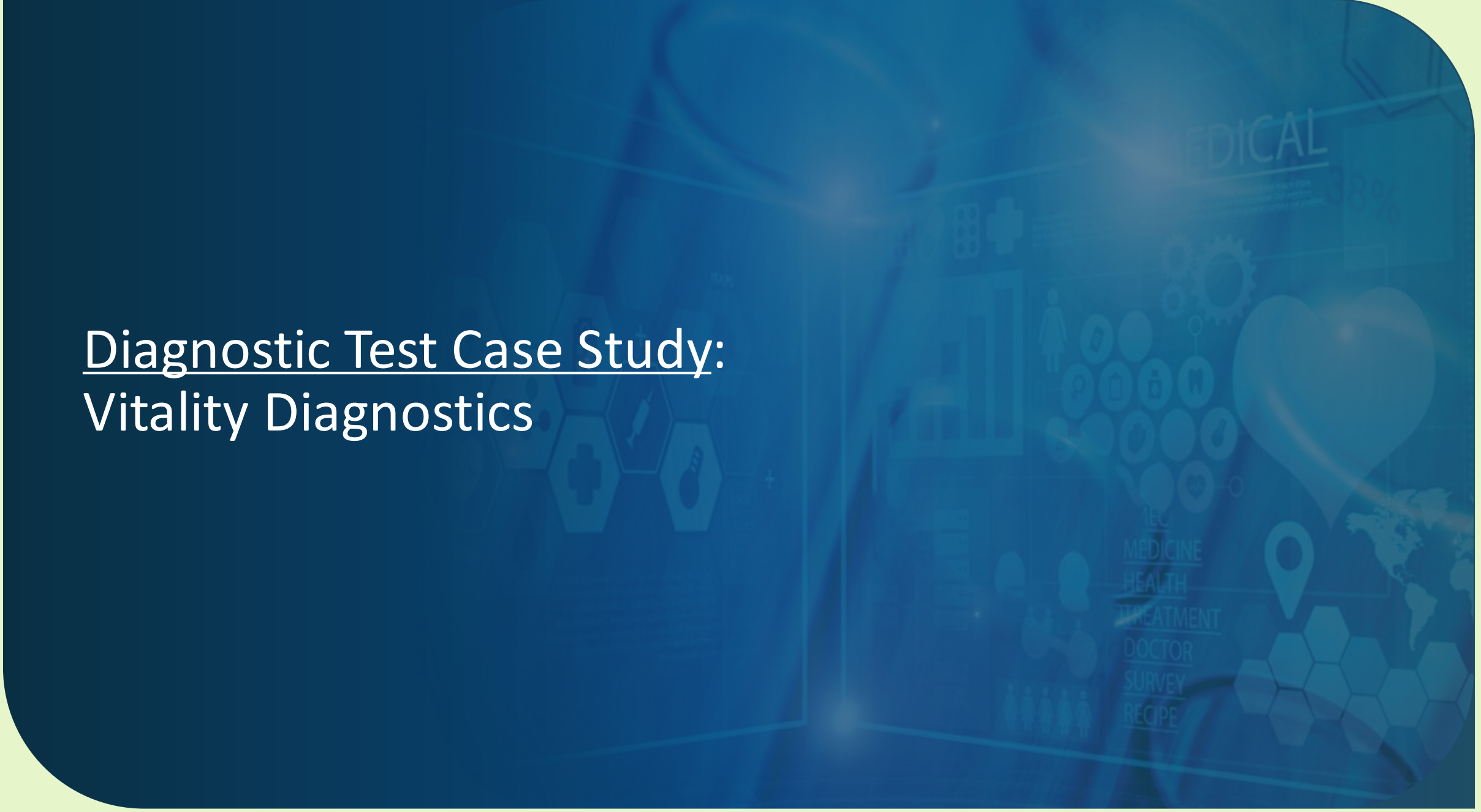
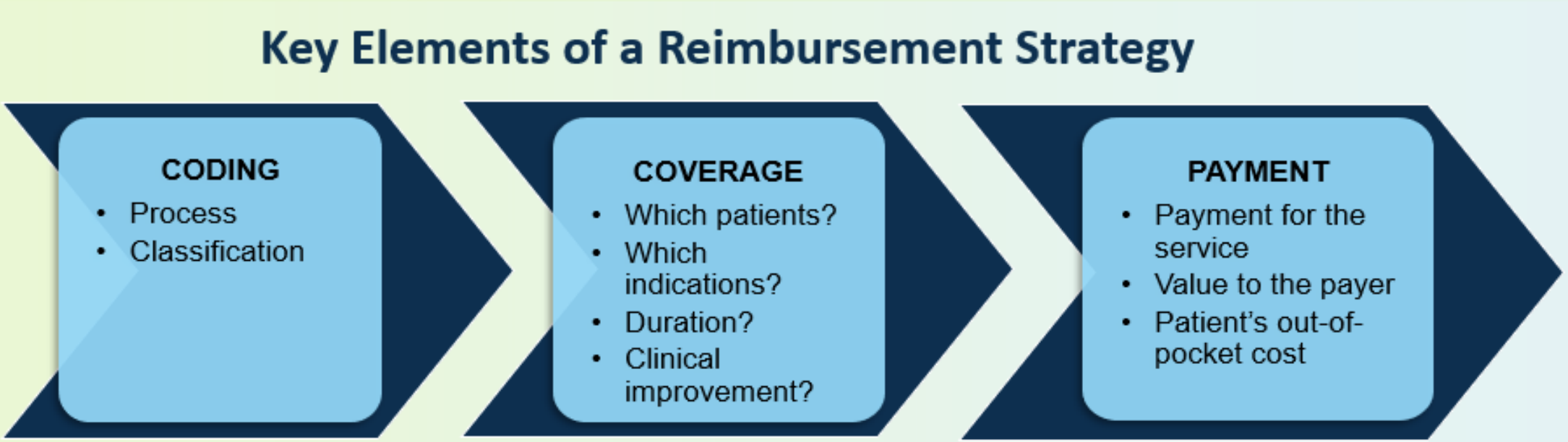
Diagnostic Test Case Study:
Vitality Diagnostics



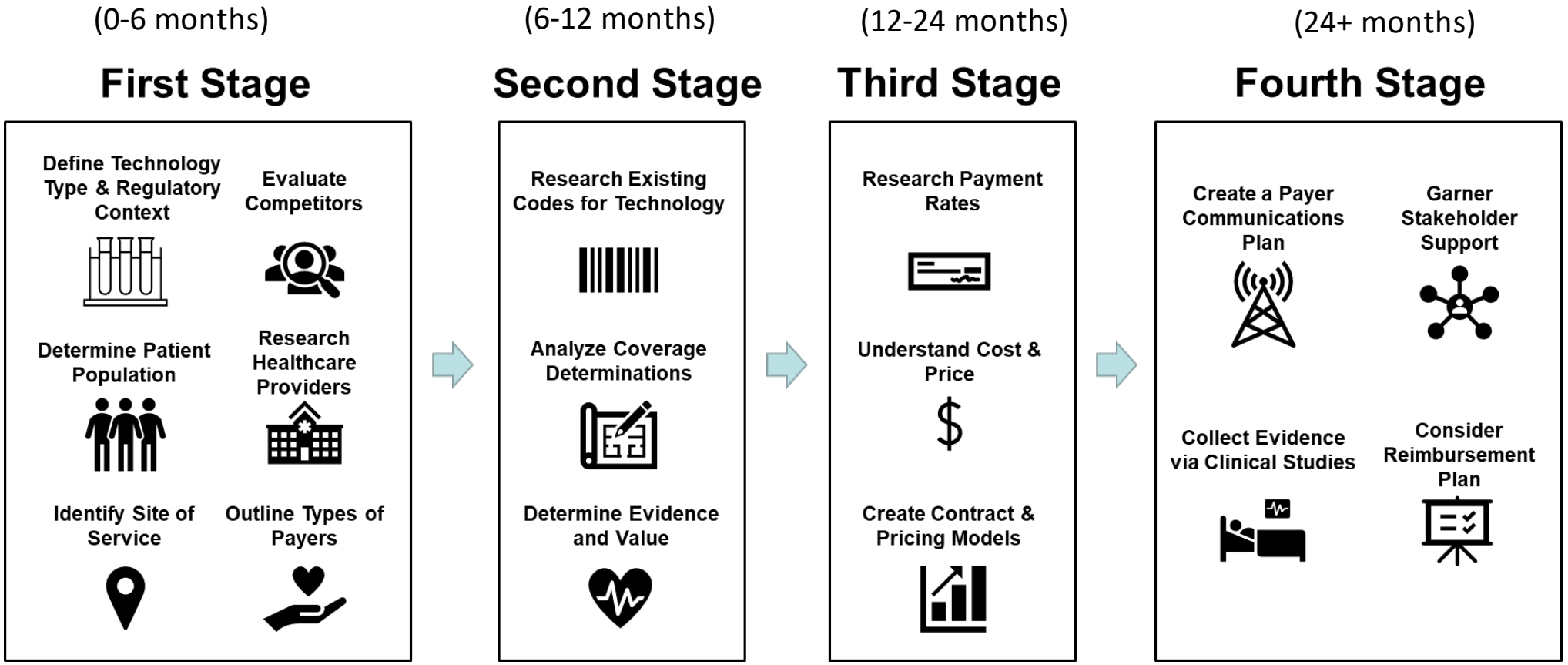
Reimbursement Overview

Bringing a diagnostic to market is a complex process. An innovator needs to understand the entire commercialization process and manage multiple tasks related to early-stage research and development, clinical studies, regulations, reimbursement and post-market surveillance. The goal of receiving Food and Drug Administration (FDA) approval is often considered the primary endpoint that leads a new diagnostic to commercial success and is often a pre-requisite for payer coverage. However, if a new diagnostic does not obtain the desired amount of reimbursement or is not even covered by payers, then physicians are highly unlikely to recommend and use the new diagnostic. Therefore, ensuring reimbursement for the new diagnostic is as important as obtaining regulatory approval.



Reimbursement Strategy Activities Roadmap

This case study breaks down the process described in our *Knowledge Guide for Diagnostic Test Reimbursement*. It will take you step-by-step through a process innovators may follow to develop a strategy for diagnostic test reimbursement. We'll walk through each step from the innovator's point of view. Aspects of the process may be conducted together, roughly in tandem.



Introduction to Vitality Diagnostics' CEO and VitalScreen

Beth is the CEO of Vitality Diagnostics – a spin-out company of Magnolia Health System. She has a novel prenatal test that she thinks will improve diagnostic accuracy for the detection of chromosome abnormalities of an unborn baby. The test, called VitalScreen, is in late stages of clinical development.

What does Beth need to do throughout product development to ensure optimal reimbursement?

Here's some background from Vitality Diagnostics' initial pitch to investors:

Product Description:

- Vitality Diagnostics is developing a Non-Invasive Prenatal Test (NIPT) called **VitalScreen**
- VitalScreen is used as a prenatal cell-free DNA (cfDNA) screening tool for the detection of chromosome abnormalities of a fetus.

Why VitalScreen?

- In 2019, there were 3.7 million births in the U.S. (per CDC data), and the NIPT market size in the U.S. was approximately 3.48 billion in 2020.
- Physicians can utilize this screening tool in an **outpatient setting** for pregnant women (as early as nine weeks gestation) – especially for high-risk pregnancies.
- Currently, there are **no FDA-approved products on the market**: all comparable prenatal screening products are Laboratory Developed Tests (developed and performed in one, single CLIA-certified laboratory.)

