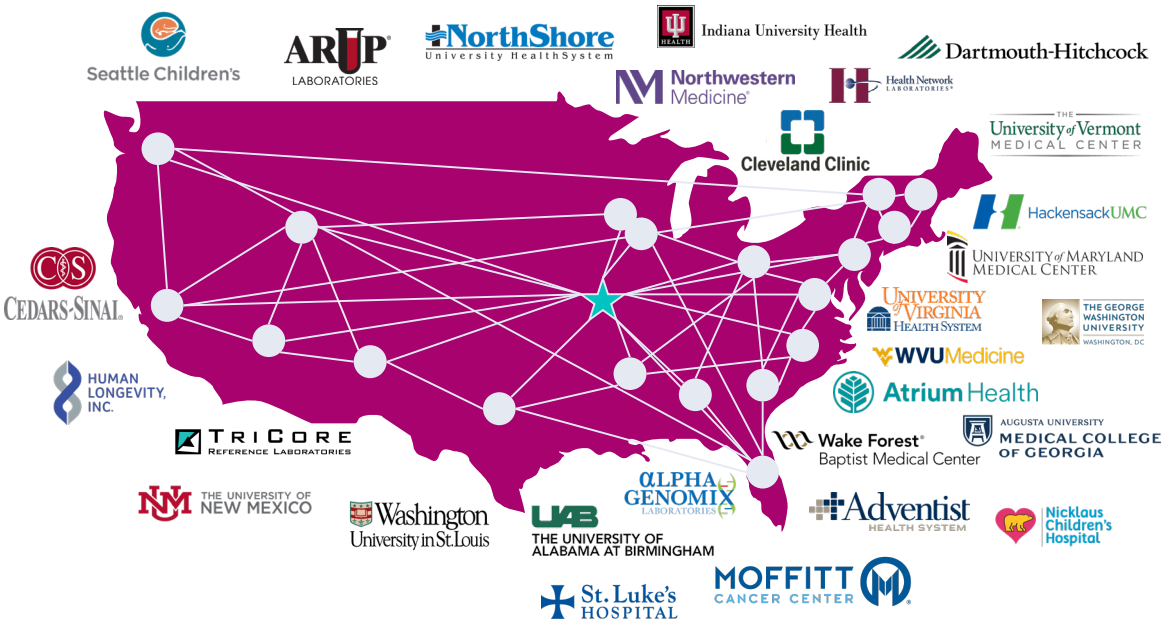
2003

WashU plays critical role in Human Genome Project.



Our Customers and Partners

The PierianDx Network



The largest clinical interpretation sharing network

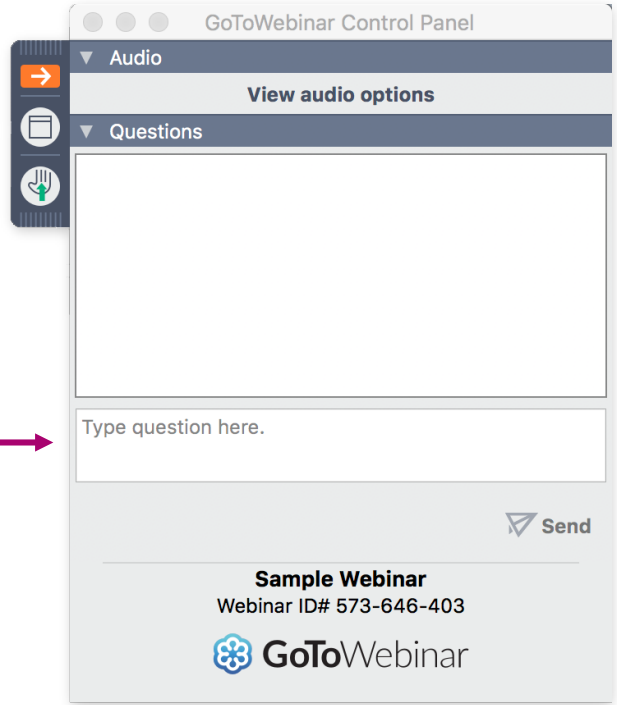
Most complete clinical genomics infrastructure

Most clinically robust knowledgebase

Most clinically experienced team

How to Submit Questions

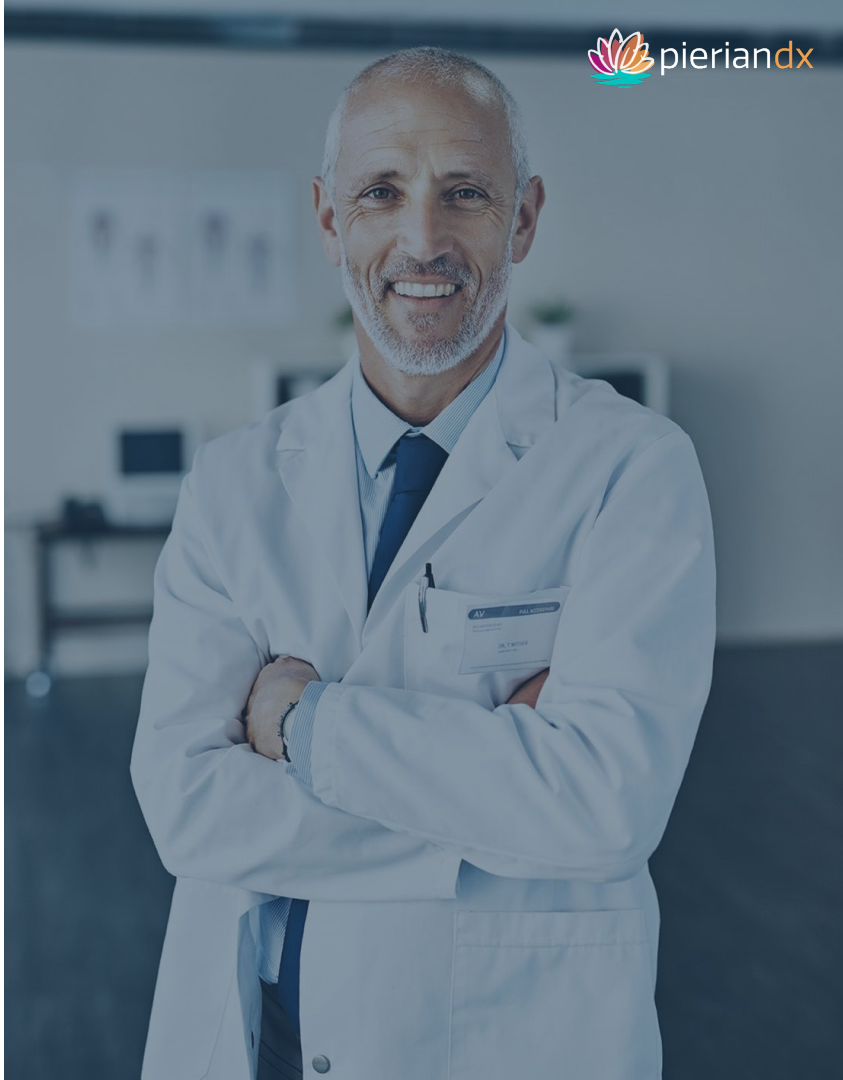
Type questions here



2020 Reimbursement Landscape

Agenda

1. Next Generation Sequencing (NGS) Market Outlook
2. NGS Payor Coverage
3. Evidence of Clinical Utility
4. NGS Coding Update
5. Payment Assignment
6. Keys to Success



