

Clinical Evaluation of a New Blood-Based Test for Colorectal Cancer Screening

Aasma Shaukat,¹⁻³ Zhen Meng,⁴ Andy Piscitello,⁴ Chuanbo Xu,⁴ Lilian C. Lee,⁴ Lance Baldo,^{4,a} Theodore R. Levin^{3,5}

¹New York University Grossman School of Medicine; New York, NY, US; ²University of Minnesota Twin Cities; Minneapolis, MN, US; ³On behalf of the PREEMPT CRC Investigators; ⁴Freenome Holdings, Inc.; South San Francisco, CA, US; ⁵Kaiser Permanente Division of Research; Pleasanton, CA, US

^aAffiliation at the time the study and/or analyses were conducted



INTRODUCTION

- Colorectal cancer (CRC) is the second most common cause of cancer-related death in the US, but is treatable when detected early¹
- Despite the proven benefits of CRC screening, greater than 40% of eligible adults at average risk for CRC in the US in 2021 were not up to date with guidelines²⁻⁴
- Low screening uptake can be partly attributed to the inconveniences associated with conventional screening methods as well as disparities in access to medical care (including CRC screening) among certain demographic groups^{2,5,6}
- Specific challenges of conventional screening methods include the bowel preparation and invasiveness associated with colonoscopy and fecal aversion associated with stool-based tests^{7,8}
- Individuals may be more receptive to blood-based tests (BBTs) compared with conventional methods, which may help individuals overcome some barriers to screening^{9,10}
- PREEMPT CRC (NCT04369053¹¹), a prospective, multicenter observational study, was conducted to validate an investigational BBT designed to detect molecular signals associated with CRC using machine learning (ML) and artificial intelligence (AI) technologies in an average-risk, screening-eligible population

OBJECTIVE

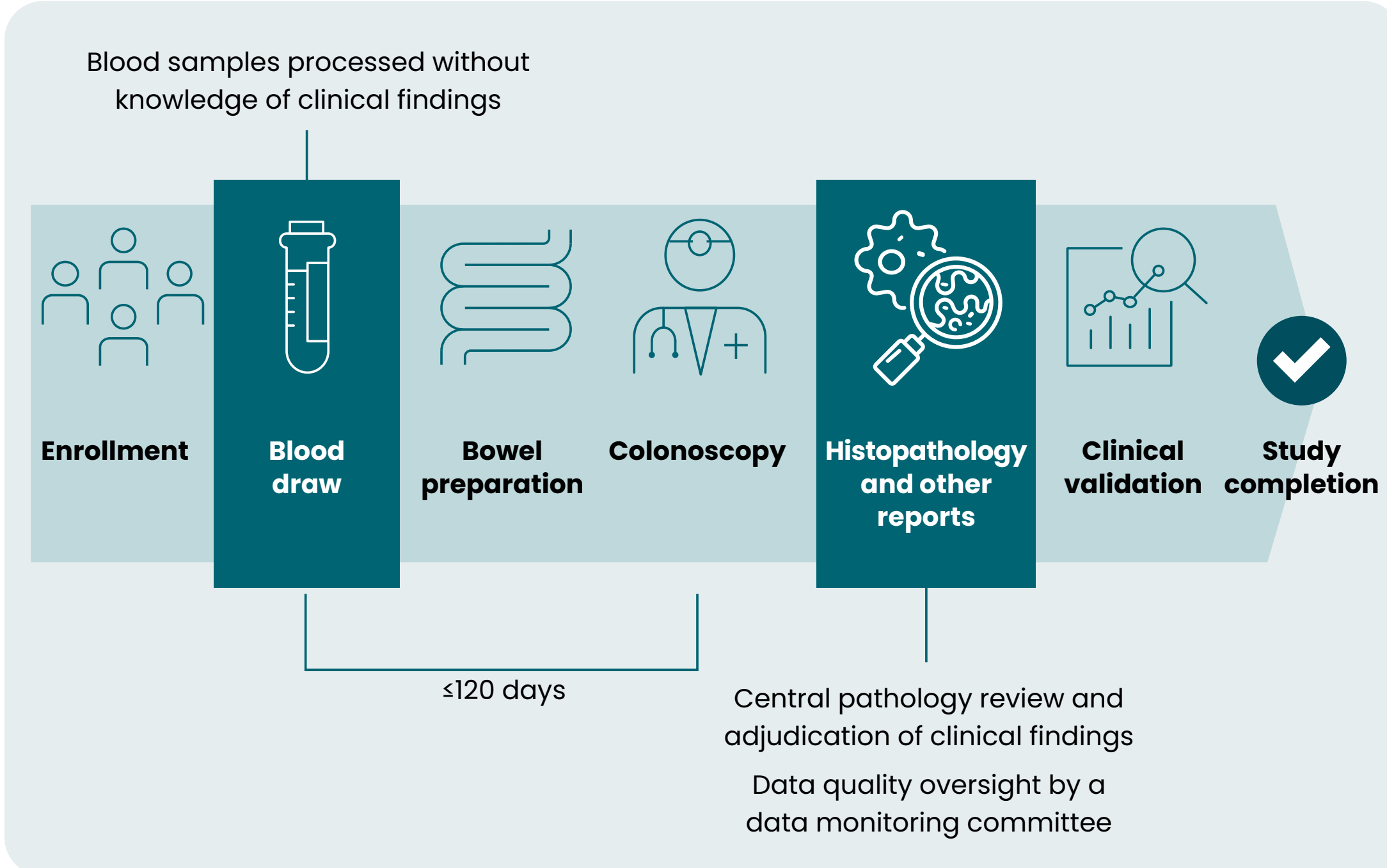
- To provide an assessment of the clinical performance of an investigational BBT evaluating molecular signals for the early detection of CRC in an average-risk population

METHODS

Study design

- Participants were 45 to 85 years of age, at average risk for CRC, and willing to undergo a standard-of-care screening colonoscopy to be eligible for enrollment
- Prior to bowel preparation for colonoscopy, participants provided a blood sample for testing
- Colonoscopy was performed within 120 days of the blood draw (Figure 1)
- Colonoscopy and applicable histopathology reports underwent central review
- A data monitoring committee had oversight of data quality
- Blood samples were processed blind to clinical findings, and all participants, research physicians, and central pathologists remained blind to the results of the blood test

