# Colon Cancer Screening Updates

**Katie Hutchins, MD, FACG**
Assistant Professor
Division of Gastroenterology

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University of Nebraska Medical Center

# Disclosures Statement

No conflicts of interest

No discussion of off-label uses

# Objectives

Review the current colorectal (CRC) screening tests

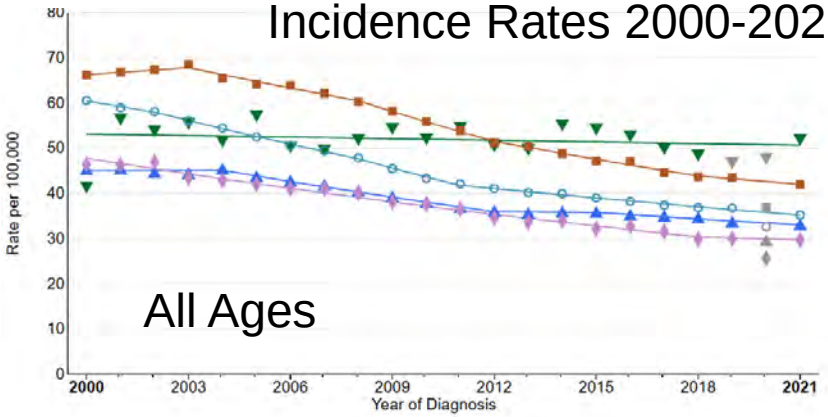
Discuss newer CRC screening tests

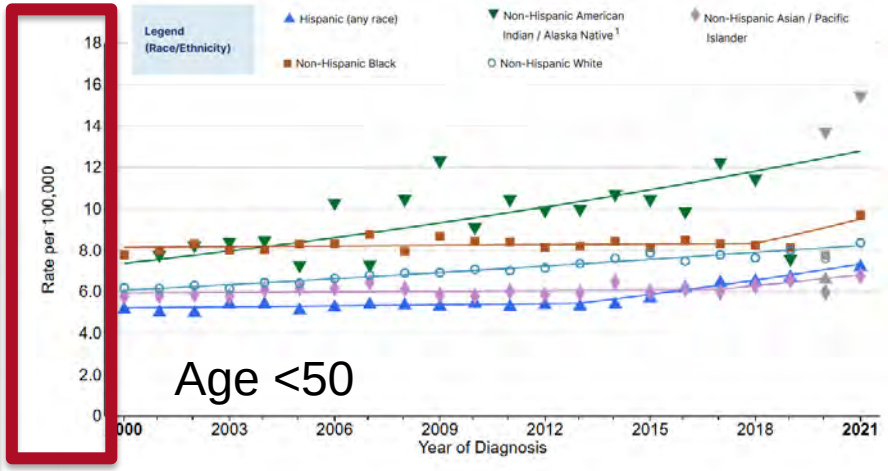
Outline strategies to improve screening rates

# Colorectal Cancer

1. #3 in new cancer & #2 deaths
2. Incidence Rate: All ages ↓
3. Incidence Rate: < 50 ↑
4. Lifetime Risk: **4%**

Incidence Rates 2000-2021




Seer.cancer.gov

# Screening Age: Average risk

**Multi-society Task Force (2022)  ACG (2021), USPSTF (2021), ACS (2018) ***

- CRC screening in all individuals aged **45 to 75**
- Individuals ages **76 to 85**, the decision to start or continue screening should be individualized and based on prior screening history, comorbidity, life expectancy, CRC risk, and personal preference
- Screening is **NOT** recommended after age 85

