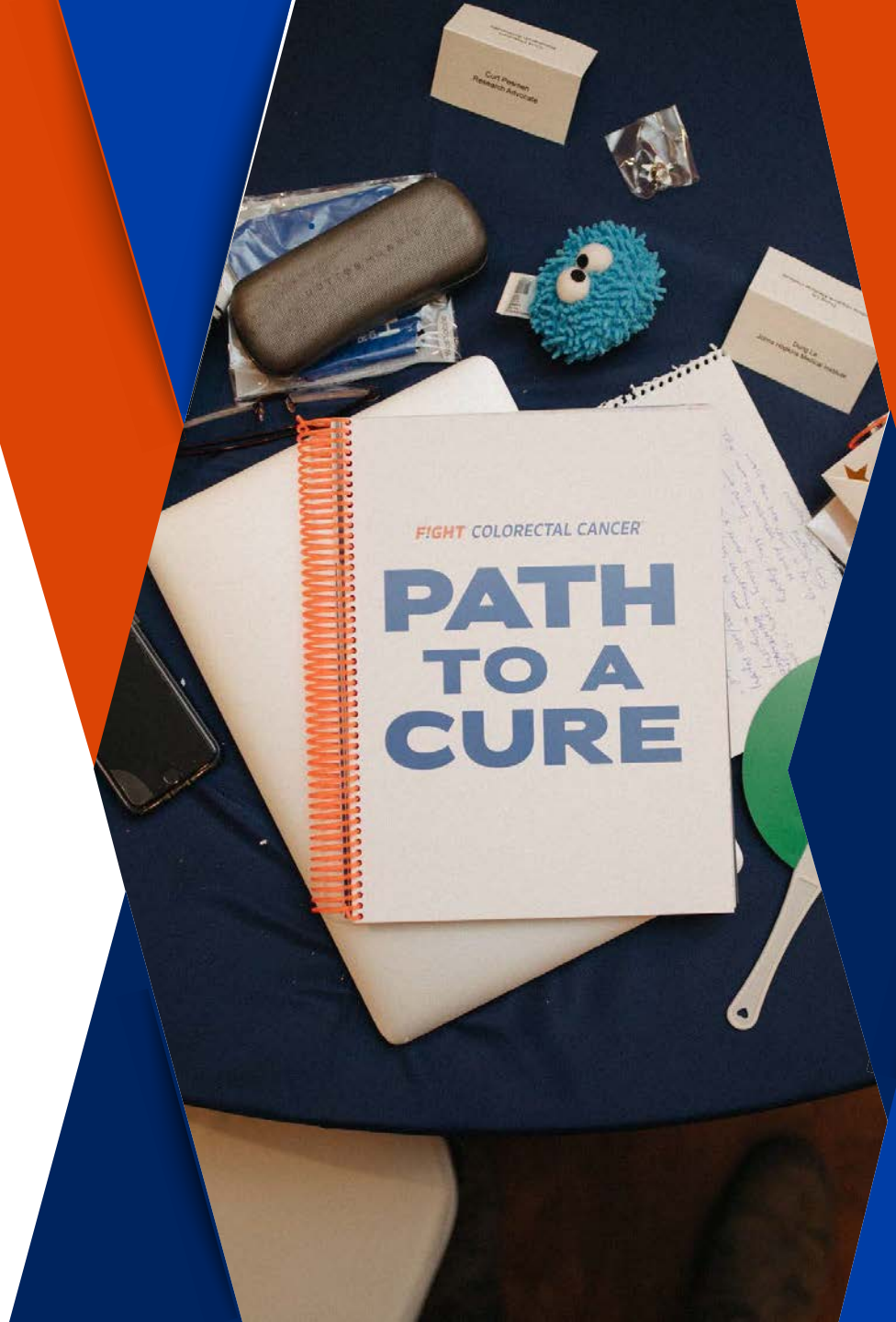
2023 EAO-CRC Think Tank
Breakout Session

Research Opportunities for Under 50 Risk Stratification and Population-based Early Intervention Strategies

FIGHT COLORECTAL CANCER™



Moderators

Josh Demb, MPH, PhD

MODERATOR

Postdoctoral Researcher, University of California

Fola May, MD, PhD, MPhil

BOARD MEMBER

MODERATOR

Fight CRC Board Member, Associate Professor of Medicine at the University of California Los Angeles (UCLA), Director of Quality Improvement in the Vatche and Tamar Manoukian Division of Digestive Diseases, Director of the May Laboratory, Associate Director of the UCLA Kaiser Permanente Center for Health Equity, and staff physician in the Veterans Affairs

Speakers

Ann Zauber, PhD

SPEAKER

Member and Attending at Memorial Sloan Kettering Cancer Center (Epi/Biostatistics Dept.)