First Stage

First Stage

- Define Technology Type & Regulatory Context
- Evaluate Competitors
- Determine Patient Population
- Research Healthcare Providers
- Identify Site of Service
- Outline Types of Payers

Second Stage

- Research Existing Codes for Technology
- Analyze Coverage Determinations
- Determine Evidence and Value

Third Stage

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- Create Contract & Pricing Models

Fourth Stage

- Create a Payer Communications Plan
- Garner Stakeholder Support
- Collect Evidence via Clinical Studies
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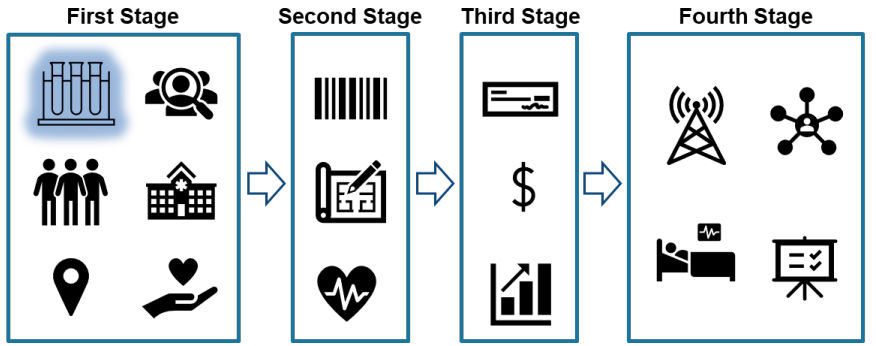
First Stage: Define the Technology Type & Regulatory Context

Beth is excited for the potential of VitalScreen to improve outcomes for families. Beth knows she needs to draft a product description based on the intended use. She also knows she needs to determine how FDA will regulate VitalScreen (which is in late stages of clinical development). She hopes that any comparable screening tools on the market will help her understand how her product can be reimbursed.

Beth drafts an intended use statement for VitalScreen based on what she envisions would go on a product label. She looked for examples on the web by searching for "NIPT" + "Intended Use." Here is what she drafted: "*VitalScreen is a diagnostic test intended for use as a prenatal cell-free DNA (cfDNA) screening tool for the detection of chromosomal anomalies from maternal peripheral whole blood specimens in pregnant women as early as 9 weeks gestation*." Beth also searches the FDA in vitro diagnostic database for the terms "prenatal" + "non-invasive" + "testing" and does not find anything similar to VitalScreen's intended use. She determines that there are no equivalent FDA-approved IVDs on the market, but there are similar products that are Laboratory Developed Tests (LDTs) – developed and performed in one, single CLIA-certified laboratory. Beth knows that most LDTs in development will not be required to receive a premarket approval or clearance from FDA because of a policy known as "enforcement discretion" – in other words, FDA has the legal authority to require premarket reviews, but has decided not to enforce that authority at this time. Even though FDA-cleared/approved devices are always preferred by payers, NIPTs (LDTs only at this time) are reimbursable and the test can be repeated for each pregnancy.



Key questions:

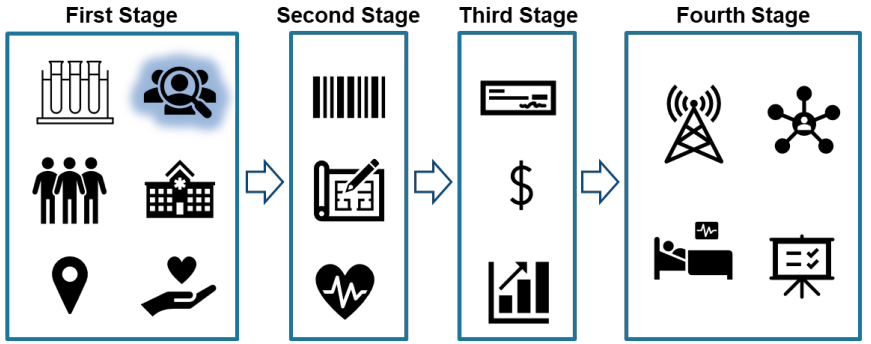
- What is the intended use?
- Is the product an FDA-regulated in-vitro diagnostic (IVD) or a CMS-regulated laboratory developed test (LDT)? Are there equivalent diagnostics on the market?
- Is this a repeat (one that can be done more than once in a lifetime) or a once-and-done test?

First Stage: Evaluate Competitors

Beth is eager to assess the company's potential competitors – their market share, and product positioning.

Based on her research, Beth notes there are several predominant players/market competitors, including Natera™ Panorama™, Integrated Genetics (LabCorp Specialty Testing Group) MaterniT® 21 PLUS, GENOME-Flex, and MaterniT® GENOME.

Beth's online research indicates that the US "NIPT market is expected to reach a valuation of USD 2.5 Billion by 2028" per this 2021 Business Wire article. Beth plans to conduct additional research on the market share of each of the market players to estimate VitalScreen's potential to saturate the market. Beth's research also shows that Natera analyzes single nucleotide polymorphisms (SNPs) like her VitalScreen test versus using whole genome sequencing (a method promoted by Illumina.) Beth's product will enter the market as a "me too" disruptor and price leader. In 2019, CDC estimated 3.7 million births in the U.S. Their test is noninvasive but requires a blood sample; the diagnostic will be used primarily in outpatient OB/GYN offices. Beth, separately, is considering whether FDA-clearance/approval for her test may give her a competitive advantage over offering the test as an LDT. She refines her competitive advantage statement based on her research findings as this may impact stakeholder uptake and coverage decisions.



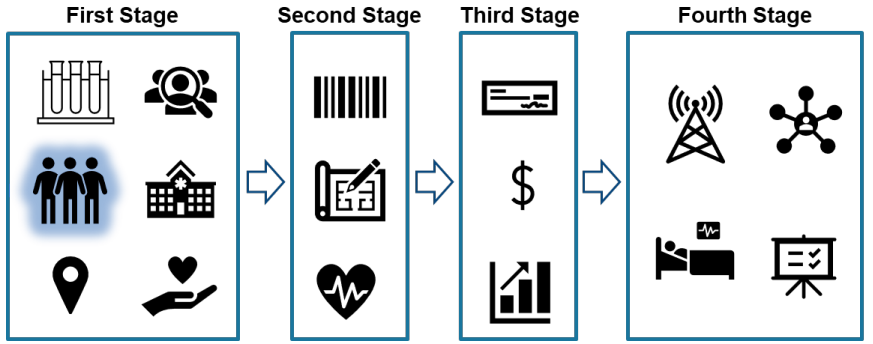
Key Questions:

- What competitor devices are on the market?
- What will differentiate Beth's product from competitors?

See Glossary for additional information.

First Stage: Determine Patient Population

Beth knows she also needs to specify the patient population for her diagnostic. She consults with her clinical team to think through who will use VitalScreen and where they will use it. This is important as this information will inform the clinical study design and data collected.



Beth is able to easily define the patient population for VitalScreen as pregnant women, particularly those with high-risk pregnancies. While an individual's childbearing age can vary and may depend on external factors (such as whether it is a natural pregnancy). Based on a preliminary web search, Beth learns that high-risk pregnancies occur in women 17 years or younger and 35 years or older. Beth decides to focus on females aged 35 and older as their pregnancies are considered high risk and as this patient population may have individual insurance plans (rather than being covered under their parent's plan.) Market research also shows trends toward older maternal age, which raises the concerns of detecting genetic abnormalities especially in this age group (35 and older). Additionally, research also indicates that NIPT in women undergoing in vitro fertilization is also a viable option of screening with or without prior preimplantation genetic testing. Forward-looking, continuous (re)assessment of market trends and target audiences will be crucial to refine market size, etc.

Key Questions:

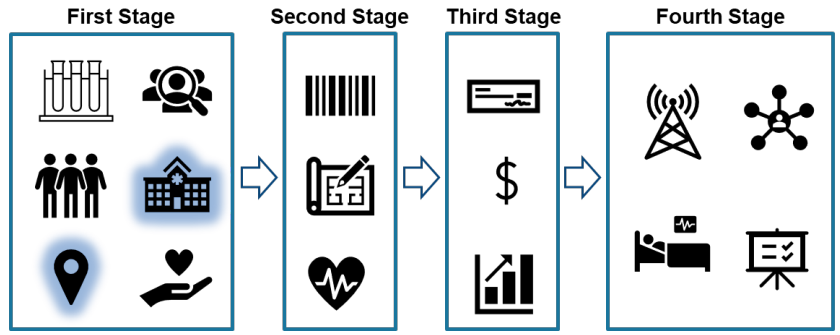
- Which patients would benefit most from the diagnostic test?
- Is there a certain age range these patients fall into?
- Is the test gender specific or agnostic?
- Which patient population offers the largest target market size, and has potentially the highest coverage rates?
- Are there certain socio-economic factors, such as high-risk populations, income, etc. that should be considered for this patient population?

See Appendix & Glossary for additional information.

First Stage: Research Healthcare Providers & Identify the Site of Service

Beth intends to determine which specific healthcare provider group would use VitalScreen. She also wants to identify the site of service based on the intended use for the identified patient population. This will inform whether the setting is considered inpatient or outpatient.

Beth talks to the healthcare providers on her board of advisors and verifies that the non-invasive test – which requires a blood sample – would be conducted by OBs in an outpatient (doctor's office) setting. Beth was concerned that for potential high-risk pregnancies the test might be administered in an inpatient setting (in a hospital). This would have meant that the test would be rolled into the total cost of care (under one MS-DRG.) In such settings, payers would reimburse the hospital in one lump-sum payment and the test would not be itemized or paid separately by insurance – not an ideal scenario. Since the test will, most likely, be paid as a separate line item, Beth can use this information when talking to healthcare providers and expects to not only break even but also have a margin (pending reimbursement rate research).



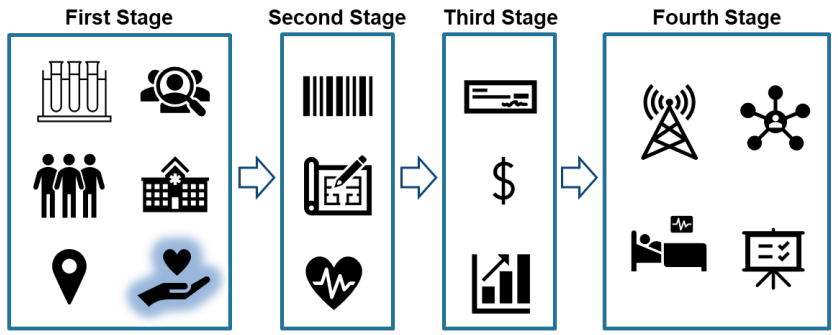
Key Questions:

- Based on the intended use and target patient population, which particular group of healthcare providers would use the diagnostic (i.e., OB/GYN, pediatrician, primary healthcare provider, cardiologist, etc.)?
- Where will the diagnostic be used – in an outpatient (doctor's office) or inpatient (hospital) setting?
- Is the diagnostic considered a standard of care (vs. an optional, add-on service)?

See Appendix & Glossary for additional information.

First Stage: Outline the Types of Payers for the Patient Population

Beth knows different types of payers - including Medicaid, Medicare, and commercial payers - should be evaluated. Not all payers may be appropriate for the target patient population of VitalScreen.



Since Beth knows that women of child-bearing age are below the age of 65, she eliminates Medicare Part B patients from her analysis. While Medicare is also for the disabled, the target population would be very low within Medicare (likely just those covered due to disability.) Additionally, Beth learned from CMS that prenatal diagnostic tests "are not relevant to a Medicare beneficiary, are not considered a Medicare benefit (statutorily excluded), and therefore will be denied as Medicare Excluded Tests."

Although Beth plans to first target mothers with commercial insurance (or employed by companies who manage their own health plans), she also considers Medicaid patients. From her advisory council, Beth understands that commercial payers often make coverage decisions based on Medicare/Medicaid coverage determinations. She creates a list of major commercial payers to target that include Aetna (including Innovation Health), Cigna, Anthem BlueCross BlueShield, CareFirst BlueCross BlueShield, and United Healthcare. She also plans to work with Medicaid Care Organizations (MCOs) to have the test included for moms using Medicaid.

Key Questions:

- Based on the age of your target patient population, should any payers be excluded from the analysis?
- Would the test be predominantly used by a patient population with a specific payer, i.e., commercial payers only?
- Would these patients be willing to pay "out-of-pocket" or a cash price for the test?
- What motivators/incentives would stimulate patients to pay out of pocket?

See Appendix & Glossary for additional information.

Second Stage

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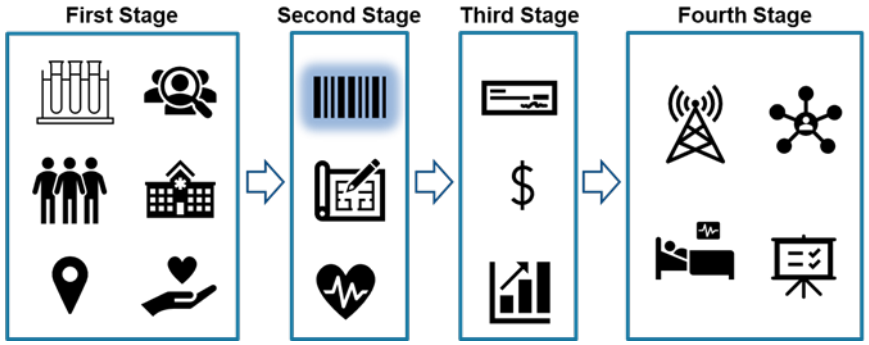
Second Stage: Research Existing Payment Codes for the Technology

Now Beth is ready to research existing Current Procedural Terminology (CPT®) codes for her technology. She wants to find references of the code(s) and diagnostic test (NIPT) in various coverage determinations and also to search the CMS lab fee schedule for payment rates.



