



Colorectal Cancer Screening for Employees

Victoria M. Raymond, MS, LCGC
Sr. Director, Medical Affairs
Guardant Health

April 3, 2023

Discussion Topics

- Colorectal Cancer (CRC) and Screening
- Challenges of CRC Screening Adherence
- Blood-based testing for CRC Screening

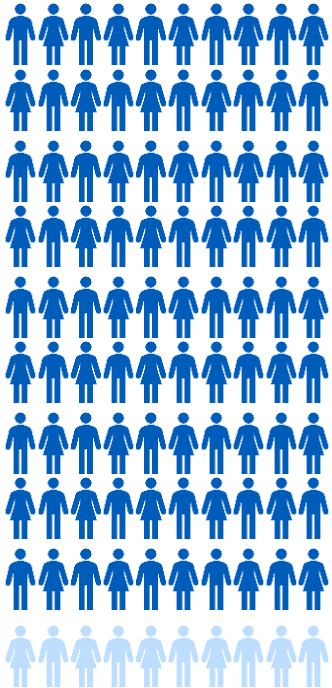
Colorectal Cancer (CRC) and Screening



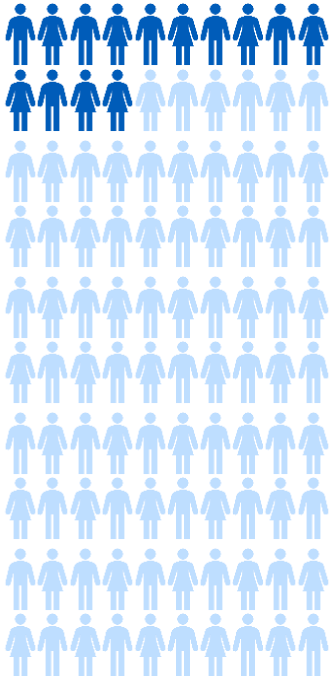
Colorectal Cancer Early Screening vs Late Diagnosis

90%

of people diagnosed with CRC in **early stages** by screening survive



VS

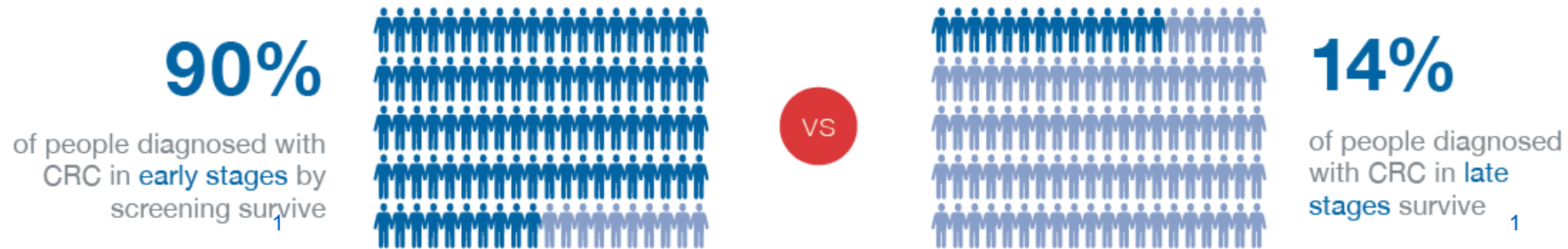


14%

of people diagnosed with CRC in **late stages** survive

National Cancer Institute. Surveillance, Epidemiology, and End Result Program website. Cancer Stat Facts: Colorectal Cancer. <https://seer.cancer.gov/statfacts/html/colorect.html>. Accessed August 16, 2019

Early-stage diagnosis significantly increases survival rates which leads to lowers treatment costs