José Perea García, MD, PhD, MSc.

SPEAKER

Chief Department of Surgery in Vithas Arturo Soria University Hospital, Professor of Surgery for the European University of Madrid, Principal Investigator in the Institute of Biomedical Research of Salamanca

Iris Lansdorp-Vogelaar, PhD

(Virtual)

SPEAKER

Professor, Department of Public Health of Erasmus MC, Erasmus MC, Rotterdam, Netherlands

Heather Hampel, MS, CGC

SPEAKER

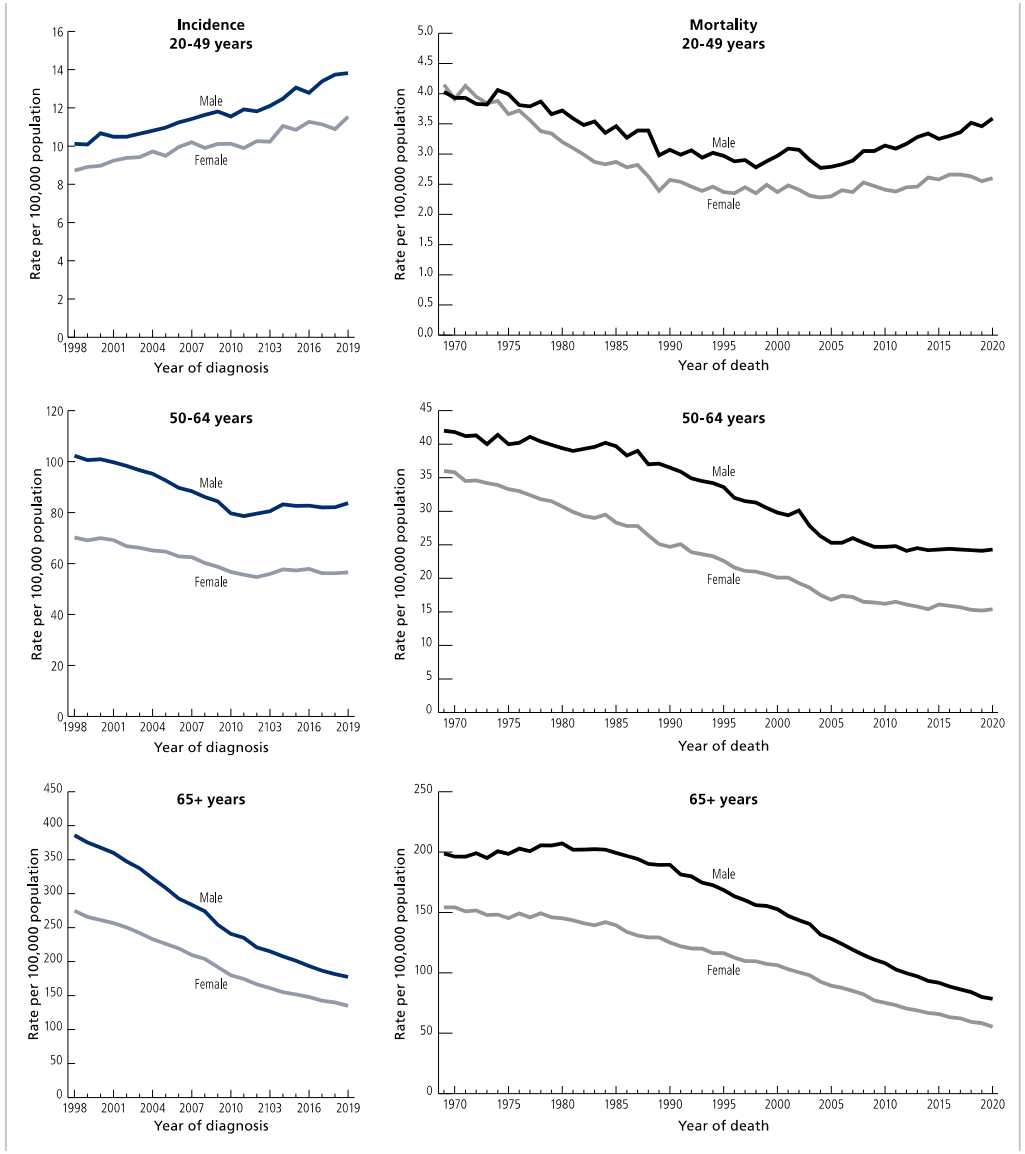
Professor in the Department of Medical Oncology and Therapeutics Research and Associate Director of the Division of Cancer Genomics at City of Hope National Cancer Center

