Updates in Colon Cancer Screening Guidelines and Novel tests

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Disclosures

- Consultant for Freenome, Motus GI, Iterative Health, UniversalDx
- Member of the USMSTF, ACG BOT

Objectives

- Review Colorectal cancer (CRC) screening in patients at average risk and family Hx
- Current Screening needs
- Future options for CRC screening
- Take home points

Case 1

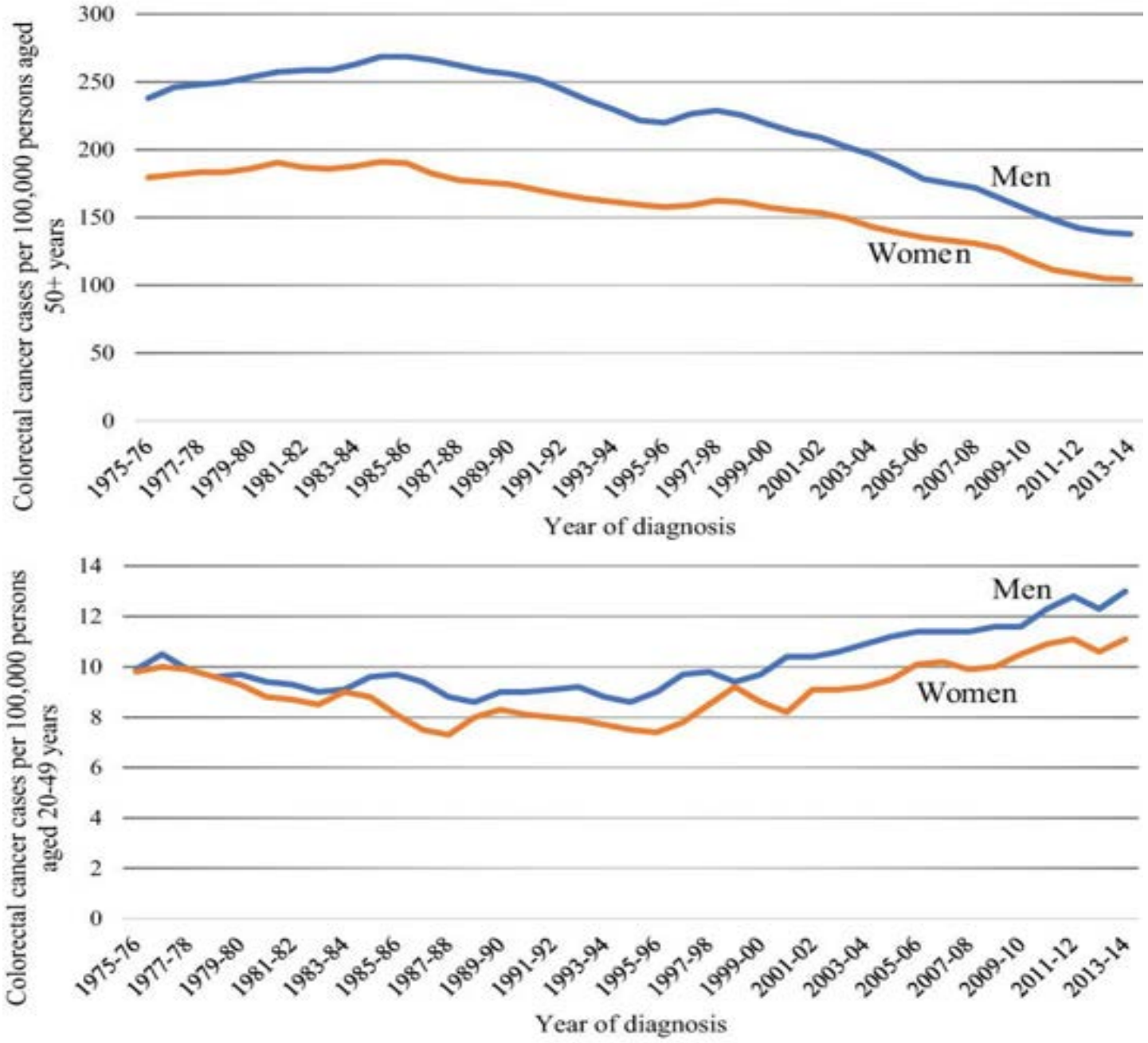
45-year-old healthy male asks about Colon cancer screening and his options. Reports no family hx of CRC or advanced polyps

- When would you recommend colorectal cancer screening?
  A. Now
  B. Age 50

- What modality would you recommend?
  A. Colonoscopy
  B. Stool-based test
  C. Patient choice