Beth searches for existing CPT codes online using search terms such as "CPT + NIPT" or "CPT + Non-invasive Prenatal Testing." Beth knows that CPT codes can be listed in commercial payers' coverage determinations, CMS lab fee schedules, etc. and that there may be one or multiple CPT codes for her test type, so she widens her search accordingly to ensure all codes have been considered. Her search returns the following NIPT codes in Cigna's coverage determination:

- 81420: Fetal chromosomal aneuploidy
- 81507: Fetal aneuploidy

Beth determines an "unlisted" procedure code such as 81479 ("Unlisted molecular pathology procedure(s)") does not need to be used. Unlisted codes are generally only applicable to tests that do not fit an existing code. Additionally, they can be more challenging to get coverage for and payment rates need to be negotiated with each potential payer. However, she determined that bringing in a Reimbursement Consultant to validate her findings and guide her next steps will be most beneficial.

Key Questions:

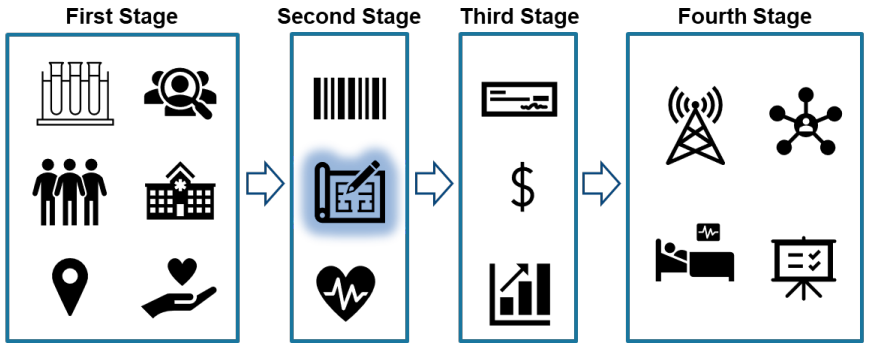
- Are there existing CPT codes for the diagnostic?
- Which CPT code best fits my test (sometimes multiple)?
- Have only "unlisted" codes been used to date?
- If so, do you want to apply for a new CPT code?

See Appendix & Glossary for additional information.

Second Stage: Analyze Coverage Determinations

With potential CPT codes in hand, Beth now wants to review and list all overage determinations for commercial payers to understand differences in coverage – i.e., when a diagnostic is deemed medically necessary vs. experimental. She wants to do the same for Medicaid and list all state-specific coverage determinations for Medicaid populations.

Beth conducts an online query using "[commercial payer name] + NIPT" and "[commercial payer name] + [CPT]" as search terms. She scans the results for references to CPT codes 81420 and 81507. *Cigna deems NIPT under both codes "medically necessary" only "to screen for fetal trisomy 13, 18 and 21 […] in a viable single or twin gestation pregnancy ≥ 10 weeks gestation." Cigna deems NIPT "experimental" for tests performed "in an out of network laboratory" and for indications not covered in "medical necessary" section.* The document also lists applicable ICD-10 diagnosis codes for which the test is deemed medically necessary. Beth knows that Medicaid coverage can vary state by state and by plan administrators (such as Amerigroup); she searches "Medicaid + NIPT" or ""Medicaid + [CPT code]" online and searches for state-specific Department of Health ordering guidelines for the test. She learns that per the Maryland Department of Health NIPT testing is a covered Medicaid benefit. This is positive news as Medicaid does not consider NIPT to be a mandatory service to be covered for all patients per this resource.



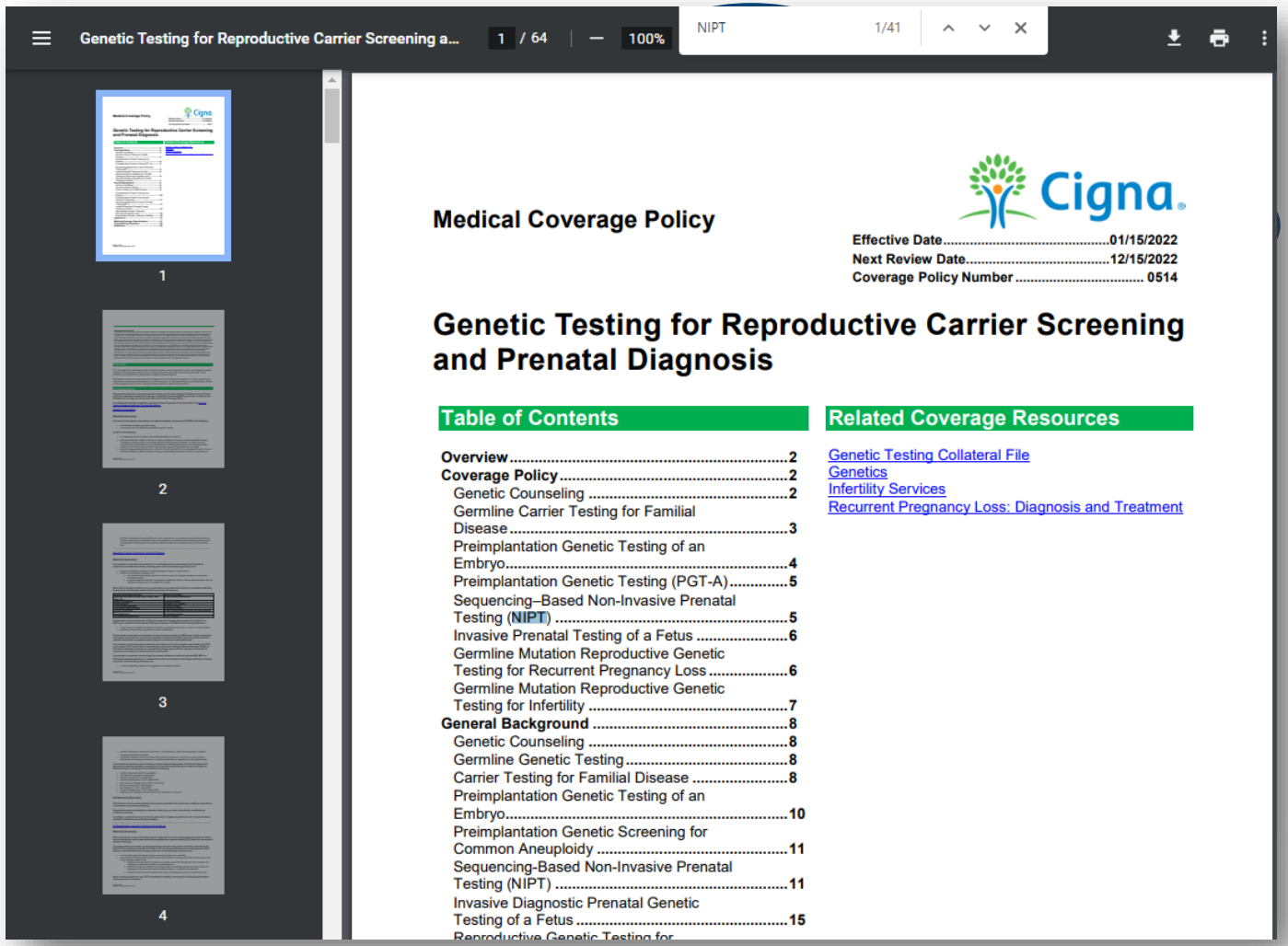
Key Questions:

- Which coverage determinations exist for both commercial payers and Medicaid the technology given the identified CPT codes? Note: Commercial payers often make coverage decisions based on Medicare / Medicaid coverage determinations.
- Is the test deemed medically necessary or experimental (or both) by the payers? Note: Only tests that are "medically necessary" are covered.
- Are there payer-specific requisitions that need be met for coverage, e.g., specific diagnosis (ICD-10 code) or genetic counseling pre- and post testing?
- Are there special coverage requirements for diagnostics, e.g., for tests without FDA approval (such as for LDTs) must the lab be CAP accredited and or must the lab be an in-network lab?

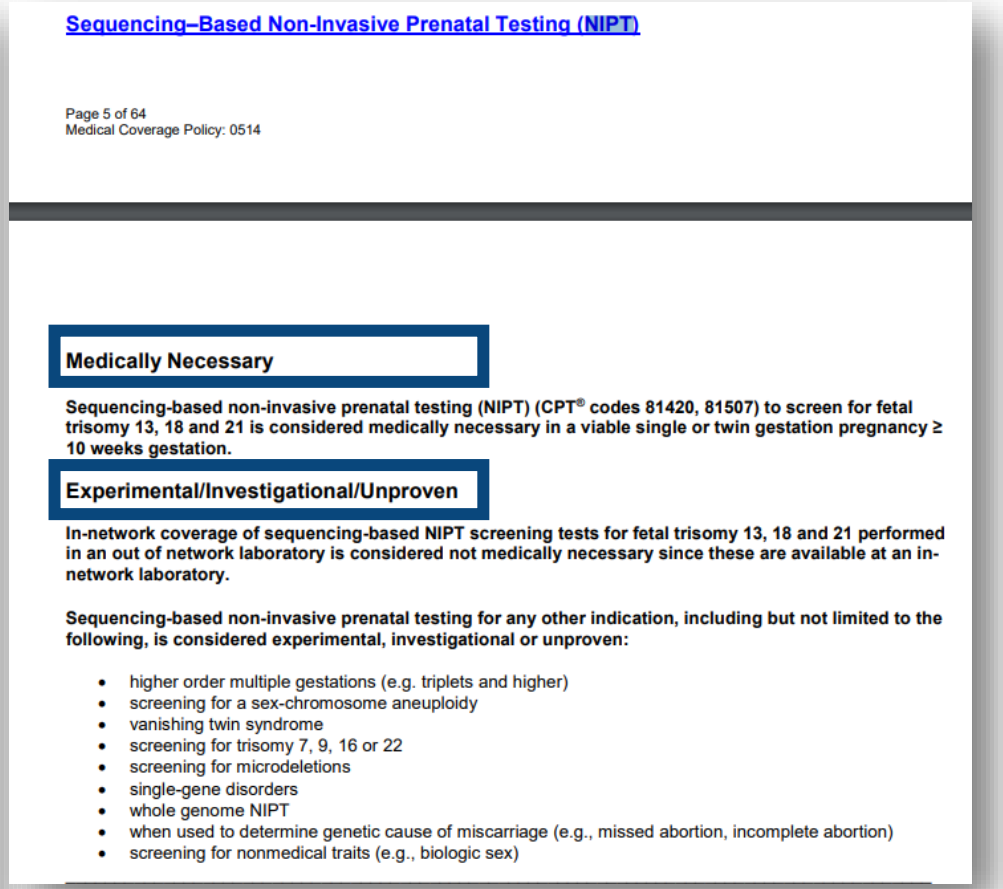
See Appendix & Glossary for additional information.

