The Benefit of 80% Adherence in All Communities:

CISNET Modeling Studies for Colorectal Cancer Screening

National Colorectal Cancer Roundtable
April 15, 2025

John Inadomi, MD University of Utah Health
Amy Knudsen, PhD Massachusetts General Hospital
Carolyn Rutter, PhD Fred Hutch Cancer Center

CRC Screening
U.S. Preventive Services Task Force

- Start and Stop in Average Risk Adults:
  - Ages 45-49 years Grade B
  - Ages 50-75 years Grade A
  - Ages 76-85 years Grade C
  - Older than 85 years: do not screen

JAMA 2021

CRC Screening
U.S. Preventive Services Task Force

- Stool Based Tests:
  - Fecal occult blood testing annually*
  - FIT-DNA testing every 1 or 3 years
- Direct Visualization Tests:
  - Sigmoidoscopy
    - Every 5 years
    - Every 10 years with annual FOBT *
  - CT colonography every 5 years
  - Colonoscopy every 10 years

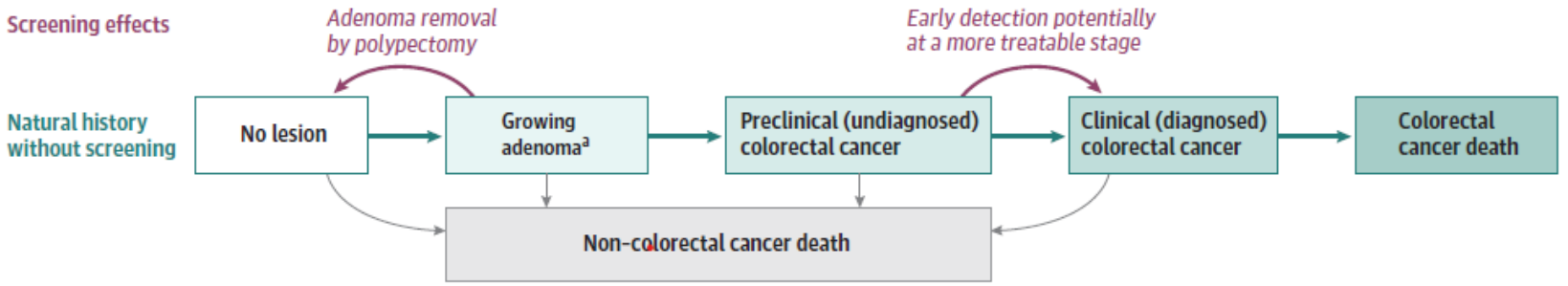
*FIT or high-sensitivity gFOBT (Hemoccult Sensa)

JAMA 2021

Cancer Intervention & Surveillance Modeling Network (CISNET)

- Funded by the National Cancer Institute since 2000
- Supports development of computer models that simulate the natural history of cancer and the effects of screening

Figure 1. Natural History of Colorectal Cancer and the Effects of Screening as Simulated by SimCRC, CRC-SPIN, and MISCAN



Knudsen et al. *JAMA* 2021; 325(19):1998-2011

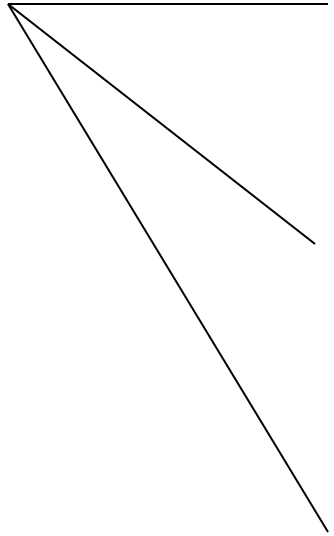
- CISNET models allow us to ask and answer “what if” questions in a quick and timely manner, relative to randomized trials

CISNET Colorectal Cancer Models

- CRC-SPIN
  - Carolyn Rutter (PI)
  - Pedro Nascimento de Lima
- MISCAN-Colon
  - Iris Lansdorp-Vogelaar (PI)
  - Chiara Bruck
  - Rosita van den Putelaar
- SimCRC
  - Karen Kuntz (PI)
  - Amy Knudsen (PI)
  - Fernando Alarid Escudero
  - Selina Pi
- Coordinating Center
  - Ann Zauber (PI)
  - John Inadomi (PI)
  - Anne Hahn