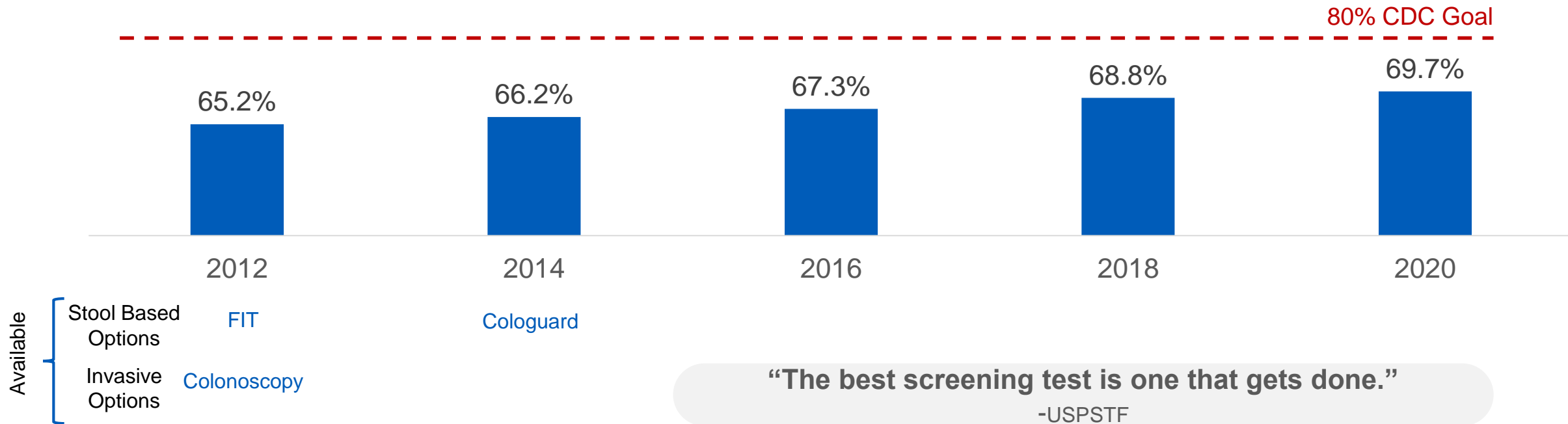


Stage IV CRC treatment is **3x greater** than the cost of Stage I CRC treatment²

1. National Cancer Institute. Surveillance, Epidemiology, and End Result Program website. Cancer Stat Facts: Colorectal Cancer. <https://seer.cancer.gov/statfacts/html/colorect.html>. Accessed August 16, 2019
Sherman B, Lynch W., "Connecting the Dots: Examining the Link Between Workforce Health and Business Performance", *The American Journal of Managed Care*, 2014, Vol. 20, No. 2. [No Time For Guesswork - CDC](#)

Despite multiple options, CRC screening rates remain stagnant, stool-based and invasive options have not moved the needle

