

Clinical Validation of a Blood-Based Test for the Early Detection of Colorectal Cancer (PREEMPT CRC)

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Disclosure information

Aasma Shaukat, MD, MPH

- I disclose the following financial relationship:
 - Consultant for Freenome Holdings, Inc. and Iterative Health

Background



Colorectal cancer is the second deadliest cancer in the US¹



Blood-based screening provides another modality to help increase screening adherence beyond colonoscopy and stool-based tests³



In the US, screening rates remain suboptimal²

of eligible individuals aged 45 years and older were up to date with CRC screening as of 2021



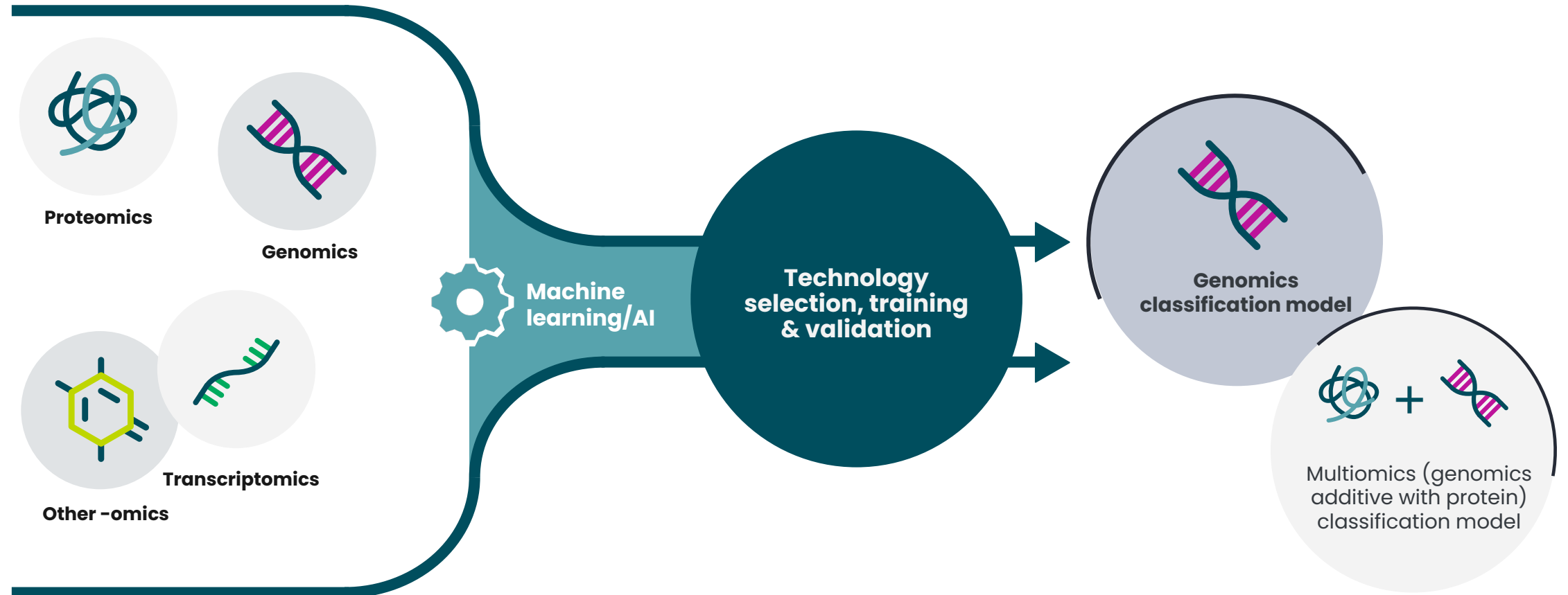
Clinical performance of an investigational blood-based test in an average-risk population was assessed in the PREEMPT CRC Study (NCT04369053)

1. American Cancer Society. *Colorectal Cancer Facts & Figures 2023-2025*. Atlanta: American Cancer Society; 2023. 2. Siegel RL, et al. *CA Cancer J Clin*. 2023;73(3):233-254. 3. Liang PS, et al. *Clin Gastroenterol Hepatol*. 2023;21(11):2951-2957.e2.