Healthcare Policy Decisions Supported by CISNET CRC Modeling

- **US Preventive Services Task Force CRC screening recommendations (2008, 2016, 2021)**



Annals of Internal Medicine

Evaluating Test Strategies for Colorectal Cancer Screening:
A Decision Analysis for the U.S. Preventive Services Task Force

US Preventive Services Task Force | MODELING STUDY

Estimation of Benefits, Burden, and Harms
of Colorectal Cancer Screening Strategies
Modeling Study for the US Preventive Services Task Force

JAMA | US Preventive Services Task Force | MODELING STUDY

Colorectal Cancer Screening
An Updated Modeling Study for the US Preventive Services Task Force

Healthcare Policy Decisions Supported by CISNET CRC Modeling

- US Preventive Services Task Force CRC screening recommendations (2008, 2016, 2021)
- **American Cancer Society CRC screening guideline (2018)**

Cancer

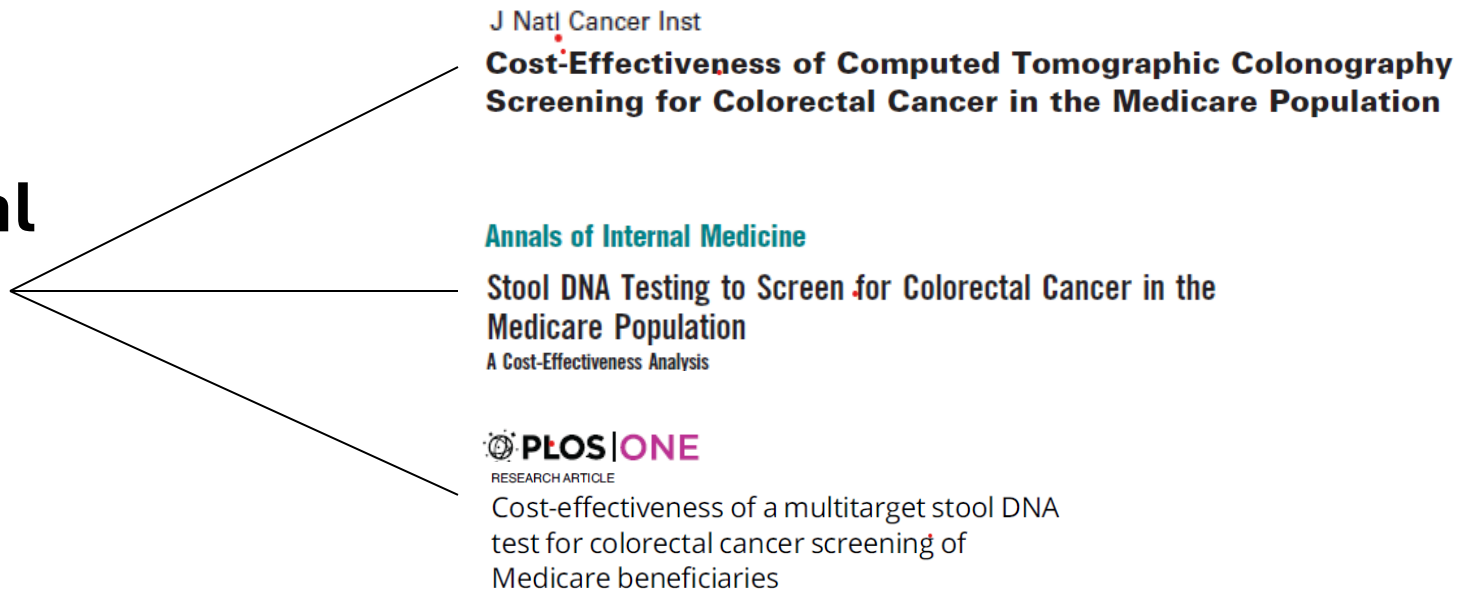
The Impact of the Rising Colorectal Cancer Incidence in Young Adults on the Optimal Age to Start Screening: Microsimulation Analysis I to Inform the American Cancer Society Colorectal Cancer Screening Guideline

