2026 Update in Colorectal Cancer Trends and Screening

UCSD Moores Cancer Center Oncology Updates: Screening & Prevention
August 19, 2026

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Health Sciences

Disclosures

Consultant/Advisor for:	Guardant Health; Geneoscopy; InterVenn; Universal Diagnostics; CellMax Life
Grant/Research support:	National Institutes of Health, National Cancer Institute; Epigenomics; Freenome
Employee of:	UC San Diego; Veterans Health Administration

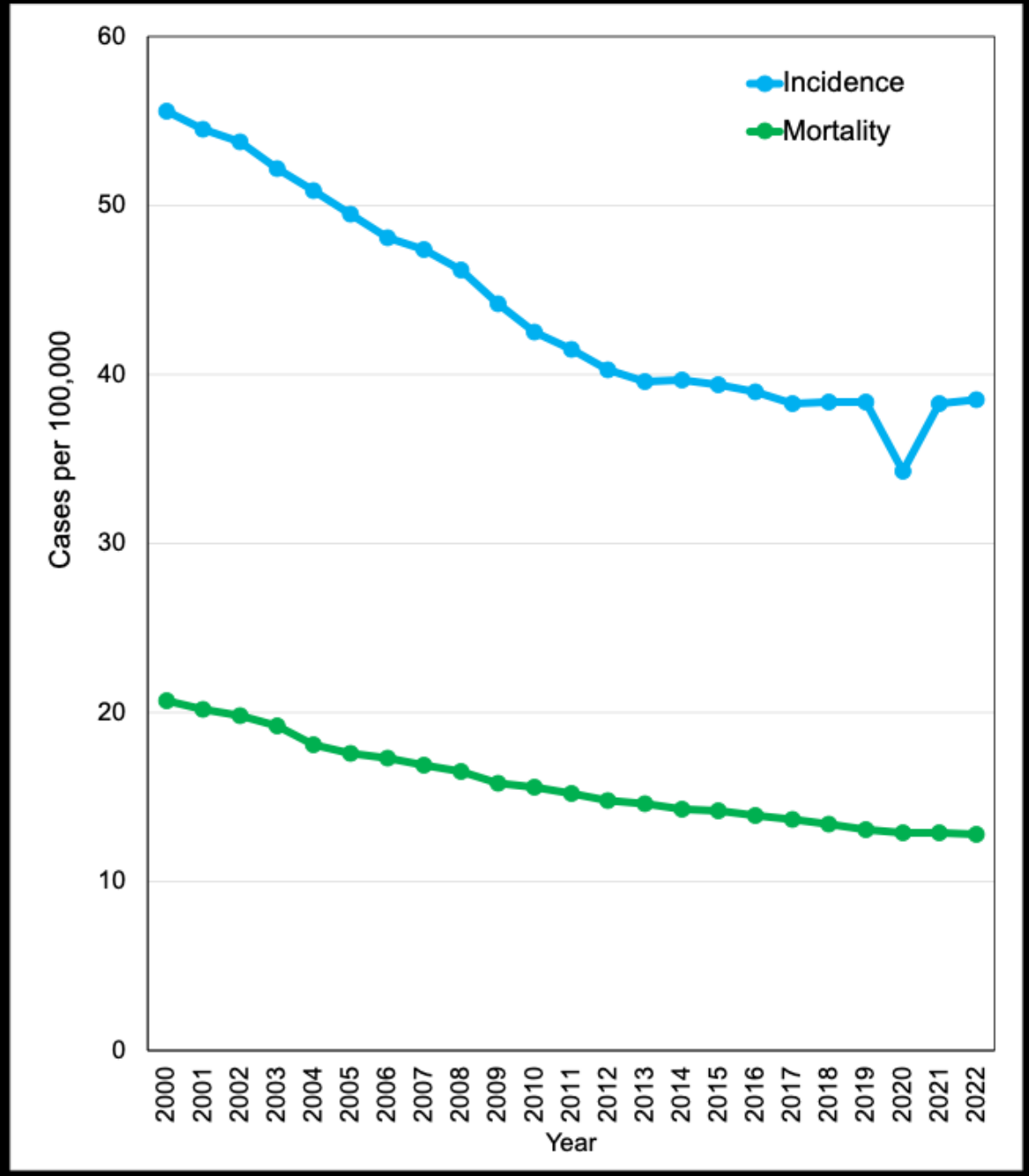
All of these companies are developing tests for colorectal cancer screening and surveillance

Agenda

- Trends in colorectal cancer epidemiology
- Novel evidence supporting screening
- 2026 American Cancer Society colorectal cancer screening guidelines

The CRC Success Story

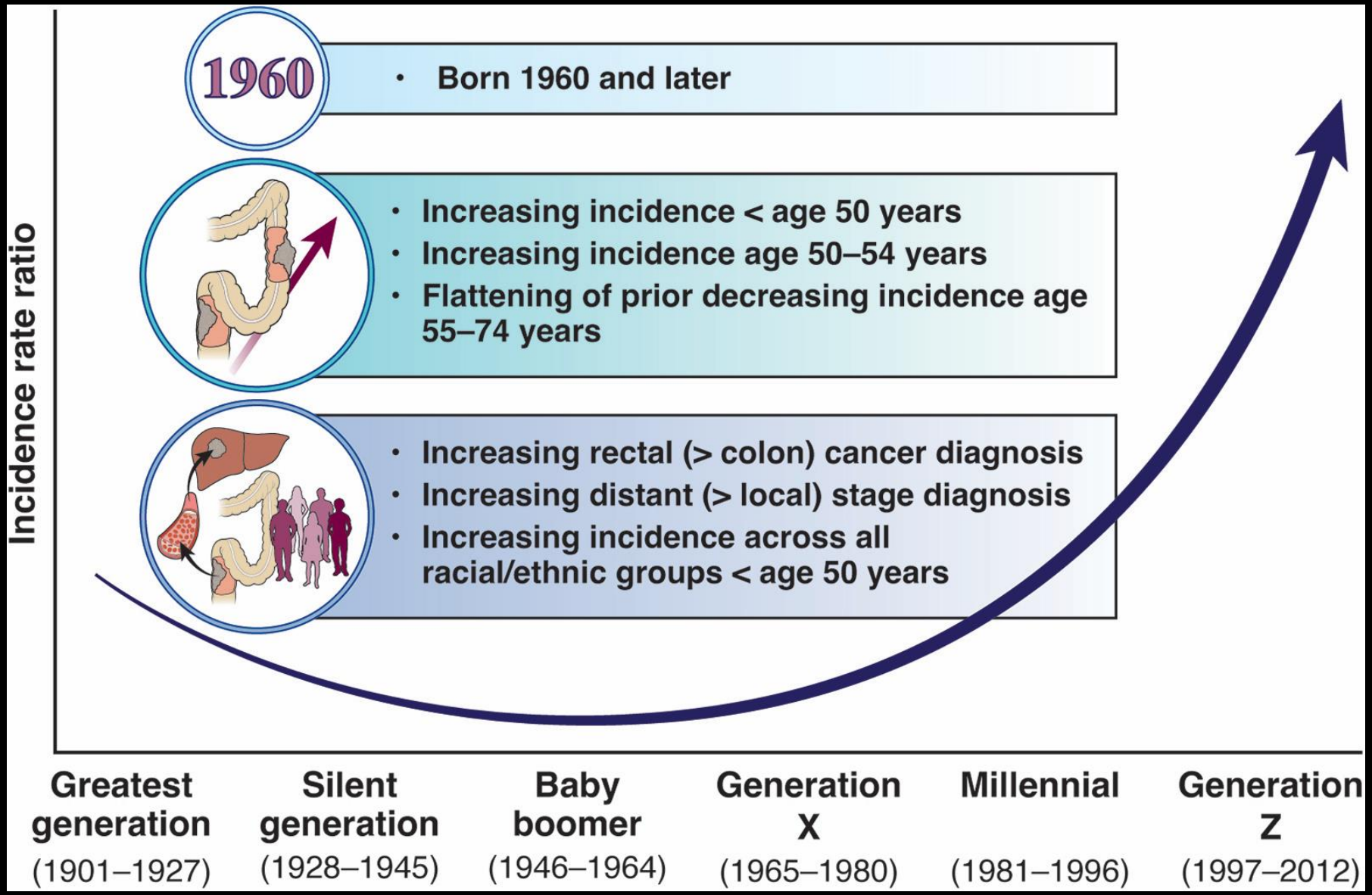
- For all groups combined, incidence and mortality have improved over time
  - Screening, risk factors, treatment
- Incomplete picture:
  - Recent annual percentage change not changing
  - #2 cause of cancer death for all ages
  - #1 cause of cancer death <age 50



Surveillance Epidemiology End Results 21 2000-2022 delay-adjusted incidence and mortality. Includes appendix. SEER*Explorer accessed 1/9/26.