Figure 1. PREEMPT CRC study schema



AI/ML model training

- A classification model was established using ML and AI technologies to derive proprietary methylated-DNA signatures associated with advanced colorectal neoplasia (ACN)
- Plasma isolated from whole blood samples was analyzed to generate a binary result by comparing with a threshold learned during model training

Test validation

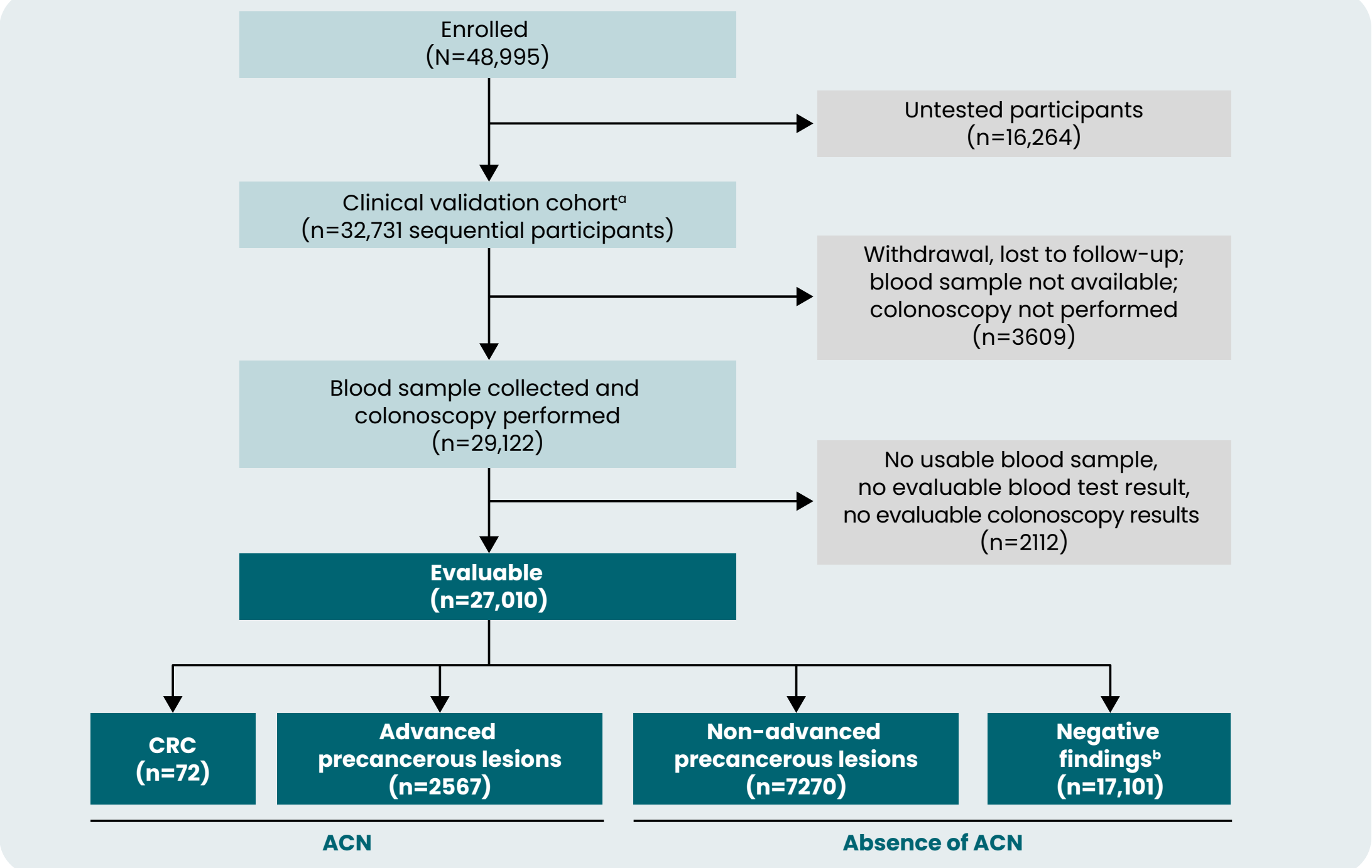
- The performance of the investigational BBT was assessed using screening colonoscopies with histopathology as the reference method
- The four prespecified primary endpoints included sensitivity for CRC, specificity for ACN, negative predictive value (NPV) for ACN, and positive predictive value (PPV) for ACN
 - ACN was composed of CRC and advanced precancerous lesions
 - Advanced precancerous lesions included carcinoma in situ or high-grade dysplasia, adenoma with villous growth pattern (≥25%), adenoma ≥1.0 cm, sessile serrated lesion with or without cytological dysplasia ≥1.0 cm, and traditional serrated adenoma
 - NPV for ACN was defined as the proportion of participants without a diagnosis of CRC or advanced precancerous lesions among those who had a negative test result
 - PPV for ACN was defined as the proportion of participants with a diagnosis of CRC or advanced precancerous lesions among those who had a positive test result
- A secondary endpoint assessed the test's sensitivity for advanced precancerous lesions

RESULTS

Participant demographics

- Of 48,995 study participants originally enrolled in PREEMPT CRC between May 2020 and April 2022, a subset of 32,731 sequentially enrolled participants were included in the clinical validation cohort (Figure 2)
 - Of these, 82.5% (n=27,010) had evaluable blood samples and colonoscopy results

Figure 2. Evaluable study participants



*The clinical validation cohort included 32,731 participants consecutively enrolled after a predetermined cutoff date that coincided with a study protocol amendment in which further COVID-19 mitigations were implemented and generally coincides with vaccine expansion to all adults in the United States.
 *Negative findings include non-neoplastic or no findings.
 ACN, advanced colorectal neoplasia; CRC, colorectal cancer.

- The mean age of evaluable participants was 58.1 years, and 55.8% were female
- The study enrolled a diverse population, with 11.2% of evaluable participants identifying as Black or African American, 8.8% identifying as Asian, and 11.8% identifying as Hispanic or Latino (Table 1)

Table 1. Baseline demographics

Demographic characteristics	Evaluable participants ^a (N=27,010)
Age (years)	
Mean (SD)	58.1 (8.2)
Median	57
Age Group, n (%)	
45-49	2968 (11.0)
50-54	8899 (32.9)
55-64	8725 (32.3)
65-74	5604 (20.7)
≥75	814 (3.0)
Biological Sex, n (%)	
Female	15,076 (55.8)
Male	11,934 (44.2)
Race, n (%)	
White	19,707 (73.0)
Black or African American	3038 (11.2)
Asian	2381 (8.8)
American Indian or Alaskan Native	78 (0.3)
Native Hawaiian or Other Pacific Islander	72 (0.3)
More than one reported	136 (0.5)
Other/unknown	1598 (5.9)
Ethnicity, n (%)	
Hispanic or Latino	3189 (11.8)
Not Hispanic or Latino	22,421 (83.0)
Unknown	1400 (5.2)

^aPercentages may not total 100 because of rounding.