*combined / summarized

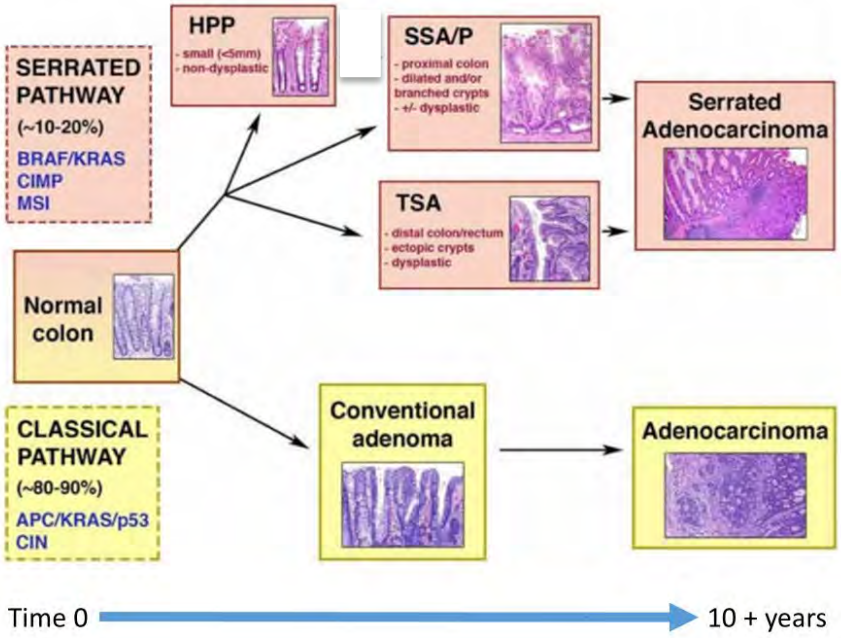
Patel, Swati G et al. Gastroenterology, 2022. V162, Issue 1, 285 – 299
USPSTF. JAMA. 2021;325:1965-1977.
Wolf, Andrew et al. CA CANCER J CLIN 2018;68:250–281

# Purpose of CRC Screening

Detection / Removal of adenoma
Detection / Removal of sessile serrated lesions

Detection of early CRC

Normal colon → Polyp → Cancer Sequence




Baker, AM. *et al. Sci Rep* **5**, 8654 (2015)

# Multi-Society Task Force ranking of CRC screening tests (2017)

| |
|---|
| Tier 1 |
| Colonoscopy every 10 years |
| Annual fecal immunochemical test |
| Tier 2 |
| CT colonography every 5 years |
| FIT-fecal DNA every 3 years |
| Flexible sigmoidoscopy every 10 years (or every 5 years) |
| Tier 3 |
| Capsule colonoscopy every 5 years |
| Available tests not currently recommended |
| Septin 9 |

**Sensitivity for CRC 48.2 – 68%**
Specificty 80 – 91%

Rex et al. AJG. 2017

# Colonoscopy: Quality Indicators Updates 2024

Joint recommendations ASGE & ACG

**Priority Quality Indicators:**

Adenoma Detection Rate (ADR) (age ≥ 45) ≥35%

Women ≥30%  Men ≥40%

Sessile Serrated Lesion Detection Rate (SSLDR)* ≥6%

Bowel Preparation Adequacy Rate ≥90%

Cecal Intubation Rate (CIR) ≥ 95%

Additional Quality Indicators (many more):

Average withdrawal time ≥8 minutes (6)

(must still measure ADR & SSLDR)

Rex, D et al. Quality Indicators for Colonoscopy. AJG. 119(9):p 1754-1780. Sept 2024.
Van Toledo et al. Lancet Gastro & Hep. 2022;7(8):747-54.

# Colonoscopy + AI

GI Genius (Medtronic) – first device

## CADe

Meta-analysis 10 RCT

- ADR RR1.43 (P<.001)
- Polyp Detection Rate 1.44

Shaukat et al: Adenoma detected / colonoscopy
True histology rate

CADe: Higher APC No decrease in THR

## CADx

Resect-and-discard OR diagnose-and-leave strategies

Huang et al. Int J colorectal Dis 2022;37: 495-506)
Samarasena, J et al.Gastroenterology, 2023: 165: 1568 – 1573
Shaukat et al. Gastroenterology. 2022; 163:732-741.