Generational trends in CRC: established and emerging

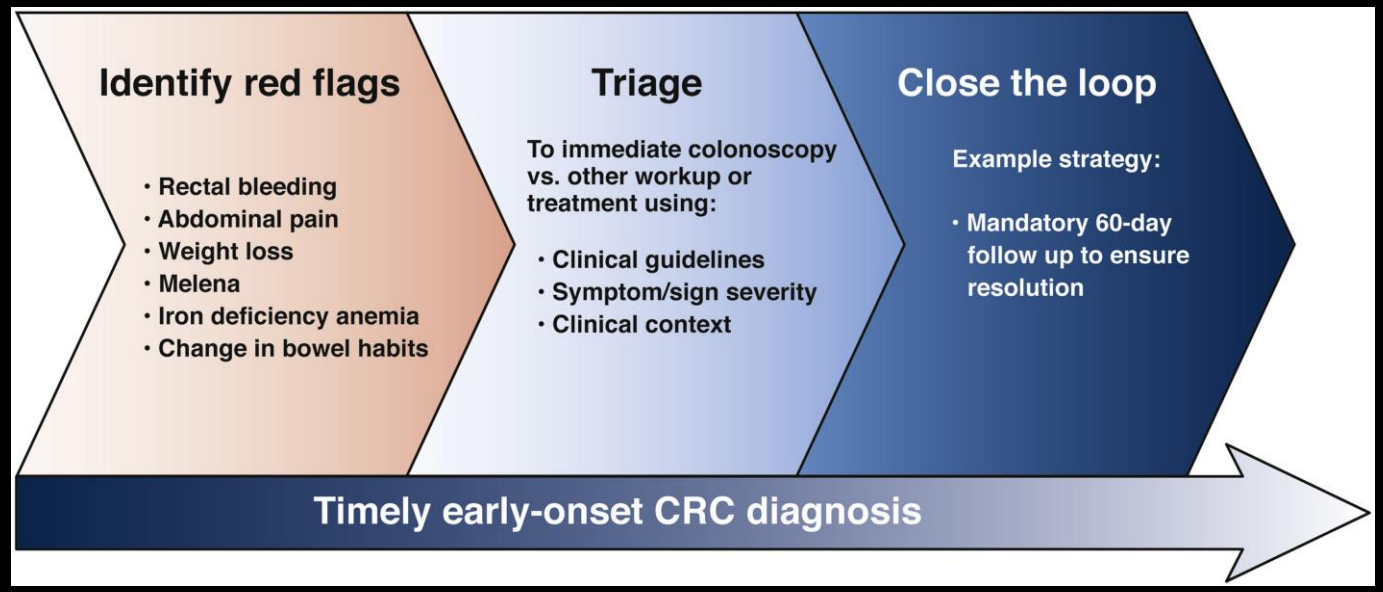
Birth Cohort
Colorectal Cancer



Gupta S; May FP; Kupfer S; Murphy CM
Clin Gastro Hep 2023

What can we do now to address changing epidemiology?

- Invest in fundamental translational epidemiologic research
  - Discover and understand drivers
- Individuals under age 45
  - Close the clinical loop on potential red-flag signs and symptoms of CRC
- Individuals age ≥45 age eligible for screening
  - ↑ Urgency to get people up to date



Burnett Hartman; A Demb; J Lee JK; Gupta S Gastro 2021; Siegel CA J Clin 2023

Screening – Recent Evidence

- Randomized trials
- Prospective observational studies of new tests

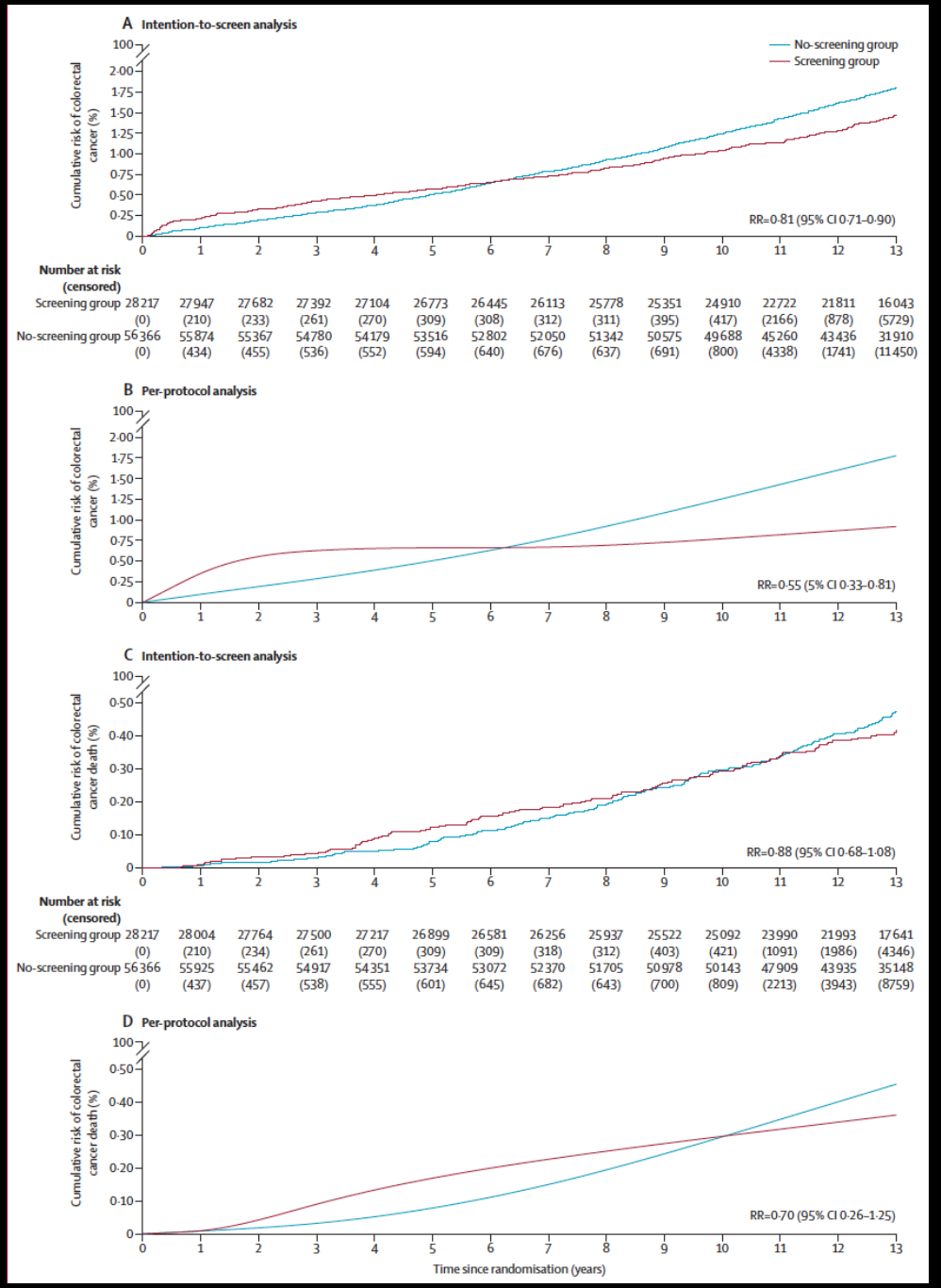
RCT: Colonoscopy vs. no invitation

- ~85,000 age 55-64 in Norway, Sweden, and Poland
- Median follow-up 13 years
- 19% relative reduction CRC incidence
- No reduction in mortality
- Per protocol:
  - 45% reduction for incidence
  - Non-significant 30% reduction for mortality