Test performance for primary and secondary outcome measures

- PREEMPT CRC met all primary endpoints (Table 2)

Table 2. Test performance for primary and secondary outcome measures

Primary endpoints	Total evaluated (n/N)	% (95% CI)
Sensitivity for CRC	57/72	79.2% (68.4%–86.9%)
Specificity for ACN	22,306/24,371	91.5% (91.2%–91.9%)
NPV for ACN	22,306/24,567	90.8% (90.7%–90.9%)
PPV for ACN	378/2443	15.5% (14.2%–16.8%)
Secondary endpoint	Total evaluated (n/N)	% (95% CI)
Sensitivity for advanced precancerous lesions	321/2567	12.5% (11.3%–13.8%)

ACN, advanced colorectal neoplasia; CRC, colorectal cancer; NPV, negative predictive value; PPV, positive predictive value.

KEY FINDINGS AND CONCLUSIONS

- PREEMPT CRC is the largest prospective study of a BBT for CRC in an average-risk population to date
- With a sensitivity for CRC of 79.2% and specificity for ACN of 91.5%, the investigational BBT met all primary endpoints
- Additionally, the investigational BBT displayed a sensitivity of 12.5% for advanced precancerous lesions
- Performance of the investigational BBT in PREEMPT CRC indicates that blood-based screening tests may offer an effective alternative to conventional methods for early CRC detection in average-risk individuals

References

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Acknowledgments

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Disclosures

AS: consultant: Freenome Holdings, Inc., Iterative Health. **ZM:** employee: Freenome Holdings, Inc. **AP:** employee: Freenome Holdings, Inc.; holds equity: Freenome Holdings, Inc. **CX:** employee: Freenome Holdings, Inc. **LCL:** employee: Freenome Holdings, Inc. **LB:** former employee: Freenome Holdings, Inc. **TRL:** employee: Kaiser Permanente; participation on a Data Safety Monitoring Board or Advisory Board: CONFIRM trial (NCT01239082); leadership or fiduciary role in other board, society, committee, or advocacy group: California Colorectal Cancer Coalition (unpaid); research funding: PCORI, Universal Diagnostics.

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- Despite the proven benefits of CRC screening, greater than 40% of eligible adults at average risk for CRC in the US in 2021 were not up to date with guidelines²⁻⁴
- Low screening uptake can be partly attributed to the inconveniences associated with conventional screening methods as well as disparities in access to medical care (including CRC screening) among certain demographic groups^{2,5,6}
- Specific challenges of conventional screening methods include the bowel preparation and invasiveness associated with colonoscopy and fecal aversion associated with stool-based tests^{7,8}
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AI/ML model training

- A classification model was established using ML and AI technologies to derive proprietary methylated-DNA signatures associated with advanced colorectal neoplasia (ACN)

Table 1. Baseline demographics

Demographic characteristics	Evaluable participants ^a (N=27,010)
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OBJECTIVE

- To provide an assessment of the investigational BBT evaluation of CRC in an average-risk population

METHODS

Study design

- Participants were 45 to 75 years old, willing to undergo a stool-based test, and eligible for enrollment
- Prior to bowel preparation, a blood sample was drawn for testing
- Colonoscopy was performed (Figure 1)
- Colonoscopy and appendectomy were reviewed
- A data monitoring committee oversaw the study
- Blood samples were processed and analyzed by participants, research staff, and research staff blind to the results of the colonoscopy

Figure 1. PREEMPT CRC study design



	(n=2567)	(n=1270)	(n=12,350)
ACN			
Absence of ACN			

^aThe clinical validation cohort included 32,731 participants consecutively enrolled after a predetermined cutoff date that coincided with a study protocol amendment in which further COVID-19 mitigations were implemented and generally coincides with vaccine expansion to all adults in the United States.
^bNegative findings include non-neoplastic or no findings.
 ACN, advanced colorectal neoplasia; CRC, colorectal cancer.

- The mean age of evaluable participants was 58.1 years, and 55.8% were female
- The study enrolled a diverse population, with 11.2% of evaluable participants identifying as Black or African American, 8.8% identifying as Asian, and 11.8% identifying as Hispanic or Latino (Table 1)

Specificity for ACN	22,306/24,371	(91.2%–91.9%)
NPV for ACN	22,306/24,567	90.8% (90.7%–90.9%)
PPV for ACN	378/2443	15.5% (14.2%–16.8%)
Secondary endpoint	Total evaluated (n/N)	% (95% CI)
Sensitivity for advanced precancerous lesions	321/2567	12.5% (11.3%–13.8%)

ACN, advanced colorectal neoplasia; CRC, colorectal cancer; NPV, negative predictive value; PPV, positive predictive value.

ZM: employee; Freenome Holdings, Inc. **LB:** former employee; Freenome Holdings, Inc. **TRL:** employee; Kaiser Permanente; participation on a Data Safety Monitoring Board or Advisory Board: CONFIRM trial (NCT01239082); leadership or fiduciary role in other board, society, committee, or advocacy group: California Colorectal Cancer Coalition (unpaid); research funding: PCORI, Universal Diagnostics.

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INTRODUCTION

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- Colorectal cancer (CRC) is the second most common cause of cancer-related death in the US, but is treatable when detected early¹
- Despite the proven benefit of early detection, only 15% of average-risk adults at average risk adhere to guidelines²⁻⁴
- Low screening uptake is associated with conventional methods, such as colonoscopy, and is more pronounced in access to medical care and in certain demographic groups⁵
- Specific challenges of colonoscopy, such as bowel preparation and fecal aversion associated with the procedure, may prevent some individuals from undergoing the procedure
- Individuals may be more likely to undergo colonoscopy if compared with conventional methods, but may still struggle to overcome some barriers
- PREEMPT CRC (NCT04369053) was conducted to evaluate a new blood-based test (BBT) to detect molecular signals associated with advanced colorectal neoplasia (ACN) using machine learning (ML) and artificial intelligence (AI) technologies in screening-eligible populations

AI/ML model training

- A classification model was established using ML and AI technologies to derive proprietary methylated-DNA signatures associated with advanced colorectal neoplasia (ACN)

Table 1. Baseline demographics

Demographic characteristics	Evaluable participants ^a (N=27,010)
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KEY FINDINGS AND CONCLUSIONS

[Click here to enlarge](#)

...pective study in an average-risk population...
 ...2% and 11.2% of the investigational population...
 ...BBT for advanced colorectal neoplasia...
 ...onal BBT in a blood-based method...
 ...ective methods for early detection...
 ...individuals...