Cancer

Optimizing Colorectal Cancer Screening by Race and Sex: Microsimulation Analysis II to Inform the American Cancer Society Colorectal Cancer Screening Guideline

Healthcare Policy Decisions Supported by CISNET CRC Modeling

- US Preventive Services Task Force CRC screening recommendations (2008, 2016, 2021)
- American Cancer Society CRC screening guideline (2018)
- **Centers for Medicare and Medicaid Services National Coverage Determinations (2009, 2010, 2019)**



Status of Colorectal Cancer and Colorectal Cancer Screening in the U.S.

Leading Sites of Cancer in the U.S., 2025

- **New cancer cases (annual)**
  1. Breast 319,750
  2. Prostate 313,780
  3. Lung 226,650
  4. **Colon & rectum 154,270**
  5. Melanoma 104,960

- **Cancer deaths (annual)**
  1. Lung 124,730
  2. **Colon & rectum 52,900**
  3. Pancreas 51,980
  4. Breast 42,680
  5. Prostate 35,770

Source: American Cancer Society. *Cancer Facts & Figures 2025*.

CRC Screening Recommendations

- US Preventive Services Task Force (USPSTF) recommends adults at average risk to undergo routine screening for CRC from ages 45 to 75
- USPSTF recommends many options for screening, including
  - Colonoscopy (COL) every 10y
  - Annual fecal immunochemical testing (FIT)
  - Multitarget stool DNA testing (mtsDNA) every 1-3y
- Blood tests for CRC are also available
  - Performed every 3y
  - Sensitivity for detecting cancer meets CMS coverage criteria
  - Low sensitivity for detecting precancerous polyps

CRC Screening in the U.S.

- 2023 National Health Interview Survey
  - **Approximately 70%** report having been **screened for CRC at least once***
  - **45%** report being **up-to-date within CRC screening***