Lancet 2026; 407: 1787–95

Long-term effects of colonoscopy screening on colorectal cancer incidence and mortality: a multicountry, population-based randomised controlled trial

*Michal F Kaminski, Mette Kalager, Magnus Løberg, Louise Emilsson, Anna Macios, Faye Samy, Joy Shi, Shona Fielding, Miguel A Hernán, Kjetil Garborg, Maciej Rupinski, Evelien Dekker, Manon Spaander, Øyvind Holme, Ann G Zauber, Nastazja D Pilonis, Joanna Didkowska, Piotr Spychalski, Geir Hoff, Jaroslaw Regula, Hans-Olov Adami, Michael Bretthauer, for the NordICC Study Group**



RCT: Colonoscopy vs. FIT

- ~57,000 age 50-69 in Spain
- Median follow-up 10 years
- No difference in incidence or mortality
- Per protocol:
  - 33% reduction for incidence
  - 83% reduction for mortality

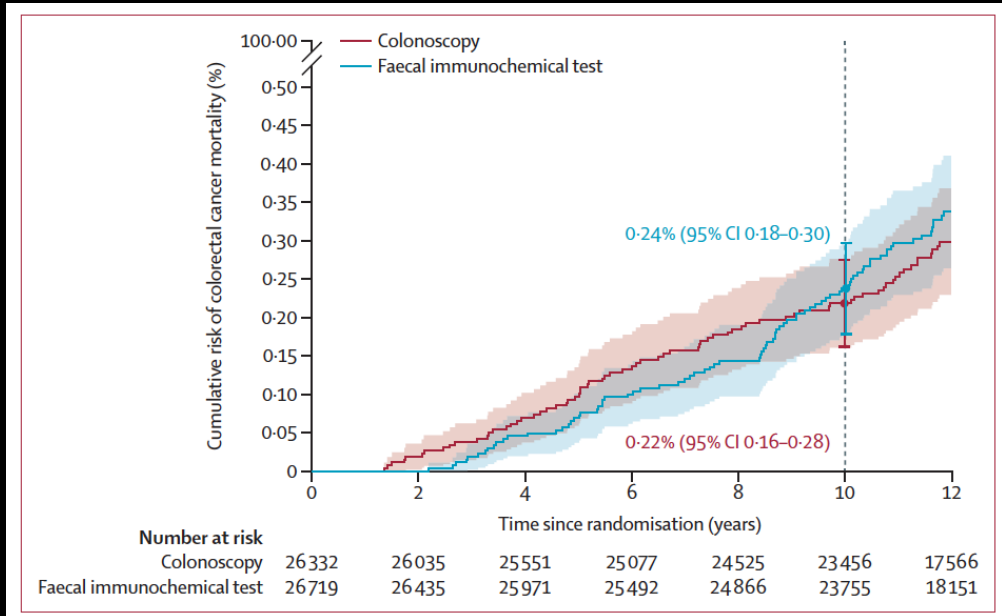
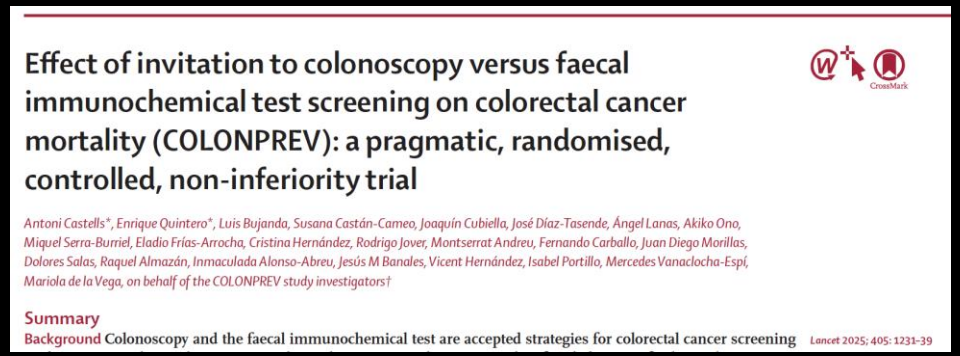


Figure 2: **Cumulative risk of colorectal cancer mortality at 10 years in the intention-to-screen analysis population**
Shaded areas indicate 95% CIs.



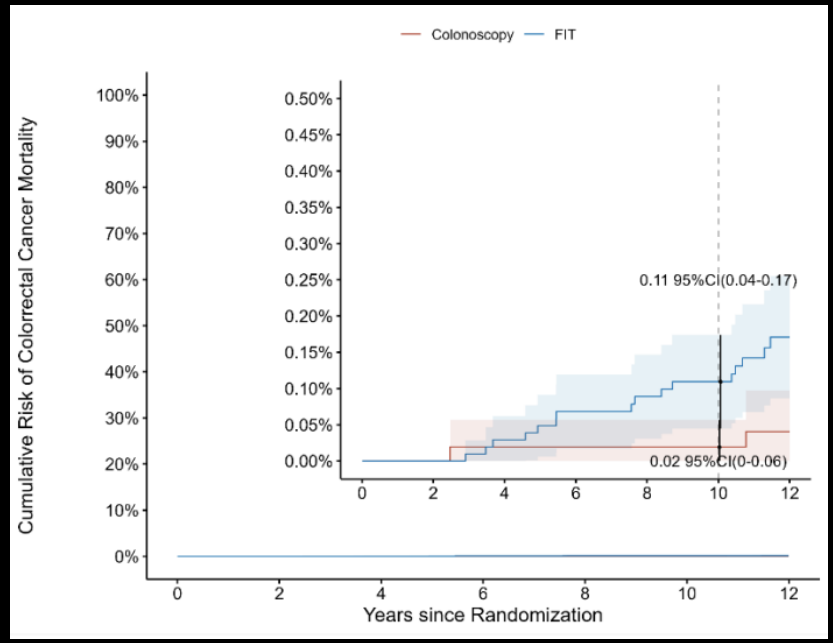
Effect of invitation to colonoscopy versus faecal immunochemical test screening on colorectal cancer mortality (COLONPREV): a pragmatic, randomised, controlled, non-inferiority trial

Antoni Castells, Enrique Quintero*, Luis Bujanda, Susana Castán-Cameo, Joaquín Cubiella, José Díaz-Tasende, Ángel Lanas, Akiko Ono, Miquel Serra-Burriel, Eladio Frías-Arrocha, Cristina Hernández, Rodrigo Jover, Montserrat Andreu, Fernando Carballo, Juan Diego Morillas, Dolores Salas, Raquel Almazán, Inmaculada Alonso-Abreu, Jesús M Banales, Vicent Hernández, Isabel Portillo, Mercedes Vanaclocha-Espí, Mariola de la Vega, on behalf of the COLONPREV study investigators†*