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METHODS

Study design

- Participants were 45 to 75 years old, willing to undergo a stool-based test, and eligible for enrollment
- Prior to bowel preparation, a blood sample was collected for testing
- Colonoscopy was performed (Figure 1)
- Colonoscopy and appendectomy were performed as needed
- A data monitoring committee oversaw the study
- Blood samples were processed and analyzed by participants, research staff, and a central pathology review committee, blind to the results of the colonoscopy

Figure 1. PREEMPT CRC study design



	(n=72)	(n=2567)	(n=1270)	(n=12,161)
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Absence of ACN				

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INTRODUCTION

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- Colorectal cancer (CRC) is the second most common cause of cancer-related death in the US, but is treatable when detected early¹
- Despite the proven benefit of colonoscopy for eligible adults at average risk, screening rates are low and do not meet current guidelines²⁻⁴
- Low screening uptake is associated with conventional barriers, including limited access to medical care and demographic disparities⁵
- Specific challenges of colonoscopy include bowel preparation and fecal aversion associated with the procedure⁶
- Individuals may be more likely to undergo colonoscopy compared with conventional methods if barriers are overcome⁷
- PREEMPT CRC (NCT04369053) was conducted to evaluate a blood-based test (BBT) to detect molecular signatures of CRC (ML) and artificial intelligence (AI) screening-eligible population

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KEY FINDINGS AND CONCLUSIONS

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prospective study in a high-risk population

2% and 10% of the investigational population

BBT for advanced colorectal neoplasia

onational BBT in a blood-based test to effectively screen individuals

METHODS

Study design

- Participants were 45 to 85 years of age, at average risk for CRC, and willing to undergo a standard-of-care screening colonoscopy to be eligible for enrollment
- Prior to bowel preparation for colonoscopy, participants provided a blood sample for testing
- Colonoscopy was performed within 120 days of the blood draw (**Figure 1**)
- Colonoscopy and applicable histopathology reports underwent central review
- A data monitoring committee had oversight of data quality
- Blood samples were processed blind to clinical findings, and all participants, research physicians, and central pathologists remained blind to the results of the blood test

OBJECTIVE

- To provide an assessment of the investigational BBT evaluation of CRC in an average-risk population

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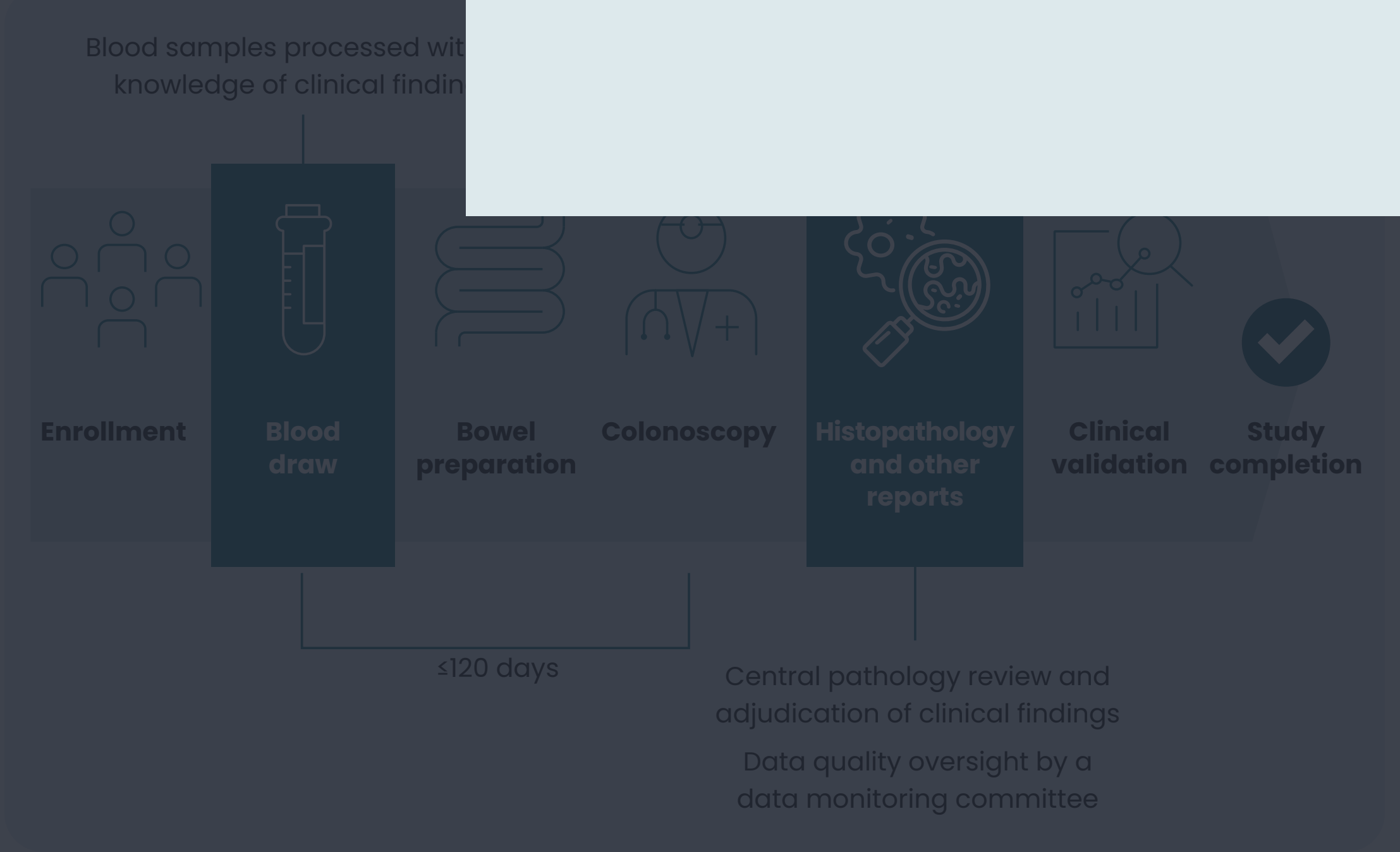
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METHODS