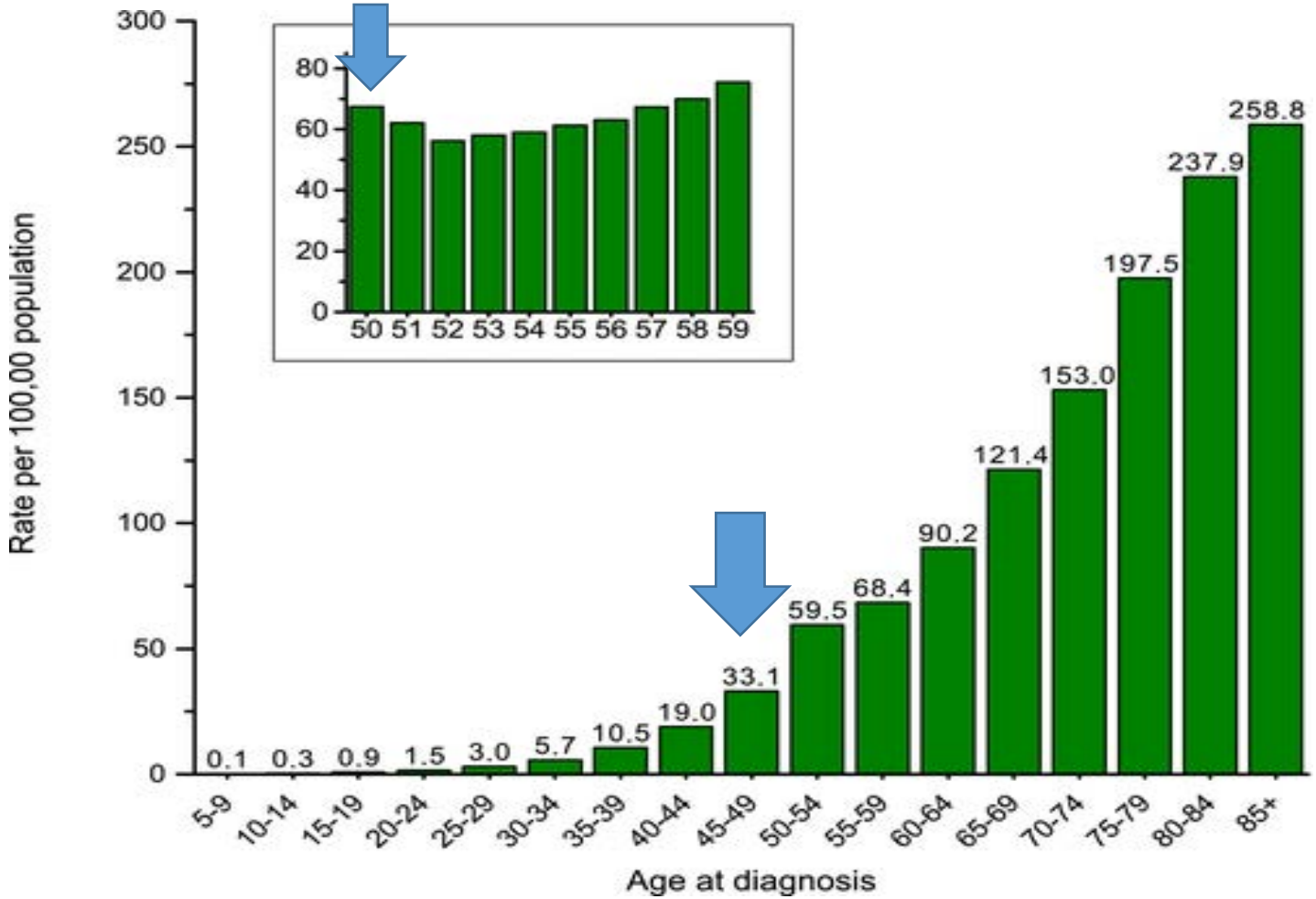
- If screening test is normal, when should he have his next screening?
  A. 5 years
  B. 10 years
  C. Age 50

CRC Incidence



Siegel RL et al. J Natl Cancer Inst. 2017;109(8):27-32

CRC Incidence over time in the US



2011-2016

Siegel R et al. CA: a cancer journal for clinicians 2020;70:145-164

ACG Clinical Guidelines: Colorectal Cancer Screening 2021

Aasma Shaukat, MD, MPH, FACG[1,2], Charles J. Kahi, MD, MSc, FACG[3-7], Carol A. Burke, MD, FACG[4], Linda Rabeneck, MD, MPH, MACG[5], Bryan G. Sauer, MD, MSc, FACG (GRADE Methodologist)[6] and Douglas K. Rex, MD, MACG[3]

1	We recommend colorectal cancer (CRC) screening in average-risk individuals between ages 50 and 75 yr to reduce incidence of advanced adenoma, CRC, and mortality from CRC
2	We suggest CRC screening in average-risk individuals between ages 45 and 49 yr to reduce incidence of advanced adenoma, CRC, and mortality from CRC
3	We suggest that a decision to continue screening beyond age 75 yr be individualized
4	We recommend colonoscopy and fecal immunochemical testing (FIT) as the primary screening modalities for CRC screening

ACG Clinical Guidelines: Colorectal Cancer Screening 2021, *The American Journal of Gastroenterology* 2021;116:458-479

USPSTF Recommendations 2021

Recommendation	GRADE	
Screen average risk men and women 50-75	A	High certainty of substantial net benefit
Screen average risk men and women starting at age 45	B	Moderate certainty of moderate net benefit
Individualize decision to screen 76-85	C	Moderate certainty of small net benefit

Recommended screening strategies include

- High-sensitivity guaiac fecal occult blood test (HSgFOBT) or fecal immunochemical test (FIT) every year
- Stool DNA-FIT every 1 to 3 years
- Computed tomography colonography every 5 years
- Flexible sigmoidoscopy every 5 years
- Flexible sigmoidoscopy every 10 years + annual FIT
- Colonoscopy screening every 10 years

- Grade A or B recs are covered by Medicare
- Other payors follow Medicare

US Preventive Services Task Force. Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement. *JAMA.* 2021;325(19):1965-1977

When Should Screening Start for CRC?

ACG

- Recommended in all adults 50 to 75 years of age
- Suggest in all average risk adults 45 to 49 years of age
- Recommend decision to screen after 75 be individualized

USPSTF

- Recommended in all adults 50 to 75 years of age
- Recommended in adults 45 to 49 years of age
- Recommended that clinicians selectively offer screening in adults 76-85 years of age

MSTF

- Suggested to all average-risk adults ages 45 to 49
- For adults ages 76 to 85, the decision to start or continue screening should be individualized and based on prior screening history, life expectancy, CRC risk, and personal preference
- Screening is not recommended after age 85

Shaukat A. et al ACG Clinical Guidelines: AJG 2021;116:458-479; USPSTF. JAMA. 2021;325:1965-1977. Patel SG, et al. Am J Gastro. 2022. 117:57-69.

ACP Guidance 2023

- Start screening at age 50 years
- Consider not screening asymptoma ages of 45 to 49
- Discuss the uncertainty around bene population
- Select among a fecal immunochemi occult blood test every 2 years, colo sigmoidoscopy every 10 years plus a years
- Clinicians should not use stool DNA, CTC, capsule endoscopy, urine, or serum screening tests for colorectal cancer