Summary

Background Colonoscopy and the faecal immunochemical test are accepted strategies for colorectal cancer screening

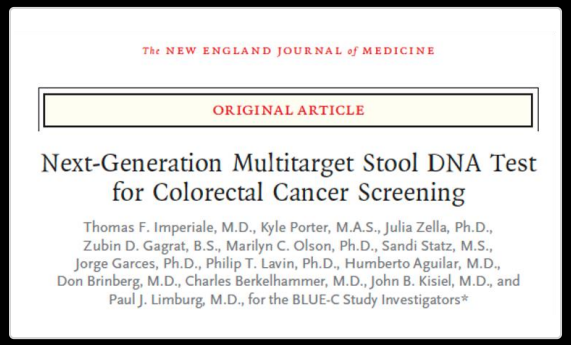
Lancet 2025; 405: 1231-39



Colonoscopy RCT take home points

- Invitation to colonoscopy:
  - Reduced incidence compared to no invitation
  - Similar incidence compared to FIT invitation
  - Similar mortality compared to FIT invitation or no invitation
- Participation in colonoscopy
  - Reduced incidence and mortality compared to FIT or no invitation
- Population level --> longer follow-up to understand colonoscopy effects
- Individual level --> colonoscopy better than no screening and FIT

Recent Evidence: FDA approved non-invasive tests


The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Next-Generation Multitarget Stool DNA Test for Colorectal Cancer Screening

Thomas F. Imperiale, M.D., Kyle Porter, M.A.S., Julia Zella, Ph.D., Zubin D. Gagrat, B.S., Marilyn C. Olson, Ph.D., Sandi Statz, M.S., Jorge Garces, Ph.D., Philip T. Lavin, Ph.D., Humberto Aguilar, M.D., Don Brinberg, M.D., Charles Berkelhammer, M.D., John B. Kisiel, M.D., and Paul J. Limburg, M.D., for the BLUE-C Study Investigators*

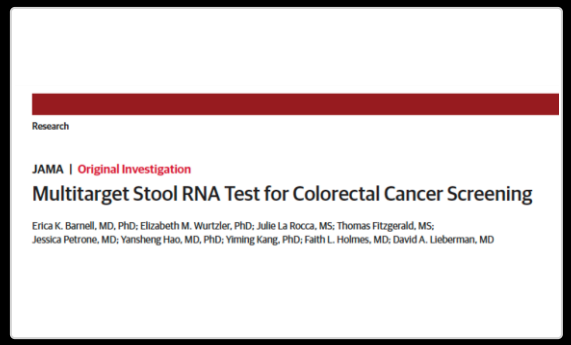
STOOL

sDNA–FIT 2.0

Cologuard Plus | Exact Sciences

Methylated DNA markers

LASS4 • LRRC4 • PPP2R5C
ZDHHC1 reference marker + FIT


Research

JAMA | Original Investigation

Multitarget Stool RNA Test for Colorectal Cancer Screening

Erica K. Barnell, MD, PhD; Elizabeth M. Wurtzler, PhD; Julie La Rocca, MS; Thomas Fitzgerald, MS; Jessica Petrone, MD; Yansheng Hao, MD, PhD; Yiming Kang, PhD; Faith L. Holmes, MD; David A. Lieberman, MD

STOOL

sRNA–FIT

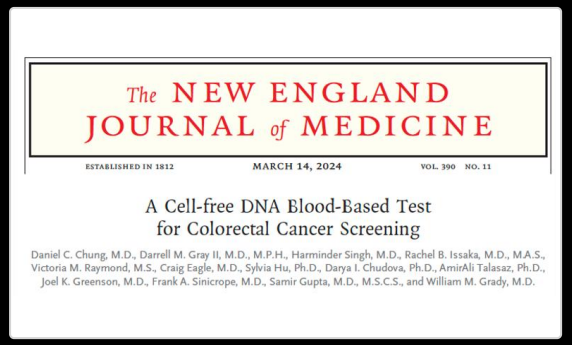
ColoSense | Geneoscopy

Eight RNA markers + FIT

GAPDH • ACY1 • AREG • TNFRSF10B
CDH1 • EGLN2 • KRAS • SMAD4

OC-Sensor FIT

Tobacco-smoking history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BLOOD

cfDNA Shield

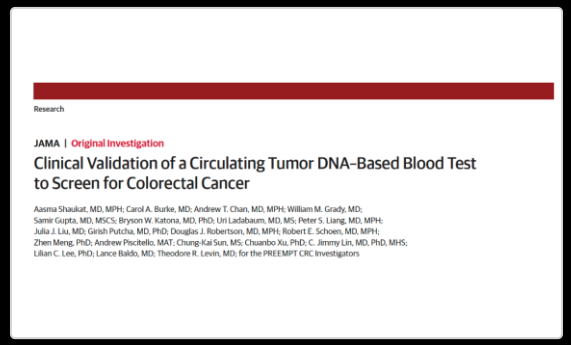
Shield | Guardant Health

cfDNA methylation

DNA methylation patterns

Aberrant fragmentation patterns

Somatic pathogenic variants: APC + KRAS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BLOOD