Second Stage: Analyze Coverage Determinations

Analyzing Medical Coverage Policies; Commercial Payer: Cigna



Source: Cigna

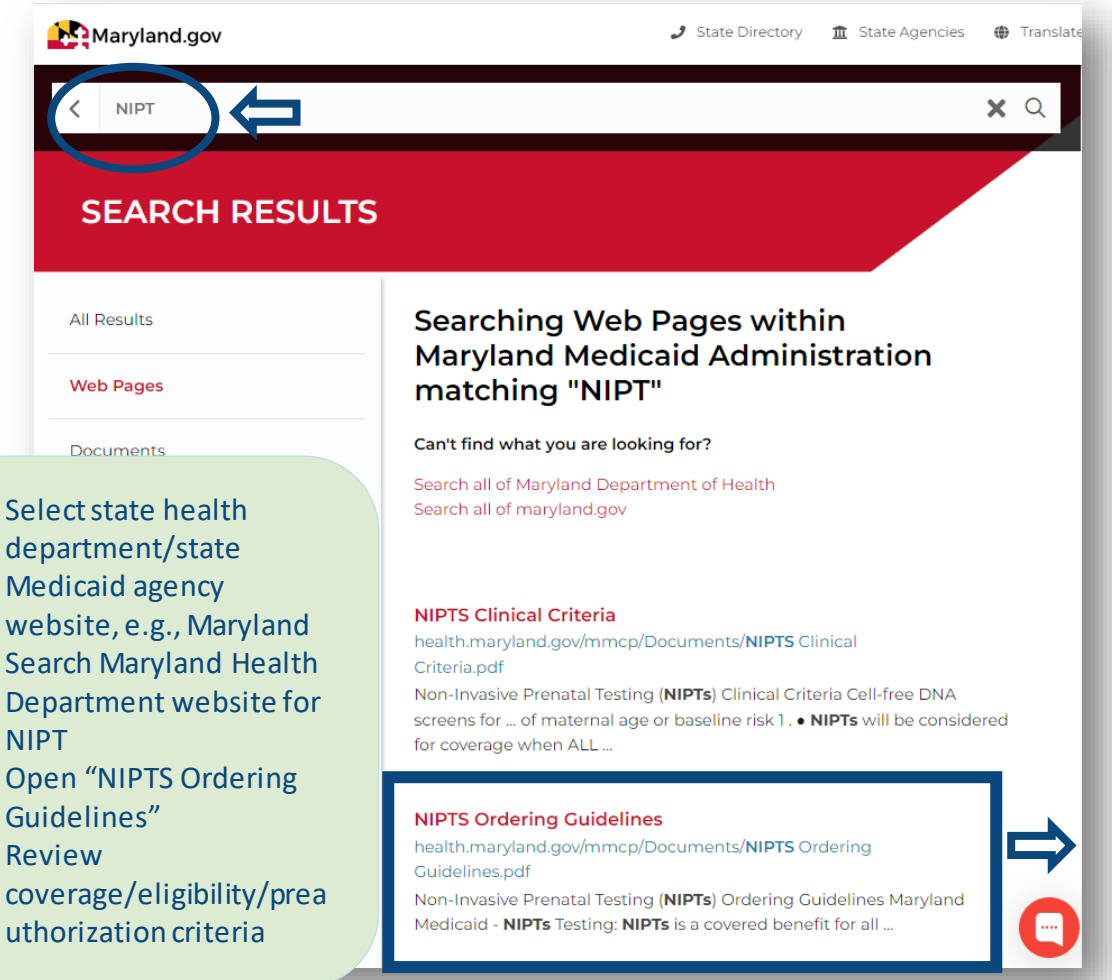


- Review sections in policy referencing NIPT
- Understand implications of coverage under "Medically Necessity" and which for which indications NIPT is considered "Experimental/Investigational"

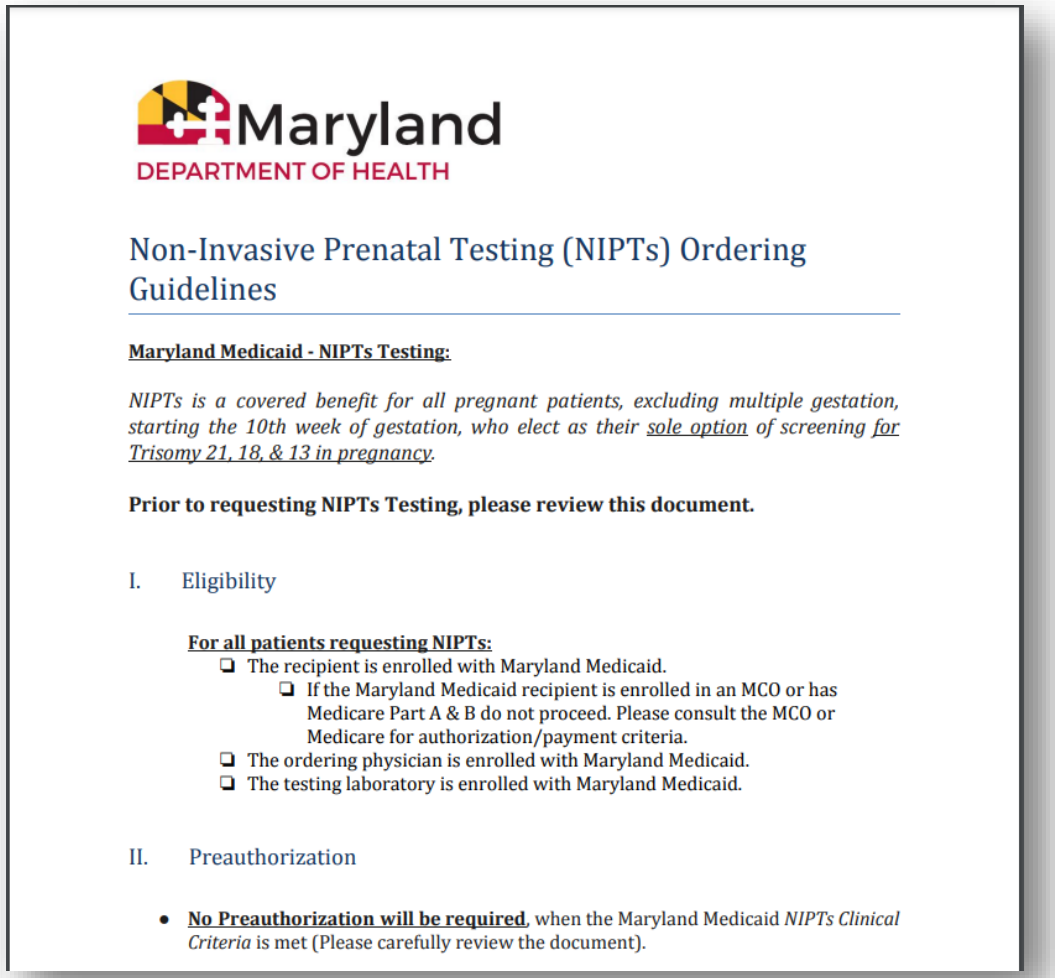
Second Stage: Analyze Coverage Determinations

Analyzing Medical Coverage Policies; CMS Medicaid: Maryland & Virginia

- Select state health department/state Medicaid agency website, e.g., Maryland
- Search Maryland Health Department website for NIPT
- Open “NIPTS Ordering Guidelines”
- Review coverage/eligibility/preauthorization criteria



Source: Maryland Department of Health



Source: Maryland Department of Health

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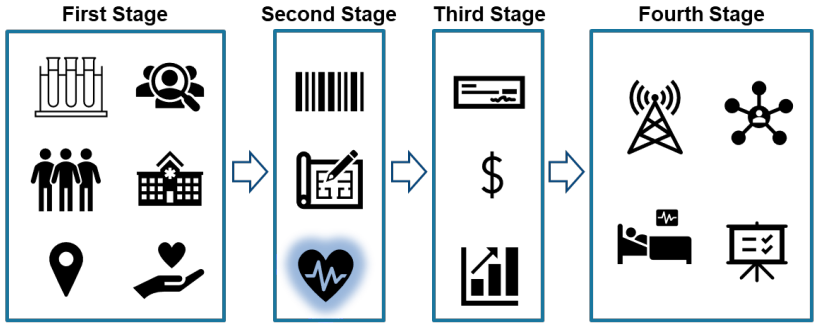
Second Stage: Determine Evidence & Value

Beth knows that well-planned **evidence** collection can show **value** and support a favorable coverage determination. Coverage determinations are based on the type of payer and related to the technology. Favorable coverage determinations are also important to potential investors.

At a conference, Beth meets the Medical Director of Aetna and asks some questions about how coverage is determined for technologies like VitalScreen. She learns that she needs to capture utilization data to define evidence to support coverage and pricing. Beth conducts an online search using "NIPT + evidence + utilization data" and finds several research articles, including a 2014 article titled "NIPT: current utilization and implications for the future of prenatal genetic counseling". Beth also discovered that the American College of Obstetricians and Gynecologists (ACOG) created an NIPT advocacy toolkit. Beth knows commercial payers will focus on the cost of the device, as captured in its coding (in addition to clinical evidence); they will look to ensure the billing codes for the procedure, service, and/or product are sufficient to cover the cost associated with the device's use. Beth plans to work directly with the different state Medicaid program SMA, MCO to determine if additional evidence is needed for coverage under local and national coverage determinations (as coverage is already established for both). Beth uses this information to build a value proposition for VitalScreen that includes established guidelines and evidence and also information on the accuracy of her test that is at the top (99%) threshold for performance (sensitivity & specificity).



Key Questions:

- Is the diagnostic considered standard of care or an optional, add-on service?
- Are there societies that advocate for NIPT?
- What evidence has been published on NIPT tests?
- Are there specific ICD-10 diagnosis codes that should be considered for evidence collection?

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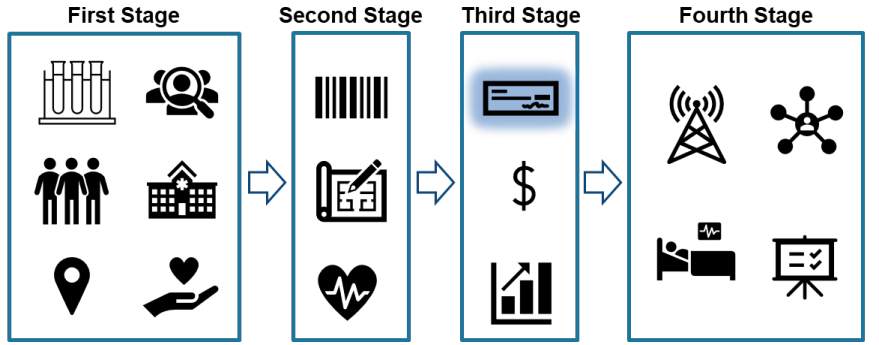
Third Stage: Research Payment Rates

With the list of potential CPT codes in hand, Beth now wants to identify publicly available payment rates for CPT codes 81420 and 81507.

Beth knows most private payers base their reimbursement rates on the CMS rates, therefore, she investigates Medicaid payment rates by following these steps:

- Look up the most current CMS "Clinical Laboratory Fee Schedule Files."
- Select File "22CLABQ2" as it has the most recent data (CY 2022 Q2 Release: Added for April 2022.)
- Click on and download the ZIP file and open the Excel spreadsheet.
- Search [CTRL+F] for preidentified CPT code(s) [81420, 81507] to see payment rates.

Based on these search criteria, she learns the 2022 Clinical Diagnostics Laboratory Fee Schedule rate for CPT 81420 is $759.05 and for CPT 81507 is $795.00. Beth notices the rates have not changed over the last three years. She also knows that even if a payment rate exists per the fee schedule, payment is based on the state specific Medicaid local coverage determinations (see coverage section). This information is very helpful, as she plans on entering the market as a price leader.