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- Colonoscopy was performed (Figure 1)
- Colonoscopy and appendectomy were performed as needed
- A data monitoring committee oversaw the study
- Blood samples were processed without knowledge of clinical findings

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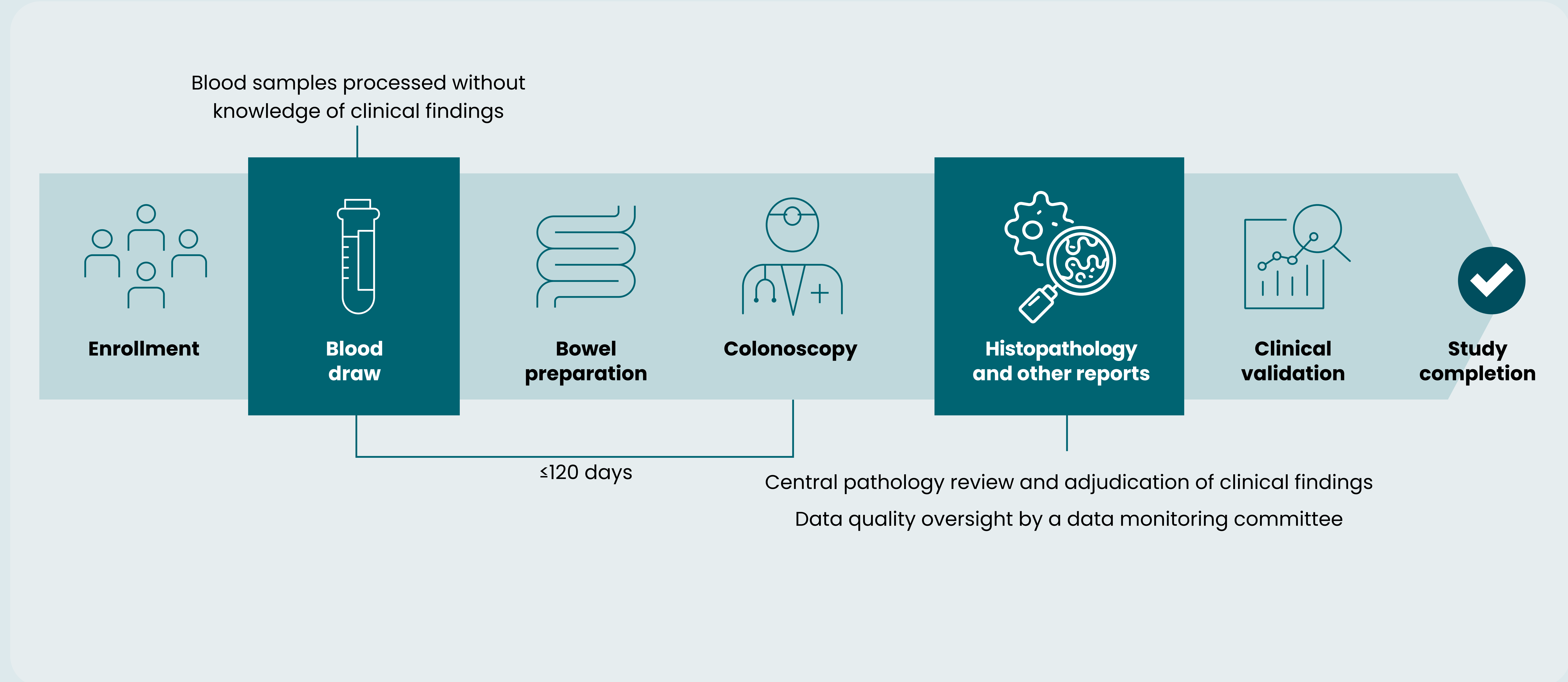
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- Despite the proven benefit of screening, only 15% of eligible adults at average risk adhere to guidelines²⁻⁴
- Low screening uptake is associated with conventional colonoscopy, including associated with convenience and access to medical care, and across demographic groups⁵
- Specific challenges of colonoscopy include bowel preparation and fecal aversion associated with the procedure⁶
- Individuals may be more likely to undergo screening compared with conventional colonoscopy, but may still face some barriers⁷
- PREEMPT CRC (NCT04330001) was a phase 2 study conducted to evaluate the ability of a blood-based test (BBT) to detect molecular signatures of advanced colorectal neoplasia (ACN) using machine learning (ML) and artificial intelligence (AI) in screening-eligible populations⁸

OBJECTIVE

- To provide an assessment of the performance of an investigational BBT evaluated against histopathology for CRC in an average-risk population

METHODS

Study design

- Participants were 45 to 75 years old, willing to undergo a stool-based test, and eligible for enrollment in the study
- Prior to bowel preparation, participants provided a stool sample for testing
- Colonoscopy was performed by a gastroenterologist (Figure 1)
- Colonoscopy and appendectomy were performed by a gastroenterologist
- A data monitoring committee was established to oversee the study
- Blood samples were processed and analyzed by a laboratory blinded to the results of the colonoscopy

Figure 1. PREEMPT CRC Study Design



AI/ML model training

- A classification model was established using ML and AI technologies to derive proprietary methylated-DNA signatures associated with advanced colorectal neoplasia (ACN)

METHODS

AI/ML model training

- A classification model was established using ML and AI technologies to derive proprietary methylated-DNA signatures associated with advanced colorectal neoplasia (ACN)
- Plasma isolated from whole blood samples was analyzed to generate a binary result by comparing with a threshold learned during model training

Test validation

- The performance of the investigational BBT was assessed using screening colonoscopies with histopathology as the reference method
- The four prespecified primary endpoints included sensitivity for CRC, specificity for ACN, negative predictive value (NPV) for ACN, and positive predictive value (PPV) for ACN
 - ACN was composed of CRC and advanced precancerous lesions
 - Advanced precancerous lesions included carcinoma in situ or high-grade dysplasia, adenoma with villous growth pattern ($\geq 25\%$), adenoma ≥ 1.0 cm, sessile serrated lesion with or without cytological dysplasia ≥ 1.0 cm, and traditional serrated adenoma
 - NPV for ACN was defined as the proportion of participants without a diagnosis of CRC or advanced precancerous lesions among those who had a negative test result
 - PPV for ACN was defined as the proportion of participants with a diagnosis of CRC or advanced precancerous lesions among those who had a positive test result
- A secondary endpoint assessed the test's sensitivity for advanced precancerous lesions

Table 1. Baseline demographics

Demographic characteristics	Evaluable participants ^a (N=27,010)
Specificity for ACN	22,306/24,371 (91.2%–91.9%)
NPV for ACN	22,306/24,567 (90.7%–90.9%)
PPV for ACN	378/2443 (15.5% (14.2%–16.8%))
Secondary endpoint	Total evaluated (n/N)
Sensitivity for advanced precancerous lesions	321/2567 (12.5% (11.3%–13.8%))

ACN, advanced colorectal neoplasia; CRC, colorectal cancer; NPV, negative predictive value; PPV, positive predictive value.