# Novel and future

Stool-based test
- mt-sRNA
- mt-sDNA 2.0

Blood-based tests
- cf-DNA (CRC specific)
- ct-DNA (CRC specific)
- multi-cancer early detection

Imaging Based:
- MR colonography
- CT capsule

# New stool-based tests

## mt-sRNA 2023

COLOSENSE

CRC PREVENT Clinical Trial

First RNA molecular test for CRC screening

FIT plus 8 specific RNA transcripts

Sensitivity st I/II vs III/IV CRC (92.3% vs 100%)

FDA approved for commercial use 2024

## mt-sDNA 2.0 (Cologuard Plus) 2024

Why: Improve specificity.

*study included individuals **40yr and older**

New molecular DNA markers (methylated DNA markers)

No head-to-head comparison Cologuard vs Cologuard+

FDA approved October 2024

Available to order March 31,2025

Barnell et al. JAMA. 2023;330(18):1760-1768
Imperiale, T et al. NEJM 2024;390:984-993

# Blood-based CRC screening
# CRC specific

## Cell Free DNA (cfDNA)

Detects **fragmented DNA** in the blood

*normal and tumor

2024Guardant Shield

First blood-based CRC test

FDA approved July 2024

Panel interrogates cfDNA

Genomic alterations

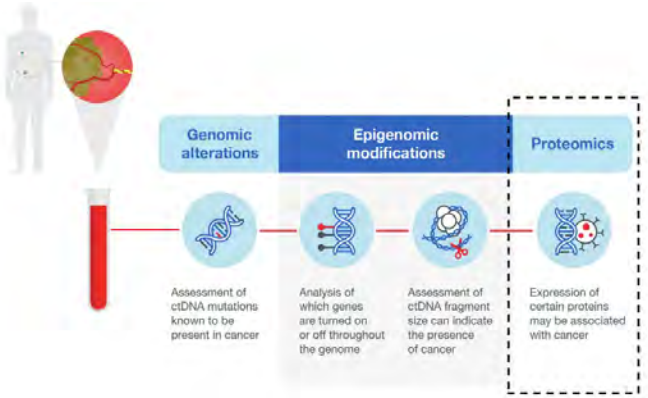
Aberrant methylation status

Fragmentomic patterns

## Circulating tumor (ctDNA)

Subset of cfDNA that specifically originates from **tumor cells**.

Designed to detect tumor:




Higher sensitivity than cfDNA blood tests

Guardant Lunar-2

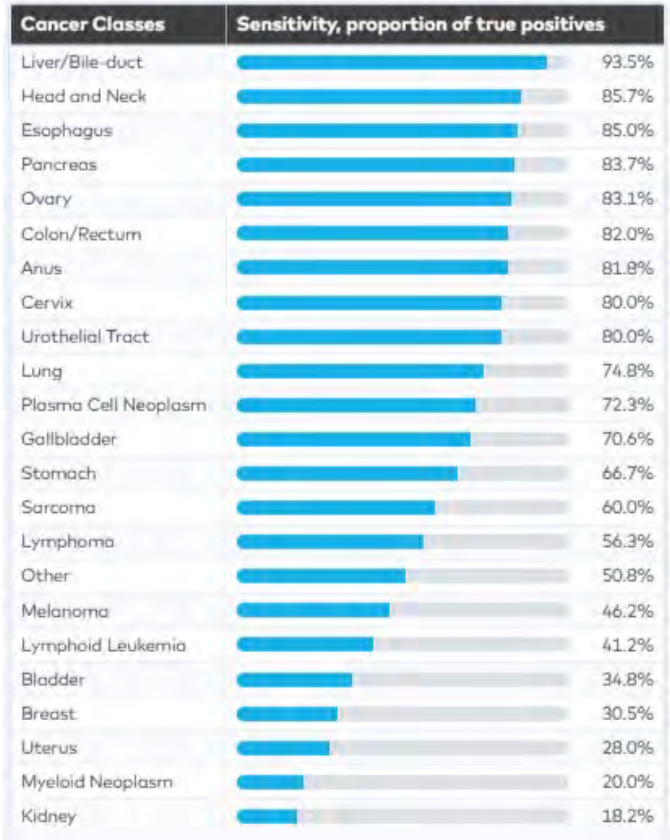
Not FDA approved

Chung et al. NEJM. 2024; 390:973-983
Bessa et al. Annals of Oncology. Oct 2023: 1187-1193

# Blood-based multi-cancer screening

CancerSEEK

GRAIL



| Cancer Classes | Sensitivity, proportion of true positives |
|---|---|
| Liver/Bile-duct | 93.5% |
| Head and Neck | 85.7% |
| Esophagus | 85.0% |
| Pancreas | 83.7% |
| Ovary | 83.1% |
| Colon/Rectum | 82.0% |
| Anus | 81.8% |
| Cervix | 80.0% |
| Urothelial Tract | 80.0% |
| Lung | 74.8% |
| Plasma Cell Neoplasm | 72.3% |
| Gallbladder | 70.6% |
| Stomach | 66.7% |
| Sarcoma | 60.0% |
| Lymphoma | 56.3% |
| Other | 50.8% |
| Melanoma | 46.2% |
| Lymphoid Leukemia | 41.2% |
| Bladder | 34.8% |
| Breast | 30.5% |
| Uterus | 28.0% |
| Myeloid Neoplasm | 20.0% |
| Kidney | 18.2% |

# Blood-based Tests

| | | |
|---|---|---|
| Freenome | cfDNA | CRC specific |
| Guardant Grail | cfDNA | CRC specific |
| | | |
| mSEPT9 | ctDNA | CRC specific |
| Guardant Lunar-2 | ctDNA | CRC specific |
| Clinical Genomics | ct DNA | CRC specific |
| | | |
| CancerSEEK | ctDNA | Multi-cancer |
| Grail | ctDNA | Multi-cancer |

# Imaging

MRI colonography (MRC)

- Non-invasive
- More prevalent in Europe. Investigational in US.
- Similar to CTC in S/S for AA, CRC
- Advantage over CTC: no radiation

CT Capsule:

- Check-Cap: prepless x-ray imaging capsule
- Small amount of contrast used.

- Emits low dose x-ray beam by a miniature electric motor as the capsule travels through the colon
- Generates a 3D reconstruction of the colon

- In development and validation stages

# Comparing Tests

| | Test | Sensitivity CRC | Sensitivity AA | Specificity |
|---|---|---|---|---|
| Visualization based | Colonoscopy | 95% | 95% | 86% |
| | CT colonography | 84% | | 88% |
| Stool based | FIT | 74% | 24% | 94% |
| | mts-DNA | 93% | 42% | 85-90% |
| | mts-RNA | 94% | 46% | 88% |
| | mts-DNA 2.0 | 94% | 43% | 91% |
| Blood based | cf-DNA | 83.1% | 13.1% | 89.6% |
| | ct-DNA | 93% | 23% | 90% |