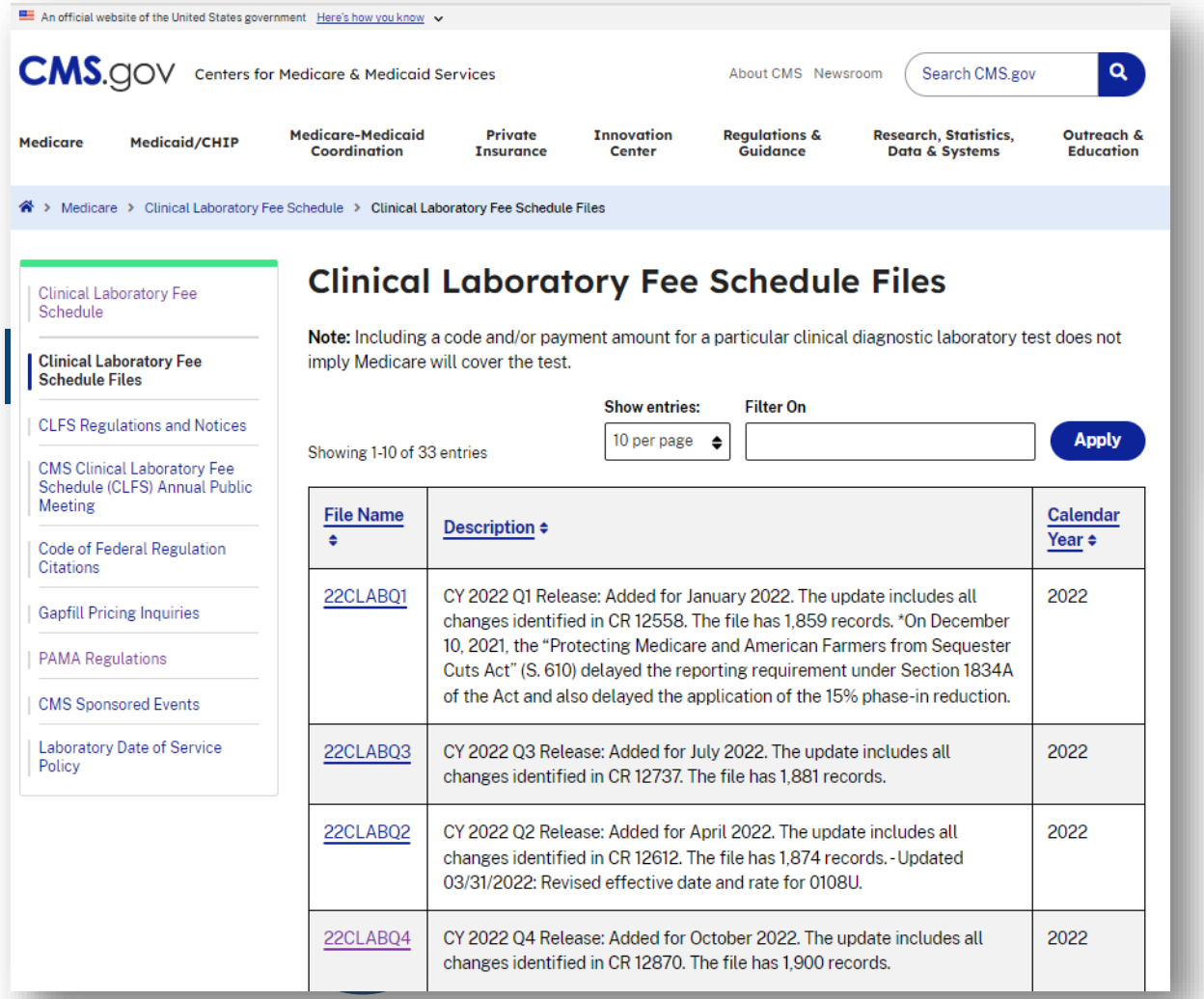


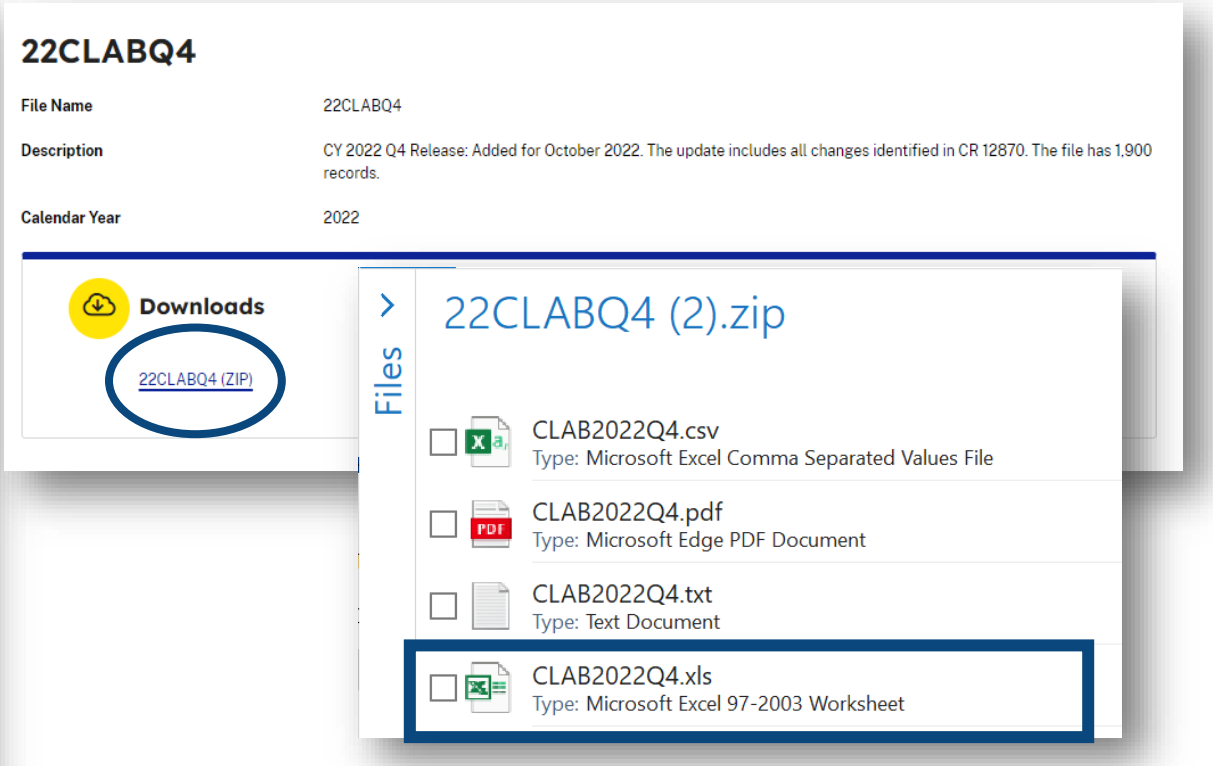
Key Question:

- Is there an existing CMS lab fee schedule? If so, what are the rates for the identified CPT codes?

Third Stage: Research Payment Rates

Navigating CMS Clinical Lab Fee Schedule Files





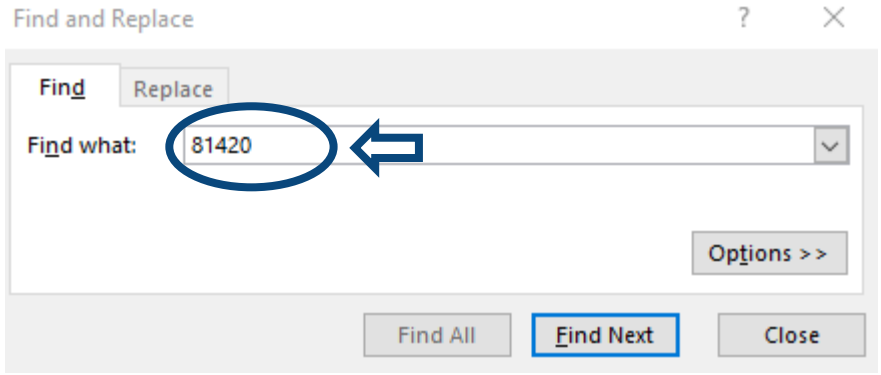
- Look up the most current CMS "Clinical Laboratory Fee Schedule Files".
- Select File "22CLABQ4" as it has the most recent data (CY 2022 Q4 Release: Added for October 2022.)
- Click on and download the ZIP file and open the Excel spreadsheet.
- Search [CTRL+F] for preidentified CPT code(s) [84484] to see payment rates.

Source: CMS

Third Stage: Research Payment Rates (cont.)

Navigating CMS Clinical Lab Fee Schedule Files

1	**2022 Clinical Diagnostic Laboratory Fee Schedule**						
2	**CPT codes, descriptions and other data only are copyright 2022 American Medical Association. All rights reserved. CPT is a registered trademark of the American Medical Association.**						
3							
4	**YEAR**	**HCPCS**	**MOD**	**EFF_DATE**	**INDICATOR**	**RATE2022**	**SHORTDESC**
689	2022	81420		20220101	N	00759.05	Fetal chrmoml aneuploidy
721	2022	81507		20220101	N	00795.00	Fetal aneuploidy trisom risk



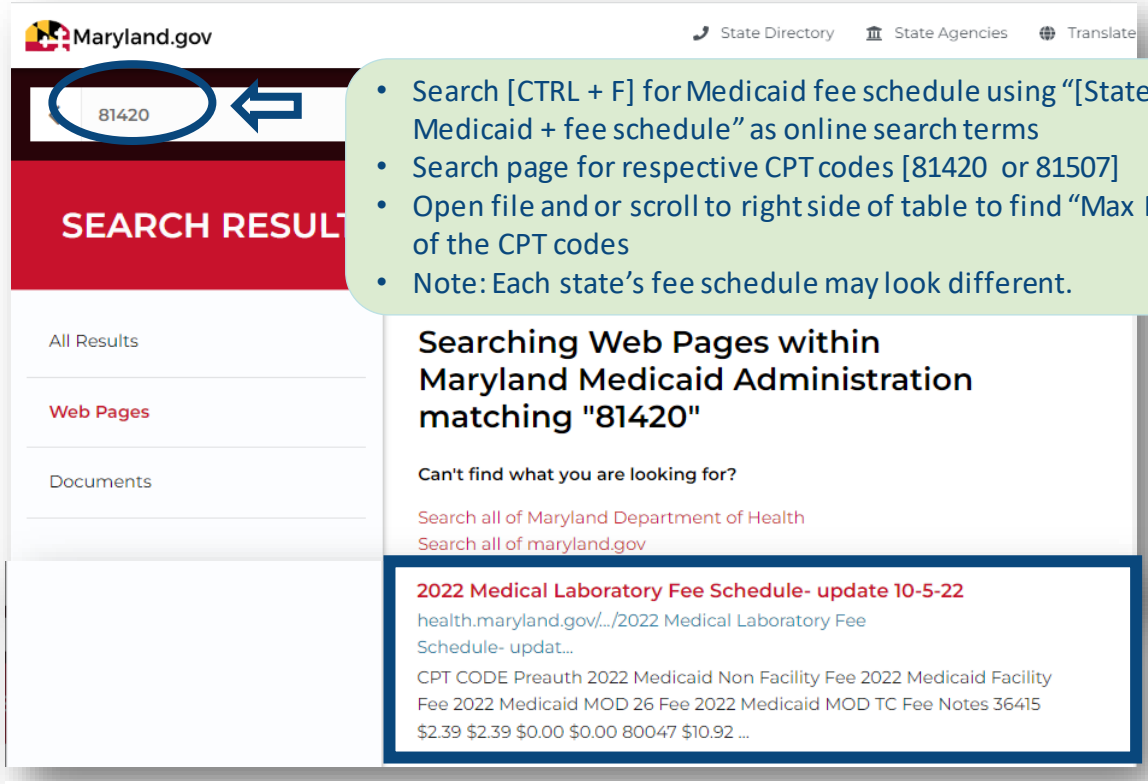
- Search [CTRL+F] for preidentified CPT code(s) [81420; 81507].
- Check "SHORTDESC" to double-check applicability of test description to your diagnostic.
- Check "RATE2022" to understand the current CMS Medicare payment rate; i.e., for CPT 81420, the rate is $759.05.
- Check prior years' fee schedule to see if there were any changes in the rates.