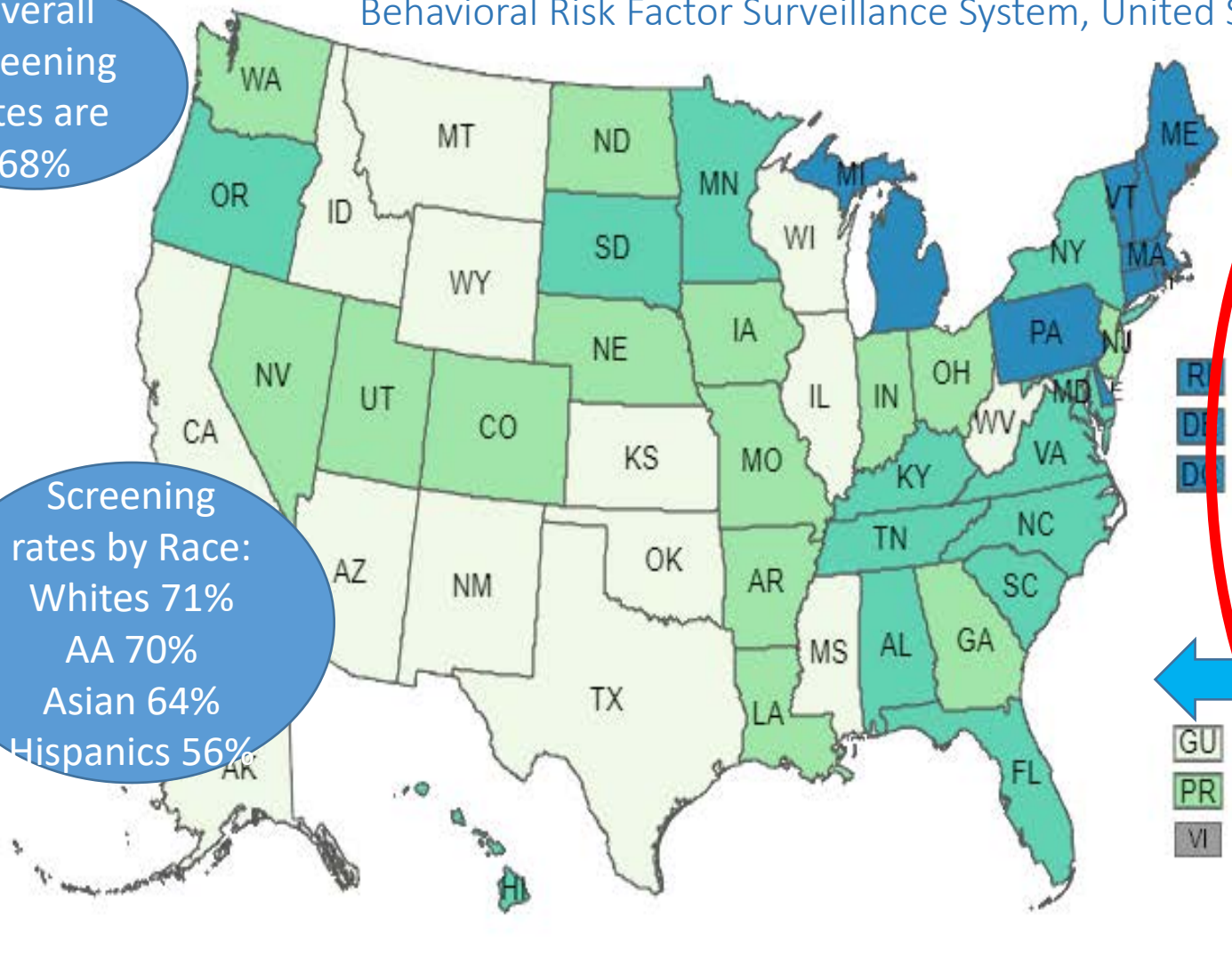
Qaseem A. et al. Screening for Colorectal Cancer in Asymptomatic Average-Risk Adults: A Guidance Statement From the American College of Physicians. Annals Int Med 2023, https://doi.org/10.7326/M23-0779

2020: Percentage of Adults 50–75 Years fully meeting USPSTF recommendation for CRC Screening, by State

Behavioral Risk Factor Surveillance System, United States, 2020

Overall screening rates are 68%

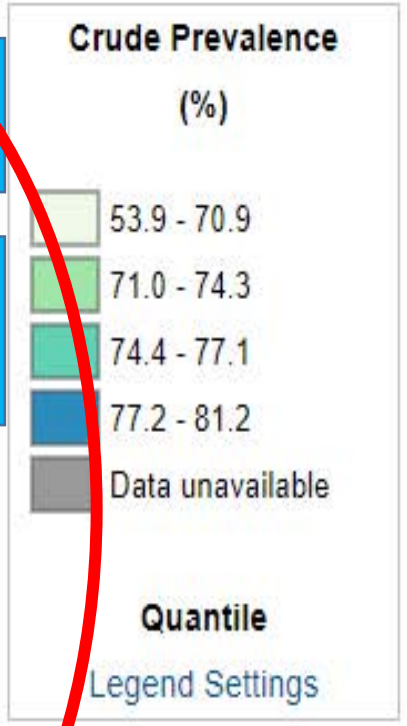
Screening rates by Race:
Whites 71%
AA 70%
Asian 64%
Hispanics 56%



Health Insurance:
Yes 71%
No 40%

Regular HCP:
Yes 73%
No 36%

21 million adults 45-49 yrs



Joseph DA, et al. MMWR Morb Mortal Wkly Rep 2020;69:253-259.

Despite existing screening options, many eligible patients are not getting screened for CRC

CRC screening rates, adults aged 45+

59%

?

80%

Colorectal cancer statistics, 2023. Siegel RL et al. CA: A Cancer J for Clinicians. 2023. doi: 10.3322/caac.21772