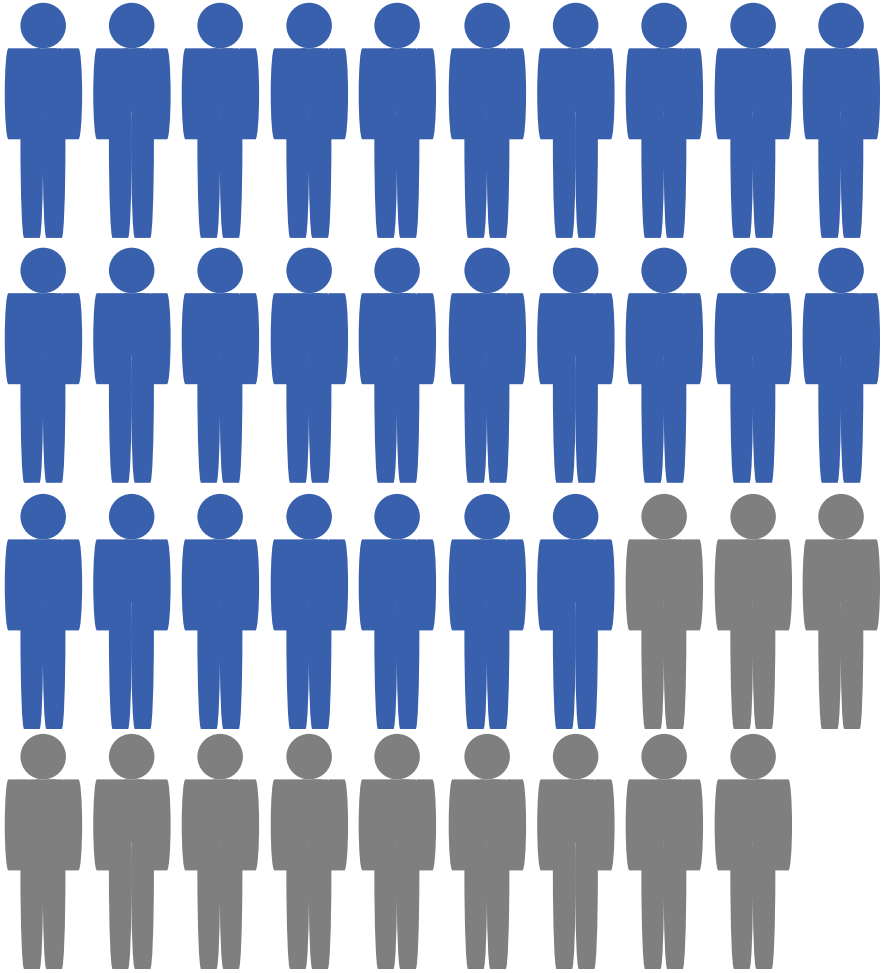
* Among respondents aged 45-75y

- What if we could increase uptake of CRC screening by 10 percentage points, to 80%?