Blood-based colorectal cancer screening test

Detecting signatures associated with advanced colorectal neoplasia (ACN) in plasma derived from whole blood samples

Development platform



AI, artificial intelligence.

PREEMPT CRC^{1,2}

The objective is to determine the performance of a blood-based test using screening colonoscopy with histopathology as the reference method

Enrollment

May 2020 through April 2022



Study population

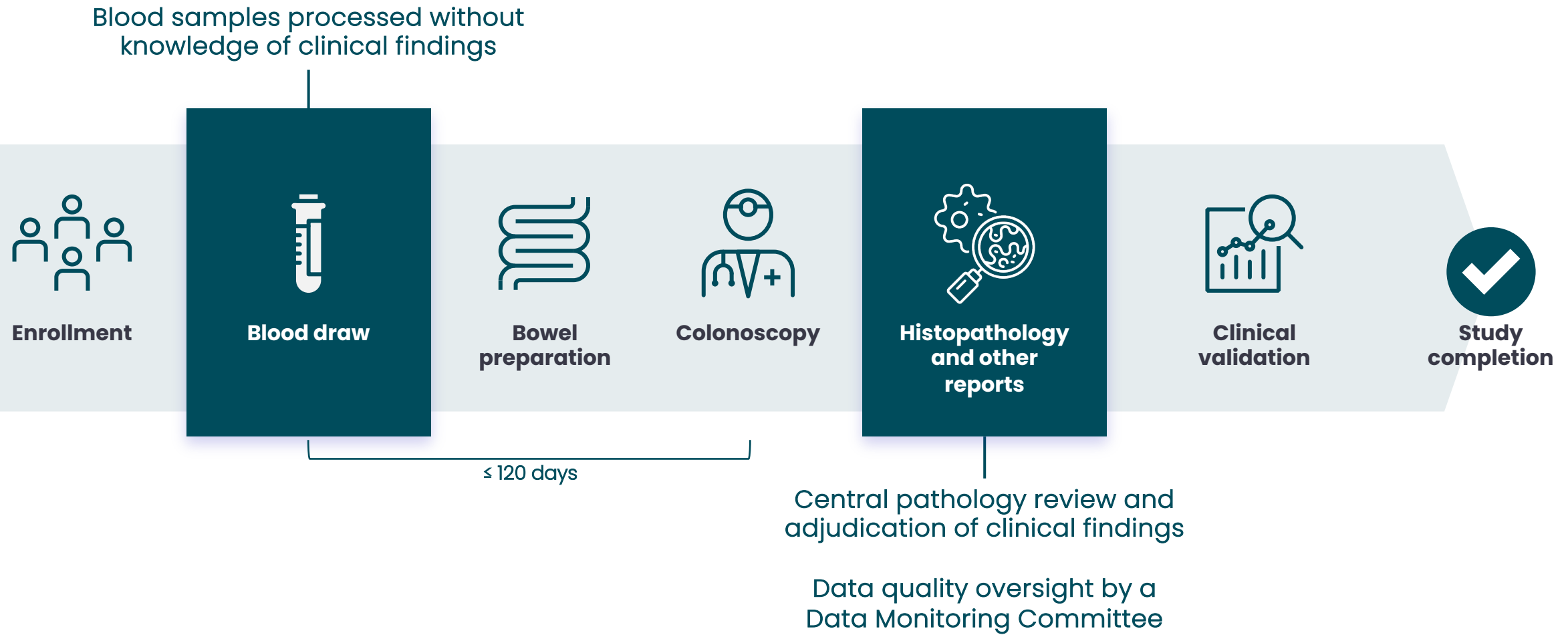
Adults aged 45–85 at average risk for colorectal cancer

- No personal history of CRC, colorectal adenoma, or inflammatory bowel disease
- No family history of CRC or hereditary gastrointestinal cancer syndromes
- Screen-eligible

CRC, colorectal cancer.

1. Shaikat A, et al. Presented at: Digestive Disease Week 2024; May 18–21, 2024; Washington, DC, USA. Abstract Sall23. 2. Cotliar J, et al. Presented at: Digestive Disease Week 2024; May 18–21, 2024; Washington, DC, USA. Abstract Sall30.