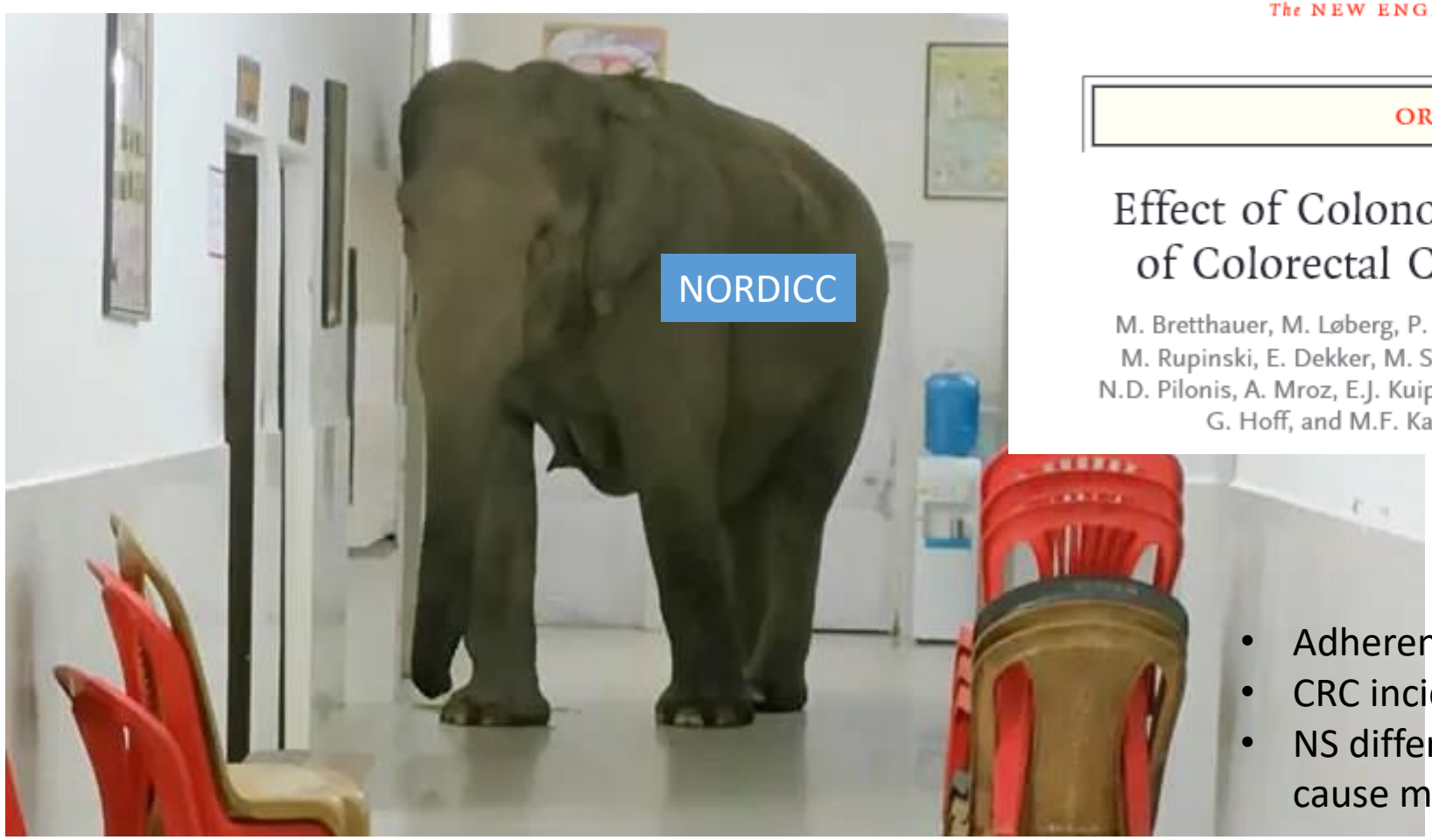
Who and how?

- **Newly Eligible + Overdue + never screened**
- **Endoscopic capacity + Access**
- **Ensuring Health Equity**

What got us here may not be enough to get us there

80% in every Community

The elephant in the Room



The NEW ENGLAND JOURNAL of MEDICINE

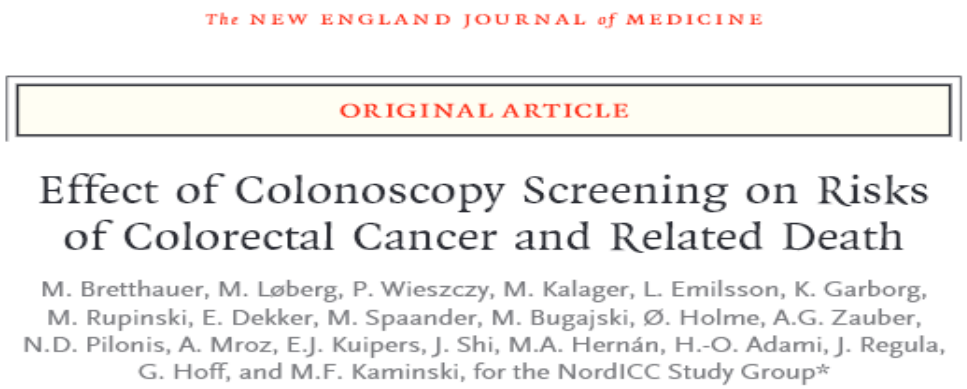
ORIGINAL ARTICLE

Effect of Colonoscopy Screening on Risks of Colorectal Cancer and Related Death

M. Bretthauer, M. Løberg, P. Wieszczy, M. Kalager, L. Emilsson, K. Garborg, M. Rupinski, E. Dekker, M. Spaander, M. Bugajski, Ø. Holme, A.G. Zauber, N.D. Pilonis, A. Mroz, E.J. Kuipers, J. Shi, M.A. Hernán, H.-O. Adami, J. Regula, G. Hoff, and M.F. Kaminski, for the NordICC Study Group*

- Adherence to colonoscopy: 42%
- CRC incidence risk reduction 18%
- NS difference in CRC mortality and all cause mortality

Putting it in context: Adherence is Key



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- Emphasizes importance of adherence
- Quality of Colonoscopy
- Underpowered for CRC Mortality difference
- Put in context with other data
- **Message**: Don’t let patients be discouraged or dissuaded

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19. We recommend organized screening programs to improve adherence to CRC screening compared with opportunistic screening.