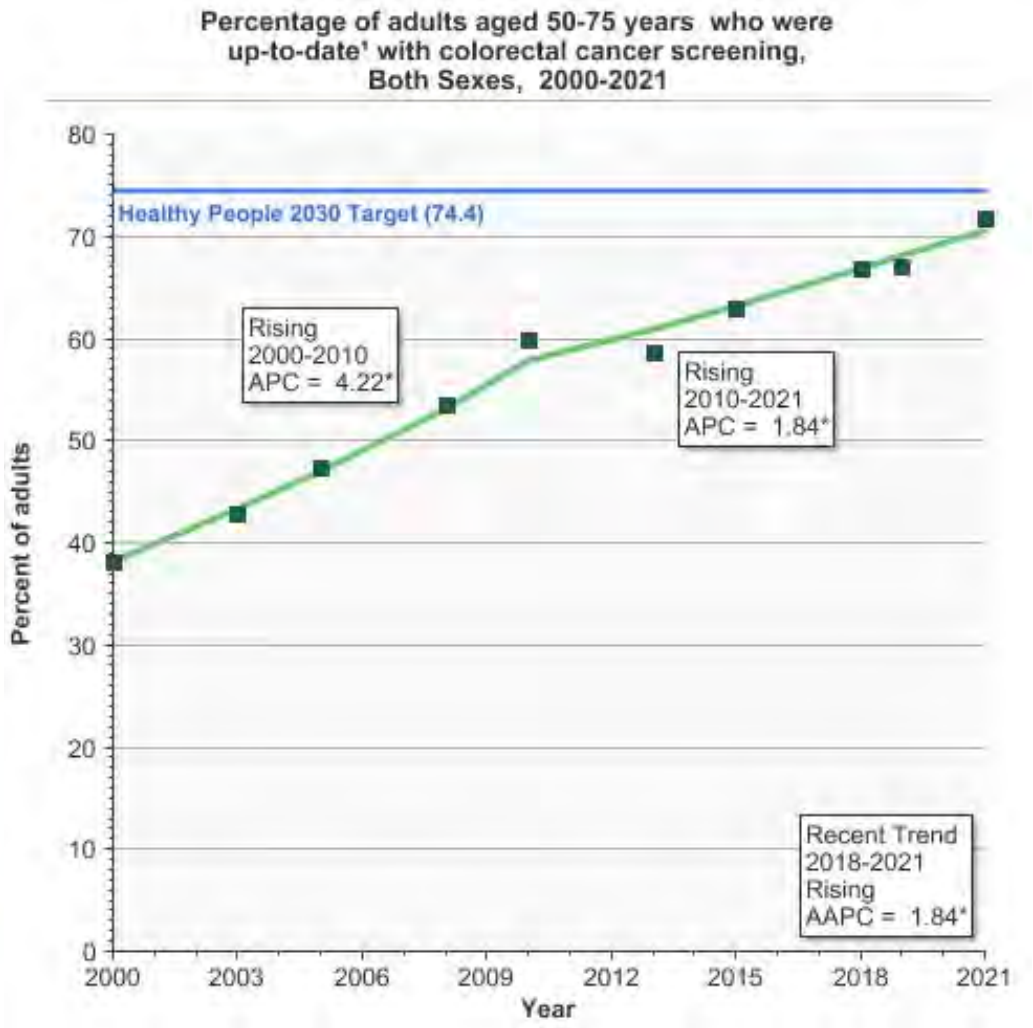
Barnell et al. JAMA. 2023. Nov 14;330 (18): 1760-1768
Bessa et al. Ann Olcol. 2023 Dec;34(12):1187-1193.
Chung et al. NEJM 2024;390:973-983
Imperiale et al. NEJM 2024/390:984-993

# Comparing Tests

| | Test | Sensitivity CRC | Cost | Frequency |
|---|---|---|---|---|
| Visualization based | Colonoscopy | 95% | varies ~$2500 | 10 yrs |
| | CT colonography | 84% | varies | 5 yrs |
| Stool based | FIT | 74% | $25 | 1 yr |
| | mts-DNA Cologuard | 93% | ~$500 | 3 yrs |
| | mts-RNA | 94% | ? | 88% |
| | mts-DNA 2.0 Cologuard + | 94% | $599 | 3 yrs |
| Blood based | Guardant Shield | 83.1% | $1495 | ? 1 yr |
| | GRAIL | 82% | $950 | ? 1 yr |

Barnell et al. JAMA. 2023. Nov 14;330 (18): 1760-1768
Bessa et al. Ann Olcol. 2023 Dec;34(12):1187-1193.
Chung et al. NEJM 2024;390:973-983
Imperiale et al. NEJM 2024;390:984-993

