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]

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

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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 early[1]
- 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 guidelines[2–4]
- 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 (NCT04369053[11]), 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

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- 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

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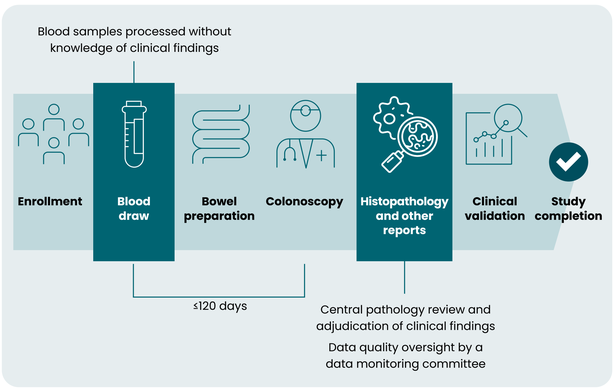
Study design

- 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

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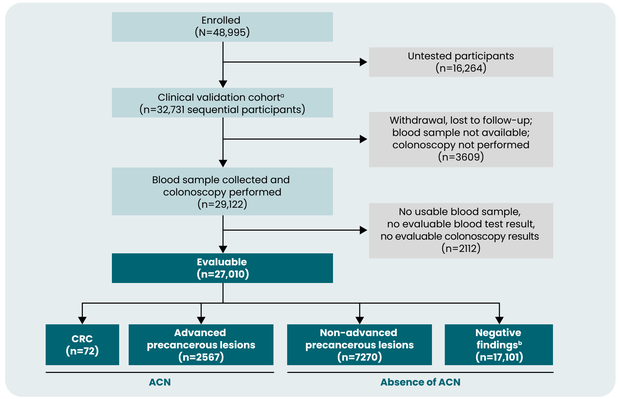
Participant demographics

- 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



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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)

[a]Percentages 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

	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%)

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KEY FINDINGS AND CONCLUSIONS

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- 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

1. Siegel RL, et al. *CA Cancer J Clin*. 2024;74(1):12-49.
2. Siegel RL, et al. *CA Cancer J Clin*. 2023;73:233-54.
3. US Preventive Services Task Force. *JAMA*. 2021;325(19):1965-1977.
4. Wolf AMD, et al. *CA Cancer J Clin*. 2018;68(4):250-281.
5. American Cancer Society. *Colorectal Cancer Facts & Figures 2023-2025*. Atlanta: American Cancer Society; 2023.
6. Musselwhite LW, et al. *Am Soc Clin Oncol Educ Book*. 2021;41:108-117.
7. Jones RM, et al. *Am J Prev Med*. 2010;38(5):499-507.
8. Kotzur M, et al. *BMJ* Open. 2022;12(9):e062738
9. Liang PS, et al. *Clin Gastroenterol Hepatol*. 2023;21(11):2951-2957.e2.
10. Coronado GD, et al. *Gut*. 2024;73(4):622-628.
11. PREEMPT CRC. ClinicalTrials.gov identifier: NCT04369053. Updated February 28, 2024. Accessed August 21, 2024. https://clinicaltrials.gov/study/NCT04369053.

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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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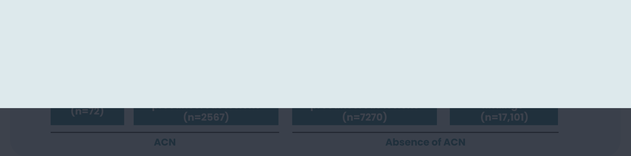

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	ACN (n=2567)	Absence of ACN (n=17,101)