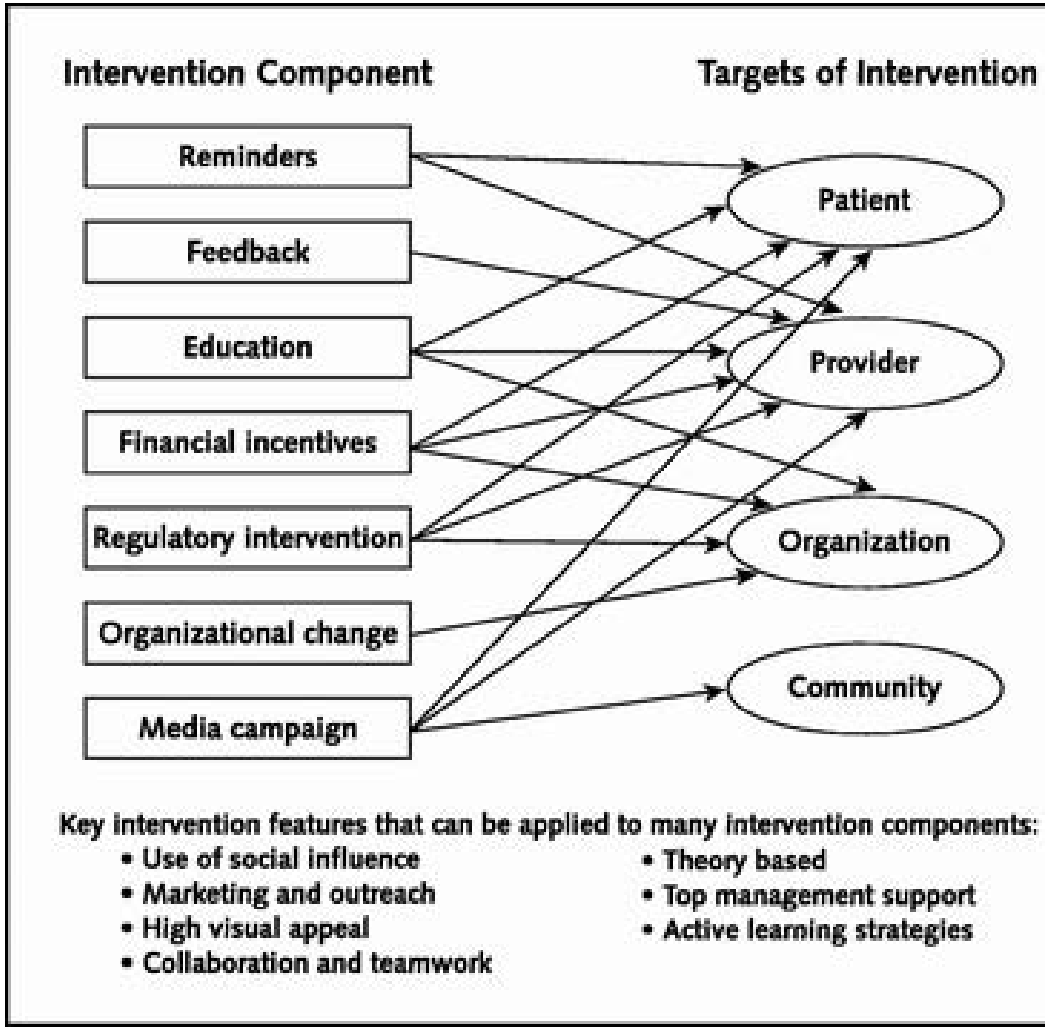
Strong recommendation; low-quality evidence

20. We suggest the following strategies to improve adherence to screening: patient navigation, patient reminders, clinician interventions, provider recommendations, and clinical decision support tools.

Conditional recommendation; very low-quality evidence

ACG Clinical Guidelines: AJG 2021;116:458-479

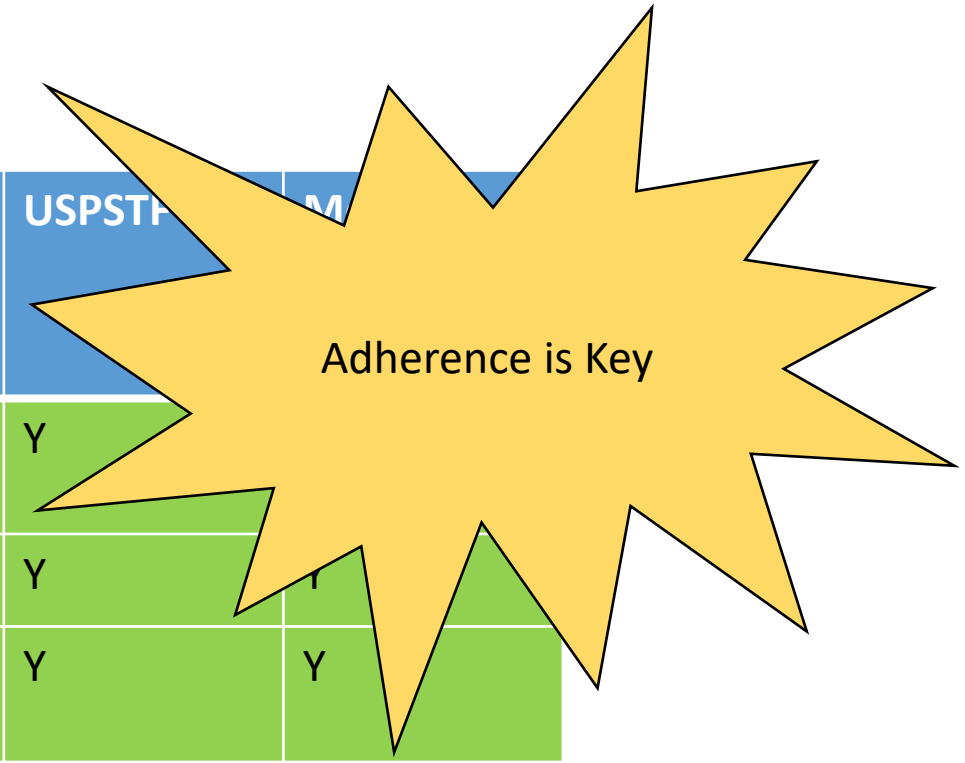
Improving Adherence



Stone EG, et al. Interventions that increase use of adult immunization and cancer screening services: A meta-analysis. Ann Intern Med. 2002;136:641-651

CRC Screening Options

Modality	Sensitivity CRC	Sensitivity AA	Specificity	Invasive	USPSTF	M
Colonoscopy	96%	95%	90%	Y	Y	
FIT	74%	24%	96%	N	Y	Y
mtsDNA stool	92%	42%	87%	N	Y	Y
Septin-9	48%	-	91%	N	N	Y
Liquid Biopsy	-	-	-	N	TBD	TBD



Organized Screening Program improves Adherence

- Kaiser Permanente Northern California
- Screening before and after proactive outreach program (FIT and colonoscopy)
- 2000 to 2015

	Before	After	Absolute change
Adherence	38%	82%	+44%
CRC incidence	95 per 100,000	71 per 100,000	-24%
CRC Mortality	30 per 100,000	14 per 100,000	-52%

Levin TR et al. Gastroenterology 2018;155:1383-91

Preferred CRC Screening Tests Among 1,000 Unscreened Americans

	US MSTF Five Recommended Tests					US MSTF Tier 1 Tests	
	MULTITARGET STOOL DNA TEST EVERY 3 YEARS	COLON VIDEO CAPSULE EVERY 5 YEARS	COLONOSCOPY EVERY 10 YEARS	FIT EVERY YEAR	COLON CT SCAN EVERY 5 YEARS	FIT EVERY YEAR	COLONOSCOPY EVERY 10 YEARS
40-49 yo	34.6%	28.2%	13.7%	12.2%	11.3%	68.9%	31.1%
≥50 yo	37.3%	22.9%	13.6%	18.7%	7.6%	77.4%	22.6%