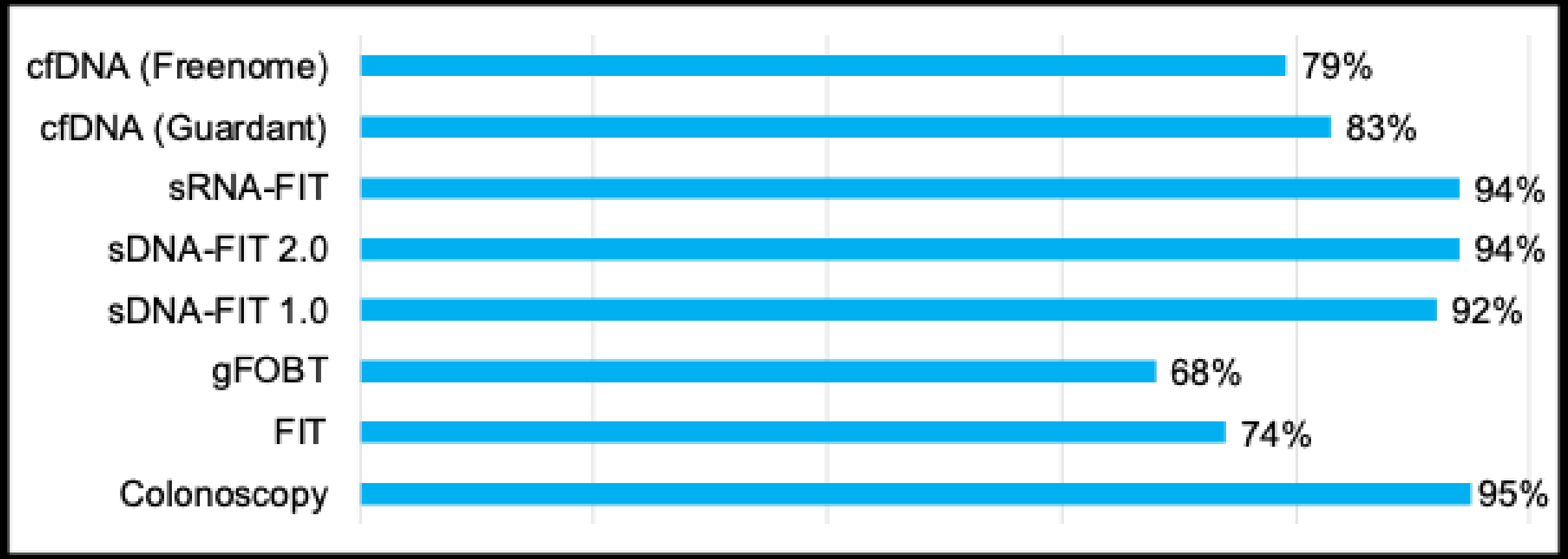
cfDNA SimpleScreen

SimpleScreen | Freenome

cfDNA methylation

DNA methylation patterns

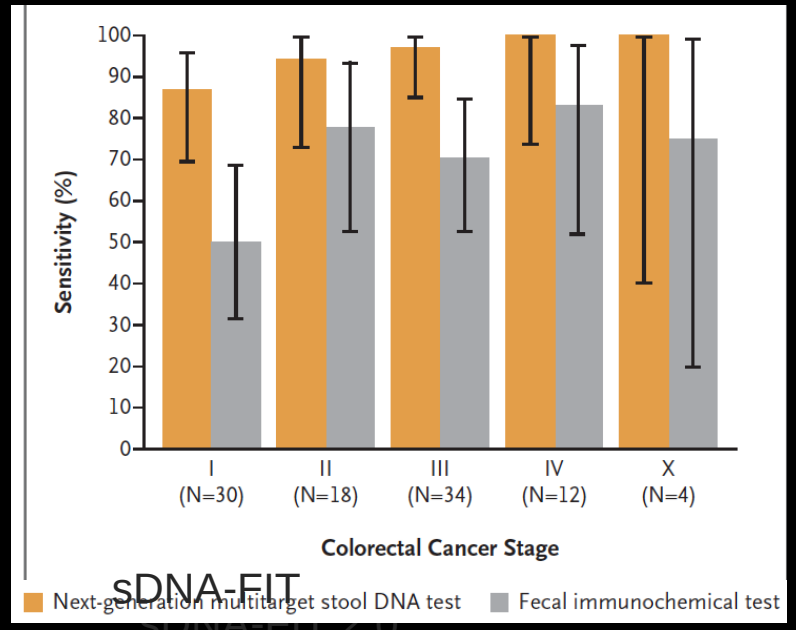
Sensitivity for CRC



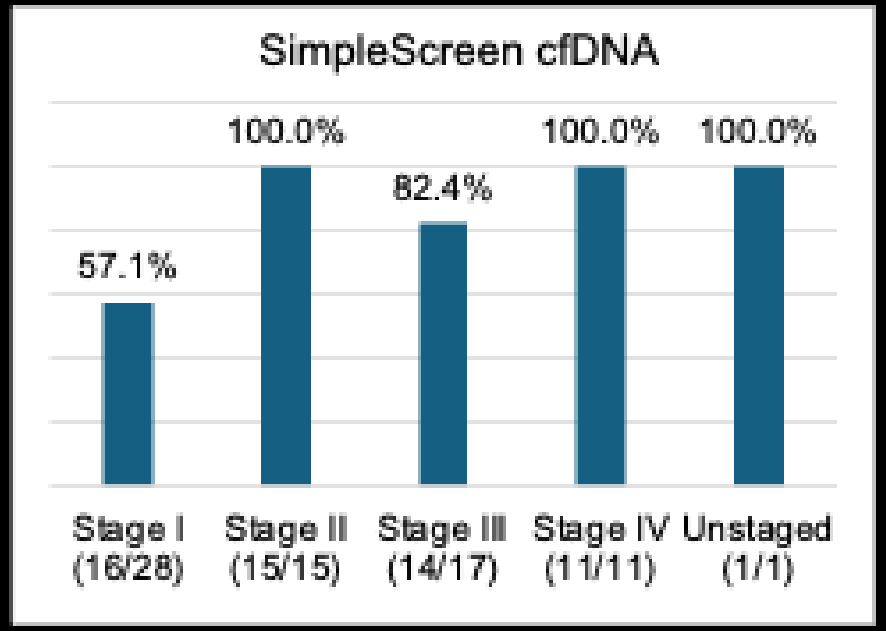
- All emerging tests have better CRC sensitivity than FIT and guaiac FOBT
- Novel fecal tests approaching colonoscopy

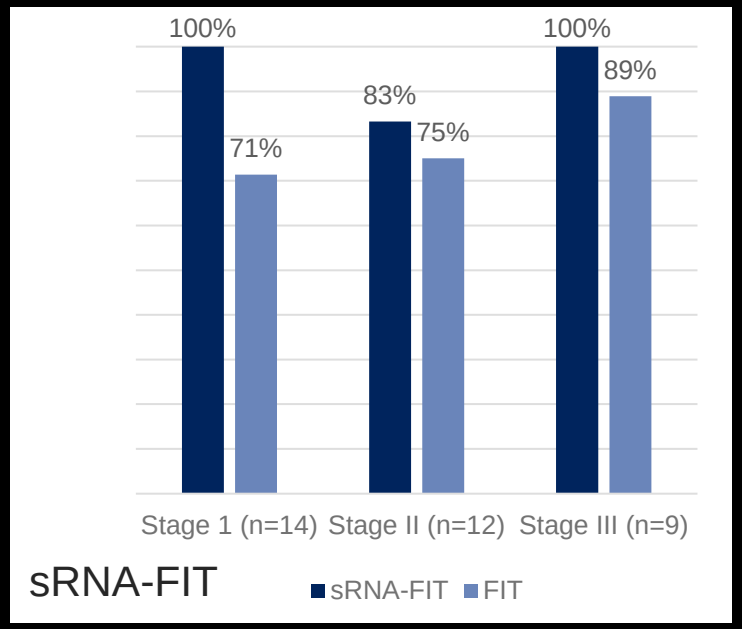
Knudsen A JAMA 2021; Knudsen AHRQ Publication No. 20-05271-EF-2 2021; Imperiale T NEJM 2014; Imperiale T NEJM 2024; Chung D NEJM 2024; Barnell E JAMA 2023