# Current Screening Rates → Goal




**Screening rates vary**

Race / Ethnicity
- Hispanic; 63.1%

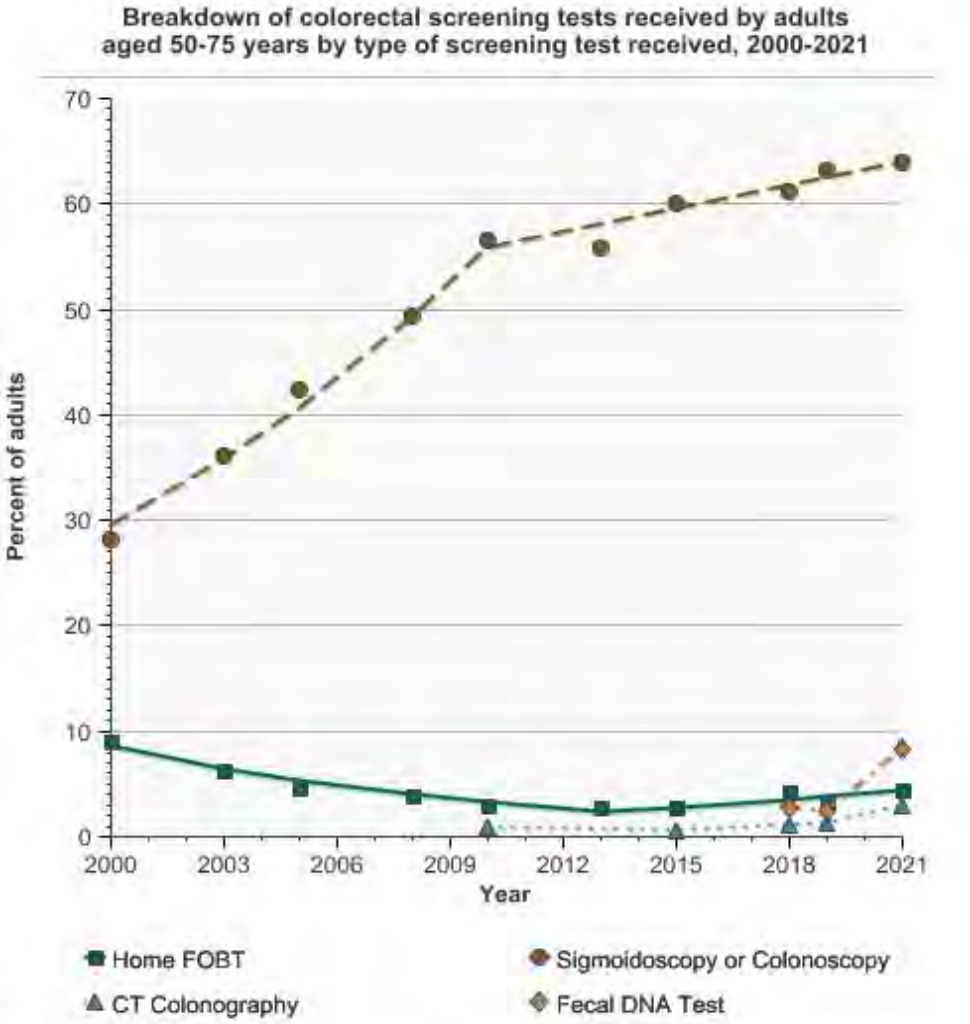
Poverty Level:
- <200% FPL: 61.1%

Education Level:
- Less than HS: 58.8%
- HS: 67.1%

**Healthy People 2030**

Cancer Trends Progress Report
National Cancer Institute, NIH, DHHS, Bethesda, MD, March 2024, https://progressreport.cancer.gov