Makaroff KE et al. Patient Preferences for Colorectal Cancer Screening Tests in Light of Lowering the Screening Age to 45 Years, *Clinical Gastroenterology and Hepatology* (2022). DOI: 10.1016/j.cgh.2022.07.012

Case 1

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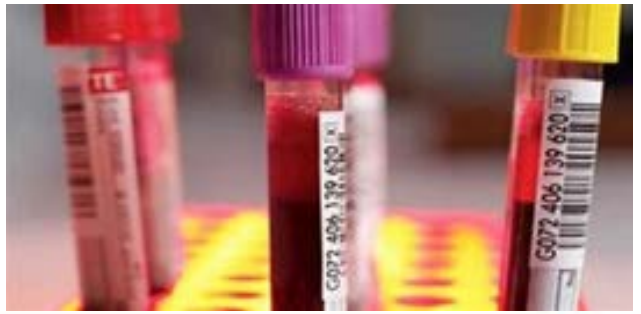
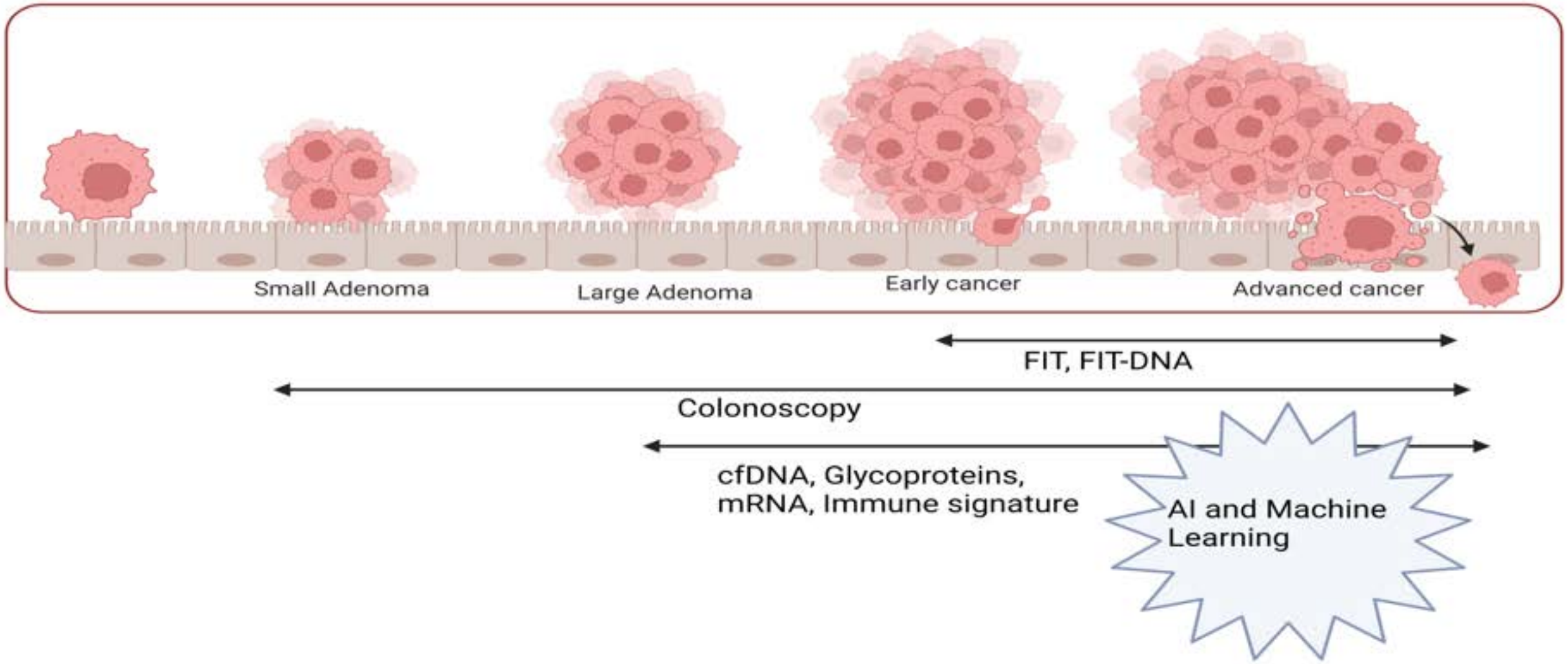
FUTURE

Blood Based CRC screening tests





Stool and Blood-based CRC Screening tests

CRC detection Test	Details of Technology	Special Considerations	Expected Completion
Stool based			
Exact	Multi-target stool DNA+FIT Version 2.0	Target recruitment 29,000	March 2023
Geneoscopy	Mts-RNA test	Target Recruitment 10,000	♦ 2022
Blood-Based			
Freenome	Cell free DNA plus artificial intelligence for CRC and AN (NCT04369053)	Aims to recruit 25,000 average risk individuals between 45-85	
Guardant	ctDNA LUNAR test to detect cell free tumor DNA in blood (NCT04136002)	Aims to recruit 10,000 average risk individuals between 45-84 years	♦ 2022

Sensitivity CRC 95%
Specificity CRC 92%
Sensitivity AA 57%

Sensitivity CRC 94%
Specificity CRC 88%
Sensitivity AA 46%

Shaukat, A., Levin, T.R. Current and future colorectal cancer screening strategies. *Nat Rev Gastroenterol Hepatol* (2022). https://doi.org/10.1038/s41575-022-00661-3