Percent of US Adults Aged 50 – 75
Up-To-Date with CRC Screening^{3*}

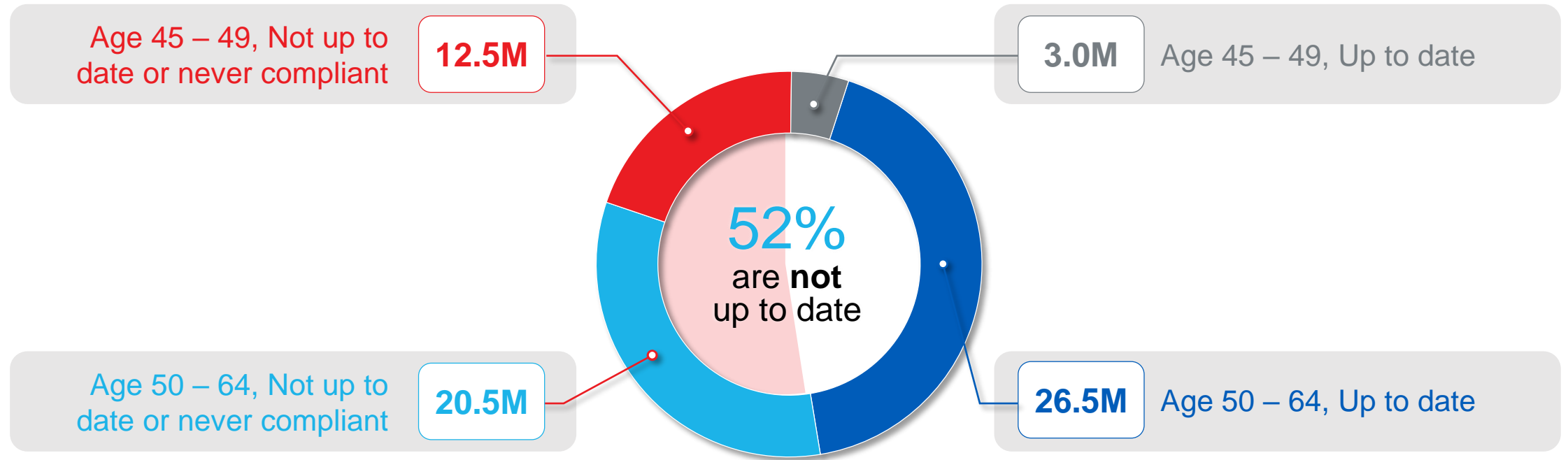


CRC = colorectal cancer; FIT = fecal immunochemical test; BRFSS = Behavioral Risk Factor Surveillance System; CTC = computed tomography colonography
 *This figure includes those up-to-date with FIT, sigmoidoscopy, or colonoscopy. In 2020, the BRFSS also measured Cologuard and CTC usage. The percentage up-to-date with CRC screening based on FIT, sigmoidoscopy, colonoscopy, Cologuard, or CTC in 2020 was **71.6%**.

1. Doubeni CA, et al. *Gastroenterology*. 2019;156(1):63-74.e6. 2. Healthy People 2030. Accessed July 14, 2021. <https://health.gov/healthypeople/objectives-and-data/browse-objectives/cancer/increase-proportion-adults-who-get-screened-colorectal-cancer-c-07> 3. <https://www.cdc.gov/cancer/colorectal/statistics/use-screening-tests-BRFSS.htm>, accessed January 5, 2022.

Compliance is more challenging in the working age population

33M average-risk patients aged 45-64 are not up to date



US Population Eligible for Noninvasive Screening, Age 45 – 64

Estimates based on ACS 2018 (BRFSS)

Colorectal Cancer Screening Compliance is hindered by the barriers patients face with current options

Many factors can prevent patient follow-through ¹⁻³

Stool-based test:

- Disgust with handling stool
- Hassle to complete
- Apprehension about accurately completing a test at home



Barriers



Colonoscopy:

- Discomfort
- Fear of an invasive procedure
- Time commitment (prep to procedure can be 2-3 days)

