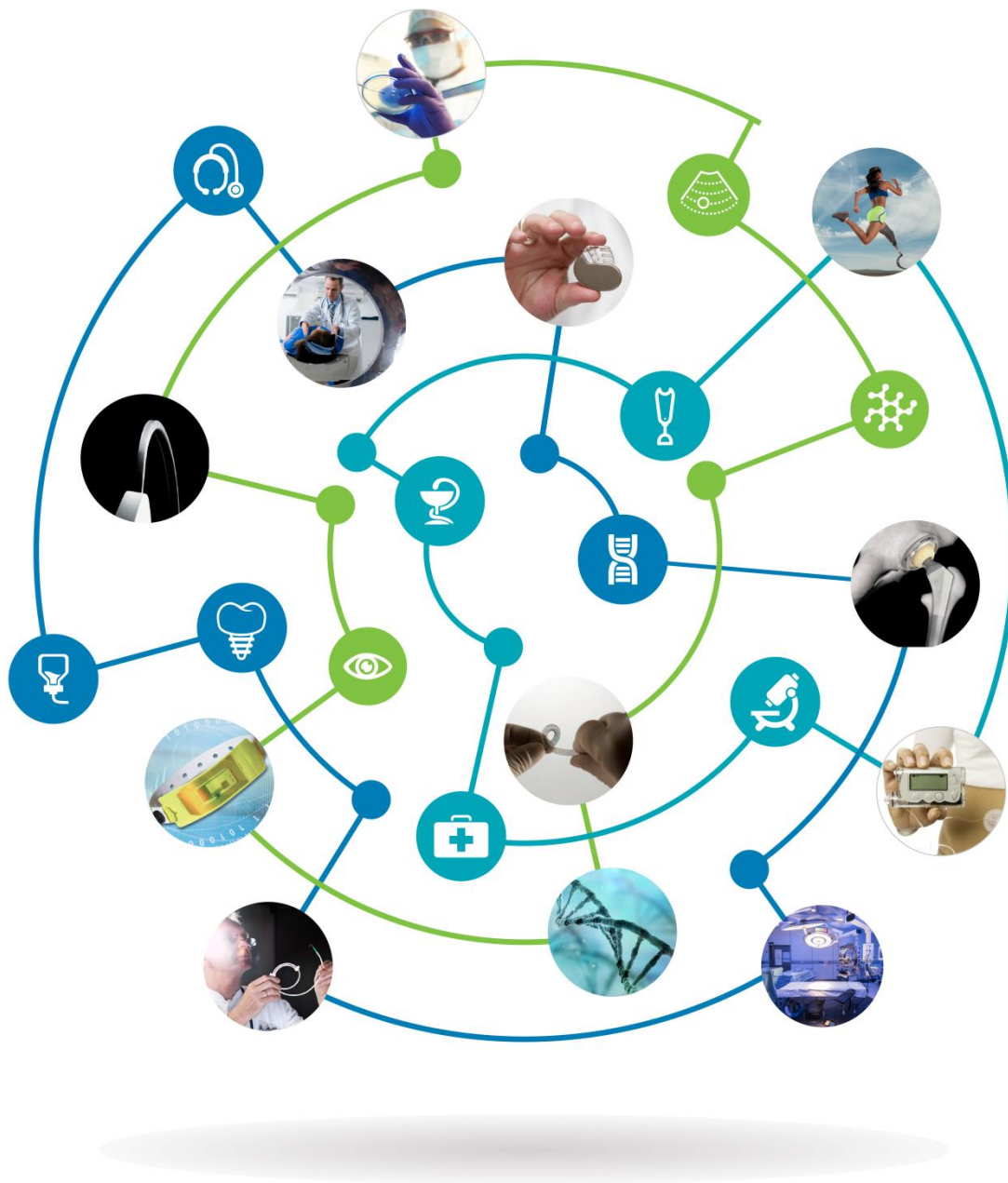


AdvaMedDx Value Assessment Framework *in Practice*



Application of the Comprehensive Assessment of the Value of Diagnostic Technologies Framework to Exact Sciences Cologuard Multi-target sDNA Test