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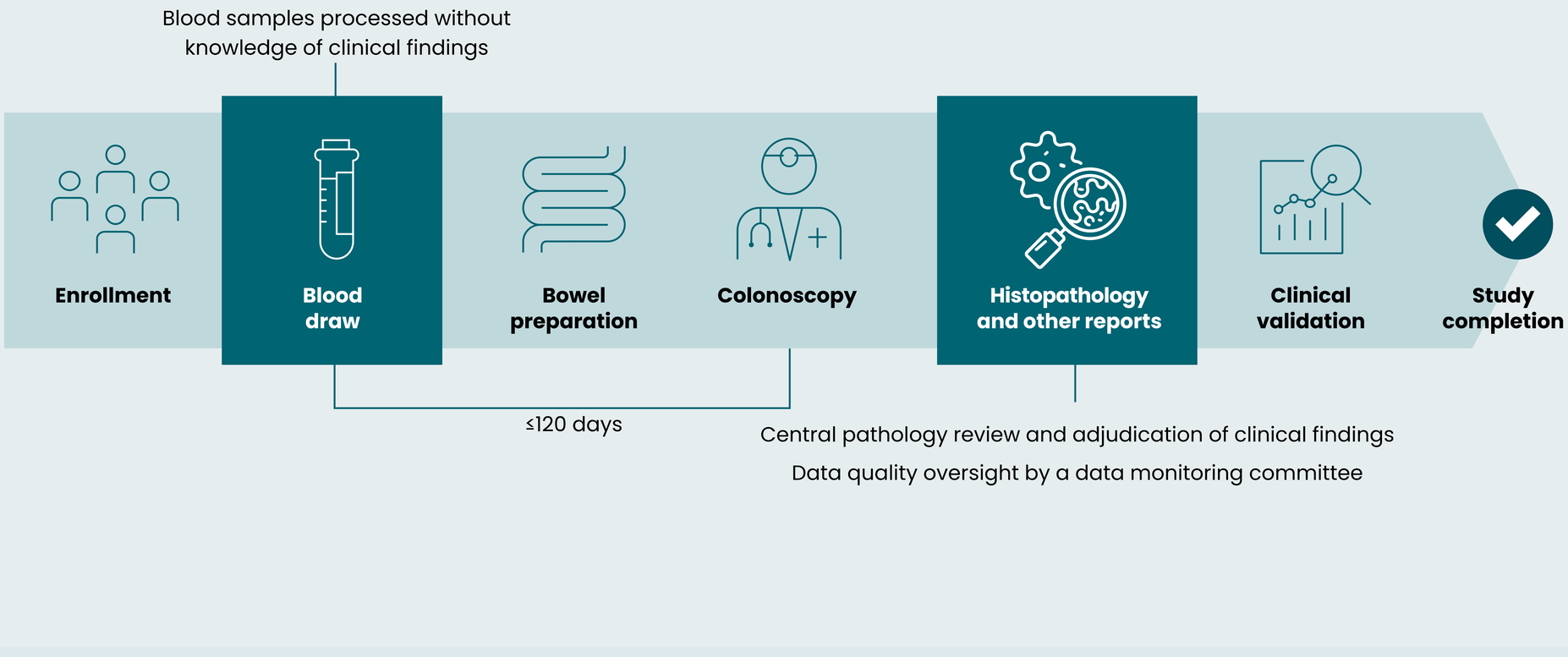

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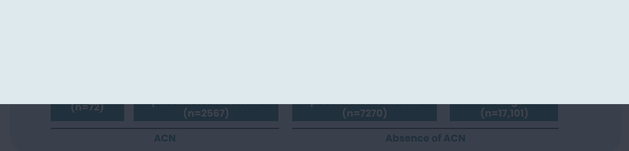

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- The four prespecified primary endpoints included sensitivity for CRC, specificity for ACN, negative predictive value (NPV) for ACN, and positive predictive value (PPV) for ACN
  - ACN was composed of CRC and advanced precancerous lesions
  - Advanced 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

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

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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 early[1]
- Despite the proven be… eligible adults at aver… date with guidelines[2–4]
- Low screening uptake … associated with conve… in access to medical … demographic groups[5]
- Specific challenges of … bowel preparation an… fecal aversion associa…
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- PREEMPT CRC (NCT043… study, was conducted … detect molecular sign… (ML) and artificial intel… screening-eligible pop…

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- To provide an assessm… investigational BBT ev… of CRC in an average-…

METHODS

Study design

- Participants were 45 t… willing to undergo a st… eligible for enrollment
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- Colonoscopy and app… review
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- Blood samples were p… participants, research… blind to the results of t…

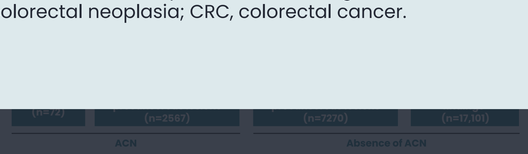
Figure 1. PREEMPT CR…

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)