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Next Generation Sequencing (NGS)

Market Outlook

Recent Trends

Biomarker and NGS Testing

Biomarker Testing

Progressive increase in oncology due to tumor agnostic biomarkers developed to inform targeted and immune therapies

Standardized testing algorithms drive biomarker testing for common tumors (NSCLC, CRC, breast) at diagnosis at many healthcare settings

NGS Testing

More laboratories performing NGS for common tumor types with approved therapies

Tumor agnostic markers, such as MSI, TMB and NTRK fusions are marked drivers of more NGS testing

Improving payor coverage with recent Medicare coverage for FDA-approved NGS tests

> "**Explosion of biomarker testing** . It's been huge in the lung field, expanded in breast and colon. I think it's being used more in thyroid. I can't speak to the other rare tumor types. I know we'll do an NGS panel on tumors when we are unclear on primary diagnosis or we are looking for targeted therapy."
>
> - Pathologist, Community Hospital

> Growth of **NGS testing for TMB, and MMR proficiency with a view towards immunotherapy** and more generally, an increase in testing to qualify patients for therapy."
>
> - Pathologist, Community Hospital

Source: BHA Analysis

Single-Marker, Tumor-Specific to Comprehensive Genomic Profiling

Oncology Testing is Evolving

Single Markers and Hotspot Panels

Specific patient populations are tested for specific biomarkers using standard methods (e.g., EGFR PCR for NSCLC)

Limits on tissue availability makes this process less viable long -term

Broad NGS Testing

NGS / CGP increasingly dominates standard methods (e.g., PCR, FISH)

Use of a single test on a single sample to obtain a comprehensive biomarker status of the patient

Multi-Modality

Mix of test methods gives best insights

Possible reflex test patterns with some tests being prioritized because of their ease of use/affordable cost

Some FDA approved; some LDTs

Informatics deployed to create genotypic and phenotypic profile of patient

Whether In-house or Send-out

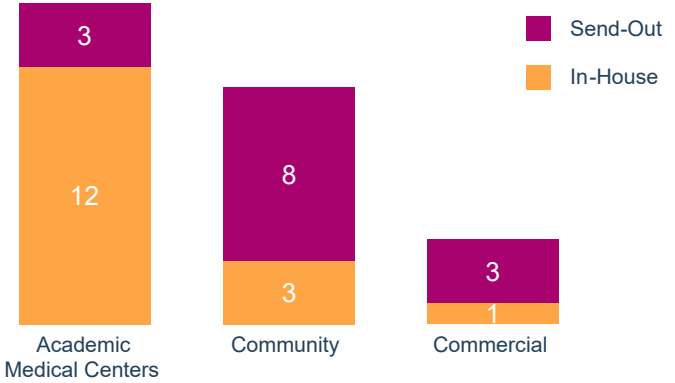
Improved Clinical NGS Access

Key Findings

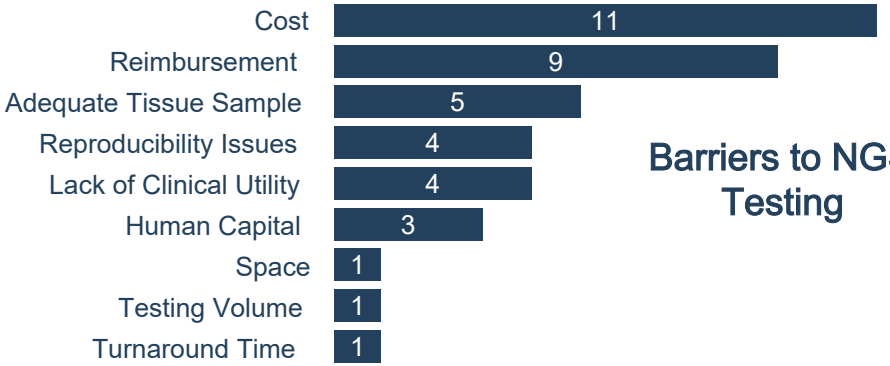
- AMCs and NCI Centers have brought clinical NGS in-house
- Physicians in community setting send -out to reference labs
- Some laboratories have implemented reflex testing for certain tumor types
- Despite improved coverage, cost, and reimbursement remain challenging

Pathologists anticipate an increase in NGS -based testing moving forward as coverage outlook continues to advance and more targeted therapies get approved

NGS Testing Capabilities



Barriers to NGS Testing



Source: BHA analysis of qualitative interviews with 30 Pathologists and/or Lab Directors

NGS Payor Coverage

Reimbursement: 3 Distinct Components

Coverage

The most common form of third -party payment for healthcare products and services in the US. Defines the range and extent of services the insurer will pay.

Coding

Universal medical alphanumeric codes that characterizes services, procedures, and products provided to patients and the case for providing them. A product will likely have different coding, coverage, and payment rates across different care settings and payors.

Payment

The process by which payments are made by an insurer for a covered product. If coverage, coding, or payment are missing, molecular diagnostics WILL NOT be covered

Source: BHA Analysis

Commercial and Government Payors

4 Ways to Achieve Coverage

Local Coverage Determination (LCD)	National Coverage Determination (NCD)	Private Payors	Medicaid
A Medicare Administrative Contractor (MAC) could review a test performed in that jurisdiction May still have significant positive carry -over benefits with private Payors	Provides access to testing for all Medicare patients nationally Could have significant positive carry -over benefits with Private Payors	Each private payor generates its own coverage policy; significant variability in coverage for the same test possible Increasingly, private payors are outsourcing coverage to genetic benefit managers (GBMs) and laboratory benefit managers (LBMs)	Oncology and biomarker tests are covered on state by state basis, coverage lags behind Medicare and other private payors

Note

For Medicare Advantage patients, coverage must follow relevant LCDs and NCDs, but for tests not covered in a NCD/LCD, independent policies can be generated