^aThe clinical validation cohort included 32,731 participants consecutively enrolled after a predetermined cutoff date that coincided with a study protocol amendment in which further COVID-19 mitigations were implemented and generally coincides with vaccine expansion to all adults in the United States.

^bNegative findings include non-neoplastic or no findings.

ACN, advanced colorectal neoplasia; CRC, colorectal cancer.

- The mean age of evaluable participants was 58.1 years, and 55.8% were female
- The study enrolled a diverse population, with 11.2% of evaluable participants identifying as Black or African American, 8.8% identifying as Asian, and 11.8% identifying as Hispanic or Latino (Table 1)

KEY FINDINGS AND CONCLUSIONS

The study was a prospective study in an average-risk population. The BBT was evaluated against histopathology as the reference method. The BBT was found to be effective for early detection of advanced precancerous lesions.

Clinical Evaluation of a New Blood-Based Test for Colorectal Cancer Screening

Aasma Shaukat,^{1,2,3} Zhen Meng,⁴ Andy Piscitello,⁴ Chuanbo Xu,⁴ Lilian C. Lee,⁴ Lance Baldo,^{4,a} Theodore R. Levin^{3,5}

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^aAffiliation at the time the study and/or analyses were conducted



INTRODUCTION

- Colorectal cancer (CRC) is the second most common cause of cancer-related death in the US, but is treatable when detected early¹
- Despite the proven benefit of colonoscopy for eligible adults at average risk, adherence to guidelines²⁻⁴ is low
- Low screening uptake is associated with convergence in access to medical care across demographic groups⁵
- Specific challenges of bowel preparation and fecal aversion associated with colonoscopy⁶
- Individuals may be more likely to undergo colonoscopy compared with conventional methods⁷
- PREEMPT CRC (NCT04339053) study, was conducted to evaluate the ability to detect molecular signatures of colorectal neoplasia (ML) and artificial intelligence (AI) screening-eligible population

OBJECTIVE

- To provide an assessment of the investigational BBT evaluation of CRC in an average-risk population

METHODS

Study design

- Participants were 45 to 75 years old, willing to undergo a stool-based test, and eligible for enrollment
- Prior to bowel preparation, participants provided a blood sample for testing
- Colonoscopy was performed by a gastroenterologist (Figure 1)
- Colonoscopy and appendectomy were performed by a gastroenterologist
- A data monitoring committee reviewed all site-reported adverse events and were supported by Freenome Holdings.

Figure 1. PREEMPT CRC study design



AI/ML model training

- A classification model was established using ML and AI technologies to derive proprietary methylated-DNA signatures associated with advanced colorectal neoplasia (ACN)

Table 1. Baseline demographics

Demographic characteristics	Evaluable participants ^a (N=27,010)
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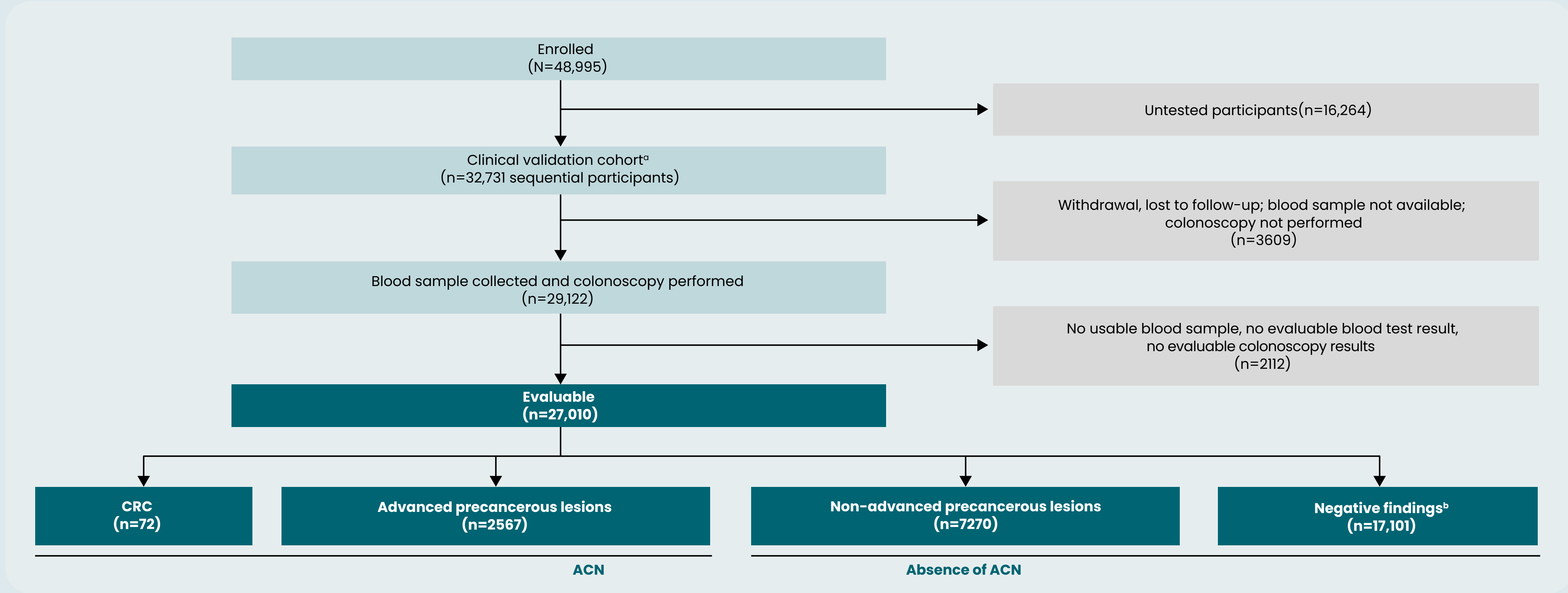
KEY FINDINGS AND CONCLUSIONS

RESULTS

Participant demographics

- Of 48,995 study participants originally enrolled in PREEMPT CRC between May 2020 and April 2022, a subset of 32,731 sequentially enrolled participants were included in the clinical validation cohort (**Figure 2**)
 - Of these, 82.5% (n=27,010) had evaluable blood samples and colonoscopy results

Figure 2. Evaluable study participants



^aThe clinical validation cohort included 32,731 participants consecutively enrolled after a predetermined cutoff date that coincided with a study protocol amendment in which further COVID-19 mitigations were implemented and generally coincides with vaccine expansion to all adults in the United States.
^bNegative findings include non-neoplastic or no findings.
 ACN, advanced colorectal neoplasia; CRC, colorectal cancer.