PREEMPT CRC study methods^{1,2}



CRC, colorectal cancer.

1. Shaukat A, et al. Presented at: Digestive Disease Week 2024; May 18-21, 2024; Washington, DC, USA. Abstract Sall23. 2. Cotliar J, et al. Presented at: Digestive Disease Week 2024; May 18-21, 2024; Washington, DC, USA. Abstract Sall30.

PREEMPT CRC endpoints

Primary endpoints

- Sensitivity for colorectal cancer
- Specificity for non-advanced colorectal neoplasia (non-ACN)*
- Negative predictive value for non-ACN
- Positive predictive value for ACN

Secondary endpoint

- Sensitivity for advanced adenoma (AA)†

*ACN comprised CRC and advanced adenoma.

†Advanced adenomas include carcinoma in situ or high-grade dysplasia, adenoma with villous growth pattern ($\geq 25\%$), adenoma ≥ 1.0 cm, sessile serrated adenoma/polyp ≥ 1.0 cm, and traditional serrated adenoma, colorectal cancer.

Clinical validation analysis



Clinical validation cohort

Consecutive participants enrolled after a predetermined cutoff date*

≥96%

Power

All primary and secondary endpoints were powered at 96% or greater



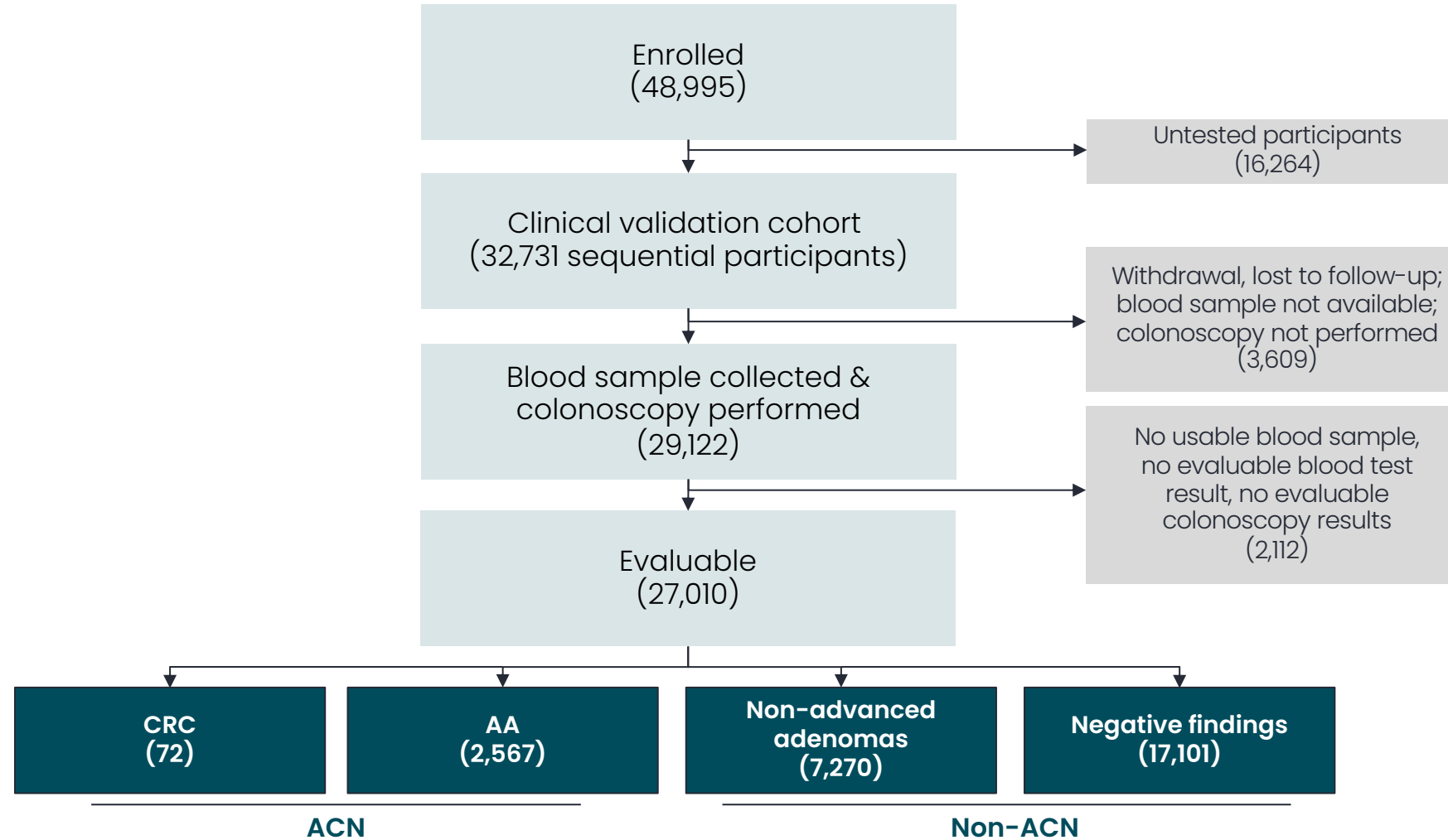