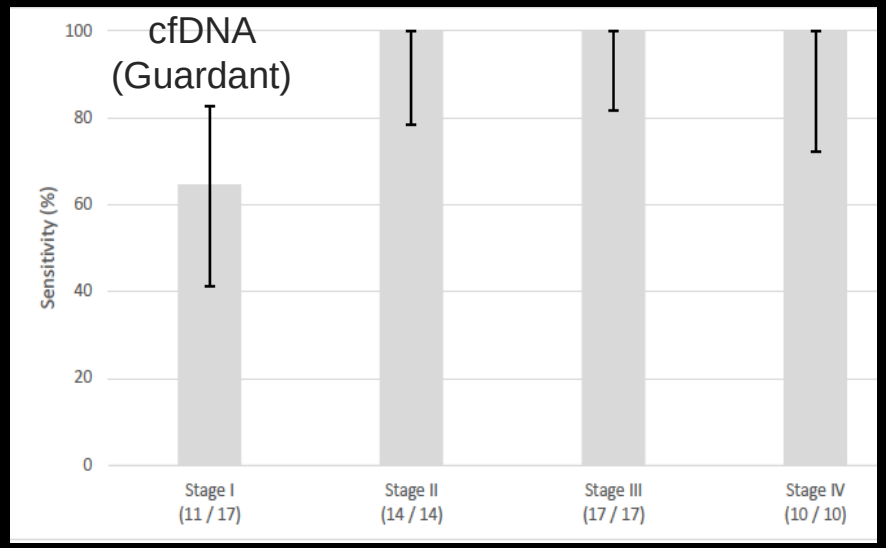
Stage-Specific Sensitivity for CRC



sDNA-FIT



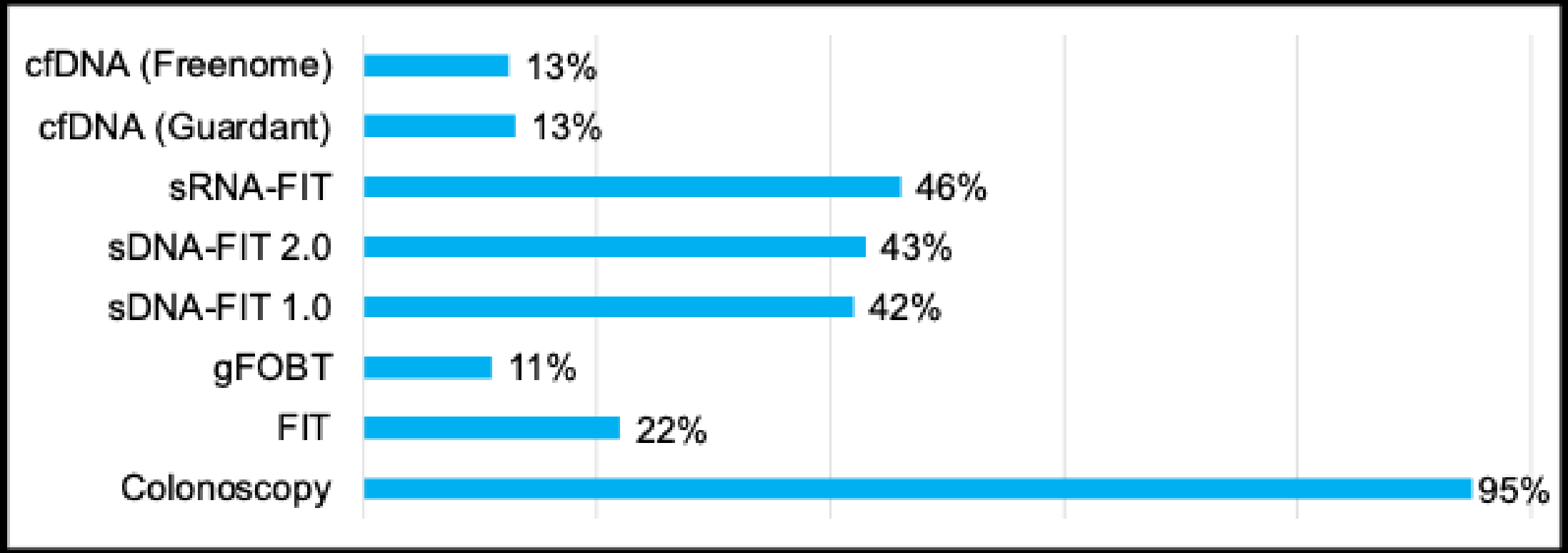




- Low sample size
- Novel stool tests:
  - Stage 1 sensitivity high and appears better than FIT
- Blood based tests:
  - Stage 1 sensitivity lower

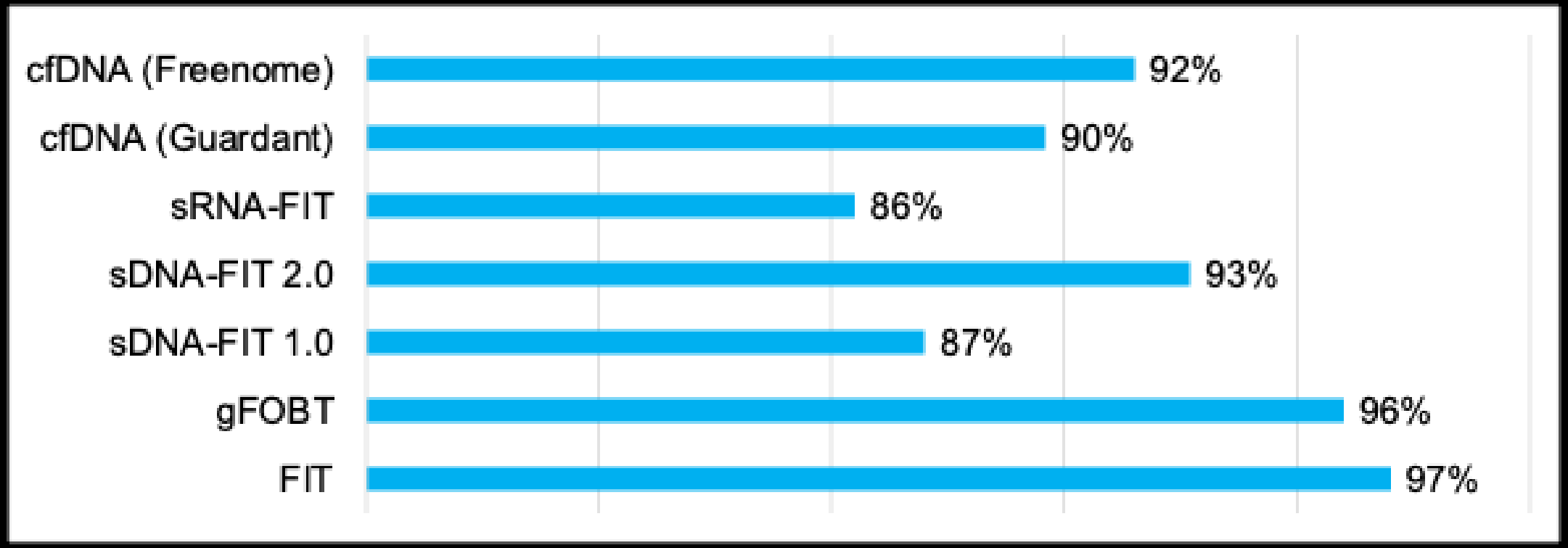
Imperiale T NEJM 2024; Chung D NEJM 2024; Barnell E JAMA 2023; Ladabaum Gastro 2024; Shaukat JAMA 2025

Sensitivity for Advanced Polyps



- All emerging tests have lower sensitivity for advanced polyps compared to colonoscopy
- Emerging stool tests have higher sensitivity than FIT
- cfDNA has lower sensitivity for advanced polyps compared to FIT, sDNA-FIT 1.0, and emerging fecal tests

Specificity in those without advanced neoplasia



- Defined by proportion of patients with non advanced adenomas, non-neoplastic findings, or negative colonoscopy who have a negative test
- Specificity remains better for FIT compared to emerging tests
  - Specificity declines with age for all novel tests but not for FIT