3.9 million U.S. 45-year-olds in 2021

= 100K

2.7 million (70%) screened for CRC at least once in lifetime

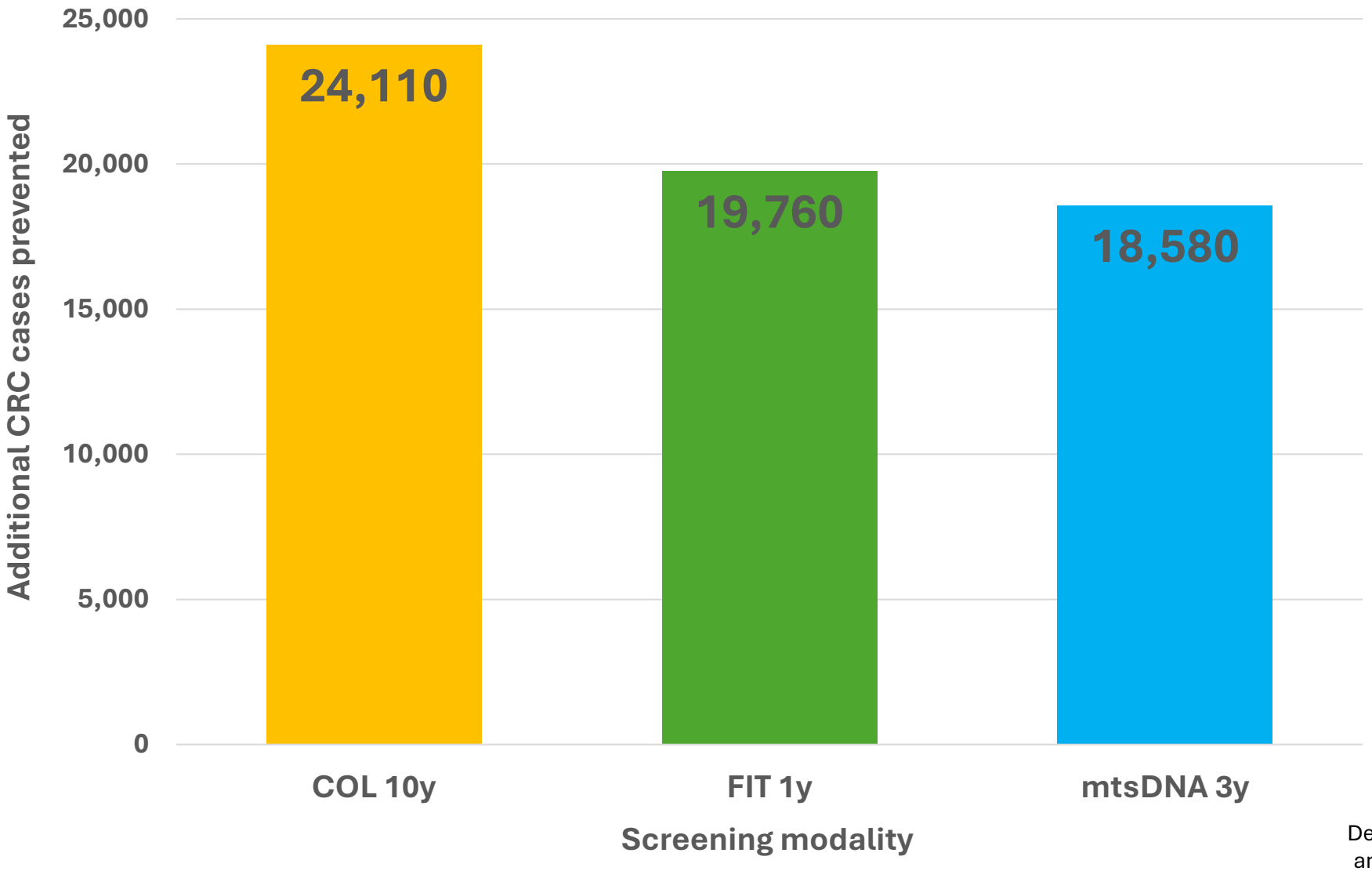


400K additional 45-year-olds screened for CRC (10 percentage point increase)

3.1 million (80%) screened for CRC at least once in lifetime

Benefits of increasing uptake of CRC screening by 10 percentage points

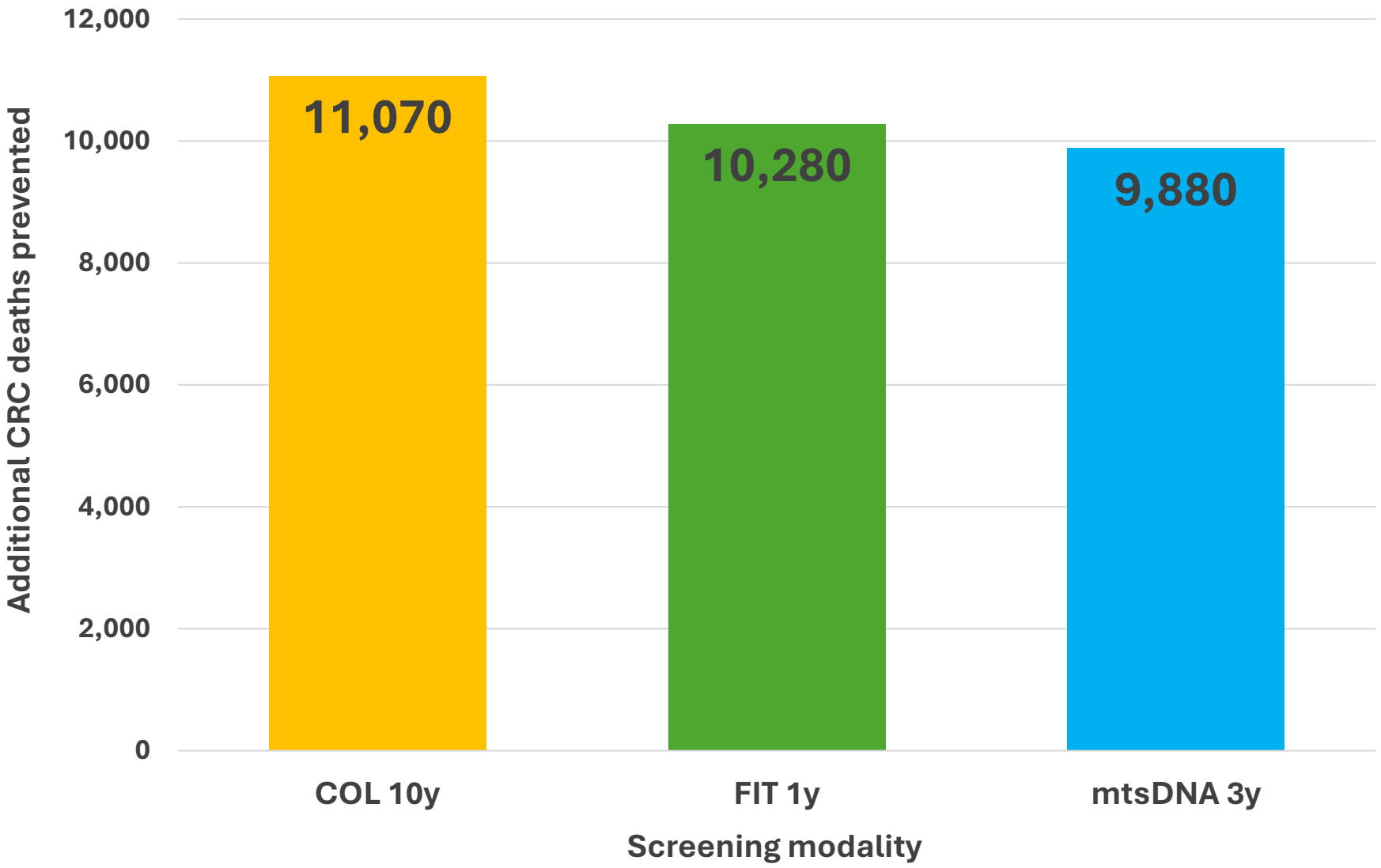
Estimated CRC cases prevented by increasing screening uptake by 10 percentage points