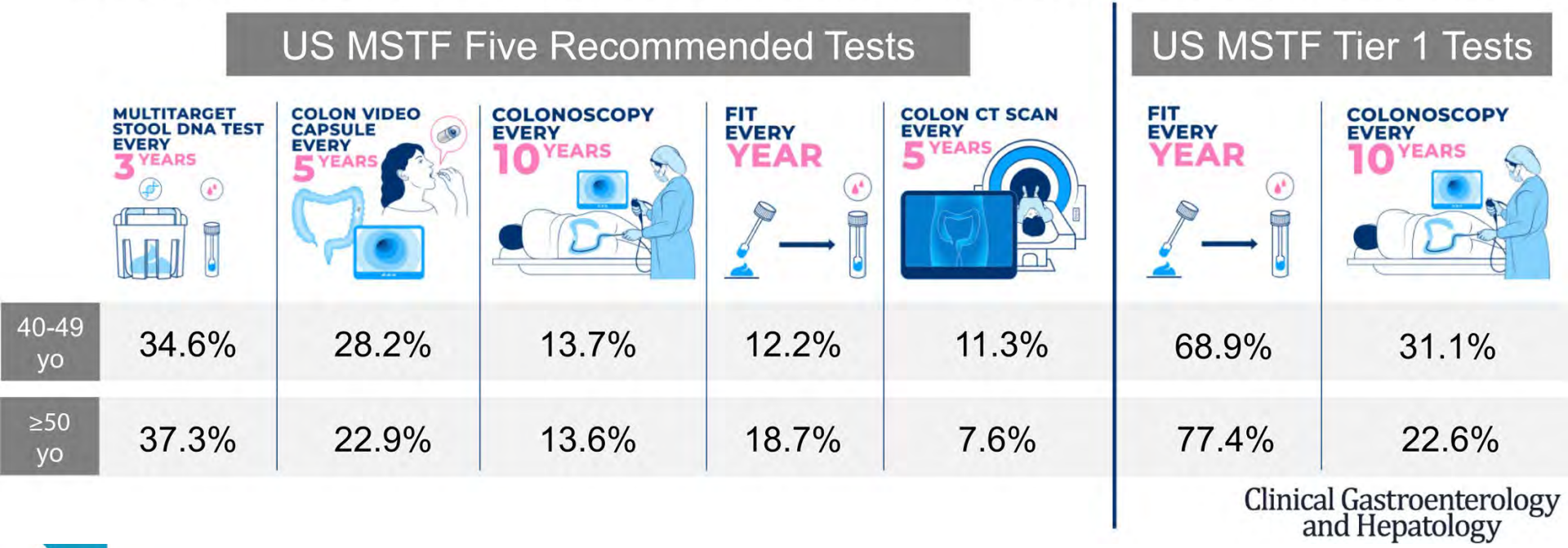
# Test Utilization




Source: Centers for Disease Control and Prevention, National Center for Health Statistics. National Health Interview Survey.
Data are age-adjusted to the 2000 US standard population using age groups: 50-64, 65-75.

# Evaluating the importance of options

## Preferred CRC Screening Tests Among 1,000 Unscreened Americans




Clinical Gastroenterology and Hepatology

Makaroff KE, et al. Patient Preferences for Colorectal Cancer Screening Tests in Light of Lowering the Screening Age to 45 Years. Clin Gastroenterol Hepatol. 2023 Feb;21(2):520-531.e10.

# Patient Favorites: Blood vs Stool?

**Overdue** for CRC (average risk)

413 patient

- 210 FIT → 88.1%
- 203 Epi proColon → 99.5%

67% of participants with (+) test in each group had or scheduled colonoscopy within 3 months of (+)

Liles EG et al.Cancer Treatment & Research Communications;10: 27-31

# Take Away Points

CRC screening is designed to identify advanced adenomas, sessile serrated lesions or early CRC

Multiple tests options exist

Test performance varies

Strategy to improve screening rates: Offer more than colonoscopy

# Questions

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