Source: CMS

Third Stage: Research Payment Rates

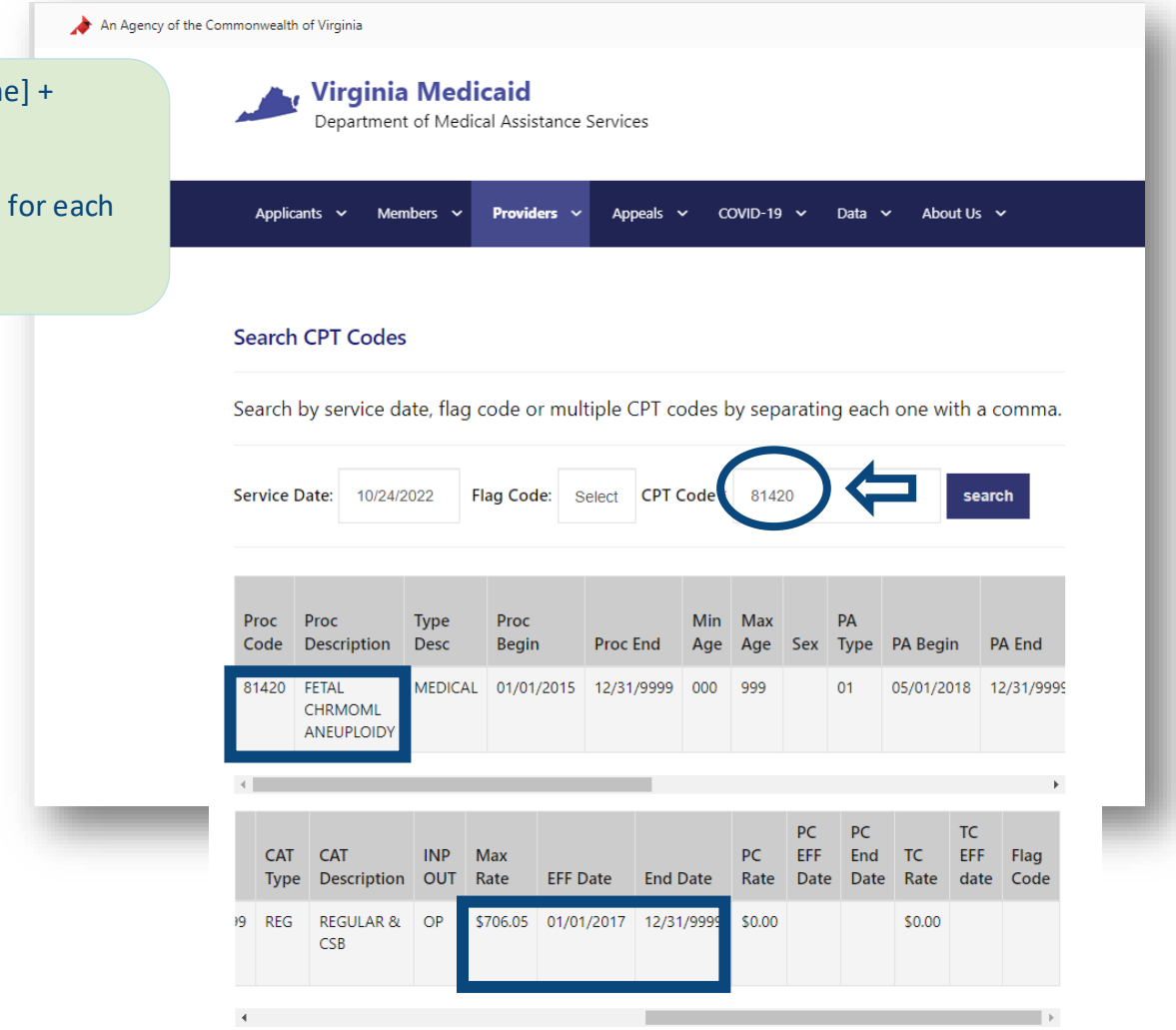
Medicaid Fee Schedules by CPT Code: Maryland & Virginia

- Search [CTRL + F] for Medicaid fee schedule using "[State Name] + Medicaid + fee schedule" as online search terms
- Search page for respective CPT codes [81420 or 81507]
- Open file and or scroll to right side of table to find "Max Rate" for each of the CPT codes
- Note: Each state's fee schedule may look different.



CPT CODE	Preauth	2022 Medicaid Non Facility Fee	2022 Medicaid Facility Fee	2022 Medicaid MOD 26 Fee	2022 Medicaid MOD TC Fee	Notes	
81420		$603.44	$603.44	$0.00	$0.00	Clinical Criteria	
81507		$632.03	$632.03	$0.00	$0.00		

Source: Maryland Department of Health



Source: Virginia Medicaid

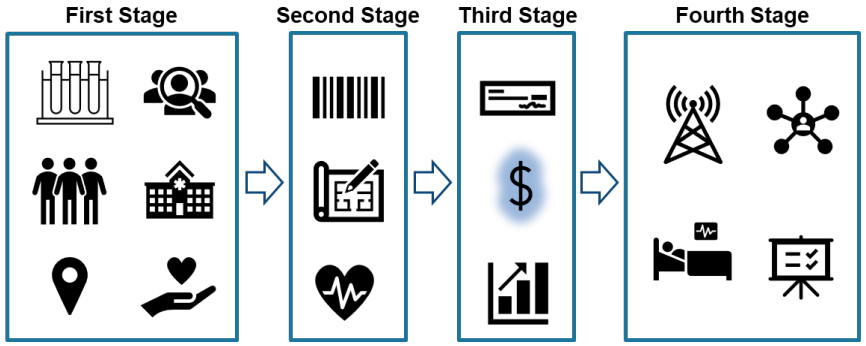
Third Stage: Research Payment Rates (cont.)

Coverage Summary Findings

Payer	CPT 81420	CPT 81507	References
CMS Medicare	***N/A***; not considered a Medicare benefit (statutorily excluded)	***N/A;*** not considered a Medicare benefit (statutorily excluded)	https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleid=58917&ver=35&keyword=prenatal&keywordType=all&areaId=all&docType=NCA,CAL,NCD,MEDCAC,TA,MCD,6,3,5,1,F,P&contractOption=all&sortBy=relevance&bc=1
CMS State Medicaid Agencies			
Maryland	✓ **$ 603.44**	✓ **$ 632.03**	https://health.maryland.gov/mmcp/Documents/2022%20Medical%20Laboratory%20Fee%20Schedule%204.27.22.pdf https://health.maryland.gov/mmcp/Documents/NIPTS%20Clinical%20Criteria.pdf
Virginia	✓ **$ 706.05**	**$ 795.00**	https://www.dmas.virginia.gov/for-providers/rates-and-rate-setting/procedure-fee-files-cpt-codes/#searchCPT
…			
Aetna	✓ *No preauthorization requirements*	✓ *No preauthorization requirements*	Per negotiated rate
Cigna	✓ *No preauthorization requirements*	✓ *No preauthorization requirements*	Per negotiated rate
United Healthcare	✓ *Preauthorization requirements*	✓ *Preauthorization requirements*	Per negotiated rate
BlueCross BlueShield of North Carolina	✓ *Preauthorization requirements*	✓ *Preauthorization requirements*	Per negotiated rate

Third Stage: Understand the Cost and Price of the Test

Beth is now ready to investigate a Medicare price and private payer charge for VitalScreen based on the total cost of the test and the market price tolerance. She knows coverage does not always equal cost coverage.



Beth first establishes the total cost of the test. Her team calculates the Cost of Goods Sold (COGS direct costs (incl. reagents, etc.) between $350 -$400 based on volume predictions of 5,000-10,000 units. Her business advisor estimates indirect costs (incl. sales force costs and other overhead) from $100-$250 per unit; for a total cost of $450 to $650. Beth wants to break even or make a profit and compares her test cost to the lowest CMS payment rate of $759.00 for the pre-selected CPT codes (81420, 81507); fortunately, the payment rate is higher than the total cost of the screening test.

Her next step is to find out what out-of-pocket costs patients, on average, incur for this services (in case their insurance does not cover the test in whole or part.) To determine the max out-of-pocket cost for the test, Beth calls current test providers and asks about costs for different insurance-coverage scenarios. Beth understands for Medicaid patients, out-of-pocket expenses would, most likely, not be affordable.

The self-pay price or "manufacturer's suggested retail" price – what individuals would pay without using their insurance – should be determined based on the total cost of the test, the current CMS payment rates, potential differences in coverage, and the varying patient populations' ability to pay for VitalScreen.

Key Questions:

- What direct costs (material and labor) are incurred producing the diagnostic? What are indirect (fixed or variable) costs – such as administrative and personnel costs – associated with the product?
- What is the existing payment rate for the test (if any)? What is the break-even point? Note: The price of a product and the payment rate are usually different.
- What are average out-of-pocket costs for the test?

See Appendix & Glossary for additional information.

Third Stage: Create Contract and Pricing Models

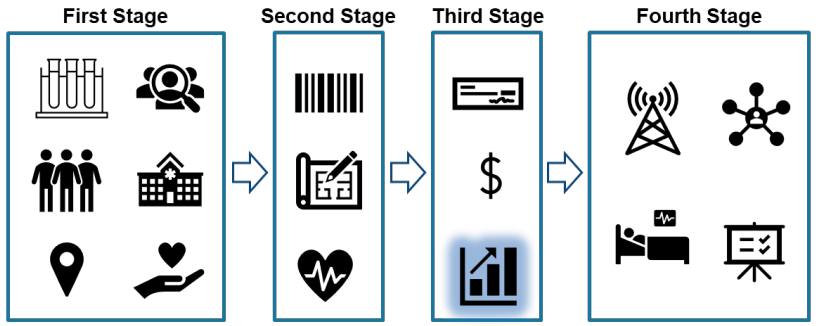
Beth knows many factors impact price, including the Cost of Goods Sold (COGS), existing (or potentially new) payment rates, the product's value proposition and differentiation, market size, the anticipated place of service (setting), and the purchasing power of distributors.

Beth understands that even if a test has an established coverage determination and average reimbursement rate, special rates may be negotiated with each payer. As a result, Beth continues her conversations with the CMOs of each of the commercial payers to enable effective contract negotiations with each when she is ready to go to market. She will use her value proposition (lower rates; high test accuracy) in support of her negotiations.

Medicaid state-by-state variances may make it difficult to evaluate coverage potential and reimbursement. However, existing national coverage determinations can make it easier to access this important patient group. Furthermore, individuals are highly unlikely to pay a self-pay price for this screening service if not covered by their plan.

Beth creates a charge/pricing matrix based for each of the following stakeholders and based on potential annual volume estimates:

- Commercial Payers (charge without contract; goal pre-negotiated rate with contract)
- Medicaid (CMS Clinical Laboratory Fee Schedule rate)
- Consumers (self-pay price without insurance; compassionate care out-of-pocket cost)



Key Questions:

- Is the diagnostic filling an unmet need? What is the product's value proposition and differentiation in comparison to other products on the market?
- What is the prevailing market price of similar products on the market (if any)?
- How big is the target market?
- What is the anticipated place of service (e.g., out-patient or in-patient)?
- Who are the purchasers of the diagnostic?

See Appendix & Glossary for additional information.

Third Stage: Understand the Cost and Price of the Test *Summary Findings*

Cost Assumptions	Value/Rate
Volume Assumption	5,000-10,000 units
Cost of Goods Sold (COGS direct costs (incl. reagents, etc.)	$350.00 - $400.00 per unit
Indirect Costs (incl. sales force costs and other overhead)	$100.00 - $250.00 per unit
TOTAL COST	**$450.00 - $650.00**
CMS Reimbursement Rate by Code	**Rate**
CMS 2022 Lab Fee Schedule	
CPT 81420	$ 759.05
CPT 81507	$ 795.00
Medicaid (Maryland example)	
CPT 81420	$ 603.44
CPT 81507	$ 632.03
Medicaid (Virginia example)	
CPT 81420	$ 706.05
CPT 81507	$ 795.00

Payer: Viable Price Range (allows for cost coverage and margin for both – Vital Diagnostics and physicians)	**CPT 81420: $603.44 – $759.05** **CPT 81507: $632.03 – $795.00** (based on vol. agreement / negotiated per unit rate)
Patient: Self-pay/Out-of-pocket Price	**CPT 81420 / 81507: $675.00**

Fourth Stage

First Stage

- Define Technology Type & Regulatory Context
- Evaluate Competitors
- Determine Patient Population
- Research Healthcare Providers
- Identify Site of Service
- Outline Types of Payers

Second Stage

- Research Existing Codes for Technology
- Analyze Coverage Determinations
- Determine Evidence and Value

Third Stage

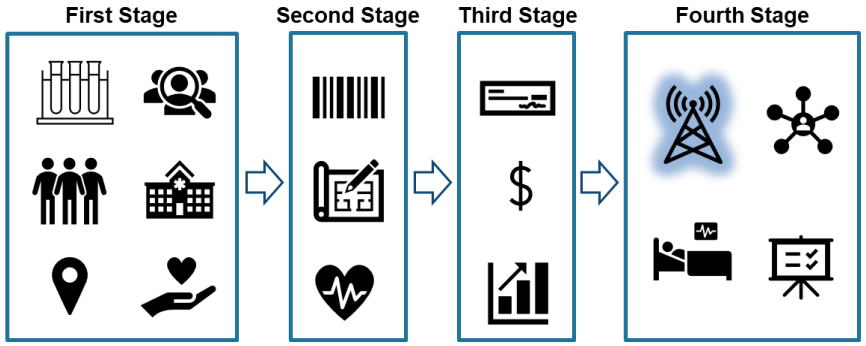
- Research Payment Rates
- Understand Cost & Price
- Create Contract & Pricing Models

Fourth Stage

- Create a Payer Communications Plan
- Garner Stakeholder Support
- Collect Evidence via Clinical Studies
- Consider Reimbursement Plan

Fourth Stage: Create a Communications Plan

Beth's final goals for her reimbursement strategy include developing a communications plan to inform stakeholders of VitalScreen's attributes, drive market adoption, and receive optimal coverage.