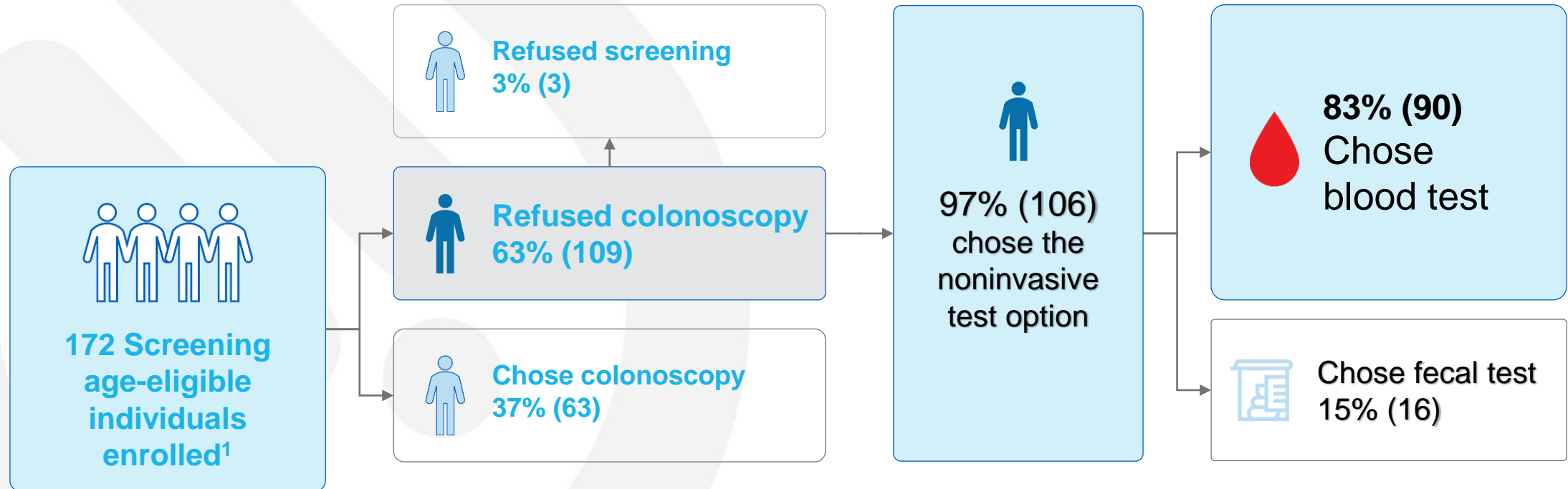


References:1. Liles EG, Coronado GD, Perrin N, et al. Uptake of a colorectal cancer screening blood test is higher than of a fecal test offered in clinic: a randomized trial. *Cancer Treat Res Comm.* 2017;10:27-31. doi:10.1016/j.ctarc.2016.12.004 2. Denberg TD, et al. *J Gen Intern Med.* 2005;20(11):989-995. 3. Parks, P. Innovation in Colorectal Cancer Screening - There Has to Be a Better Way. *AJMC.* <https://www.ajmc.com/view/innovation-in-colorectal-cancer-screening-there-has-to-be-a-better-way>. Accessed September 17, 2021.

A New Blood-based Test for CRC Screening



Noninvasive, blood-based testing is a more acceptable option for patients who refuse colonoscopy¹




Individuals who refuse colonoscopy are more willing to have a blood test than take a stool sample at home^{2,3}

1. Adler A, et al. *BMC Gastroenterol.* 2014;14:183. 2. Roth JA, et al. *Am Health Drug Benefits.* 2019;12(5):256-262. 3. Liles EG, et al. *Cancer Treat Res Comm.* 2017;10:27-31.

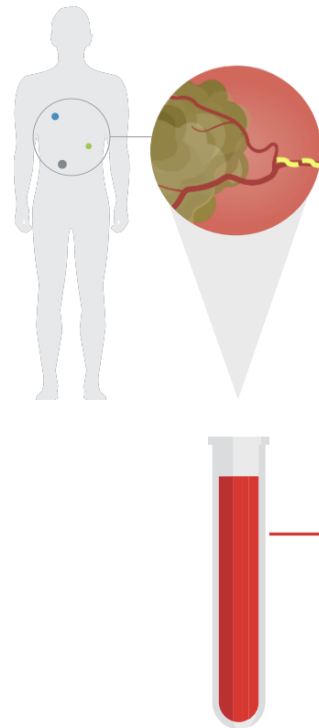
Patient survey demonstrates preference for blood test over stool and colonoscopy methods (n=559)



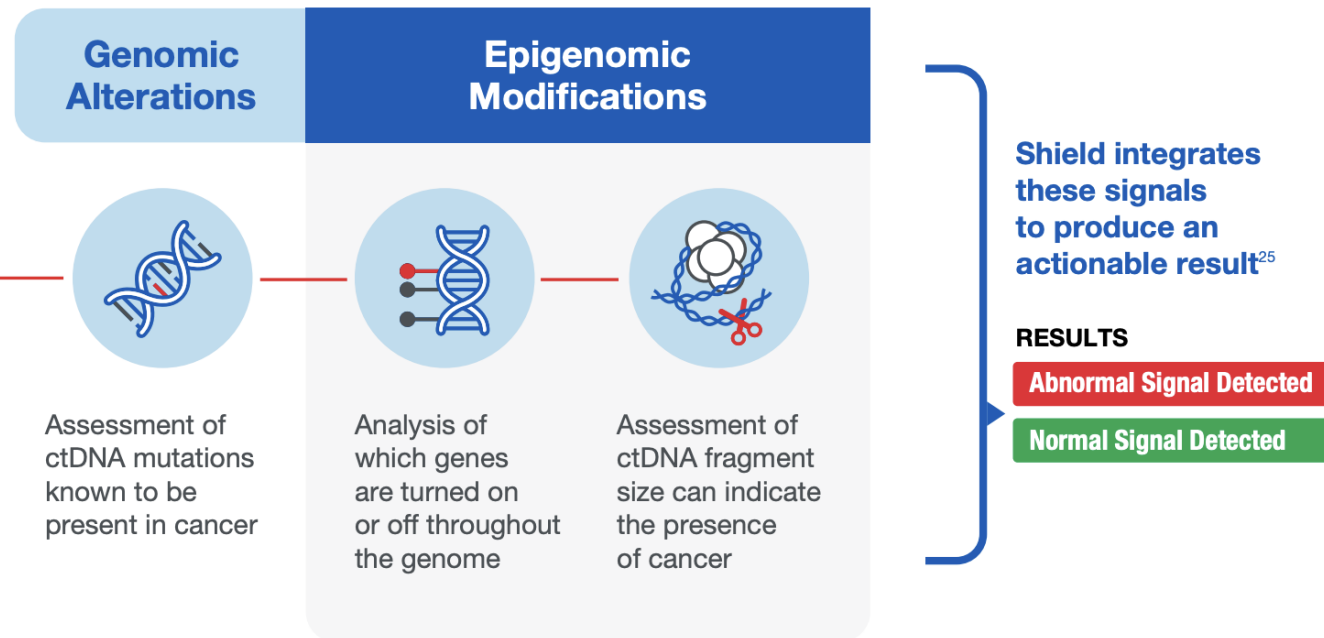
Of patients who have never been screened, a blood test was preferred almost 5:1 over a stool-based test