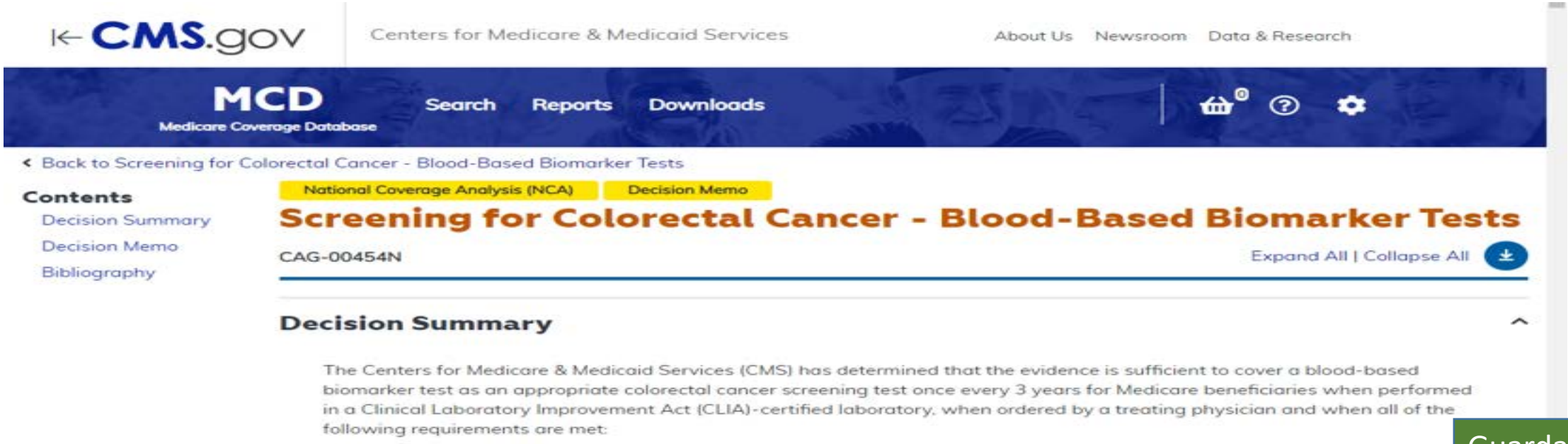

eneoscopy
Transforming Gastrointestinal Health


INTERVENN


CellMax Life


Universal
DIAGNOSTICS

Setting the Bar: CMS National Coverage Decision



Sensitivity for CRC	74%
Specificity for CRC	90%
FDA approval	✓

Guardant
N=20,000
CRC Sensitivity: 83%; CRC Specificity 90%;
AA sensitivity: 13%

Practical questions

- How ordered?→information required
- How completed?→Navigation or not
- How collected?→ clinic, commercial lab, mobile phlebotomy, home
- How Processed?→ Commercial lab, central lab, regional labs
- Require interpretation?→Clinician or staff?

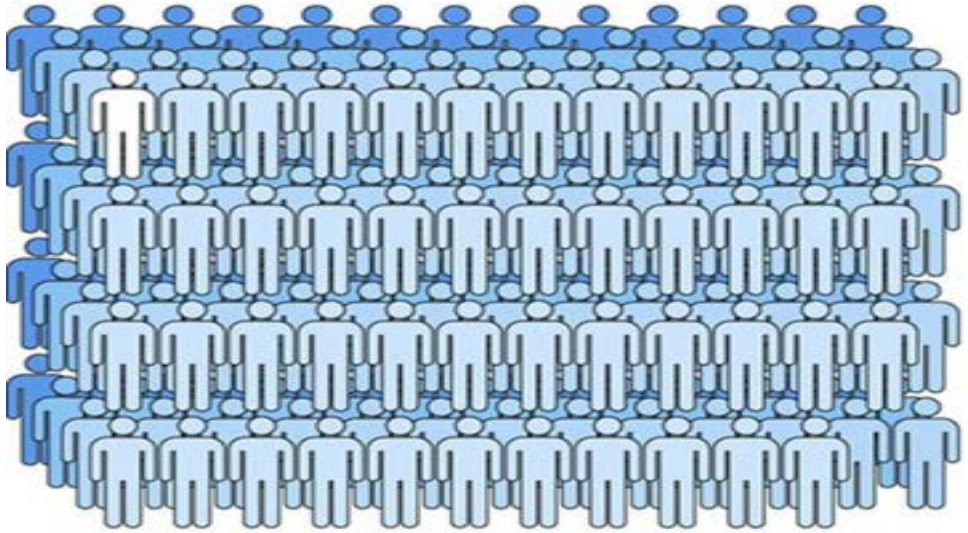
Bigger questions

- Repeat interval?→Data, company, experts, modelling
- Long term outcome→?Association with CRC incidence and mortality
- Follow up of false positives?
- Comparative effectiveness?
- Availability
- Cost
- Adherence to the two steps?