Value Framework Overview

In response to the growing need to demonstrate how diagnostic tests and technologies fit into the emerging value-based paradigm for providers, payers, and patients, AdvaMedDx launched a Strategic Value Initiative to develop an approach to value assessment for diagnostic tests and technologies that can be used by Medical technology companies as well as by health systems, payers, and other stakeholders.¹

The AdvaMedDx Value Assessment approach goes beyond traditional Health Economic Outcomes Research (HEOR) and clinical efficacy metrics to assess the value that diagnostic tests and technologies may contribute to improving patient care and experience, economic outcomes, and the overall health of populations. This approach uses four broad categories, or “value drivers,” to describe the value of diagnostic tests and technologies: clinical impact, non-clinical patient impact, care delivery revenue and cost impact, and public/population impact relevant to an array of stakeholders who may evaluate and measure value differently.

The AdvaMedDx Value Assessment approach can be used to guide the development of a value proposition that successfully communicates the full breadth of expected impacts offered by diagnostic tests and technologies while taking into account the demands of the changing health care ecosystem. The collection of information associated with the value drivers reflects quantitative and qualitative metrics of value, gives appropriate weight to patient experience and societal impacts, and also accounts for the consideration of evidence collected through a variety of methods. An illustration highlighting the value drivers and components of AdvaMed’s approach is on the following page.

In order to demonstrate the application of this framework across different types of diagnostic tests and technologies, AdvaMedDx has partnered with member companies to develop use cases. These use cases address the clinical need for the diagnostic test or technology, alternative and existing technologies on the market, the expected impacts of the diagnostic test or technology, and the evidence to support such a value assessment. The use cases have been developed as a way to directly demonstrate the application of the AdvaMedDx Value Framework to the featured diagnostic test and should not be construed as an endorsement or promotion thereof.

Exact Sciences

This use case demonstrates the value of Exact Sciences’ Cologuard test across all of the identified value drivers and for a range of stakeholders. Cologuard works by detecting altered DNA or excess hemoglobin in the abnormal cells shed into the colon, where they are picked up by stool. This method can also identify abnormal precancerous cells before they are detectable in the bloodstream.

Illustration of AdvaMedDx Value Assessment Approach

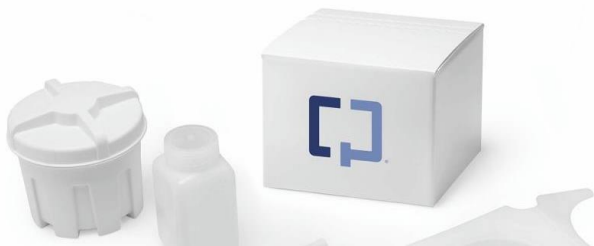


Source: "A Framework for Comprehensive Assessment of the Value of Diagnostic Tests", co-developed with Deloitte Consulting LLP

Exact Sciences Cologuard multi-target sDNA test

Medtech companies with a new product concept in development should start early, not only to address the FDA requirements, but also the value proposition that the technology conveys to patients, providers, and the health care system.

Exact Sciences' Cologuard multi-target sDNA test demonstrates value across all of the drivers and serves as an example of the appropriate application of the Advamed value assessment approach in establishing value for a range of stakeholders.



Exact Sciences manufactures the FDA-approved Cologuard multi-target sDNA test that provides a simple, low-risk, noninvasive method to detect both pre-cancer and cancer in a specimen that can be taken in the patient's home. Cologuard is prescribed and then the test kit box is shipped directly via UPS to a patient's home where the patient follows the directions to collect a fecal sample in a purpose-designed collection container, which is then placed back in the box, picked up by UPS using a pre-paid label, and delivered to Exact Sciences Laboratories LLC. Exact Sciences Laboratories then reports the findings back to the patient's doctor.

Cologuard detects 11 biomarkers that can be associated with colorectal cancer and pre-malignant lesions (9 DNA markers, one DNA reference gene, and one fecal hemoglobin marker) which are used together to calculate a single biomarker score using a logistic regression formula.