Secondary endpoint	Total evaluated (n/N)	% (95% CI)
Specificity for ACN	22,306/24,371	91.2%–91.9%
NPV for ACN	22,306/24,567	90.8% (90.7%–90.9%)
PPV for ACN	378/2443	15.5% (14.2%–16.8%)
Sensitivity for advanced precancerous lesions	321/2567	12.5% (11.3%–13.8%)

ACN, advanced colorectal neoplasia; CRC, colorectal cancer; NPV, negative predictive value; PPV, positive predictive value.

- The mean age of evaluable participants was 58.1 years, and 55.8% were female
- The study enrolled a diverse population, with 11.2% of evaluable participants identifying as Black or African American, 8.8% identifying as Asian, and 11.8% identifying as Hispanic or Latino (**Table 1**)

Clinical Evaluation of a New Blood-Based Test for Colorectal Cancer Screening

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^aAffiliation at the time the study and/or analyses were conducted



INTRODUCTION

Colorectal cancer (CRC) is the second most common cause of cancer-related death in the US, but is treatable when detected early¹

Despite the proven benefit of colonoscopy for eligible adults at average risk, screening rates are low²⁻⁴

Low screening uptake is associated with convergence in access to medical care across demographic groups⁵

Specific challenges of bowel preparation and fecal aversion associated with colonoscopy may prevent some individuals from undergoing the procedure⁶

Individuals may be more likely to undergo colonoscopy compared with conventional stool-based tests⁷

PREEMPT CRC (NCT04333001) was conducted to evaluate the ability of the PREEMPT CRC (ML) and artificial intelligence (AI) to detect molecular signatures of advanced colorectal neoplasia (ACN) in screening-eligible populations

OBJECTIVE

To provide an assessment of the performance of the investigational BBT compared with conventional stool-based tests in an average-risk population

METHODS

Study design

- Participants were 45 to 75 years old, willing to undergo a stool-based test, and eligible for enrollment in the study
- Prior to bowel preparation, a blood sample was collected for testing
- Colonoscopy was performed on all participants (Figure 1)
- Colonoscopy and appendectomy were performed as needed
- A data monitoring committee reviewed all data
- Blood samples were processed and analyzed by participants, research staff, and research staff blind to the results of the colonoscopy

Figure 1. PREEMPT CRC Study Design



AI/ML model training

- A classification model was established using ML and AI technologies to derive proprietary methylated-DNA signatures associated with advanced colorectal neoplasia (ACN)

RESULTS

- The mean age of evaluable participants was 58.1 years, and 55.8% were female
- The study enrolled a diverse population, with 11.2% of evaluable participants identifying as Black or African American, 8.8% identifying as Asian, and 11.8% identifying as Hispanic or Latino (**Table 1**)

Table 1. Baseline demographics

Demographic characteristics	Evaluable participants ^a (N=27,010)
Age (years)	
Mean (SD)	58.1 (8.2)
Median	57
Age Group, n (%)	
45–49	2968 (11.0)
50–54	8899 (32.9)
55–64	8725 (32.3)
65–74	5604 (20.7)
≥75	814 (3.0)
Biological Sex, n (%)	
Female	15,076 (55.8)
Male	11,934 (44.2)
Race, n (%)	
White	19,707 (73.0)
Black or African American	3038 (11.2)
Asian	2381 (8.8)
American Indian or Alaskan Native	78 (0.3)
Native Hawaiian or Other Pacific Islander	72 (0.3)
More than one reported	136 (0.5)
Other/unknown	1598 (5.9)
Ethnicity, n (%)	
Hispanic or Latino	3189 (11.8)
Not Hispanic or Latino	22,421 (83.0)
Unknown	1400 (5.2)

^aPercentages may not total 100 because of rounding.

Secondary endpoint	Total evaluated (n/N)	% (95% CI)
Specificity for ACN	22,306/24,371	91.5% (91.2%–91.9%)
NPV for ACN	22,306/24,567	90.8% (90.7%–90.9%)
PPV for ACN	378/2443	15.5% (14.2%–16.8%)
Sensitivity for advanced precancerous lesions	321/2567	12.5% (11.3%–13.8%)

ACN, advanced colorectal neoplasia; CRC, colorectal cancer; NPV, negative predictive value; PPV, positive predictive value.

KEY FINDINGS AND CONCLUSIONS

The PREEMPT CRC (ML) and AI model demonstrated high specificity and NPV for ACN compared with conventional stool-based tests in an average-risk population.

The study enrolled a diverse population, with 11.2% of evaluable participants identifying as Black or African American, 8.8% identifying as Asian, and 11.8% identifying as Hispanic or Latino.

The mean age of evaluable participants was 58.1 years, and 55.8% were female.

The study was supported by Freenome Holdings, Inc. and Kaiser Permanente.