Adherence to Blood based tests

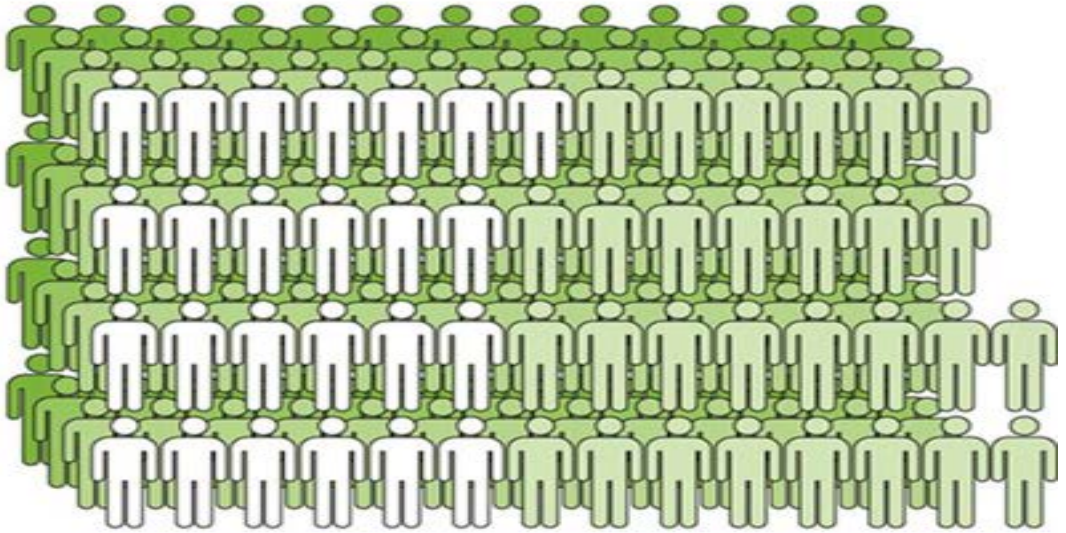
413 randomized adults

Blood Test Arm



99.5% (CI95: 97.3%-100%)
completed test

FIT Arm

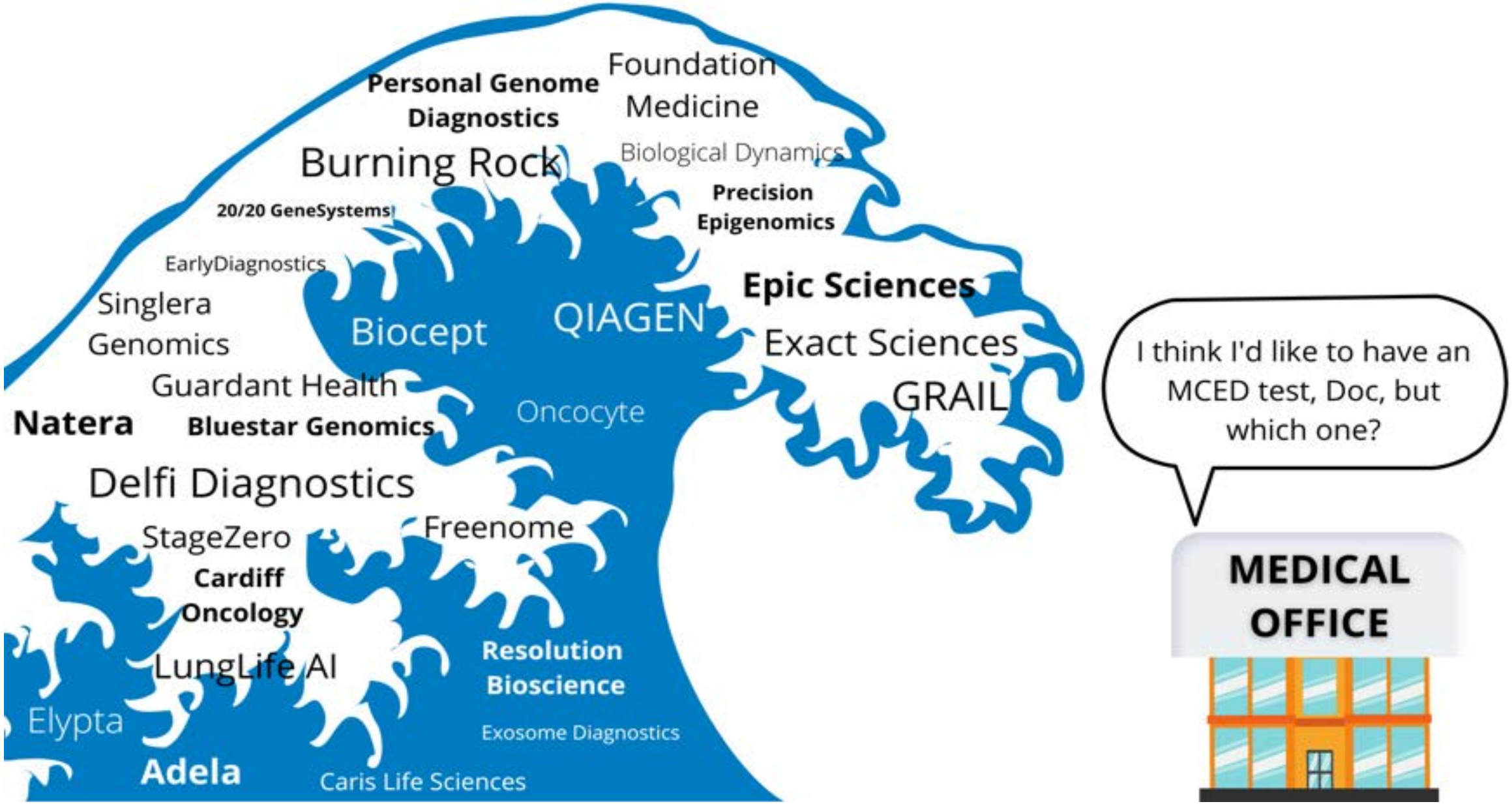


88.1% (CI95: 83.0%-91.8%)
completed test

= a difference of **11.4%** (CI95: 6.9%-15.9%, p<.001)

Liles EG et al. Uptake of a colorectal cancer screening blood test is higher than of a fecal test offered in clinic: A randomized trial. 2017 Cancer Treatment and Research Communications;10: 27-31

Multi Cancer Tests: Pathway to Population Screening


Personal Genome Diagnostics
Foundation Medicine
Burning Rock
Biological Dynamics
20/20 GeneSystems
Precision Epigenomics
EarlyDiagnostics
Epic Sciences
Singlera Genomics
Biocept
QIAGEN
Exact Sciences
Guardant Health
GRAIL
Natera
Bluestar Genomics
Oncocyte
Delfi Diagnostics
Freenome
StageZero
Cardiff Oncology
LungLife AI
Resolution Bioscience
Elypta
Exosome Diagnostics
Adela
Caris Life Sciences
I think I'd like to have an MCED test, Doc, but which one?
MEDICAL OFFICE

Natural History of the Targeted Cancers

- Knowledge of natural history is best for cancers we are already screening
  - Breast, lung, prostate, colon
- Limited for others that are a target of MCEDs:
  - Pancreatic, liver
- Without knowledge of the natural history, hard to predict degree of stage shift

The ability to confirm a cancer signal

- Anxiety associated with a positive test impairs quality of life
- Single cancer screening tests: image guided biopsies or colonoscopy
- Imaging tests can be imperfect
- MCED-may lead to whole body scanning-risk for incidentalomas
- What to do about false positives?
- Will need guidance on algorithms to approach +MCED tests
- Burden of confirming MCED test results will be the costliest aspect of population screening

Published Nov 4, 2021

San Francisco Rapper & Cannabis Entrepreneur, Berner, 40, Shares That His Cancer Surgery 'Went Well,' But 'We Still Have a Battle to Fight'

Berner revealed last month that doctors discovered his cancer after a series of blood tests.

Sydney Schaefer

Details

Do Blood Tests to Detect Cancer Actually Work?

These tests are in market now, as LDTs

- Galleri being sold for $949 per test, but not covered by insurance
- Guardant Shield (CRC specific test) is also available to order now ($895)

- Release of these tests into the market will get ahead of the trials

Summary

- Average risk individuals: Start screening at 45
- Improve screening efforts with emphasis on adherence
- Organized Programs, patient navigation are effective strategies
- Promising blood-based markers for CRC under development, need thorough evaluation

Thank you!

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