The test provides a single qualitative patient result of Positive or Negative. The test detects increased levels of these biomarkers when they are released into stool from cells being shed from the colorectal epithelium and epithelial lesions. In contrast, peripheral blood-based DNA biomarkers are not elevated in pre-malignant disease and are rare to absent in early stage disease. Stool is a rich source of DNA biomarkers, allowing for high levels of early stage colorectal cancer detection and the detection of significant pre-malignant polyps (adenomas).

The Cologuard test is a comprehensive screening system which includes a nationwide patient compliance program to improve the patient experience and to bolster high rates of successful screening. This system includes a staff-based welcome call, reminder calls and letters, and a 24/7 patient support line, all designed to improve patient compliance and satisfaction.



Unmet Need

AdvaMedDx's assessment process begins with understanding and addressing the unmet need and value imparted through the new diagnostic test.

Unmet patient need can be framed in terms of clinical validity, clinical utility, access, patient preferences, costs, quality of care, ease of use, etc.

Colorectal cancer (also referred to as colon cancer or CRC) is the second most common cause of cancer death among cancers affecting both men and women. In 2016, there were an estimated 135,000 new cases of colorectal cancer diagnosed and 49,000 deaths from colorectal cancer in the United States.² The relative 5-year survival rate of colorectal cancer is 94% if diagnosed while in its earliest stage, compared to only 11% if found after the cancer has metastasized.³ Often, colorectal cancer has no symptoms until it is in an advanced stage. Regular screening and early diagnosis are critical to survival. Currently, greater than 23 million Americans are eligible for, but are not participating in, CRC screening.⁴

Test methods for colorectal cancer screening include a multi-target stool DNA test (Cologuard®), fecal occult blood tests, endoscopy (colonoscopy or flexible sigmoidoscopy), imaging tests such as CT colonography (virtual colonoscopy), and peripheral blood tests for circulating biomarkers. Except for screening colonoscopy itself, all screening tests are followed by a diagnostic colonoscopy to evaluate abnormal results. Some patients have an aversion to screening colonoscopies due to the preparation requirements, sedative risk, and the invasive nature of the procedure. Consequently, many patients have avoided colorectal cancer screening because of the lack of acceptable alternatives to a colonoscopy. As of 2016, only 62% of average-risk individuals 50 years old and older were up to date with recommended colorectal cancer testing.⁵



Patient Populations

Assessments should consider the extent to which a diagnostic test may be more or less effective for various patient populations and align with the population focus of the stakeholder evaluating the test.

This section demonstrates the value of the diagnostic test to patients by addressing the need for the test in the context of the affected patient sub-population and the available alternatives to treat their condition.

The timing of colorectal cancer diagnosis affects treatment options and greatly impacts survival. Cologuard addresses the need for accurate and noninvasive colorectal cancer screening in patients age 50 and older.

Cologuard offers a simple, low-risk, noninvasive test that encourages greater compliance with screening recommendations due to its ease of use. The Cologuard test has minimal administration time and unlike colonoscopy does not require changes in lifestyle or a preparation process. The Cologuard sample can be obtained during one typical bowel movement and requires only a few additional minutes to prepare the sample for shipping afterwards. This is significantly shorter than the time required for a colonoscopy, which can require up to 24 hours of preparation before the procedure, 30 minutes to one hour for the procedure itself, and potentially several hours of recovery before discharge.

Cologuard is also able to detect precancerous lesions, allowing the physician receiving the results to alert the patient of the need to seek a follow-up colonoscopy or surgical procedure to remove polyps that, left undetected and intact, could eventually become cancerous. This means that colorectal cancer can be prevented from developing, thereby reducing the potential for more costly colorectal cancer treatment.



Time Frames

The assessment should identify time frames that are important in understanding the value of the diagnostic test.

There are four stages of colorectal cancer: ^{6 7}

- Stage 1: Stage 1 colorectal cancer has not spread beyond muscular layers of the colon. If diagnosed during this stage, the 5-year survival rate is 94%.
- Stage 2: In Stage 2, the cancer has spread beyond the muscular layers and into the surrounding tissue. At this stage, the survival rate is 82%.
- Stage 3: At Stage 3, colorectal cancer is considered to be “advanced” and has spread to the local lymph nodes. During this stage, the 5-year survival rate is 67%.
- Stage 4: Stage 4 cancer has spread to other organs. Only 11% of patients diagnosed in this stage survive for 5 years after diagnosis.