Source: BHA Analysis

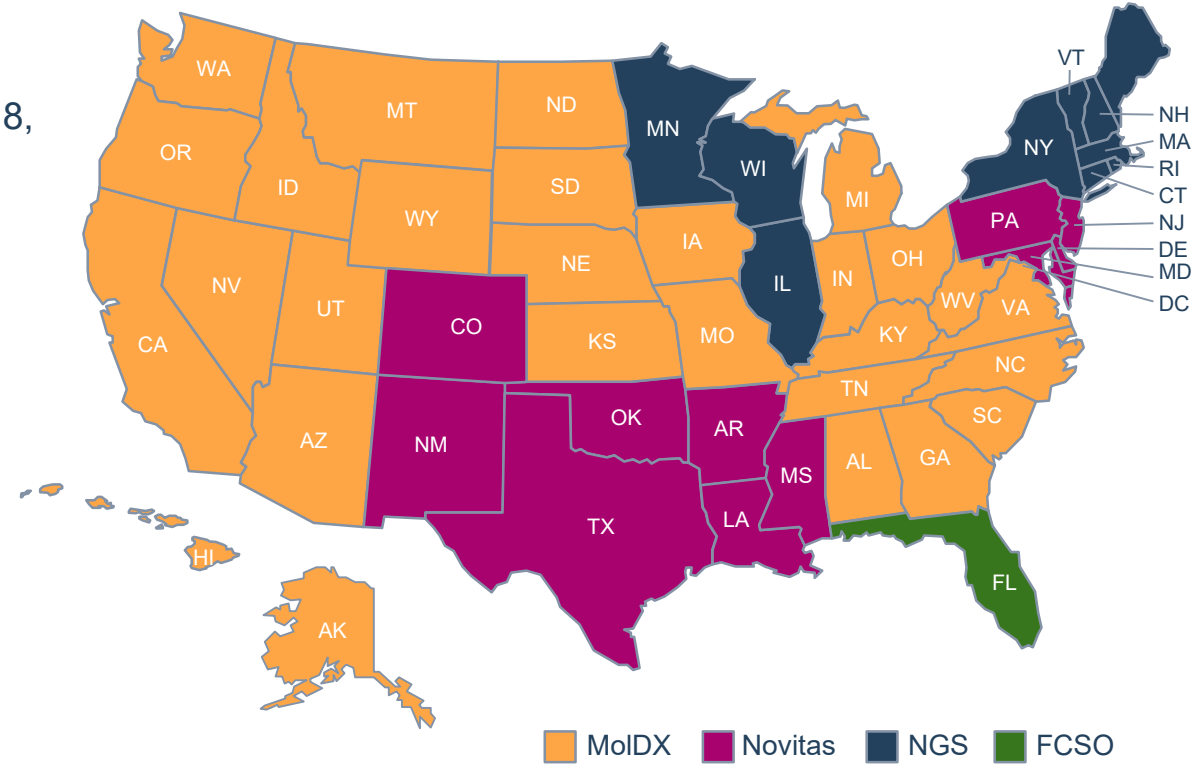
Geography Determines Requirement

MolDX Determines Coverage in Majority of States

The MolDX Program currently covers Jurisdictions JE, JF, JM, J15, J5, and J8, which includes half of US states

MACs covering these jurisdictions are Noridian Healthcare Solutions, Palmetto GBA, WPS Government Health Administrators, and CGS Administrators

Mainly, coverage of advanced diagnostics falls under four MACs: MolDX, Novitas, National Government Services, and First Coast Service Options



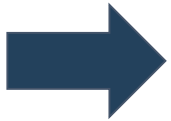
Source: BHA Analysis

A Requirement for Novel Molecular Assays

MolDX Technology Assessment for Medicare

Technology Assessment Requirements

1. Executive summary with description of assay, intended patient populations and purpose
2. Analytical validity evidence (published or in-house)
3. Clinical validity evidence (published)
4. Clinical utility (published)
5. Copies of all supporting documentation



Final Coverage Decisions May Include

- Coverage
- Limited Coverage
- Coverage with Data Development (CDD)
- No Coverage

Source: BHA Analysis

Coverage Varies Across Private Insurers

The lack of continuity across Medicare and commercial coverage decisions for advanced diagnostics highlights the existing difference in evidence requirements for Payors

- Insurers can create an explicit positive coverage policy, explicit negative coverage policy, or forego developing a policy for a diagnostic assay
- A coverage policy may address an entire category of diagnostic tests (e.g., all NGS-based tests) or or one specific diagnostic test
- Commercial insurers use a variety of tools to evaluate clinical utility, and their ultimate coverage decisions may not reflect those made by MolDX

Clinical Utility Assessment Tools used by Private Payors

1. Published Studies
2. Health Technology Assessment
3. Guideline Society Recommendations
4. Medicare Coverage Decisions

Source: BHA Analysis

Coverage Management and Utilization of Diagnostics

Payors are Turning to Third Parties

- Payors leverage third parties to control spending on advanced testing

  → United Healthcare and Anthem, through AIM Specialty Health have implemented prior authorization programs

- Payors are increasingly relying on Genetic/Lab Benefit Managers to control spending on advanced testing

  → HCSC has contracted with Evicore to manage outpatient genetic and molecular testing

GBMs/LBMs will enforce evidence -based policies and ensure that laboratory -based testing is medically necessary, increasing the need for adequate clinical evidence

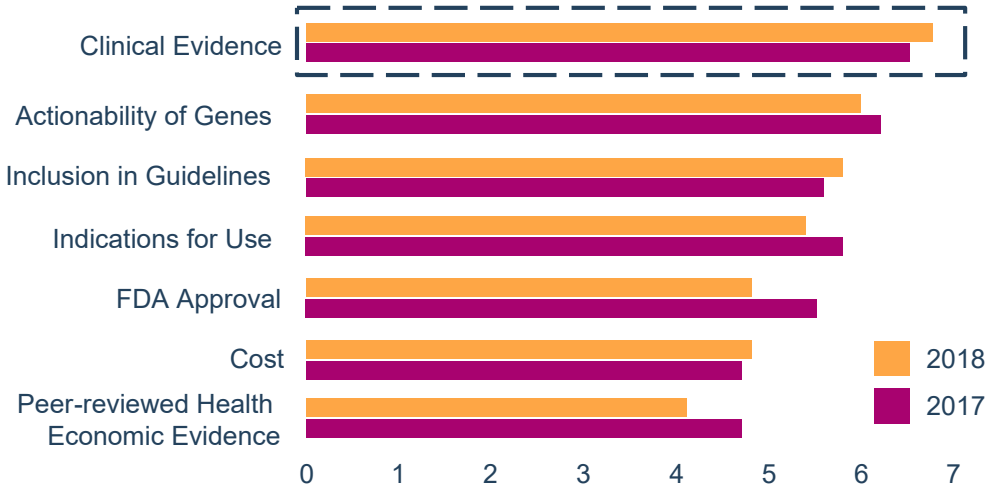
Source: BHA Analysis

Coverage for a Molecular Diagnostic

Clinical Evidence Most Influential

Impact on a Health Plan's Coverage and Reimbursement Decision

(1 = No Impact, 7 = High Impact)