Previous Screening Modality	Future Screening Modality		
	 shield™	Stool	olonoscopy
olonoscopy only	42	5	53
ologuard only	51	29	17
F F B only	56	26	15
Ne er screened	65	14	21

Shield™ is an accurate blood test that uses a multimodal approach to detect CRC Technology^{2,16,22}



Shield assesses for DNA shed by tumors, called circulating tumor DNA (ctDNA) to detect colorectal cancer through a simple blood draw²²



2. Kim ST, Raymond VM, Park JO, et al. Combined genomic and epigenomic assessment of cell-free circulating tumor DNA (ctDNA) improves assay sensitivity in early-stage colorectal cancer (CRC). *Cancer Res.* 2019;79(suppl 13):916. doi:10.1158/1538-7445.AM2019-916 16. Westesson O, Axelrod H, Dean J, et al. Integrated genomic and epigenomic cell-free DNA (cfDNA) analysis for the detection of early-stage colorectal cancer. *Cancer Res.* 2020;80(suppl 16):2316. doi:10.1158/1538-7445.AM2020-2316 22. Lee J, Kim HC, Kim ST, et al. Multimodal circulating tumor DNA (ctDNA) colorectal neoplasia detection assay for asymptomatic and early-stage colorectal cancer (CRC). *J Clin Oncol.* 2021;39(15_suppl):3536. doi:10.1200/jco.2021.39.15_suppl.3536 25. The genetics of cancer. American Society of Clinical Oncology. Updated March 2018. Accessed April 6, 2022. <https://www.cancer.net/navigating-cancer-care/cancer-basics/genetics/genetics-cancer>

ECLIPSE Validates Shield™ as a high-sensitivity blood test for CRC screening that is easy to complete*

Sensitivity^{27*†}

83%

CRC Overall

Specificity^{27*‡}

90%



ECLIPSE is one of the largest studies and the first of its kind to validate a blood test that detects CRC with high sensitivity³⁰

- Validated Shield in over 10,000 patients¹⁷
- Included a diverse population representative of US demographics with broad ethnic and socioeconomic backgrounds^{27,30§}
- Patients aged 45 to 84 at average risk for CRC^{30†}

*The ECLIPSE study (NCT04136002) is comparing the sensitivity and specificity of cfDNA only Shield with findings from subsequent colonoscopy in over 10,000 average-risk patients.^{17,27}