Classification models

Endpoints of both models were pre-specified to be evaluated in sequence: respective evaluation criterion must be met before proceeding with the next evaluation



*April 5, 2021; corresponding to expanded eligibility of COVID-19 vaccination for the overall population and a return to more normal office visits.

Study participants



AA, advanced adenomas; ACN, advanced colorectal neoplasia; CRC, colorectal cancer.

Study participants

Demographic characteristics	Evaluable (n=27,010)	
Age (years)		
Mean (SD)	58.1 (8.2)	
Median	57	
	n	%
Age Group		
45-49	2,968	11.0
50-54	8,899	32.9
55-65	8,725	32.3
65-74	5,604	20.7
≥ 75	814	3.0
Biological Sex		
Female	15,076	55.8
Male	11,934	44.2
Race		
White	19,707	73.0
Black or African American	3,038	11.2
Asian	2,381	8.8
American Indian or Alaska Native	78	0.3
Native Hawaiian or Other Pacific Islander	72	0.3
More than one reported	136	0.5
Other/unknown	1,598	5.9
Ethnicity		
Hispanic or Latino	3,189	11.8
Not Hispanic or Latino	22,421	83.0
Unknown	1,400	5.2

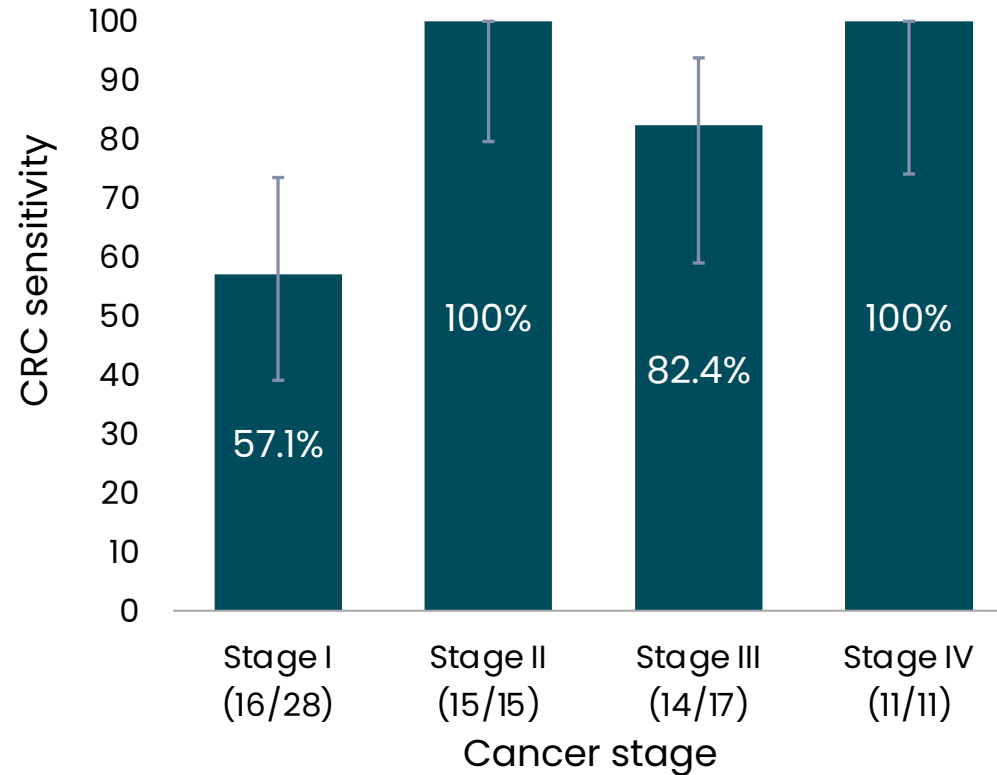
Percentages may not total 100 because of rounding.