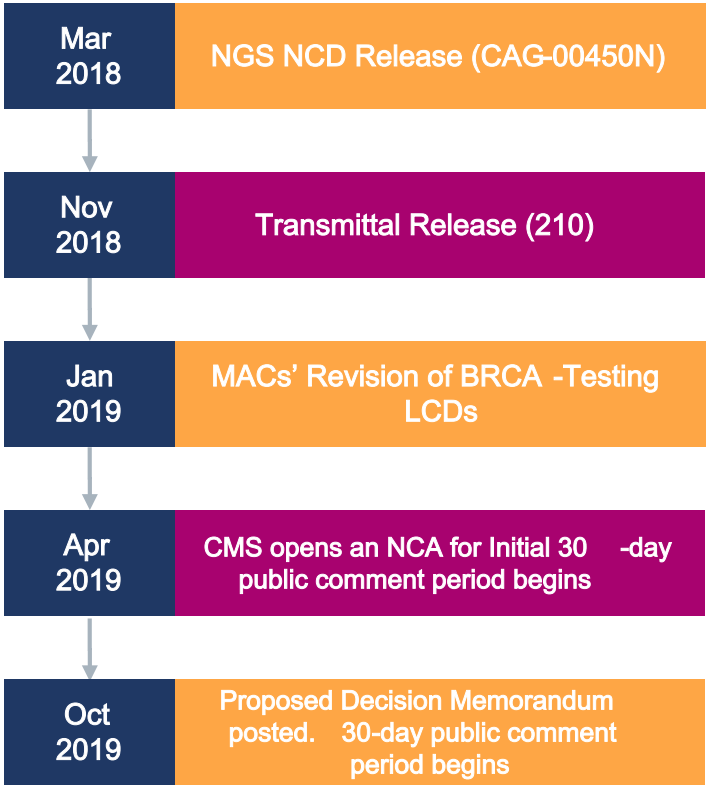
Considerations

- Clinical evidence supporting the validity and utility of the test was rated as most influential in coverage determination
- While ratings remain similar YoY, the importance of FDA approval decreased slightly from last year
- Health economic evidence was noted as least influential in coverage decisions

Source: BHA - Qualitative interviews with 20 payors

For NGS Advanced Cancer Testing

CMS' NCD Proposal



CMS states NGS is covered nationally for FDA-approved companion diagnostics tests performed in a CLIA laboratory for patients with advanced cancers with an FDA-approved therapy

- MACs have authority to decide if other NGS tests are covered in their jurisdictions

CMS clarifies to MACs that only NGS testing allowed by the NGS NCD is covered (e.g., FoundationFocus™CDxBRCA, F1CDx)

Palmetto and MolDXcontractors revise LCDs to take a non-coverage stance if patients with early stage cancers (e.g., stage 1 or 2) undergo NGS BRCA germline tests

- It is unclear whether it was CMS's intention to prevent coverage of germline BRCA testing

CMS received a total of 82 comments by the close of the comment period

New proposed decision memo published which distinguishes between national and local coverage of NGS testing (somatic and/or germline)

Source: Proposed Decision Memo for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG-00450R) CMS. Oct 2019

Proposed Changes to NCD to Expand Coverage

NGS Germline Testing

		National Coverage	Local Coverage
Original NCD	Patient Criteria	• Recurrent, relapsed, refractory, metastatic, or advanced stage III or IV cancer • Not been previously tested using the same NGS test for the same primary cancer diagnosis • Decided to seek further cancer treatment	Same as National Coverage
	Test Criteria	• FDA approved or cleared approval or clearance as a CDx in the patient's cancer • Results are provided to the treating physician for management of the patient using a report template to specify treatment options	• Other NGS tests that do not fall under the NCD (e.g., LDTs)
Proposed Addition	Patient Criteria	• Ovarian or breast cancer • Clinical indications for germline (inherited) testing • Risk factors for germline (inherited) cancer breast or ovarian cancer • Not been previously tested using NGS	• A cancer diagnosis other than breast or ovarian • Clinical indications for germline testing • Risk factors for germline breast or ovarian cancer • Not been previously tested using NGS
	Test Criteria	• FDA approved or cleared • An FDA approved or cleared indication for use in that patient's cancer • Results provided to the treating physician for management of the patient using a report template to specify treatment options.	• Other NGS tests that do not fall under the NCD (e.g., LDTs)

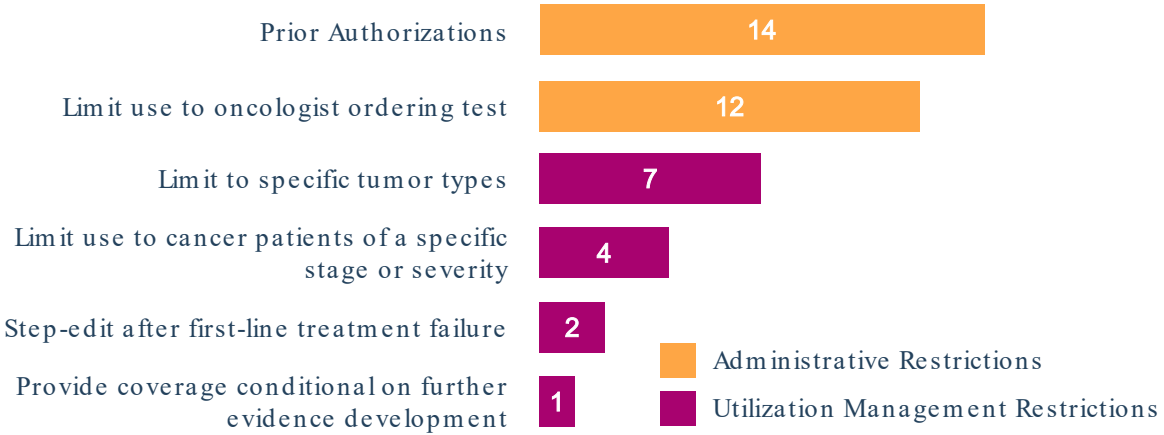
Note: All relevant patient and test criteria must be met for testing to be eligible for national/local coverage

Source: Proposed Decision Memo for Next Generation Sequencing (NGS) for Medicare Beneficiaries with Advanced Cancer (CAG -00450R). CMS. Oct 2019

Commercial Payors Not Significantly Influenced (Yet)

Medicare NCD on NGS has not strongly influenced commercial coverage decisions, but rather has acted as another reason to reconsider policy. Many Payors maintain restrictions on use of NGS tests

NGS Restrictions Utilized by Payors, cited by Pathologists



"**We cover CGP in five instances** : 1) In **lung cancer** 2) in patients who have **failed standard treatment** who are interested in participating in trials 3) in patients who have **failed all available treatment options** and are still interested in getting additional chemo 4) in patients who have **cancers of unknown primary** , and 5) in patients in whom there is **inadequate tissue** ."

- AVP, Medical Affairs

"We employ step-therapy from other treatments. **We want patients to try first - line treatment based on NCCN guidelines first before they try CGP** ."