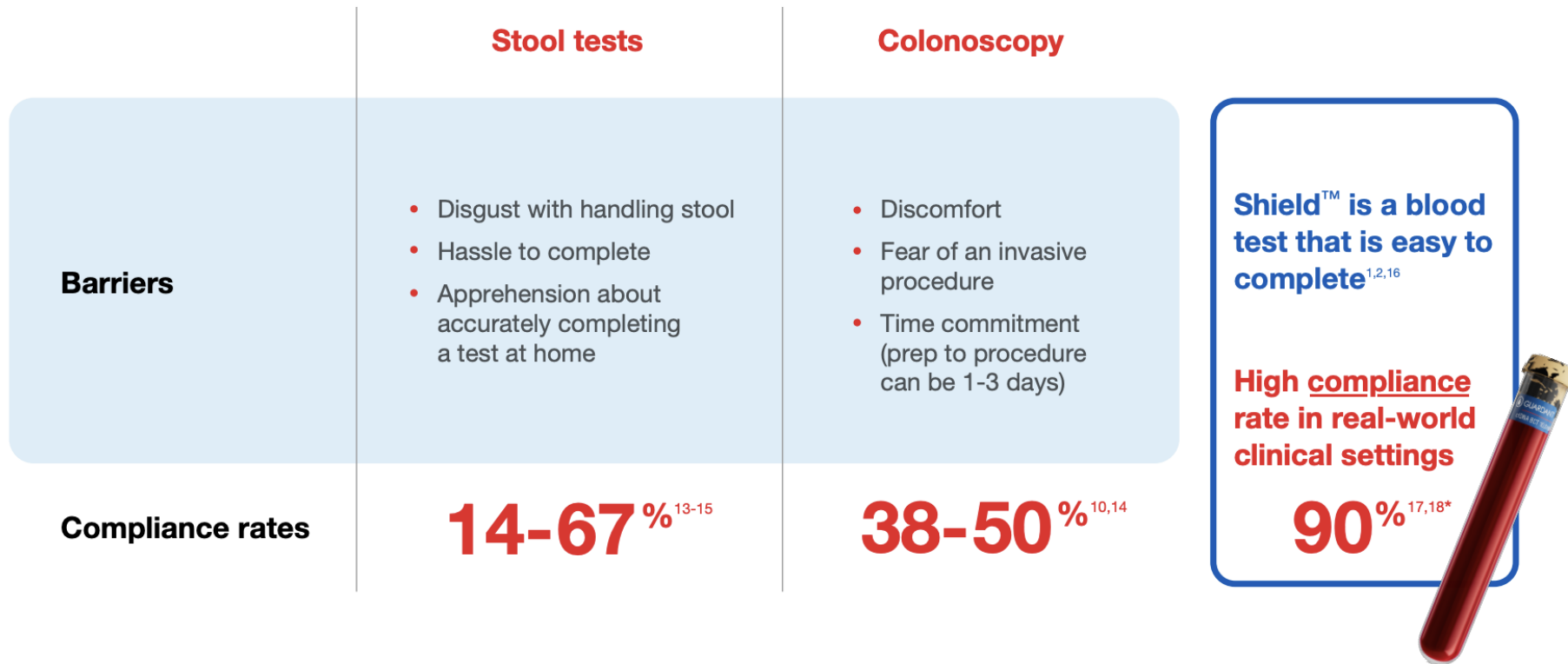
†Patients had no prior diagnosis of CRC, inflammatory bowel disease, or family history of genetic risk for CRC (eg, Lynch syndrome).³⁰

‡Specificity detected for advanced neoplasia defined in ECLIPSE as CRC or advanced adenomas.^{17,30}

§With more than 200 clinical trial sites in rural and urban communities across 34 states, study participant demographics included 13% Black, 15% Hispanic, and 7% Asian American populations. The study achieved above-average enrollment among Black Americans for a clinical trial.^{27,31}

Compliance Rates Remain Stagnant and Low with Current Stool Tests and Colonoscopy⁸

Many factors can prevent patient follow-through for more conventional methods⁹⁻¹²





*Compliance rate for the first 8,000 patients that were prescribed Shield and completed it.¹⁸