Beth's outreach to multiple stakeholders clarifies she will need a **communication plan** to differentiate VitalScreen from other products on the market in the minds of her customers. She personalizes messaging for the following stakeholder groups:

- **Payers:** To communicate the product value, test accuracy, and high-level pricing information; with available utilization data either from VitalScreen or competitors (if available). This could also include the analytical validation data and test accuracy information and patient testimonials in support of the screening test.
- **Patients:** As patients form the basis of the clinical need and, along with patient advocacy groups, can be important drivers of the adoption of screening tests such as VitalScreen, they play a vital role in driving demand and advocating for (additional) coverage of the test.
- **Physicians & Health Provider Systems:** Sharing cost-benefits information on implementing VitalScreen (over other screening tests on the market) and advocating for its adoption with their employers and peers to support market demand will be crucial. The favorable real-world evidence study outcomes conducted by Harvard Pilgrim Health Care and Illumina can be used as a foundation for these discussion and to "pitch" similar studies. Also, physicians need to be equipped to talk about VitalScreen to patients in a persuasive manner.
- **Professional medical societies:** For this group information dissemination will aid in including new and innovative products, such as VitalScreen, in their guidelines.

Key Questions:

- Who are the key decisions makers for the determinants of providers, commercial payers, and Medicaid that set reimbursement rates, collect payments, process claims, and pay provider claims?
- Can we claim that the new device provides payers with both, clinical and economic benefits over currently available alternatives?

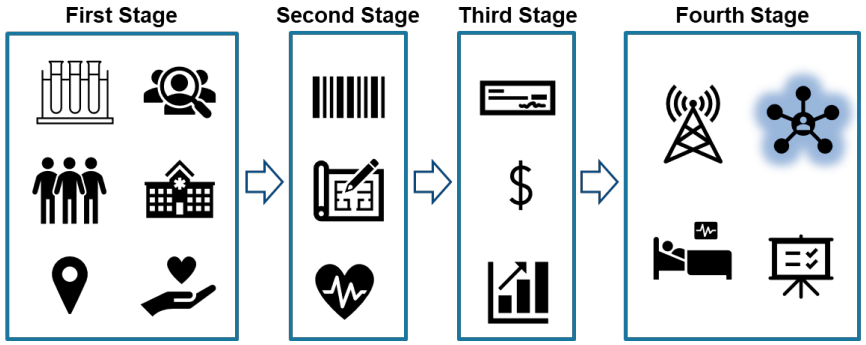
See Glossary for additional information.

Fourth Stage: Garner Stakeholder Support

Beth knows she will need stakeholder support for her reimbursement strategy for VitalScreen, to drive market adoption and receive coverage.

Beth will need to engage early and establish long term relationships with key stakeholders and product champions. Each stakeholder plays an important role in the successful commercialization of VitalScreen. Stakeholders include:

- **Patients** form the basis of the clinical need and, along with patient advocacy groups, can be important drivers of the adoption of VitalScreen.
- **Physicians** have to be willing to use the test in real-world clinical practice, as well as advocate for its adoption with their employers and peers.
- **Health Provider Systems**, including hospitals and clinics, have to be willing to try VitalScreen (over other screening tests on the market), these stakeholders will pay particular attention to potential burdens a new test may add to their clinical and administrative staff.
- **Professional medical societies** must be open to updating their guidelines to include new and innovative products, such as VitalScreen, once sufficient evidence has been provided, as this is a huge driver in securing coverage from payers.



Key Questions:

- Who is on my list of stakeholders?
- Which stakeholder group has impact on coverage; which on payment rates?
- What role do patients and consumers play; do they have an impact on coverage decisions?

See Glossary for additional information.

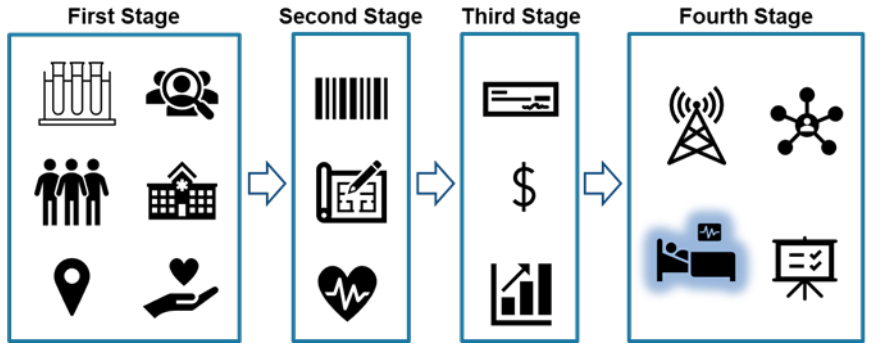
Fourth Stage: Collect Clinical Evidence by Conducting Clinical Studies

Beth assesses whether a clinical study is needed to collect evidence needed for favorable coverage.

Although Beth knows clinical studies do not need to be conducted for LDTs, in order to bring her screening test to market she is contemplating feedback she received from CMOs of commercial payers pertaining to her 99% accuracy claim. She is also evaluating the information in the recent FDA Safety Communication on the topic of "Genetic Non-Invasive Prenatal Screening Tests May Have False Results." FDA's notion of appropriate use of cell-free DNA tests as screening and not diagnostic tests needs to be considered in the value equation. Beth wants to demonstrate the clinical utility of the test by showing the test is accurate enough to be used in making treatment decisions.

If Beth were considering applying for a new CPT code to get a higher reimbursement rate, a clinical study would most likely be needed. In that scenario, FDA-clearance/ approval would be another factor impacting the decision to establish a new CPT code and reimbursement rate. Beth plans to meet with a Reimbursement Consultant to weigh her options pertaining to CPT code applications for a Category I or III CPT code.

For now, Beth is planning on analyzing the analytical real world performance data (including monitoring of potential false positives) of VitalScreen to build upon the 99% accuracy claim for her LDT. As none of the currently available NIPTs have yet been authorized, cleared, or approved by the FDA, this could help differentiate VitalScreen.



Key Questions:

- Is a clinical study needed to collect evidence; if yes, under which circumstances?
  - Note: LDTs – unlike IVDs – only require analytical not clinical validation. Hence, clinical studies are not required for LDTs.
- Has the product produced better results toward existing population to include the real-world patient population?
- How can you expand the number of hospital sites performing the screening test and case volume to show clinical utility?

See Appendix & Glossary for additional information.

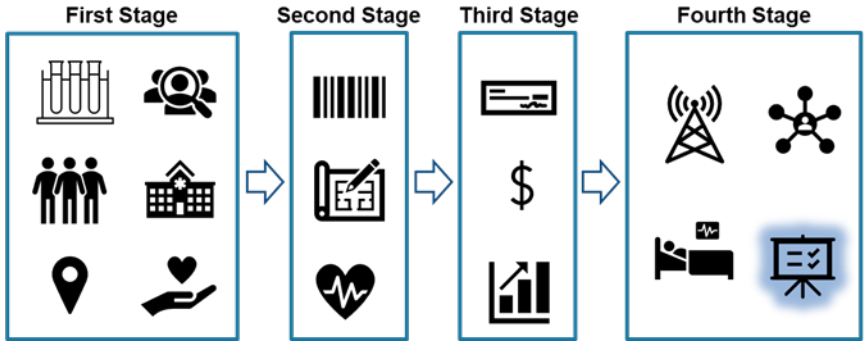
Fourth Stage: Consider Reimbursement Plan for a New Diagnostic

Beth also acknowledges that there may be a future need to consider additional evidence collection for new reimbursement vehicles and to request a novel CPT code for VitalScreen. She plans to integrate this into her reimbursement strategy to meet potential future unmet needs for VitalScreen and drive market adoption.

She includes a plan to strengthen the medical necessity criteria by creating supporting evidence for **new reimbursement** mechanisms thereby improving the value proposition for VitalScreen.

As VitalScreen may undergo technological and analytical changes in the future, she may decide to submit the test for FDA-clearance/approval. If that happens, a new CPT code may be required to capture the differentiation of the regulated test.

Beth integrates her thinking in her reimbursement plan and will research detailed requirements on requesting a new CPT code in the coming months; her reimbursement plan includes an addendum with a timeline and resource requirements for obtaining a new CPT code.



Key Questions:

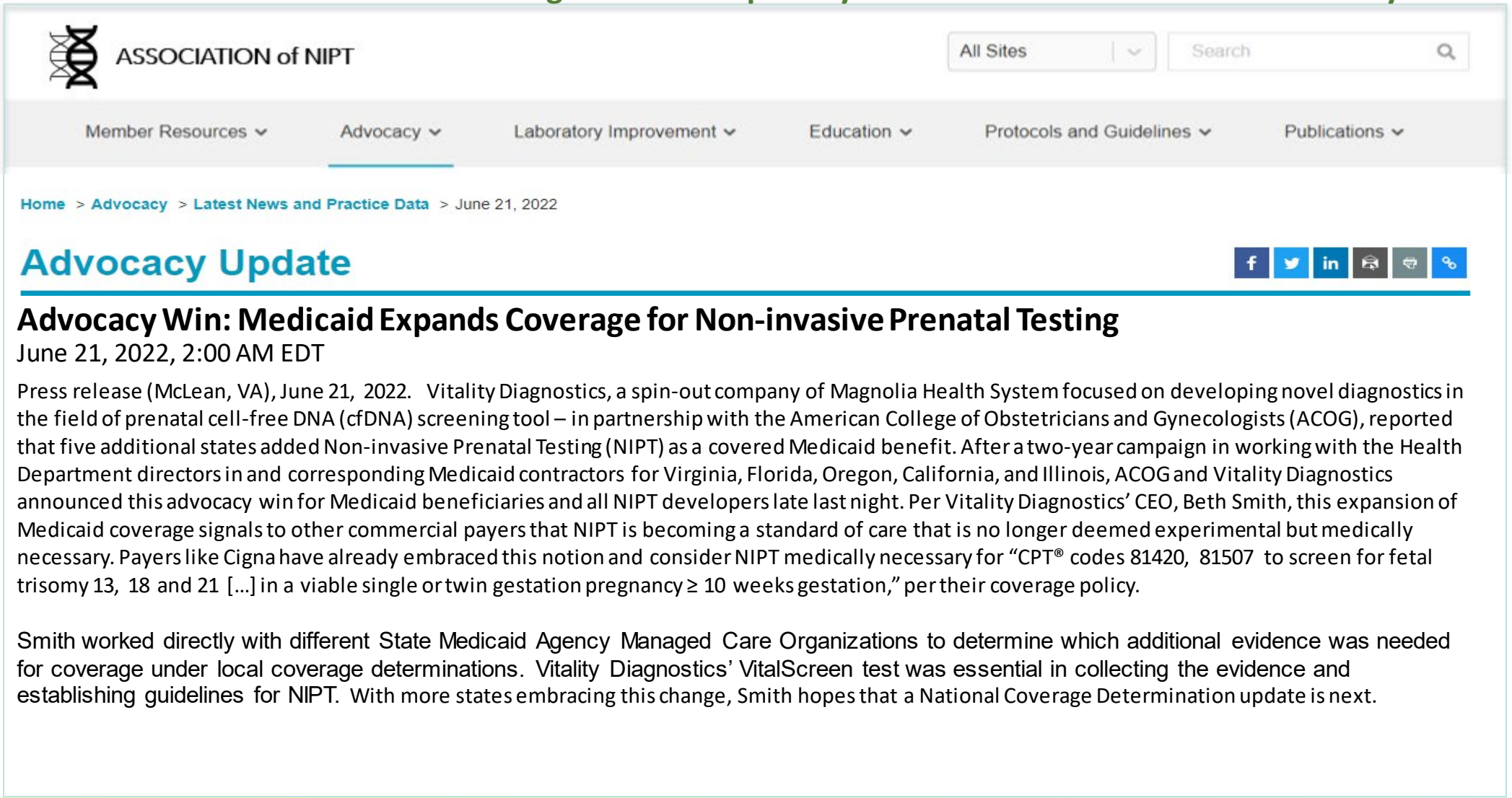
- Will technological changes be made to my test in the future; will it be considered a new diagnostic?
- If so, what are the pros and cons of applying for a new CPT code?
- What steps do I need to take to obtain coverage for my new diagnostic?

See Glossary for additional information.