- Director, Pharmacy Benefits

Source: BHA analysis of qualitative interviews with 30 Pathologists and/or Lab Directors

Evidence of Clinical Utility

Critical to Positive Coverage Decisions

Robust Evidence Development

Analytical Validity

Ability to accurately and reliably measure the genotype of interest

★ Clinical Validity

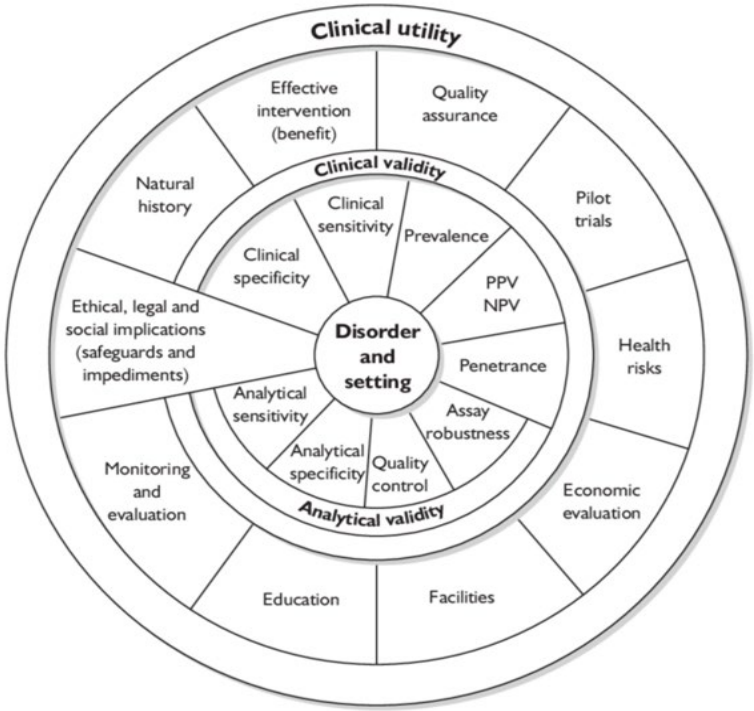
Test's ability to detect associated disorder (phenotype)

★ Clinical Utility

Risks and benefits associated with test's introduction into routine practice, including health outcomes

★ Payors expect novel diagnostics to be supported by appropriate clinical validity and utility evidence

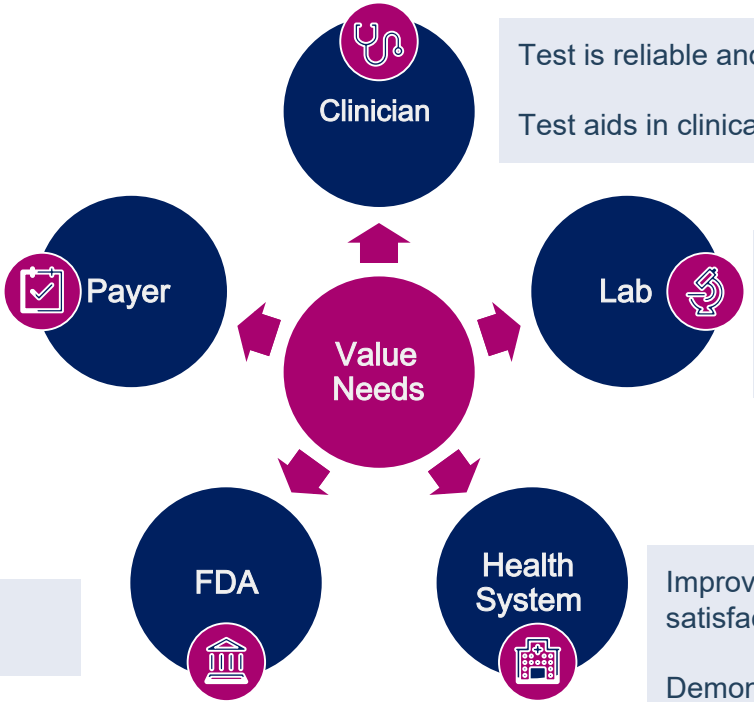
ACCE Evaluation Process for Genetic Testing



Source: BHA Analysis

Stakeholder Evidence Needs for Successful Strategy

Evidence Strategy



Test is reliable and accurate

Test aids in clinical management

Informs clinical management in an unbiased real -world setting

Management informed by test results in improved clinical outcomes

Preferably results in downstream cost-savings

Test is reliable and accurate

Better workflow / efficiency (turnaround time)

Test is accurate

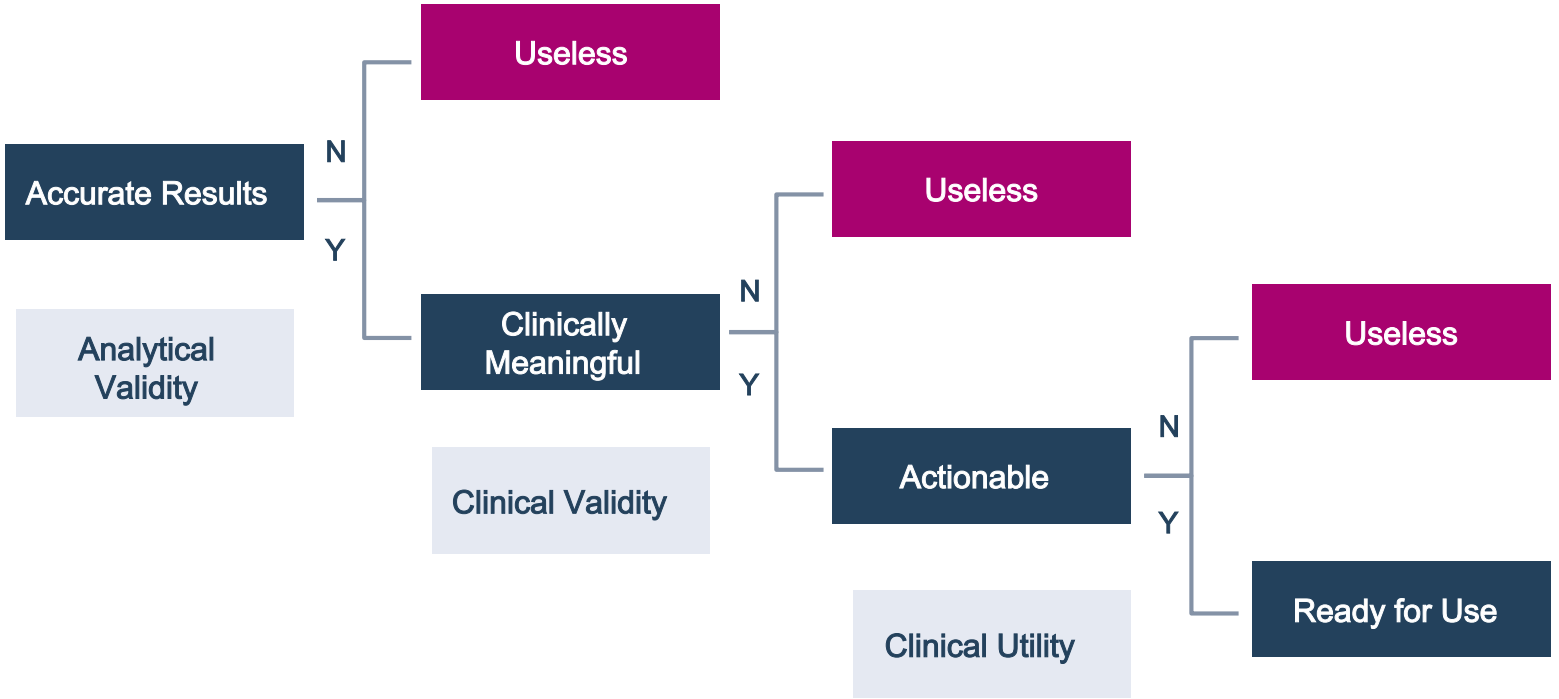
Improves quality of care and patient satisfaction