Colorectal cancer is highly treatable when diagnosed early. Stage 1 and the majority of Stage 2 colorectal cancer, both considered localized disease, can be successfully treated by surgical removal of the affected part of the colon and lymph nodes. After Stage 1, chemotherapy and/or radiation may be considered in addition to surgery but are generally reserved for regional (Stage 3) and distant (Stage 4) disease. Early diagnoses allows for better treatments and better outcomes. However, only about 40% of colorectal cancers are found during Stage 1 or 2, before the cancer has spread beyond the colon.⁸ Once the cancer has spread, treatments become more complicated and survival rates decrease.

The high percentage of colorectal cancer diagnoses after Stage 1 are likely or in part due to the failure of patients to follow colorectal cancer screening recommendations.⁹ Patients diagnosed with Stage 3 or 4 disease may have avoided screening and therefore presented after they developed symptoms, which are more commonly associated with late disease.¹⁰

Cologuard allows for the detection of colorectal cancer in its earliest stages, when treatments are shorter and less expensive, and patient survival rates are much greater, meaning the

patient is more likely to be able to continue in or return to the workforce and avoid further health system costs. Productivity loss due to cancer in general has been estimated to be \$19,900/100 employees per year as not only is productivity lost for the cancer patient, but also through changes in productivity among their co-workers — a ripple-effect.¹¹



Stakeholders

The intended audience for a value assessment affects the framing of the assessment and the drivers and metrics that could be highlighted.

Both the intended audience/stakeholders and the purpose of the assessment should dictate which types of value are considered and emphasized via the assessment process, as well as the types and quality of evidence needed to support evidence development needs and appropriate strategies for collecting annual performance information.

It is important for stakeholders to consider the full range of value drivers and impacts.

The chart on the following page highlights potential value for various stakeholders based on use of the Cologuard test in screening for colorectal cancer.

Cologuard Test Value Drivers Impact by Stakeholder

	Clinical Impact	Non-Clinical Impact	Care Delivery Revenue and Cost Impact	Public/Population Impact
Patient	<ul style="list-style-type: none"> 92% sensitivity in detecting CRC stages 1-4 (compared to 74% with fecal immunochemical tests (FIT))¹² 94% sensitivity in detecting surgically curable stage cancers (I and II) 69% sensitivity in detecting highest risk pre-cancers¹³ Insignificant risk of adverse reaction from the test itself No sedation required No preparation or physical discomfort 	<ul style="list-style-type: none"> Ability to collect a sample at home Requires no training to obtain samples Higher patient compliance with screening recommendations (67%) Under ACA and CMS preventive benefit – no out of pocket costs for screening tests Higher patient satisfaction with testing method No preparation required Results delivered quickly 	<ul style="list-style-type: none"> Reduced office visits Reduces the need for colonoscopy by limiting colonoscopy to diagnostic use as opposed to screening 	<ul style="list-style-type: none"> No work missed No caregiver needed (as with colonoscopy) so no caregiver work missed Lower overall healthcare cost with lower cost testing method & potentially earlier treatment
Doctor	<ul style="list-style-type: none"> Provides ability to detect CRC earlier and intervene earlier The balance of benefits to harms are equivalent or superior to all other USPSTF-recommended screening strategies Little to no risk of adverse reaction No sedation required 	<ul style="list-style-type: none"> Fewer office visits Patient compliance program that ensures patients more likely to follow through with screening than with other test methods Less follow up required Easy to order via fax or portal 	<ul style="list-style-type: none"> Reduced office visits Informs need for additional procedures Included in HEDIS measures and CMS STARS programs, quality credit for a 3-year lookback period during HEDIS audits Patient compliance program reduces administrative burden of ensuring compliance and follow-up National database can be checked at any time for current or past patient results 	<ul style="list-style-type: none"> Lower overall healthcare cost with lower cost testing method & potentially earlier treatment
Hospital/Outpatient Clinic	<ul style="list-style-type: none"> Ability to produce and report Patient Reported Outcomes for quality metrics Manage most at-risk patients effectively, eliminating unexpected outcomes 			

	Clinical Impact	Non-Clinical Impact	Care Delivery Revenue and Cost Impact	Public/Population Impact
Insurer	<ul style="list-style-type: none">• Manage most at-risk patients effectively, eliminating unexpected outcomes			<ul style="list-style-type: none">• Lowers overall healthcare costs• Lower rehabilitation costs crucial• Quicker return to work• Coordinated care among the stakeholders



Evidence Across the Value Drivers

Diagnostic test innovators must determine the best way to show value with evidence. This can vary based upon the type of test.