Comparative Effectiveness

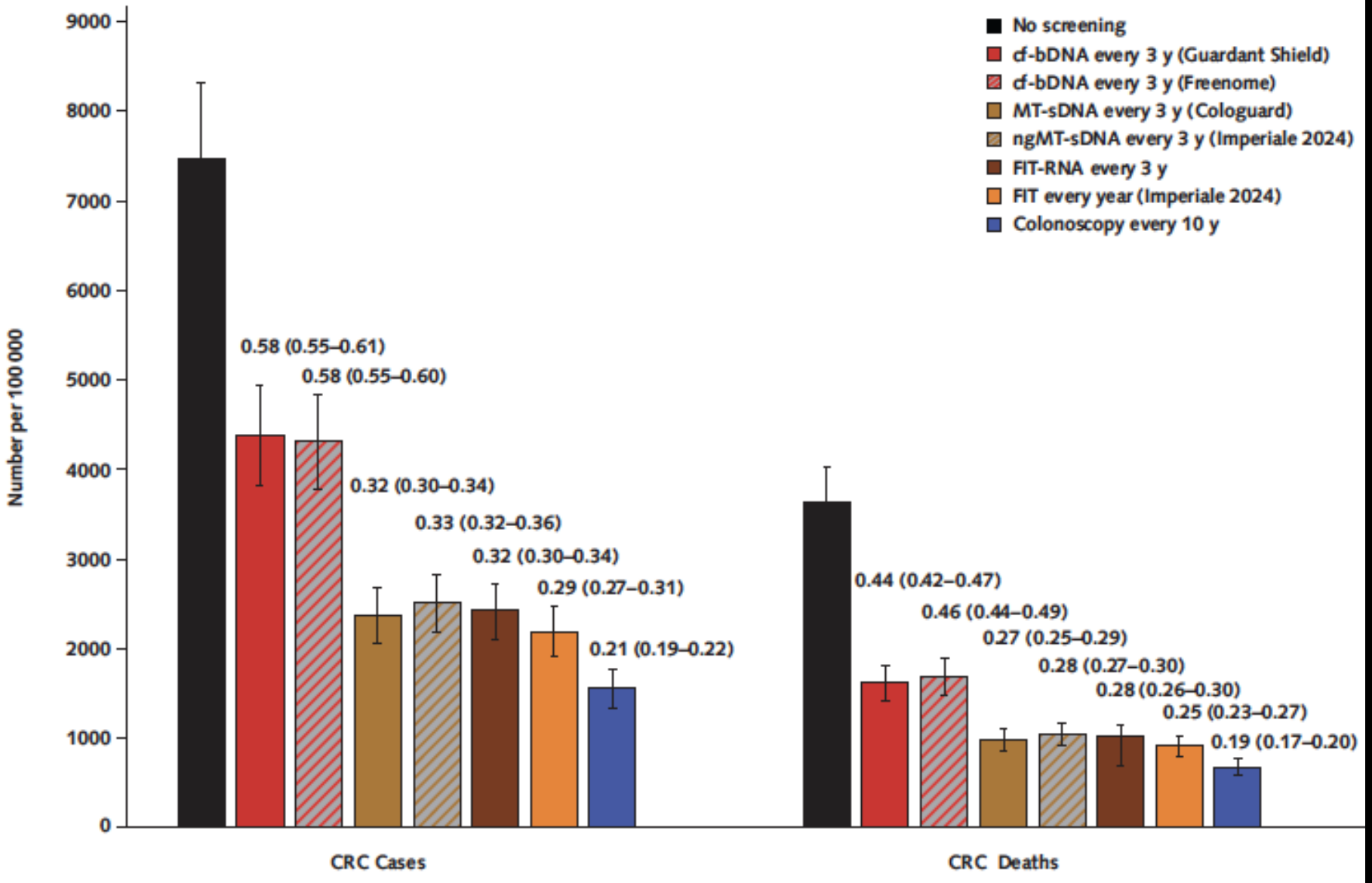
- Modelling study
- Gradient of predicted risk reduction colonoscopy > fecal tests > blood tests

ORIGINAL RESEARCH Annals of Internal Medicine

Projected Impact and Cost-Effectiveness of Novel Molecular Blood-Based or Stool-Based Screening Tests for Colorectal Cancer

Uri Ladabaum, MD, MS; Ajitha Mannalithara, PhD; Robert E. Schoen, MD, MPH; Jason A. Dominitz, MD, MHS; and David Lieberman, MD

Figure 1. Clinical outcomes with emerging and established CRC screening strategies.



2026 American Cancer Society Guidelines

Recommended Age: ≥ 45 years for individuals with average risk

Preferred Options

Direct Visual Exams

- Colonoscopy every 10 years
- Sigmoidoscopy every 5 years
- CT colonography every 5 years

High-Sensitivity Stool Tests

- FIT annually
- Guaiac FOBT annually
- Multi-target DNA-FIT every 3 years (Cologuard)
- Multi-target RNA-FIT every 3 years (Colosense)

Non-Preferred but Acceptable

- For those who decline or do not complete a preferred test

Blood-based tests

- Cell-free DNA every 3 years (Shield or SimpleScreen)

Colorectal cancer screening: An update to the American Cancer Society guideline, 2026

CA Cancer J Clin. 2026;e70083.
https://doi.org/10.3322/caac.70083

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Elena B. Elkin PhD, MPA[7] | Ruth Etzioni PhD[8] | Abbe Herzig PhD[9] |
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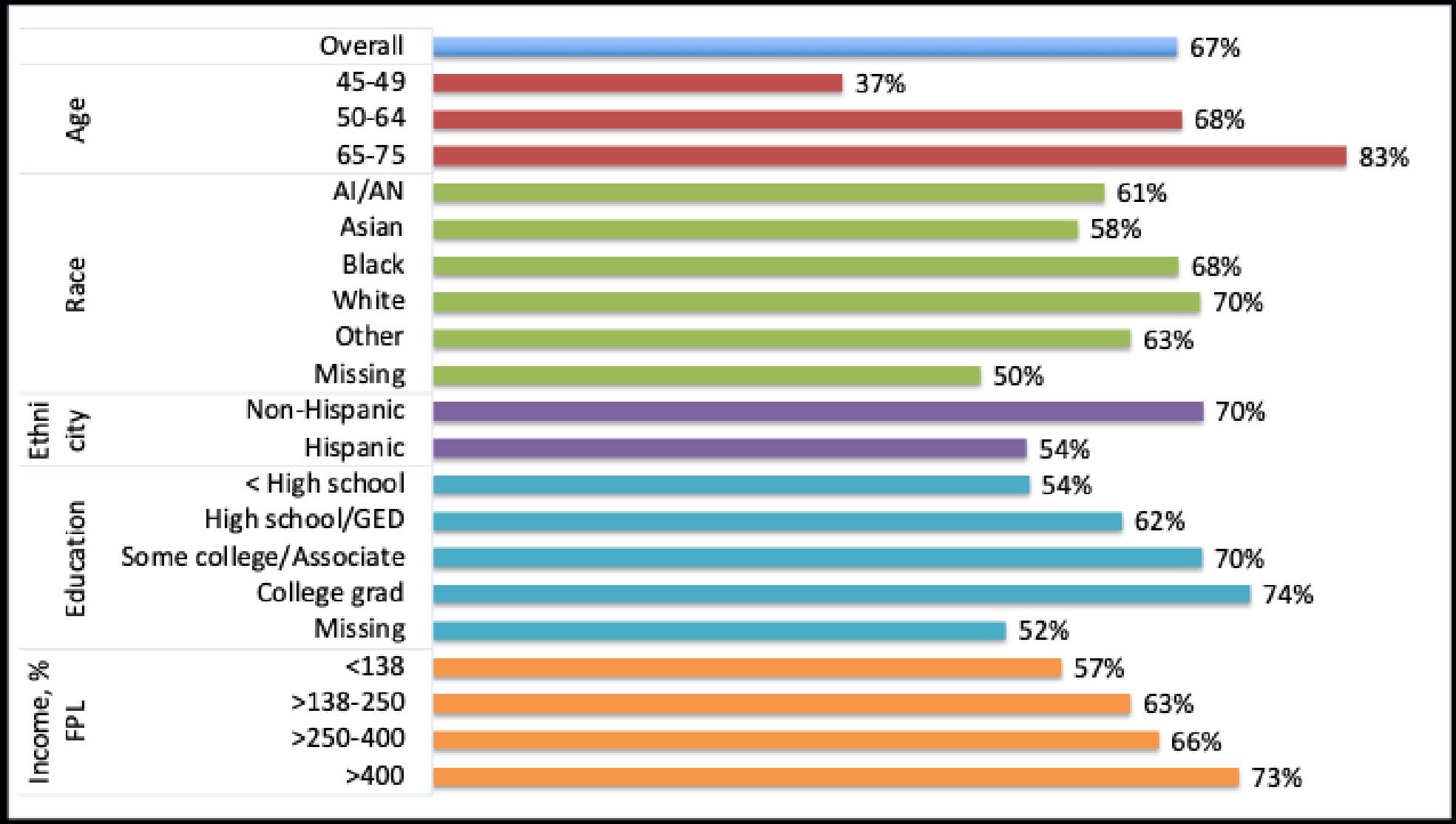
Sana Raoof MD, PhD[12] | Ya-Chen Tina Shih PhD[13] | Steven J. Skates PhD[14] |
Tyler B. Kratzer MPH[15] | Deana Manassaram-Baptiste PhD, MPH[16] |
Robert A. Smith PhD[16]