References: 9. Liles EG, Coronado GD, Perrin N, et al. Uptake of a colorectal cancer screening blood test is higher than of a fecal test offered in clinic: a randomized trial. *Cancer Treat Res Commun.* 2017;(10):27-31. doi:10.1016/j.ctarc.2016.12.004 10. Denberg TD, Melhado TV, Coombes JM, et al. Predictors of nonadherence to screening colonoscopy. *J Gen Intern Med.* 2005;20(11):989-995. doi:10.1111/j.1525-1497.2005.00164.x 11. Parks P. Innovation in colorectal cancer screening - there has to be a better way. *Am J Manag Care.* Published October 9, 2017. Accessed September 17, 2021. <https://www.ajmc.com/View/innovation-in-colorectal-cancer-screening-there-has-to-be-a-better-way> 12. Colonoscopy. American Society of Clinical Oncology. Updated December 2019. Accessed December 7, 2021. <https://www.cancer.net/navigating-cancer-care/diagnosing-cancer/tests-and-procedures/colonoscopy> 13. Gellad ZF, Stechuchak KM, Fisher DA, et al. Longitudinal adherence to fecal occult blood testing impacts colorectal cancer screening quality. *Am J Gastroenterol.* 2011;106(6):1125-1134. doi:10.1038/ajg.2011.11 14. Inadomi JM, Vijan S, Janz NK, et al. Adherence to colorectal cancer screening: a randomized clinical trial of competing strategies. *Arch Intern Med.* 2012;172(7):575-582. doi:10.1001/archinternmed.2012.332 15. Exact Sciences. Third quarter 2019 webcast and conference call. Updated October 29, 2019. Accessed December 17, 2021. <https://investor.exactsciences.com/investor-relations/events-and-presentations/event-details/2019/Third-Quarter-2019-Webcast-Conference-Call/default.aspx> 16. Westesson O, Axelrod H, Dean J, et al. Integrated genomic and epigenomic cell-free DNA (cfDNA) analysis for the detection of early-stage colorectal cancer. *Cancer Res.* 2020;80(suppl 16):2316. doi:10.1158/1538-7445.AM2020-2316 17. Data on File. Guardant Health. 18. Guardant Health. Q3 2022 Earnings Call. Accessed November 30, 2022. https://s26.q4cdn.com/594050615/files/doc_financials/2022/q3/Q3-2022-Earnings-Presentation-Final.pdf

Effectiveness Analysis Suggests that Shield would Dramatically Improve Real-World CRC Detection

1 Adherence by modality

2 Performance (Sensitivity-Specificity)

	Adherence	Sensitivity	Specificity	Effective Sensitivity	Lifetime CRCs detected per million ⁸
 shield™	90% ¹	83% ⁵	90% ⁵	75%	30k
 cologuard [®]	65% ²	92% ⁶	87% ⁶	60%	24k
FIT	43% ³	74% ⁶	95% ⁶	32%	13k
Colonoscopy	42% ⁴	95% ⁷	94% ⁷	40%	16k

1. Shield LDT Internal Data 2. EXACT Sciences Q2 2022 Earnings 3. Jensen CD, Corley DA, Quinn VP, et al. Fecal immunochemical test program performance over 4 rounds of annual screening: a retrospective cohort study. Ann Intern Med. 2016;164(7):456-63 4. Bretthauer M, Loberg M, Wieszczy P, et al: Effect of colonoscopy screening on risks of colorectal cancer and related death. 5. Guardant Press ECLIPSE Press Release 6. Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. Multitarget stool DNA testing for colorectal-cancer screening. 7. JAMA March 9, 2021 Volume 325, Number 10. 8. Lifetime CRC incident 4 in 100, <https://seer.cancer.gov/staffacts/html/colorect.html>

Summary

- ECLIPSE study validates Shield for blood-based CRC screening with comparable performance to currently available stool-based screening options
- Real-world adherence to Shield, > 90%, far exceeds adherence rates with the options available today (~67%)
- A CRC screening strategy that leverages blood-based testing with performance such as seen in Shield and high adherence has the potential to significantly positively impact the CRC screening ecosystem



Shield™ Patient Result Explainer



Shield LDT | Patient Result Explainer

PaulsonzTK, Andrew

Patient MRN: MRNAUT6774661

DOB: Oct-19-1966

Biological Sex: Female

SPECIMEN INFORMATION		AUTHORIZING PHYSICIAN	
Order ID:	ORSQA0000016489	Provider Name:	RUTH ABRAMS
Collection Date:	Nov-02-2022	Facility/Clinic:	AUT-Grand Health Hospital
Receipt Date:	Nov-02-2022	Address:	876 California 49
Report Date:	Nov-02-2022		Angels Camp CA US 95222
Specimen Type:	Blood	Phone:	408-480-3731
Status:	FINAL	Account ID:	GHSA-00010950

Result: Normal Signal Detected

What Does the Result Mean?

Your Shield LDT test result indicates a signal associated with a colorectal tumor was not detected.

What are the Next Steps?