It is critical to identify and evaluate the quantity and quality of available types of evidence for the diagnostic test early in product development and on an ongoing basis to determine how it can be used across the relevant drivers to offer robust evidentiary support.

Exact Sciences has evidence on the ability of Cologuard to detect colorectal cancer before it is present in the blood stream and would be detectable via other test methods. Exact Sciences conducted a pivotal clinical study of 10,000 patients in the U.S. that is published in the New England Journal of Medicine.¹⁴ The study determined the effectiveness of Cologuard in the detection of colorectal cancer and precancerous lesions compared to fecal immunochemical tests (FIT) using colonoscopy as the reference method on all subjects. Several other studies have been conducted to further investigate Cologuard.

Cologuard use helps eliminate costly rescreening and the complications inherent in colonoscopy screening programs. The Cologuard pivotal study shows that for every 1,000 patients screened with Cologuard only 160 are referred for further evaluation with colonoscopy— of whom only 70 will be found to have negative colonoscopies.¹⁵ By contrast, in a colonoscopy screening program 640 out of 1,000 patients will have negative colonoscopies with no cancerous or pre-cancerous growths—negating any benefit from the more-invasive procedure.¹⁶

The insurer economics of screening may be best served by looking at the single use comparison between Cologuard at \$649 (national list price) and colonoscopy at an average cost of \$1,600-\$3,000 per procedure. From the perspective of a third party payer, full value of the expense of screening only accrues when the patient remains in the “plan” for the duration of the screening interval— 3 years in the case of Cologuard and ten years for screening colonoscopy. Even with a conservative estimate of annual patient turnover of 15%, the likelihood that the full benefit of the colonoscopy-related expense will accrue to the initial payer is small when compared to the chance of a patient remaining in “plan” for three years. Additionally, patients are commonly rescreened via colonoscopy before the ten-year interval has expired, raising costs and risks for patients from complications with little potential increase in benefit.¹⁷ As a single source provider of Cologuard, Exact Sciences Laboratories has a national patient registry of all Cologuard tests and users, which can be managed across the country and across insurers and systems and can assist in ensuring appropriate utilization by only rescreening negative patients when they are due for their next screen.

Cologuard also offers the scalability, safety, precision, and compliance support of a single national laboratory test facility with a controlled analytic environment where test performance and compliance are carefully tracked and managed. This laboratory-based systematic approach to screening has driven initial screening compliance rates to 67% of kits returned. In a highly-regarded screening study (that did not include Cologuard) only 38% of colonoscopy referrals were completed within 12 months of an order.¹⁸ The combination of high compliance and high sensitivity drives clinical screening system performance and reveals that a 92% sensitivity¹⁹ test for cancer used by 67% of patients will detect more cancers in a screening population than a 95% sensitive²⁰ colonoscopy-based approach used by fewer than 50% of patients.²¹

The chart on the following page applies to the population of patients identified for colorectal cancer screening with Cologuard:

Cologuard Test Value Drivers Impact by Evidence Source

Evidence	Type of Evidence	Clinical Impact	Non-Clinical Impact	Care Delivery Revenue and Cost Impact	Public/Population Impact
U.S. Pivotal Clinical Study Published)²²	Cross-sectional	<ul style="list-style-type: none"> Low risk Higher sensitivity than FIT (92% vs 74%) for detecting CRC 94% sensitivity in detecting surgically curable stage cancers (I and II) Higher sensitivity than FIT (69% vs 46%) detecting pre-cancer most at risk for progression (high-grade dysplasia) 	<ul style="list-style-type: none"> Noninvasive No dietary or medication restrictions required 	<ul style="list-style-type: none"> More cost-effective than other common screening methods (Pap smear, Mammography)²³ With a 16% positivity rate, Cologuard can lower colonoscopy demand created by colonoscopy based primary screening programs by 84%. 	<ul style="list-style-type: none"> May improve uptake and adherence to screening guidelines.
U.S. Clinical Confirmatory Study (Published)²⁴	Cross-sectional	<ul style="list-style-type: none"> Low risk Overall, screening-relevant colorectal neoplasia (SRN) detection by sDNA testing was superior to that by FIT – 49% vs. 28% (P<.001) Higher sensitivity than FIT – 100% vs. 80% Lower specificity than FIT – 93% vs. 96% 	<ul style="list-style-type: none"> Noninvasive No dietary or medication restrictions required 	<ul style="list-style-type: none"> More cost-effective than other common screening methods (Pap smear, Mammography) 	<ul style="list-style-type: none"> May improve uptake and adherence to screening guidelines.
Multi-Year Interval Testing Analysis (Modeling Published)²⁵	Descriptive Analysis	<ul style="list-style-type: none"> Use of DNA stool testing every 3 years (3y) generates more than 90% of the life-years gained with screening colonoscopy Results meet USPSTF criteria for a recommendation 		<ul style="list-style-type: none"> DNA stool testing maximizes screening effectiveness in reducing CRC incidence and mortality, lowering downstream treatment costs 	
Patient Perception and Preferences Study (Published)²⁶	Self-reported Survey Analysis		<ul style="list-style-type: none"> Of the 423 survey respondents, 75% of them found stool testing more suitable than colonoscopy Adjusting for covariates revealed no significant racial differences in the perception of and preference for stool testing for colon screening 		<ul style="list-style-type: none"> Interventions aimed at increasing the uptake of stool DNA testing may help reduce racial disparities in CRC

Evidence	Type of Evidence	Clinical Impact	Non-Clinical Impact	Care Delivery Revenue and Cost Impact	Public/Population Impact
Review of the United States Preventive Services Draft Guidelines (Published)²⁷	Descriptive Analysis	<ul style="list-style-type: none"> Patients formerly non-compliant with screening, ages 50-74, compromise a significant portion (42%) of stool test users In a population of 1,000 screened individuals, 3-year stool testing yielded a median of 226 life-years gained, 20 CRC deaths averted, and a 76% reduction in CRC mortality 	<ul style="list-style-type: none"> Stool testing provides an opportunity to increase the quality of screening among those choosing non-invasive procedures 		<ul style="list-style-type: none"> Stool testing provides an opportunity to expand the pool of screened patients and prevent CRC and CRC-related mortality
Review of Screening in Medicare Patients (Published)²⁸	Retrospective Cohort Study	<ul style="list-style-type: none"> The availability of multitarget stool DNA colorectal cancer screening led to high screen compliance (88%) and diagnostic colonoscopy compliance on positive test cases (96%) in a cohort of previously screening non-compliant Medicare patients ages 50-85 years 			<ul style="list-style-type: none"> Demonstrated high value with 4 of 4 cancers detected at early stage and 21 cases of advanced precancerous adenomas found among the 49 positive patients



Expected Impacts (Value)

The value assessment should clearly demonstrate the impact of the diagnostic test across select value drivers including clinical impact, non-clinical patient impact, care delivery revenue and cost impact, and patient/population impact.

These impacts would be offset by the cost of acquiring the technology to derive the total expected value impacts.

Clinical Impact Value – The Exact Sciences Cologuard test provides benefits to both the patient using the test and the clinician overseeing the patient's care. Cologuard offers a simple, high sensitivity and high compliance noninvasive option for colorectal screening that does not require patient sedation or any pre-test dietary restrictions, making the test method more desirable and increasing the number of people following screening guidelines. The risk of adverse reactions to the test is low and the sensitivity is significantly higher than other fecal test methods. Cologuard allows for an earlier cancer diagnosis, which allows for an earlier intervention with better outcomes. Additionally, the use of Cologuard every three years generates more than 90% of the life-years gained with screening colonoscopy and meets the USPSTF criteria for a recommendation.