SUMMARY

VitalScreen Success*

*The following is a fictional portrayal of what success for VitalScreen may look like



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Advocacy Update

Advocacy Win: Medicaid Expands Coverage for Non-invasive Prenatal Testing

June 21, 2022, 2:00 AM EDT

Press release (McLean, VA), June 21, 2022. Vitality Diagnostics, a spin-out company of Magnolia Health System focused on developing novel diagnostics in the field of prenatal cell-free DNA (cfDNA) screening tool – in partnership with the American College of Obstetricians and Gynecologists (ACOG), reported that five additional states added Non-invasive Prenatal Testing (NIPT) as a covered Medicaid benefit. After a two-year campaign in working with the Health Department directors in and corresponding Medicaid contractors for Virginia, Florida, Oregon, California, and Illinois, ACOG and Vitality Diagnostics announced this advocacy win for Medicaid beneficiaries and all NIPT developers late last night. Per Vitality Diagnostics' CEO, Beth Smith, this expansion of Medicaid coverage signals to other commercial payers that NIPT is becoming a standard of care that is no longer deemed experimental but medically necessary. Payers like Cigna have already embraced this notion and consider NIPT medically necessary for "CPT® codes 81420, 81507 to screen for fetal trisomy 13, 18 and 21 […] in a viable single or twin gestation pregnancy ≥ 10 weeks gestation," per their coverage policy.

Smith worked directly with different State Medicaid Agency Managed Care Organizations to determine which additional evidence was needed for coverage under local coverage determinations. Vitality Diagnostics' VitalScreen test was essential in collecting the evidence and establishing guidelines for NIPT. With more states embracing this change, Smith hopes that a National Coverage Determination update is next.

Summary Findings: By Phase

First Phase

- Technology Type & Regulatory Context: diagnostic test/prenatal cell-free DNA screening; LDT under FDA enforcement discretion
- Competitors: Natera™ Panorama™, Integrated Genetics (LabCorp Specialty Testing Group) MaterniT® 21 PLUS, GENOME-Flex, and MaterniT® GENOME
- Patient Population: Pregnant women, particularly those with high-risk pregnancies; women undergoing in vitro fertilization
- Healthcare Providers & Site of Service: Obstetricians in an outpatient setting
- Types of Payers: Commercial insurance; Medicaid

Second Phase

- Existing Payment Codes: 81420: Fetal chromosomal aneuploidy; 81507: Fetal aneuploidy
- Coverage Determinations: Cigna deems NIPT under both codes "medically necessary" only for certain indications; Maryland Department of Health NIPT testing is a covered Medicaid benefit
- Evidence and Value: Capture utilization data to define evidence to support coverage and pricing – e.g., 2014 article titled "NIPT: current utilization and implications for the future of prenatal genetic counseling"

Third Phase

- Payment Rates: 2022 CMS Clinical Diagnostics Laboratory Fee Schedule rate for CPT 81420 is $759.05 and for CPT 81507 is $795.00.
- Cost and Price: Total cost of $450 – $650; enter market as price leader; determine max out-of-pocket and self-pay price for patients based on average $795 reimbursement rate and total cost of test.
- Contract and Pricing Models: Create charge/pricing matrix for Commercial Payers, Medicaid, and Consumers

Fourth Phase

- Communications Plan: Personalize messaging for stakeholder groups: Payers, Patients, Physicians/Health Systems, Professional medical societies
- Stakeholder Support: Establish long term relationships with key stakeholders and find product champions
- Clinical Evidence Curation/Clinical Studies: Lean into 99% accuracy claim - analyzing the analytical real world performance data; integrate potential FDA Safety Communication into value proposition; consider of clinical study in support of applying for a new CPT code
- Reimbursement Plan for New Diagnostic: FDA-clearance/approval should be considered; new CPT code may be required to capture differentiation of regulated test

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GLOSSARY

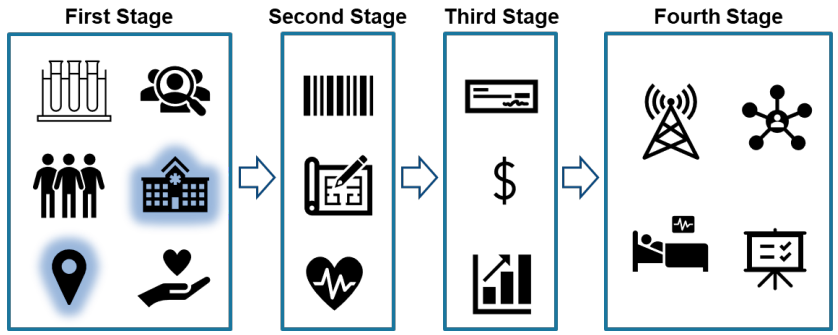
Glossary

- **AMA**: American Medical Association
- **cfDNA**: Cell-free DNA
- **CMS**: Centers for Medicare and Medicaid
- **CLIA**: Clinical Laboratory Improvement Amendments Certified
- **COGS**: Cost of Goods Sold
- **CED**: Coverage with Evidence Development
- **CPT®**: Current Procedural Terminology
- **CAP**: College of American Pathologists Accreditation
- **ICD-10**: International Classification of Diseases diagnosis codes
- **IVD**: In-vitro diagnostic
- **MCO**: Managed Care Organization
- **MS-DRG**: Medicare Severity Diagnosis. Related Groups
- **MAAA**: Multianalyte Assays with Algorithmic Analyses codes
- **NCD**: National Coverage Determination
- **LDT**: Laboratory developed test
- **NIPT**: Non-Invasive Prenatal Test
- **OB/GYN**: Obstetrician/Gynecologist
- **PLA**: Proprietary Laboratory Analyses codes
- **SNPs**: Single nucleotide polymorphisms
- **SMA**: State Medicaid Agency

APPENDIX

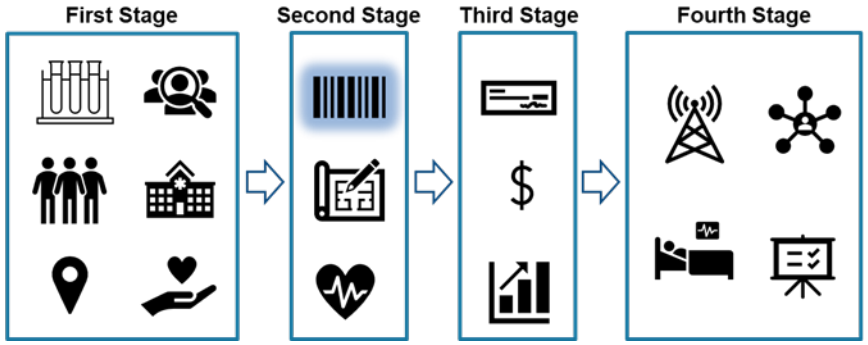
First Stage: Research Healthcare Providers & Identify the Site of Service

Additional Information



- Medical services can either be provided in an inpatient or an outpatient setting (usually not both). It is crucial to understand which one of the settings the diagnostic would fall into.
- Inpatient: If the test falls into this category, the cost of the test will be rolled into an MS-DRG (inpatient testing) where all costs of care for the episode will be paid in one lump-sum payment (and the test would not be itemized or paid separately by insurance.) Here, the cost of the test is very important (the lower the better) as the healthcare provider (organization) must evaluate the value against the cost of the test.
- Outpatient: If the test falls into this category, the diagnostic would be paid separately. If there are existing coverage determinations, the test would be paid based on a specific CMS lab fee schedule or a negotiated commercial payer rate.
    - Exceptions: Some specialty programs, such as orthopedics, participate in bundled-payment programs for which reimbursement is capped. Evaluating the cost of the diagnostic against the value is crucial in this setting.
- Based on the patient population identified in step #2, you may want to think about when and where your diagnostic would be used – i.e., where and when the results would be used to make treatment decisions. You can use like-products to verify your determination by conducting an online search.
- Goal: At the end of this exercise, you should have been able to determine which site of service best fits your test. Use this information to shape your marketing plan, to determine your price and to evaluate which payment rate will lead to a break-even point.

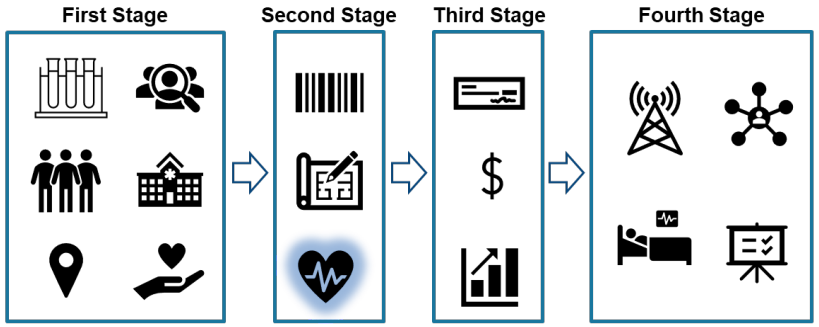
Second Stage: Research Existing Payment Codes for the Technology



Additional Information

- For molecular diagnostics, there are also Multianalyte Assays with Algorithmic Analyses (MAAA) codes and Proprietary Laboratory Analyses (PLA) codes – a subset of CPT codes – that exist just for these types of tests. She found a general overview of these codes on the American Medical Association (AMA) website.
- Beth also searched those sets of codes. She understands that when a PLA code for the test exists, the rule is that one does not use the CPT Category I code.
- Based on CMS material (that since has been superseded but offers helpful background information), Beth learned that: "*Many applications of the molecular pathology procedures are not covered services given a lack of benefit category (e.g., preventive service or screening for a genetic abnormality in the absence of a suspicion of disease) and/or failure to meet the medically reasonable and necessary threshold for coverage (e.g., based on quality of clinical evidence and strength of recommendation or when the results would not reasonably be used in the management of a beneficiary).*" This is why it is extremely important to not only understand existing payment codes but also have foresight to plan for potential payment code changes.

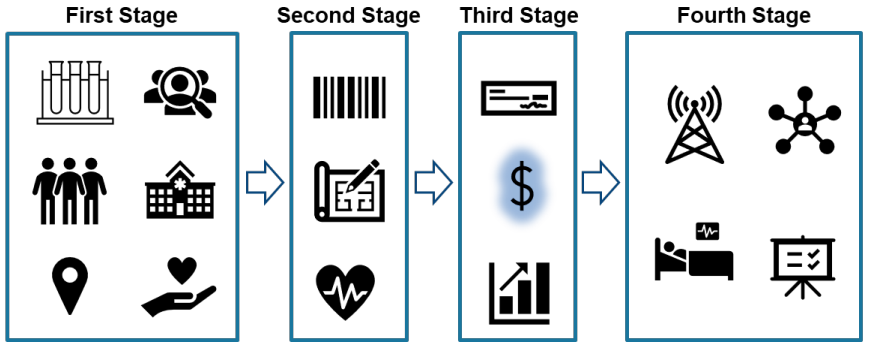
Second Stage: Determine Evidence & Value



Additional Information

- Based on this ACOG report, Beth understands that NIPTs are considered medically necessary by some private payers (and may need prior authorization from a physician before coverage) but are not yet considered standard of care for all patients.
- However, a recent FDA Safety Communication on the topic of "Genetic Non-Invasive Prenatal Screening Tests May Have False Results" must also be incorporated into the value equation – especially, when considering stakeholder communication plans.
- Go-to-market strategy: You may find you have to adjust your go-to-market strategy (market size and target market) based on existing coverage determinations. E.g., you may have to focus on only high-risk pregnancies if NIPT coverage for average-risk pregnancies is non existing or sparce.
    - Search for potential articles that offer insights into potential future coverage landscape, e.g., article here.

Third Stage: Understand the Cost and Price of the Test



Additional Information

- To determine the "cash price" for test, Beth does on the ground research by calling current test providers and inquiring what her max out-of-pocket charge would be based on different insurance-coverage scenarios. She asks her associated to collect this information on all players on the market to understand the market. Information is collected from articles, by making calls, patient advocacy groups/blogs, etc. This may take some time but is important in determining where your test lays with regard to market pricing (lower or upper end of price spectrum) and to determine potential "out-of-pocket" expenses for patients if commercial payer does not cover test (or parts of test).
- Beth also learned from her prior research that competitors like Natera have in-network agreements for their lab/LDT in place with most major private payers. However, on their website Natera states that this "does NOT mean that 100% of the cost of testing will be covered."
- She also saw that companies like Natera offer compassionate care programs capping out-of-pocket expenses at, e.g. $149 for qualifying patients.
- Some companies offer patients the option to choose between billing the patient's insurance and paying the self-pay price. Depending on the insurance, coverage, and contractual rate agreements, the out-of-pocket costs for the patient may be higher than the self-pay price.