PREEMPT CRC met all pre-specified primary endpoints

Endpoint	Genomics (N=27,010)		Multiomics (N=26,931)	
	Fraction (n/N)	Value (95% CI)	Fraction (n/N)	Value (95% CI)
Sensitivity for CRC	57/72	79.2% (68.4%, 86.9%)	56/72	77.8% (66.9%, 85.8%)
Specificity for non-ACN	22,306/24,371	91.5% (91.2%, 91.9%)	22,762/24,301	93.7% (93.4%, 94.0%)
Negative predictive value for non-ACN*	22,306/24,567	90.8% (90.7%, 90.9%)	22,762/25,061	90.8% (90.7%, 91.0%)
Positive predictive value for ACN	378/2,443	15.5% (14.2%, 16.8%)	331/1,870	17.7% (16.1%, 19.4%)

*Non-ACN was defined as the absence of CRC or advanced adenoma.
ACN, advanced colorectal neoplasia; CRC, colorectal cancer.

Sensitivity for CRC by stage (genomics)



All CRCs were staged except for one case (1/1 detected)*

*Stages as defined by the American Joint Committee on Cancer Staging System, 8th edition.
Error bars indicate 95% confidence interval.
CRC, colorectal cancer.

Sensitivity for advanced adenoma (genomics)

Sensitivity	Fraction (n/N)	Value (95% CI)
Advanced adenoma	321/2,567	12.5% (11.3%, 13.8%)
High-grade dysplasia or carcinoma in situ*	32/110	29.1% (21.4%, 38.2%)

*Pre-specified analysis supportive of secondary endpoint.

Adjustment to CMS NCD specificity cutoff

	Genomics (N=27,010)	Multionics (N=26,931)
Endpoint	Observed	Observed
Sensitivity for CRC	79.2%	77.8%
Specificity for non-ACN	91.5%	93.7%
Sensitivity for AA	12.5%	10.8%

AA, advanced adenoma; ACN, advanced colorectal neoplasia; CMS, Centers for Medicare and Medicaid Services; CRC, colorectal cancer; NCD, National Coverage Determination.

Adjustment to CMS NCD specificity cutoff

Endpoint	Genomics (N=27,010)	Multiomics (N=26,931)	Genomics (N=27,010)	Multiomics (N=26,931)
	Observed	Observed	Adjusted	Adjusted
Sensitivity for CRC	79.2%	77.8%	79.2%	80.6%
Specificity for non-ACN	91.5%	93.7%	90.0%	
Sensitivity for AA	12.5%	10.8%	14.8%	16.4%

- When specificity was adjusted to the CMS NCD cutoff of 90%, there was a corresponding modest increase in the sensitivity for AA while maintaining CRC sensitivity for the genomics model
- With the addition of protein, an improved sensitivity for both CRC (80.6%) and AA (16.4%) at the 90% cutoff was observed

Limitations



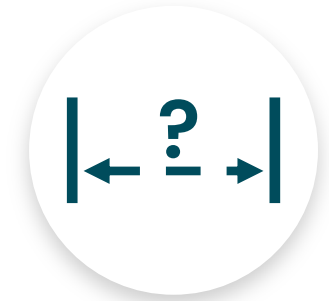
Incidence and mortality impact

The study was not designed to assess the impact of this blood-based test on CRC incidence and mortality



Test comparison

The study was not designed to compare adherence and effectiveness of different CRC screening tests