Non-Clinical Impact Value – Cologuard also produces beneficial non-clinical impacts for a range of stakeholders including patients, doctors, employers and insurers. The ease of the at-home test and patient support program impacts patient compliance with colorectal cancer screening recommendations. Patients experience greater satisfaction with a test method that is noninvasive and does not require a trip to the doctor. The Patient Perception and Preferences Study analysis supports this position: 75% of survey participants found stool testing more suitable than colonoscopy.²⁹

Additionally, patients may experience lower out-of-pocket expenses compared to costlier screening methods. For doctors, there is less follow-up required. Publicly available data from Exact Sciences shows 90% overall satisfaction among Cologuard users— with the test meeting or exceeding the expectations of 98% of the ordering providers.

Care Delivery Revenue and Cost Impact Value – Cologuard may generate both short- and long-term healthcare system cost savings. Cologuard impacts cost and care delivery by reducing the need for doctors' visits, make doctors ordering more efficient due to high compliance, and reduces the need for a colonoscopy, a comparatively expensive procedure.³⁰ It also lowers health care costs by detecting colorectal cancer early while it is still treatable. By maximizing screening effectiveness, Cologuard ultimately reduces CRC incidence and mortality, lowering downstream treatment cost.

Public/Population Impact Value – Cologuard creates beneficial societal impacts through eliminating visits to the doctor so that patients and caregivers do not miss work and decreases morbidity associated with the treatment of advanced disease, and through decreasing the impact of CRC on patients, families and communities. There is also the potential for racial disparities in CRC populations to be eliminated. Finally, Cologuard provides an opportunity to expand the pool of screened patients and prevent CRC and CRC-related mortality.

¹ "A Framework for Comprehensive Assessment of the Value of Diagnostic Tests", co-developed with Deloitte Consulting LLP, available at www.advamed.org and co-developed with Deloitte Consulting LLP

² "Cancer Stat Facts: Colon and Rectum Cancer." National Cancer Institute: Surveillance, Epidemiology, and End Results Program (2014).

³ Lansdorp-Vogelaar et al. "Effect of Rising Chemotherapy Costs on the Cost Savings of Colorectal Cancer Screening." *Journal of the National Cancer Institute* 101.20 (2009): 1412-1422.

⁴ "Colorectal cancer screening rates remain low." Centers for Disease Control and Prevention (CDC) (2013).

⁵ "National Health Interview Survey Results." Centers for Disease Control and Prevention (CDC) Morbidity and Mortality Weekly Report (2006-2017).

⁶ Lansdorp-Vogelaar et al. "Effect of Rising Chemotherapy Costs on the Cost Savings of Colorectal Cancer Screening." *Journal of the National Cancer Institute* 101.20 (2009): 1412-1422.

⁷ "Colon Cancer Stages." Cologuard.

⁸ "Colorectal Cancer Facts & Figures 2014-2016." American Cancer Society (2016).

⁹ Ibid.

¹⁰ Ibid.

¹¹ Bryla. "Cancer Presents Complex Workplace Challenges – According to IBI Research." Integrated Benefits Institute (2014).

¹² Imperiale et al. "Multitarget Stool DNA Testing for Colorectal-Cancer Screening." *The New England Journal of Medicine* 370 (2014): 1287-1297.

¹³ Ibid.

¹⁴ Imperiale, Thomas F. et al. "Multitarget Stool DNA Testing for Colorectal-Cancer Screening." *The New England Journal of Medicine*. 2014; 370:1287-1297.

¹⁵ Ibid.

¹⁶ The adenoma detection rate (ADR) seen in Imperiale et al. was 36%, therefore 64%, or 640/1000 colonoscopies, were "negative" and free of cancer or precancerous polyps (adenomas).

¹⁷ Cyhaniuk et al. "Longitudinal Adherence to Colorectal Cancer Screening Guidelines." *The American Journal of Managed Care* 22.2 (2016): 105-111.

¹⁸ Inadomi et al. "Adherence to Colorectal Cancer Screening: A Randomized Clinical Trial of Competing Strategies." *Archives of Internal Medicine* 172.7 (2012):575-582.