[a]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.
[b]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**)

Specificity for ACN	22,306/24,371	… (91.2%–91.9%)
NPV for ACN	22,306/24,567	90.8% (90.7%–90.9%)
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KEY FINDINGS AND CONCLUSIONS

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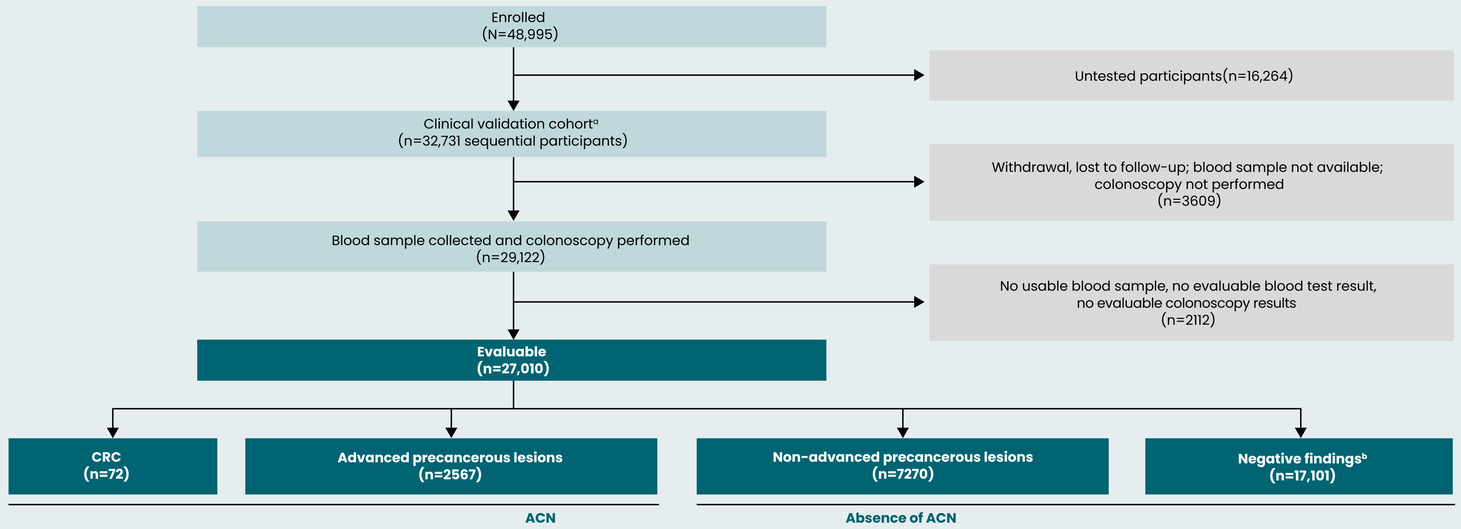
RESULTS

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



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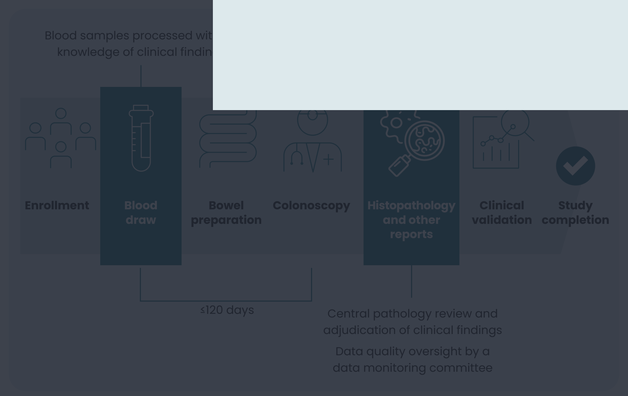

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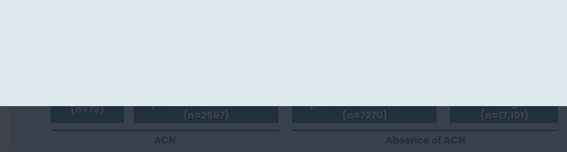

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Table 1. Baseline demographics

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)

[a]Percentages may not total 100 because of rounding.

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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%)
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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

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