Demonstrate budget impact (decrease costs)

Helps expand service line (increase revenue)

Source: BHA Research and Analysis

Policy



Payor Coverage

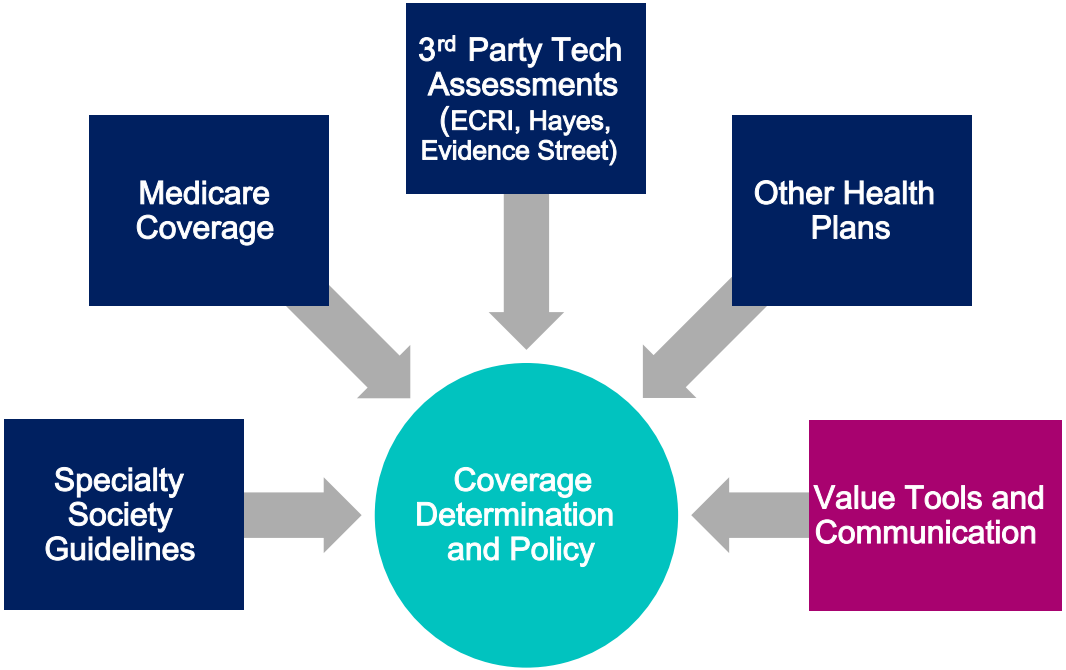
As evidence of utility and familiarity with the technology increases, payors are becoming more receptive to covering tests

	Key Findings	Change from Previous Year
Receptiveness to Coverage	• Payor receptiveness to CGP testing has increased over the last year • To further drive coverage, many payors seek evidence of clinical utility in driving meaningful changes in treatment decision -making • Inclusion in guidelines will be a catalyst to more broad coverage	Positive Change
Importance of FDA Approval	• For many payors, FDA approval is still an important condition for coverage of CGP assays • Notably, those who were more familiar with CGP tended to place less emphasis on FDA approval	Minimal Change
Primary Challenges	• The biggest hurdle for payors surrounds “diagnostic creep”, or the idea that uncovering mutations for which little is known	No Change

Source: Qualitative Interviews with 20 payers

Coverage Determination Process

Developing and deploying a robust evidence development and value communication strategy consisting of effective tools is key to payor coverage



Value Communication Tools

- Value Dossier
- Payor Value Deck
- Payor Data Binder
- Budget-impact Models

Source: BHA Research and Analysis

Driving Coverage

Developing Value Messages

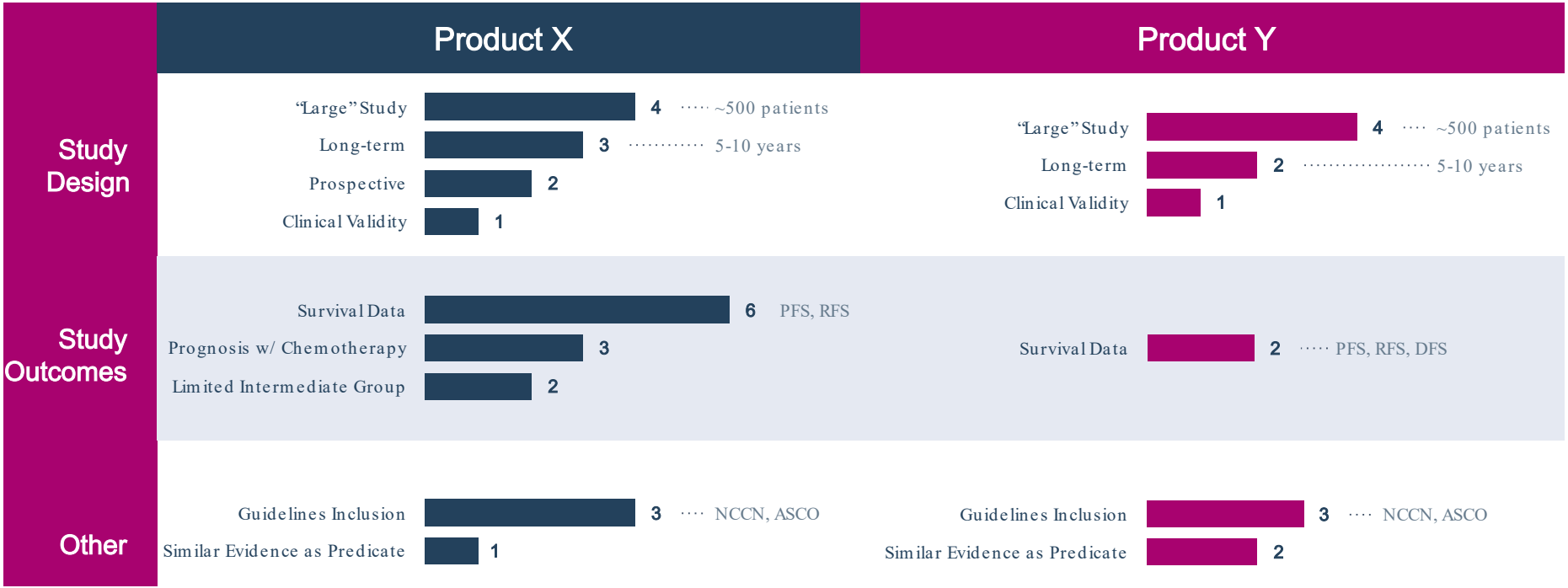
Value Components	Descriptions / Sample Value Messages
Analytical Validity and Quality	■ Test accurately measures the analytes/biomarkers of interest ■ Test is more accurate than currently available standard of care, thus reducing misdiagnosis rates
Clinical Validity	■ Test detects disease-relevant biomarkers and/or predicts the presence, absence, or risk of a specific disease ■ Test informs disease prognosis and/or risk of disease recurrence
Clinical Utility	■ Test informs an appropriate / safe and effective intervention ■ Intervention informed by the test leads to improved patient outcomes and/or reduces adverse events ■ Use of test avoids use of ineffective and potentially harmful treatment
Practice / Workflow	■ Test improves physician or laboratory practice practice and/or workflow efficiency such as TAT, TTR, or earlier intervention ■ Test reduces diagnostic odyssey and helps avoid unnecessary tests and procedures
Payer and Provider Economics	■ Test has a positive impact on hospital, clinician, or laboratory economics, both revenue and cost ■ Test shows a positive payer budget impact / cost -effectiveness ■ Test helps reduce cost associated with unnecessary tests, procedures and treatments
Patient Experience and Economics	■ Test is more accessible than alternatives and/or reduces burden on patient or caregiver ■ Test provides clarity thus reducing patient and family anxiety ■ Test report is easy to interpret thus empowering the patient with more information