The testing intervals

The study was not designed to determine the testing interval

Conclusions and future directions



PREEMPT CRC is the largest study evaluating a blood-based CRC screening test and enrolled a diverse US population



PREEMPT CRC successfully met the primary endpoints demonstrating **79.2% sensitivity for CRC** and **91.5% specificity for non-ACN**



This new blood-based test may provide a convenient and effective option for CRC screening in the intended use population



Work is currently ongoing to enhance the clinical performance of the test

The manufacturer looks forward to working with regulators to provide people with a convenient and accessible screening option

Acknowledgments

We thank the PREEMPT CRC:

- Study participants
- Investigators and site staff
- Data Monitoring Committee
- Study team and study partners

Healthcare Consultancy Group provided editorial assistance and creative design, funded by Freenome Holdings, Inc.

PREEMPT CRC study sites (1/2)*

Intermountain
Paragon Rx Clinical - Santa Ana
Texas Gastroenterology Consultants
Gastroenterology Associates, PC
Northlake Gastroenterology Associates
Associated Gastroenterologists of Central New York, PC
Susquehanna Research Group, LLC
Advanced Research Institute
Great Lakes Gastroenterology Research, LLC
Louisiana Research Center, LLC
Digestive Healthcare Center
Universal Axon Clinical Research
Gastro Care Institute
Southeast Valley Gastro (SEVG)
Gastroenterology Partners of North Houston
Syracuse Gastroenterological Associates
University of Minnesota
Gastroenterology Associates of Mississippi
Blair Gastroenterology Associates
GI Partners of Illinois - Southwest Gastroenterology
Knowledge Research Center
IHS Health
Paragon Rx Clinical - Garden Grove
Tri-State Gastroenterology Associates, PSC
Gastroenterology Consultants
Chevy Chase Clinical Research
DSI Research
Mark Coronel, MD
Springfield Clinic, LLP
North Jersey Gastroenterology
Birmingham Gastroenterology Associates
Hope Digestive and Liver Disease Clinic of Houston
ENCORE Borland Groover Clinical Research
Gastroenterology Consultants of Augusta

Gastroenterology Associates of New Jersey
Metro Atlanta Gastroenterology, LLC
Consultants in GI
Sutter Institute For Medical Research
Eastern Pennsylvania GI & Liver Specialists
Gastroenterology Associates of New Jersey
Digestive Health Research of North Texas
University of Chicago
Miller BioConnect - CA location (Ascada Research)
Ocala GI Research
Hackensack Digestive Disease Associates
Gastro Center of Maryland
Hillel Cohen
UPMC Digestive Diseases Ctr GAS
Advanced Gastroenterology
Northlake Gastroenterology Associates
South Suburban Gastroenterology
Oregon Health & Science University
Cary Gastro
Gastroenterology Associates of NJ (GANJ)
Sam Moskowitz, MD
Digestive Diseases Consultants of Kankakee
Gastroenterology Associates of New Jersey
Kaiser Permanente Northern California
Morehouse
Associated Gastroenterology Medical Group
Woodholme Gastroenterology Associates
Pharmax Research Clinic
Digestive and Liver Disease Specialists, Ltd.
Los Angeles Gastroenterology Institute
William S. Silver MD & Eric L. Tatar MD PC
Inland Empire GI
Central Florida Gastro Research

Princeton GI Associates
Precision Research Institute, LLC
Massachusetts General Hospital
Mercy Washington
University of California San Diego Medical Center
AIG Digestive Disease Research
Beth Israel Deaconess Medical Center
Teaneck Gastroenterology Associates
The Oregon Clinic, P.C.
Valley Gastroenterology Associates
American Health Network of Indiana, LLC
Advanced Gastroenterology Group
Hospital of the University of Pennsylvania
Suburban Gastroenterology
Delaware Center for Digestive Care
Mohan, Uma Yanamadala
Long Island Gastrointestinal Specialists
Digestive Disease Research Center
Digestive Research Alliance of Michiana
Gastrointestinal Associates, S.C.
Gastrointestinal Associates of Rockland
Summit Medical Group Oregon - BMC
IACT Health
Gastroenterology Associates, PA
Tri-Cities Gastroenterology
Precision Research Institute, LLC
Gastroenterology Consults
Digestive Health Associates
Cotton-O'Neil Clinical Research Center, Digestive Health
Gastrointestinal Specialists of Georgia
Digestive Health Services/GI Partners of Illinois
Valley Gastroenterology Associates
Bay Pines VA Healthcare System
Naugatuck Valley GI Consultants

*In the order of enrollment.