- If you have any questions, please get in contact with the healthcare provider who ordered this test.
- Follow your doctor's instructions to remain up to date with guideline-recommended screening programs.
- You can also check educational resources on our online portal GuardantGo.com/Patient

Methods and Limitations

The Shield LDT test is a combination of a next generation sequencing (NGS)-based assay and a protein assay for the qualitative detection of colorectal neoplasia-derived tumor signal in the blood of patients at average-risk for colorectal cancer (CRC). Cell-free DNA (cfDNA) is extracted from plasma, sequenced, and the data analyzed for the presence of genomic and epigenomic alterations in CRC. Protein signal is analyzed by an immunoassay. Based on this analysis, the Shield LDT test returns a binary result of either: Abnormal Signal Detected or Normal Signal Detected. Patients with an Abnormal Signal Detected result should be referred for colonoscopic evaluation. A Normal Signal Detected result does not preclude the presence of colorectal neoplasia, and patients should continue participating in guideline recommended screening programs. The Shield LDT test is not validated for stand-alone use in the diagnosis of cancer, but is instead intended to complement standard of care screening modalities in patients who are at average risk for CRC.

About the Test

The Shield LDT test was developed and its performance characteristics were determined by Guardant Health, Inc. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). This test may be used for clinical purposes and should not be regarded as investigational or for research only.

Guardant Health's clinical laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical laboratory testing. The results should be interpreted in the context of other clinical information and laboratory, pathology, and imaging studies by a qualified medical professional prior to initiating or changing a patient's treatment plan.

Testing performed at: Guardant Health, Inc. | 505 Penobscot Drive | Redwood City, CA 94063 | USA
Laboratory Director: Martina Lefterova, MD PhD | CLIA ID: 05D2070300 | CAP #: 8765297

REC-REG-000438 R3



Shield LDT | Patient Result Explainer

Hunter, Levi

Patient MRN: N/A

DOB: Oct-31-1965

Biological Sex: Male

SPECIMEN INFORMATION		AUTHORIZING PHYSICIAN	
Order ID:	ORSQA0000016296	Provider Name:	Sean Paul
Collection Date:	Nov-01-2022	Facility/Clinic:	Stanford Hospital
Receipt Date:	Nov-01-2022	Address:	2020 BLVD Street 600
Report Date:	Nov-01-2022		SANTA MONICA CA US 90404
Specimen Type:	Blood	Phone:	408-480-3731
Status:	FINAL	Account ID:	GHSA-00005258

Result: Abnormal Signal Detected ⚠️

What Does the Result Mean?

This result raises concern for the presence of a colorectal tumor and should be discussed with a physician. A diagnostic colonoscopy may be necessary to determine whether colorectal cancer is present.

What are the Next Steps?

- If you haven't already, please get in contact with the healthcare provider who ordered this test.
- A Patient Navigator from Guardant Health with specialized experience in screening and education, is available to address your questions and can be contacted at 855.722.7335 or ScreeningPatient@guardanthealth.com
- You can also check educational resources on our online portal GuardantGo.com/Patient

Methods and Limitations

The Shield LDT test is a combination of a next generation sequencing (NGS)-based assay and a protein assay for the qualitative detection of colorectal neoplasia-derived tumor signal in the blood of patients at average-risk for colorectal cancer (CRC). Cell-free DNA (cfDNA) is extracted from plasma, sequenced, and the data analyzed for the presence of genomic and epigenomic alterations in CRC. Protein signal is analyzed by an immunoassay. Based on this analysis, the Shield LDT test returns a binary result of either: Abnormal Signal Detected or Normal Signal Detected. Patients with an Abnormal Signal Detected result should be referred for colonoscopic evaluation. A Normal Signal Detected result does not preclude the presence of colorectal neoplasia, and patients should continue participating in guideline recommended screening programs. The Shield LDT test is not validated for stand-alone use in the diagnosis of cancer, but is instead intended to complement standard of care screening modalities in patients who are at average risk for CRC.

About the Test

The Shield LDT test was developed and its performance characteristics were determined by Guardant Health, Inc. This test has not been cleared or approved by the U.S. Food and Drug Administration (FDA). This test may be used for clinical purposes and should not be regarded as investigational or for research only.

Guardant Health's clinical laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA) as qualified to perform high complexity clinical laboratory testing. The results should be interpreted in the context of other clinical information and laboratory, pathology, and imaging studies by a qualified medical professional prior to initiating or changing a patient's treatment plan.

Testing performed at: Guardant Health, Inc. | 505 Penobscot Drive | Redwood City, CA 94063 | USA
Laboratory Director: Martina Lefterova, MD PhD | CLIA ID: 05D2070300 | CAP #: 8765297

REC-REG-000438 R3