Challenges and future directions

- Participation
- Abnormal test follow up

Uptake is suboptimal, and varies greatly across the population



Up-to-Date with Screening, National Health Interview Survey, 2023 Sabatino Prev Chron Dis 2023

Opportunities for addressing screening rates

- Multiple evidence-based interventions exist
  - Test choice
    - E.g. colonoscopy and at least one non-invasive (e.g. FIT or sDNA-FIT)
  - Mailed FIT outreach
    - Mailed invitation, including a FIT kit, +/- reminders
    - 22% absolute increase in screening participation over usual care

Inadomi J Arch Int Med 2012; Dougherty MK. JAMA Int Med 2018; Issaka RB Prev Med 2018; Gupta S; CA Cancer J Clin 2020; Coronado CEBP 2022; Raich CEBP 2022; Green BB J Am B Fam Med 2014; Selby Ann Int Med 2017; Selby Clin Transl Gastro 2019; Castaneda….Gupta AJPH 2020; Doubeni NEJM 2022; McClellan CCC 2024

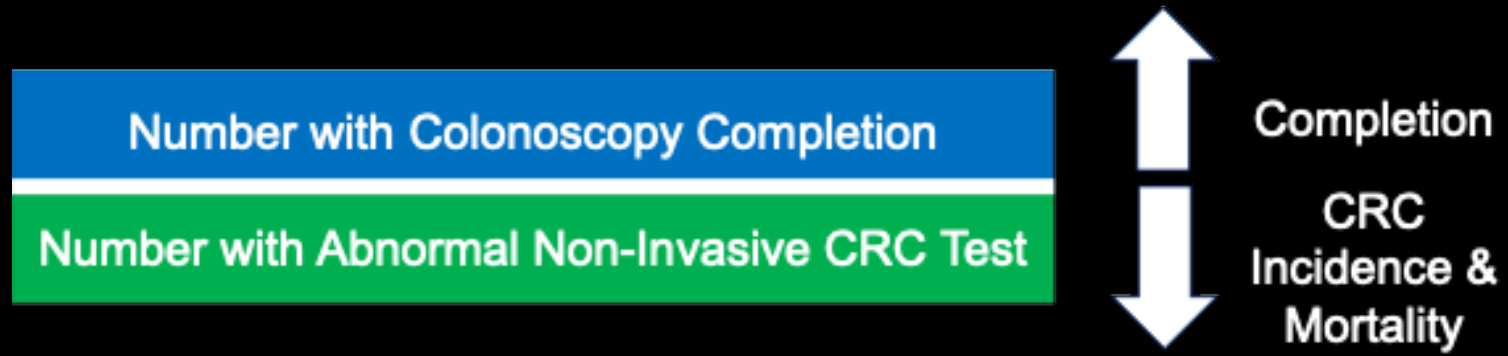
Follow up of abnormal tests is suboptimal

- Colonoscopy completion after abnormal FIT varies 18%-69% nationally
  - Cologuard f/u nationally 62%
  - cfDNA (Shield) f/u 56%
- Goal is 80%
- Lack of colonoscopy completion after abnormal FIT associated with 2.5 fold increased risk for CRC death
  - 1 in 20 have cancer
  - 1 in 4 have a large polyp

Lee YC JNCI 2017; Jimbo M Ann Fam Med 2009; Humphrey LL JGIM 2011; Rao SK JGIM 2009; Chubak J CEBP 2016; Gupta S Nodora J JNCI 2017; San Miguel Y….Gupta S May FP Gastro 2020; Bharti…Gupta Cancer 2019; Lovett Am J Gastro 2018; Jetelina JGIM 2019 Issaka Am J Gastro 2017; Issaka JAMA Netw Open 2021; Mohan GIE 2022; Mohl MT JAMA Net Open 2023; Zaki Gastro 2025

Opportunities for addressing non-invasive test follow up

- Patient-level: navigation
- Provider-level: reminders and performance feedback
- System-level: automated referrals; pre-colonoscopy calls; patient registries; problem list/coding
- Dissemination of new HEDIS (Healthcare Effectiveness Data and Information Set) quality metric



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Scorecard: where are we and where do we need to go?

Current State	Future State
• Epidemiology of CRC is changing • ↑ Early and middle age onset	• Discover etiologic drivers • High rates of screening participation • High awareness/diagnostic resolution of symptoms
• RCTs: Similar FIT and colonoscopy outcomes on intent to screen but different per protocol	• Results of ongoing studies with longer follow up
• Multiple established and emerging tests without RCTs • Highly variable sensitivity	• Comparative studies of participation, including of replacement of established tests by emerging tests
• Abnormal test follow up suboptimal	• Novel interventional trials • Quality metric that promotes tracking and follow up

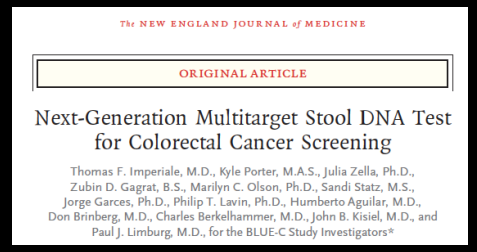
Thank you!

- Grant Support:
  - Curebound Cancer Health Equity Grant
  - Sam M. Walton family

Contact: s1gupta@health.ucsd.edu

End

Recent Evidence: FDA approved non-invasive tests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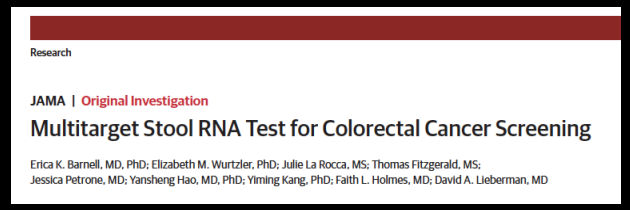
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JAMA | Original Investigation

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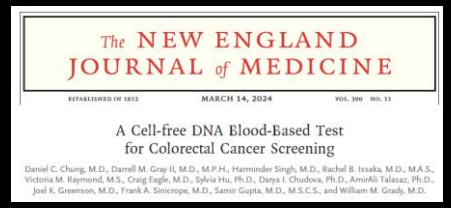
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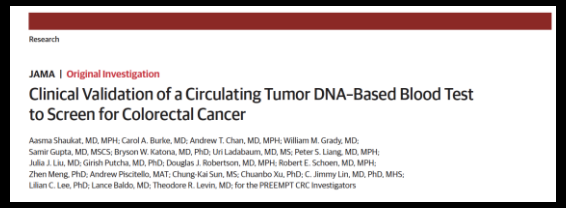
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Test	Approach
sDNA-FIT 2.0 (Cologuard Plus, Exact Sciences)	• Methylated DNA markers: LASS4, LRRC4, PPP2R5C, ZDHHC1 (ref marker) • FIT
sRNA-FIT (Colosense, Geneoscopy)	• RNA markers: GAPDH, ACY1, AREG, TNFRSF10B, CDH1, EGLN2, KRAS, SMAD4 • OC Sensor FIT* • History of tobacco smoking
cfDNA (Shield, Guardant Health)	• DNA methylation patterns • Aberrant fragmentation patterns • Somatic pathogenic variants in APC and KRAS
cfDNA (SimpleScreen, Freenome)	• DNA methylation

Imperiale T NEJM 2024; Barnell E JAMA 2023; Chung D NEJM 2024; Shaukat A JAMA 2025