Source: BHA Research and Analysis

Driving Adoption

Clinicians Also Need Compelling Evidence

N = 40 physicians



PFS = Progression Free Survival DFS = Disease Free Survival RFS - Relapse Free Survival
NCCN = National Comprehensive Cancer Network ASCO = American Society of Clinical Oncology

Source: BHA Analysis

NGS Coding Update

Diagnostic Tests

CPT Codes

Code Type	Description	Example Code
Genomic Sequencing Procedures	Include DNA or RNA sequence analysis methods that simultaneously assay multiple genes or genetic regions	81445 – Panels of 5-50 genes 81455 – Panels of > 50 genes
Molecular Pathology Tier 1/2	Tier 1: Assays performed at "significant" volumes Tier 2: Assays with lower volumes/adoption test	81235 – EGFR 81210 – BRAF
MAAA	Unique to a single clinical lab/manufacturer Represent algorithmically combined results of multiple analytes to obtain a risk score	81519 – Oncotype DX® Breast
PLA	New code set introduced in 2017 Code specific to a test provided by a sole -source laboratory, or licensed or marketed to multiple providing laboratories	0037U – FoundationOne ® CDx 0022U - Oncomine™ Dx Target Test, Thermo Fisher Scientific
Miscellaneous	Non-specific code without assigned value, requiring individual claim processor review May be used in combination with a Z -code to help identify lab	81479

Source: BHA Analysis

Multiple Coding Approaches

Codes	Description	Medicare Reimbursement Level
Proprietary Laboratory Analysis (PLA)	New set of codes created which are specific to a test and manufacturer/provider	FoundationOne CDx: $3,500 Oncomine Dx Target: $1,950 MSK-IMPACT: $2,920
Genomic Sequencing Procedures (GSP)	Relatively new codes created in 2014 Different codes for 5 -50 gene panels and >50 -gene panels	5-50 gene panel: $597 >51 gene panel: $2,920
Stacked	Labs bill for individual genes included in NGS panel Commonly used by labs to maximize payment but restrictions on code stacks by Medicare from 2019	Depends on panel size and genes billed for $3,000 to $5,000 possible
Miscellaneous	Typically used by sole -source labs that only offer NGS testing	No fixed payment

Source: BHA Analysis

Payment Assignment

Available to Laboratories

Wide Array of Payment Approaches

Payment Type	Description	Separate Payment
Fee-schedule	Negotiated per test payment rates Most prevalent means of payment for outpatient testing	Yes
Usual, customary or reasonable charges	Historic per test payment method based off of an arbitrary prevailing rate	Yes
Client/ Professional Billing	Payment is secured from physician practice or hospital instead of 3rd party insurers More recently, Medicare's 14-day rule has broadened the definition of episode of care which requires hospital to pay for some outpatient testing	From provider not payor
Capitated contract	A contract between reference lab and plan in which a lump sum is paid to that lab to provide laboratory services for all plan members	No
Exclusive contract	Variation on capitated contract in which the lab is the sole provider of services but there is per test payment	No
"Pass-through" or "carve -out"	Relationship between labs in which a sample is handed off to another lab to perform testing. The lab performing the test can bill or have the referring lab bill on its behalf	Yes
Global payment	Typically associated with payment for inpatient testing (through DRG)	No

Source: BHA Analysis

Establishing Payment for Laboratory Tests

Each year new or substantially revised codes can be either crosswalked or gap -filled to determine payment on the Clinical Lab Fe e Schedule

	Description	Advantages	Disadvantages
Crosswalk	CMS assigns a value to the new code by linking the payment rate to an existing test comparators of similar clinical value	Definitive payment rate is assigned and available immediately Crosswalk meeting provides opportunity for manufacturers to recommend specific crosswalk methodologies	Valuation may not result in increased differential payment for the new code
Gap-Fill	CMS does not assign a value Mean of MAC determined gap -fill rates are calculated and CMS finalizes the national rates effective Jan. 1 of following year	Opportunity for greater differential payment if value story is demonstrated to MACs	National payment rate is unavailable for commercial Payors to benchmark from until one year after code is effective Valuation may not result in increased differential payment for the new code

Protecting Access to Medicare Act (PAMA)

Laboratories, including physician office laboratories, are required to report private Payor rate and volume data if they:

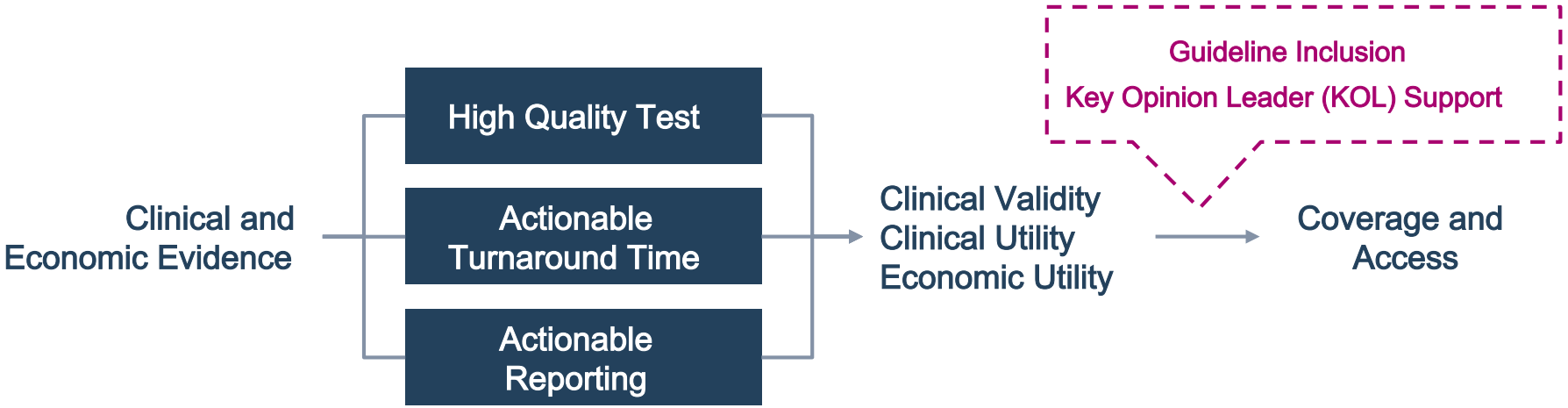
- Have more than $12,500 in Medicare revenues from laboratory services on the CLFS and have received more than 50 percent of their Medicare revenues from laboratory and physician services during a data collection period