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- ¹⁹ Morikawa et al. "A comparison of the immunochemical fecal occult blood test and total colonoscopy in the asymptomatic population." *Gastroenterology* 129.2 (2005): 422-428.
- ²⁰ Zauber et al. "Evaluating Test Strategies for Colorectal Cancer Screening – Age to Begin, Age to Stop, and Timing of Screening Intervals." Agency for Healthcare Research and Quality (2009).
- ²¹ At a prevalence of 65 CRC/10,000 screens; $(65 \times 0.67 \times 0.92 = 40 \text{ CRC detected})$ vs $(65 \times 0.95 \times 0.5 = 31 \text{ CRC detected})$
- ²² Imperiale et al. "Multitarget Stool DNA Testing for Colorectal-Cancer Screening." *The New England Journal of Medicine* 370 (2014): 1287-1297.
- ²³ Ibid.
- ²⁴ Redwood et al. "Stool DNA Testing for Screening Detection of Colorectal Neoplasia in Alaska Native People." *Mayo Clinic Proceedings* 91.1 (2016): 61-70
- ²⁵ Berger et al. "USPSTF Colorectal Cancer Screening Guidelines: An Extended Look at Multi-Year Interval Testing." *The American Journal of Managed Care* 22.2 (2016): 77-81.
- ²⁶ Abola et al. "Stool DNA-based versus colonoscopy-based colorectal cancer screening: Patient perceptions and preferences." *Family Medicine and Community Health* 3.3 (2015): 2-8.
- ²⁷ Berger et al. "Multitarget stool DNA for colorectal cancer screening: A review and commentary on the United States Preventive Services Draft Guidelines." *World Journal of Gastrointestinal Oncology* 8.5 (2016): 450-458.
- ²⁸ Prince et al. "Multitarget stool DNA tests increases colorectal cancer screening among previously noncompliant Medicare patients." *World Journal of Gastroenterology* 23.3 (2017): 464-471.
- ²⁹ Abola et al. "Stool DNA-based versus colonoscopy-based colorectal cancer screening: Patient perceptions and preferences." *Family Medicine and Community Health* 3.3 (2015): 2-8.
- ³⁰ Ladabaum et al. "Colorectal Testing Utilization and Payments in a Large Cohort of Commercially Insured US Adults." *The American Journal of Gastroenterology* 109.10 (2014): 1513-525.

AdvaMedDx Value Assessment Framework *in Practice*

Exact Sciences: Cologuard Multi-target sDNA Test

Colorectal cancer is the second most common cause of cancer death among cancers affecting both men and women. The relative 5-year survival rate for colorectal cancer is 94% if diagnosed while in its earliest stage, compared to only 11% if found after the cancer has metastasized. Regular screening and early diagnosis are critical to survival. Currently more than 23 million Americans are eligible for, but are not participating in, colorectal cancer screening.

Patient Needs



New Dx Test/Technology



Stakeholders



Patient



Physician



Hospital



Clinical Labs



Payer



Government



Employer

Stakeholders

Value Drivers

Clinical Impact

- High sensitivity in detecting CRC stages 1-4
- Low risk of adverse reaction
- No sedation required

Non-Clinical Patient Impact

- Sample can be collected at home
- Higher patient compliance with screening
- No prep required



Test Type

Value Drivers

Care Delivery Revenue and Cost Impact

- Reduced office visits
- Reduced need for colonoscopy
- Compliance program reduces administrative burden of ensuring compliance

Public/Population Impact

- Lower cost testing method and lower overall health costs
- No missed work for patient or caregivers
- Potentially earlier treatment



Patient Populations

- Low-risk patients age 50 and over



Evidentiary Support

- US Pivotal Study
- US Confirmatory Study
- Multi-year Interval Testing Analysis
- Patient Perceptions and Preferences Study
- Review of USPSTF Guidelines
- Review of Screening in Medicare Patients



Time Frames

- Diagnosis of CRC
 - Stage 1
 - Stage 2
 - Stage 3
 - Stage 4



Expected Impacts (Value)

- Increased compliance
- Low risk of adverse reaction
- High sensitivity in detecting CRC
- Increases patient satisfaction
- Lower out-of-pocket costs
- Fewer follow-up visits
- Reduced administrative burden
- Reduced screening costs
- Reduced healthcare costs
- Fewer missed work days
- Reduction in racial disparity related screening rates