PREEMPT CRC study sites (2/2)*

Palmetto Research, LLC
Kansas Gastroenterology, LLC
Gastroenterology Associates of Wyoming
Digestive System Healthcare
Delta Research Partners - Monroe
Panamericana Family Medicine Clinic
Acadiana GI Associates - Louisiana
South Island Gastro
GastroCare LI
Ocean Family Gastroenterology
Delta Research Partners - Bastrop
Citrus Valley Gastroenterology
Premier Gastroenterology Associates - Arkansas
Carolinas GI Research, LLC
Advanced Research Institute
University of Kansas Medical Center (KUMC)
Cleveland Clinic Foundation
Southeast Medical Research II, LLC
Gastroenterology Practice Associates
East Tennessee Research Institute
Edward Hines, Jr. VA Hospital
University of North Carolina
Kansas City VA Medical Center
Texas Oncology Tyler
Gastrointestinal Associates
Trinity Health Center Medical Arts
Advanced Gastroenterology PC
Emory University School of Medicine
Florida Medical Clinic, LLC
VA Sierra Nevada
VA Southern Nevada
ARCare Center of Clinical Research
Augusta University
Pinnacle Research Group LLC

Pramukh Clinical Research
Vanderbilt University Medical Center
The Center for Gastrointestinal Disorders
Clinical Research of California LLC
Quincy Medical Group
Greater Boston Gastroenterology
Gastroenterology Associates of New Jersey
NorthShore University Health System
Icahn School of Medicine at Mount Sinai
Cincinnati GI
Drs. Howard N. Guss and Gagan Beri
Cleveland Clinic Abu Dhabi
Central Texas GI Consultants
St. John's Center for Clinical Research
University of Texas MD Anderson Cancer Center
GI Associates and Endoscopy Center
LV Gastroenterology Associates
University of Alabama at Birmingham
Washington Gastroenterology - Tacoma Clinic
Gastroenterology Consultants of SW Virginia
Kaiser Permanente Southern California
Texas Oncology - Amarillo
Gastroenterology Associates of New Jersey
Veterans Affairs Medical Center
Duke Clinic
Center for Digestive Diseases
University of Texas Health Science Center at Tyler
Gastrointestinal Associates
Matrix Clinical Research
Virginia Mason Hospital
Birmingham VA Medical Center - Alabama
Denver Digestive Health Specialists
AMR West Wichita, formerly Heartland Associates
West Wichita, an AMR Company

Rio Grande Gastroenterology
Center for Digestive Health
Ochsner Clinic Foundation
PMG Research of Winston-Salem, LLC
St. Joseph Heritage Healthcare
UW Medical Center
Thomas Jefferson University Hospital
Biopharma Informatic, Inc. Research Center
The Ohio State University Wexner Medical Center
Prisma Health Cancer Institute
Sean Lacey MD
Medical University of South Carolina (MUSC)
Digestive Disease Center of New Jersey
East Bay Center for Digestive Health
Hope Research Institute
UCSF Mount Zion Medical Center
NYU Grossman School of Medicine
Gastroenterology Associates of Cleveland, Inc.
Ertan Digestive Disease Center
Samuel S. Stratton VA Medical Center
Meharry Medical College
George Washington University
Gastroenterology Associates
AMR Newton, formerly Heartland Associates Newton
Southeast Georgia Gastroenterology, P.C.
UCLA Medical Center
Northwest Cancer Specialists
Texas Oncology - McKinney/Allen
Illinois Cancer Specialists
Gastroenterology Medical Associates
Gastroenterology Consultants of Brooklyn
Allied Gastrointestinal Associates P.A.
Science 37 (Decentralized Enrollment Platform)

*In the order of enrollment.

Thank you