Source: BHA Analysis

Keys to Success

Success Driven by Multifactorial Process

Must Balance Payor and Physician/Patient Needs



Key to Successful Commercialization

Strategic development of clinical and economic evidence that clearly communicate the test's value story

Source: BHA Analysis

Compelling Communication Tools

Payor Tool	Description
Payor Coverage Presentation	30-min slide presentation which succinctly makes the case for coverage Shown to payor medical directors by payor relations group, medical science liaison, local KOL physician supporters
Payor Monograph, Dossier	White paper type document which explains issues with current treatment paradigm and describes the test's impact on treatment
Payor Data Binder	Binder containing the key supportive studies and clinical trial information
Cost/Budget Impact Models	Spreadsheet model which shows savings to payor or benefit to physician in financial terms over 2-3 year timeframe (i.e., avoided treatment costs, etc.)
Payor Profiling	Database of account level information about major relevant payors which can be used to create account-specific tactics for driving positive coverage

Source: BHA Analysis

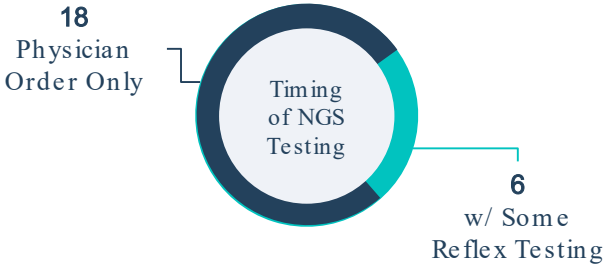
Engage Payors Strategically

	Overview	Goal	Tools
Top Down (Policy level)	Direct engagement with key decision makers (Medical Director or Tech Assessment Influencer) Payor education for access expansion Leveraging KOL support Driving policy change through evidence and/or guidelines inclusion	Positive coverage policy that can be leveraged by sales force as evidence of assured reimbursement	Payor value dossier/presentation, account profiling, etc.
Bottom Up (Claims level)	Working at the grassroots level to ensure each test request is maintained by supporting medical necessity documentation Managing/Guiding prior authorization requests with physicians Align with payor on preferred coding approach (e.g., code stacks vs. GSP codes) Leveraging denied/claims paid to create enough interest in test to encourage Payors to generate a policy and pay for the test	Maximize the number of claims paid, build interest in the test at Payor level	Medical necessity documentation, appeals A defined coding strategy: Z-codes should be applied for in advance

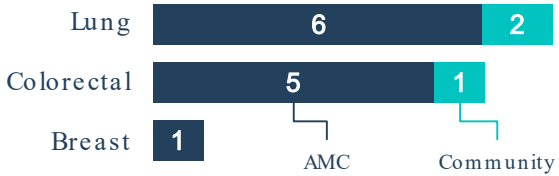
Source: BHA Analysis

Strong Relationships are Critical

Most NGS testing is at the request of the oncologist or treating physician



Reflex testing employed in specific tumor types is a mix of single biomarkers and panels



Many labs indicate NGS testing may be done at initial diagnosis or upon disease progression depending on tumor type/stage

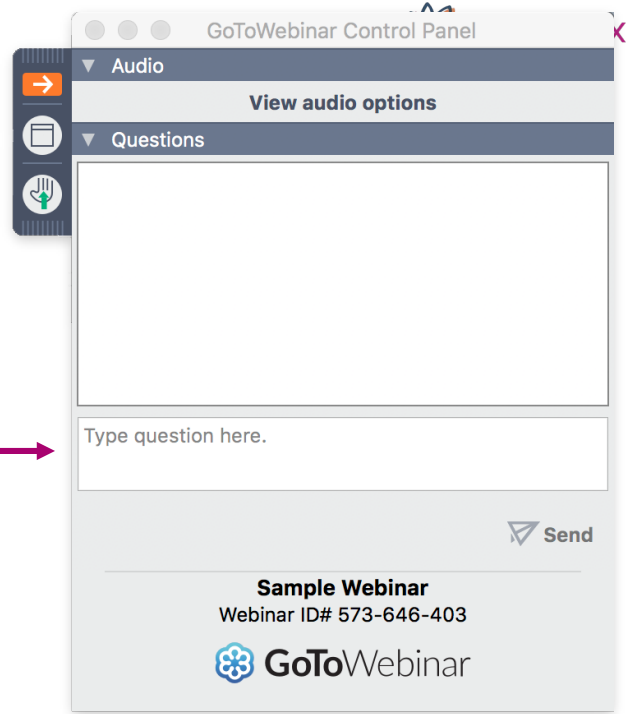
Source: BHA analysis of qualitative interviews with 30 Pathologists and/or Lab Directors

Keys to Success

1. Strong value and quality story
2. Develop compelling communication tools
3. Engage clinicians and payors early
4. Focus on key administrative elements

Thank You

Q&A



Type questions here

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Appendix

Eligibility Requirement Must be Met

CMS Coverage Pathways, NGS -Based Tests

	Local (MAC)	National (NCD)
Test Criteria	Test is performed in a CLIA-certified laboratory, **AND** Ordered by a treating physician	FDA **approval** or **clearance** as a companion in vitro diagnostic, **AND** An FDA approved or cleared indication for use in that patient's cancer, **AND** Results provided to the treating physician for management of the patient using a report template to specify treatment options
Patient Criteria	Patient has advanced cancer[1]; **AND** Patient has either not been previously tested using the same NGS test for the same primary diagnosis of cancer or repeat testing using the same NGS test only when a new primary cancer diagnosis; **AND** Patient has also decided to seek further cancer treatment.	
Scope of Coverage	For sole source, independent labs: National For hospital-based labs: Local MAC For reference labs: Local MAC	National
Coding	Existing HCPCS/CPT codes assigned by the MAC on test-by-test basis	CMS may allow labs to use existing CPT codes or will create temporary HCPCS codes to describe testing
Payment	Based on clinical lab fee schedule.	Once coding is determined, payment for individual tests will be based on the Clinical Lab Fee Schedule

1 Defined as "either recurrent, relapsed, refractory, metastatic, or advanced stages III or IV cancer."