Outcomes are over the lifetimes of ~400K US 45-year-olds in 2021 who uptake CRC screening consistent with USPSTF recommendations.

Derived from Knudsen et al. *JAMA*. 2021:325(19);1998-2011 and Knudsen et al. *JAMA Netw Open*. 2023:6(11):e2344698

Estimated CRC deaths prevented by increasing screening uptake by 10 percentage points



Outcomes are over the lifetimes of ~400K US 45-year-olds in 2021 who uptake CRC screening consistent with USPSTF recommendations.

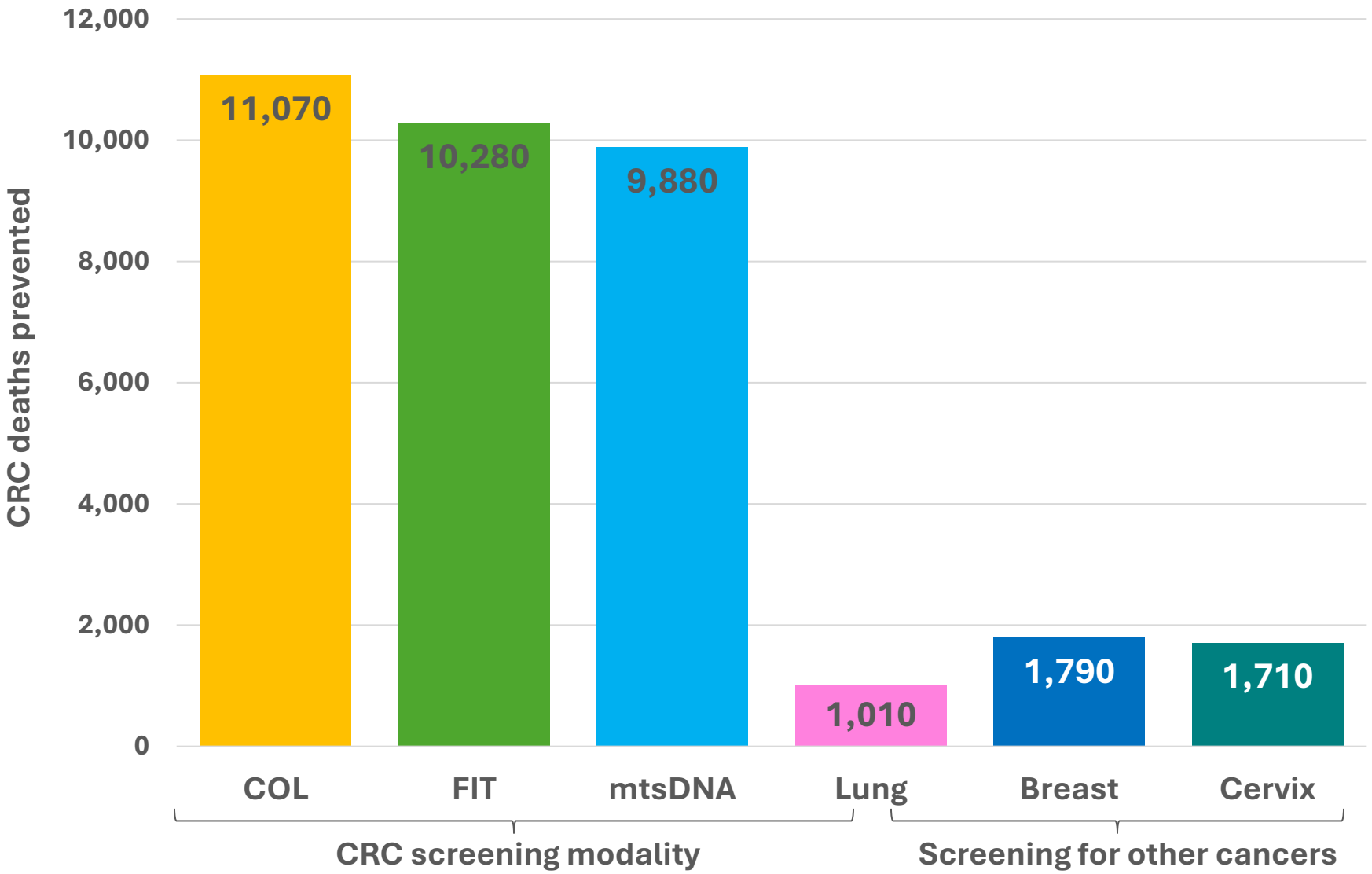
Knudsen et al. *JAMA Netw Open*. 2023:6(11);e2344698.