Clinical Evaluation of a New Blood-Based Test for Colorectal Cancer Screening

Aasma Shaukat,^{1,2,3} Zhen Meng,⁴ Andy Piscitello,⁴ Chuanbo Xu,⁴ Lilian C. Lee,⁴ Lance Baldo,^{4,a} Theodore R. Levin^{3,5}

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INTRODUCTION

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- Colorectal cancer (CRC) is the second most common cause of cancer-related death in the US, but is treatable when detected early¹
- Despite the proven benefit of CRC screening, only 15% of eligible adults at average risk adhere to guidelines²⁻⁴
- Low screening uptake is associated with convergence of barriers, including limited access to medical care and demographic groups⁵
- Specific challenges of bowel preparation and fecal aversion associated with colonoscopy⁶
- Individuals may be more likely to undergo screening compared with conventional methods, but may still face some barriers⁷
- PREEMPT CRC (NCT04369053) study, was conducted to evaluate a new blood-based test (BBT) to detect molecular signatures (ML) and artificial intelligence (AI) screening-eligible population

OBJECTIVE

- To provide an assessment of the investigational BBT evaluation of CRC in an average-risk population

METHODS

Study design

- Participants were 45 to 75 years old, willing to undergo a study procedure, and eligible for enrollment
- Prior to bowel preparation, a blood sample was collected for testing
- Colonoscopy was performed (Figure 1)
- Colonoscopy and appendectomy were performed as needed
- A data monitoring committee oversaw the study
- Blood samples were processed and analyzed by participants, research staff, and research staff, who were blind to the results of the test

Figure 1. PREEMPT CRC Study Design



AI/ML model training

- A classification model was established using ML and AI technologies to derive proprietary methylated-DNA signatures associated with advanced colorectal neoplasia (ACN)

Table 1. Baseline demographics

Demographic characteristics	Evaluable participants ^a (N=27,010)
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KEY FINDINGS AND CONCLUSIONS

[Click here to enlarge](#)

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RESULTS

Test performance for primary and secondary outcome measures

- PREEMPT CRC met all primary endpoints (Table 2)

Table 2. Test performance for primary and secondary outcome measures

Evaluable participants (N=27,010)		
Primary endpoints	Total evaluated (n/N)	% (95% CI)
Sensitivity for CRC	57/72	79.2% (68.4%–86.9%)
Specificity for ACN	22,306/24,371	91.5% (91.2%–91.9%)
NPV for ACN	22,306/24,567	90.8% (90.7%–90.9%)
PPV for ACN	378/2443	15.5% (14.2%–16.8%)
Secondary endpoint	Total evaluated (n/N)	% (95% CI)
Sensitivity for advanced precancerous lesions	321/2567	12.5% (11.3%–13.8%)

ACN, advanced colorectal neoplasia; CRC, colorectal cancer; NPV, negative predictive value; PPV, positive predictive value.

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- The clinical validation cohort included 32,731 participants consecutively enrolled after a predetermined cutoff date that coincided with a study protocol amendment in which further COVID-19 mitigations were implemented and generally coincides with vaccine expansion to all adults in the United States.
- Negative findings include non-neoplastic or no findings.
- ACN, advanced colorectal neoplasia; CRC, colorectal cancer.
- The mean age of evaluable participants was 58.1 years, and 55.8% were female
- The study enrolled a diverse population, with 11.2% of evaluable participants identifying as Black or African American, 8.8% identifying as Asian, and 11.8% identifying as Hispanic or Latino (Table 1)

...ZM: employee: Freenome
...olds equity: Freenome
...LI: employee: Freenome
...Holdings, Inc. LB: former employee: Freenome Holdings, Inc. TRL: employee: Kaiser
...Permanent; participation on a Data Safety Monitoring Board or Advisory Board:
...CONFIRM trial (NCT01239082); leadership or fiduciary role in other board, society,
...committee, or advocacy group: California Colorectal Cancer Coalition (unpaid);
...research funding: PCORI, Universal Diagnostics.

Clinical Evaluation of a New Blood-Based Test for Colorectal Cancer Screening

Aasma Shaukat,^{1,2,3} Zhen Meng,⁴ Andy Piscitello,⁴ Chuanbo Xu,⁴ Lilian C. Lee,⁴ Lance Baldo,^{4,a} Theodore R. Levin^{3,5}

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^aAffiliation at the time the study and/or analyses were conducted



INTRODUCTION

[Click here to enlarge](#)

- Colorectal cancer (CRC) is the second most common cause of cancer-related death in the US, but is treatable when detected early¹
- Despite the proven benefit of colonoscopy for average-risk individuals at average risk, low screening uptake is associated with colorectal cancer in access to medical care across demographic groups²⁻⁴
- Specific challenges of colonoscopy include bowel preparation and fecal aversion associated with discomfort and time
- Individuals may be more likely to undergo colonoscopy compared with conventional methods, but may overcome some barriers
- PREEMPT CRC (NCT0439053) study, was conducted to evaluate the performance of a blood-based test (BBT) to detect molecular signatures of advanced colorectal neoplasia (ACN) and artificial intelligence (AI) and artificial intelligence (AI) screening-eligible population

AI/ML model training

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Table 1. Baseline demographics

Demographic characteristics	Evaluable participants ^a (N=27,010)
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KEY FINDINGS AND CONCLUSIONS

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KEY FINDINGS AND CONCLUSIONS

- PREEMPT CRC is the largest prospective study of a BBT for CRC in an average-risk population to date
- With a sensitivity for CRC of 79.2% and specificity for ACN of 91.5%, the investigational BBT met all primary endpoints
- Additionally, the investigational BBT displayed a sensitivity of 12.5% for advanced precancerous lesions
- Performance of the investigational BBT in PREEMPT CRC indicates that blood-based screening tests may offer an effective alternative to conventional methods for early CRC detection in average-risk individuals

OBJECTIVE

- To provide an assessment of the performance of an investigational BBT evaluated against colonoscopy for early detection of CRC in an average-risk population

METHODS

Study design

- Participants were 45 to 75 years old, willing to undergo a stool-based test, and eligible for enrollment
- Prior to bowel preparation, a blood sample was collected for testing
- Colonoscopy was performed (Figure 1)
- Colonoscopy and appendectomy were reviewed
- A data monitoring committee oversaw the study
- Blood samples were processed and analyzed by participants, research staff, and research staff, blind to the results of the colonoscopy

Figure 1. PREEMPT CRC study design



	(n=27,010)	(n=25,672)	(n=1,270)	(n=12,306)
ACN				
Absence of ACN				

^aThe clinical validation cohort included 32,731 participants consecutively enrolled after a predetermined cutoff date that coincided with a study protocol amendment in which further COVID-19 mitigations were implemented and generally coincides with vaccine expansion to all adults in the United States.
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053. Updated February 28, 2023. <https://www.clinicaltrials.gov/study/NCT04369053>.

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 were provided by Harrison
 and were supported by
 Freenome Holdings.

TM: employee; Freenome Holdings, Inc. LB: former employee; Freenome Holdings, Inc. TR: employee; Kaiser Permanente; participation on a Data Safety Monitoring Board or Advisory Board; CONFIRM trial (NCT01239082); leadership or fiduciary role in other board, society, committee, or advocacy group; California Colorectal Cancer Coalition (unpaid); research funding: PCORI, Universal Diagnostics.