10 Percentage Point Increase in Screening:
8-16% Fewer Cancers, 15-21% Fewer Cancer Deaths

- ACS: 154,270 new CRC cases, 52,900 CRC deaths in 2025

CRC cases if trends continue (A)	CRC deaths if trends continue (B)	Screening Strategy	CRC cases prevented (C)	Reduction in CRC cases (C/A)	CRC deaths prevented (D)	Reduction in CRC deaths (D/B)
154,270	52,900	Colonoscopy	24,110	16%	11,070	21%
		FIT	19,760	13%	10,280	19%
		mtsDNA	18,580	12%	9,880	19%

Cancer deaths prevented from a 10-percentage point increase in CRC screening vs. other types of cancer screening



Why are so many more CRC deaths prevented from a 10-percentage point increase in uptake of screening?

Explanations include:

- No sex- or smoking-based eligibility criterion for CRC screening
- CRC (and cervical cancer) can be prevented by removal of pre-cancerous lesions at screening

Knudsen et al. *JAMA Netw Open*. 2023:6(11);e2344698.

CRC Screening Access

- AGA, ACS, Fight CRC
  - Met with CMS
  - Followed up with HHS, DOL, Treasury, IRS
- 1/10/2022 released guidance for commercial payers:

Are plans and issuers required to cover, without the imposition of any cost sharing, a follow-up colonoscopy conducted after a positive non-invasive stool-based screening test or direct visualization test (e.g., sigmoidoscopy, CT colonography)?

Yes. A plan or issuer must cover and may not impose cost sharing with respect to a colonoscopy conducted after a positive non-invasive stool-based screening test or direct visualization screening test for colorectal cancer for individuals described in the USPSTF recommendation.

The Impact of 80% CRC Screening: Take-home Points

- **Higher Screening Rates Save Lives**
  - A 10-percentage point increase (from 70% to 80%) can reduce CRC deaths by 15-21%, making it one of the most impactful cancer screening interventions
- **Follow-up Colonoscopy is Critical**
  - Screening tests (FIT, mtsDNA, blood tests) only work if abnormal results are followed by a colonoscopy
- **CRC Screening Prevents Cancer**
  - Unlike most other cancer screenings (breast, lung, prostate), CRC screening can detect and remove precancerous polyps, stopping cancer before it starts
  - A 10-percentage point increase (from 70% to 80%) can prevent 8-16% of CRC cases
- **We need to preserve and increase CRC screening**
  - Insurance benefit and no patient costs for the screening continuum