Aasma Shaukat, MD, MPH

SPEAKER

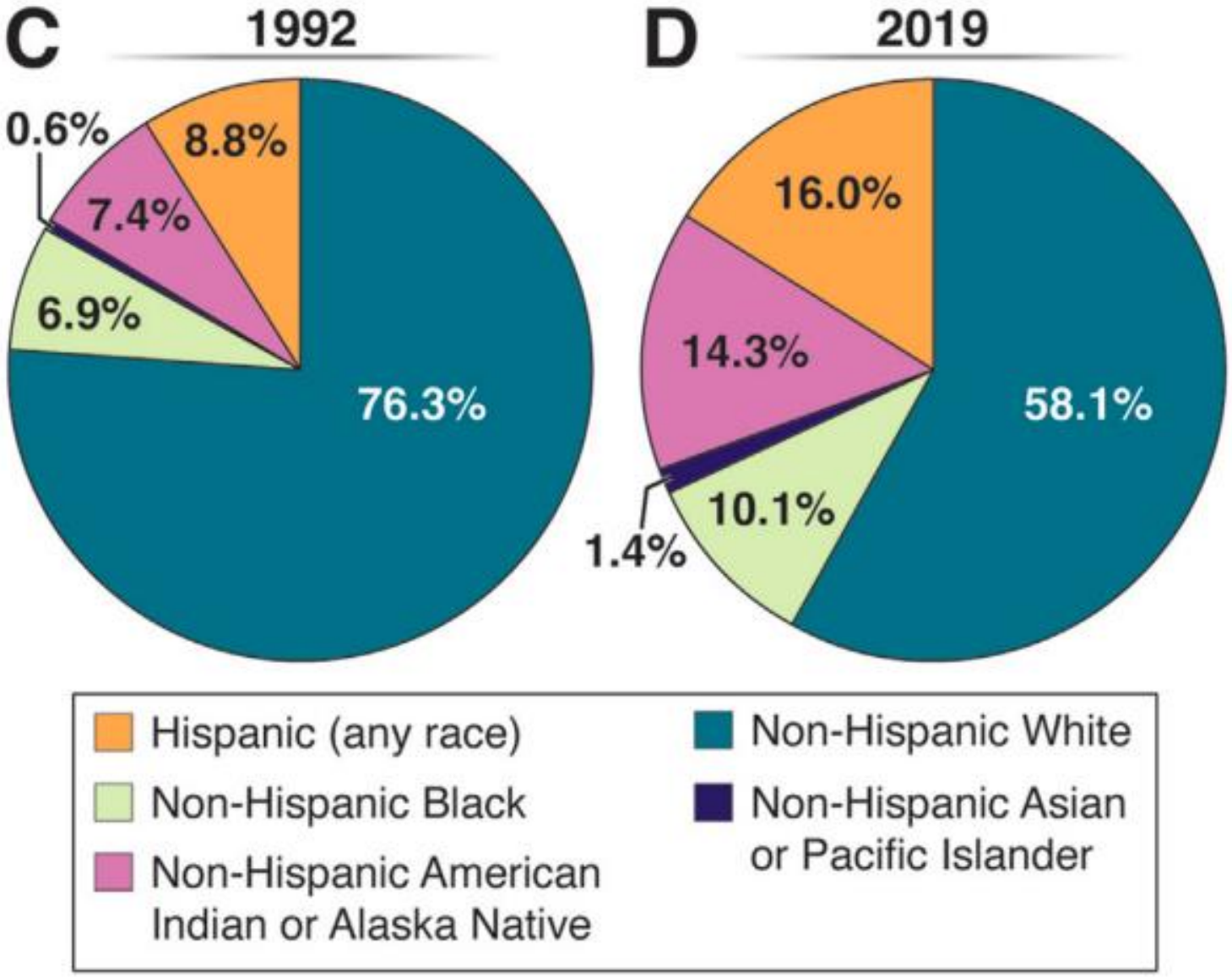
Professor of Medicine, NYU

Age-based trends in CRC Incidence



American Cancer Society. Colorectal Cancer Facts & Figures 2023-2025.

Disparities in CRC Incidence



SEER 12, 1992-2019.

Contrasting Colorectal Cancer Screening Guidelines Worldwide

Ann Zauber, PhD

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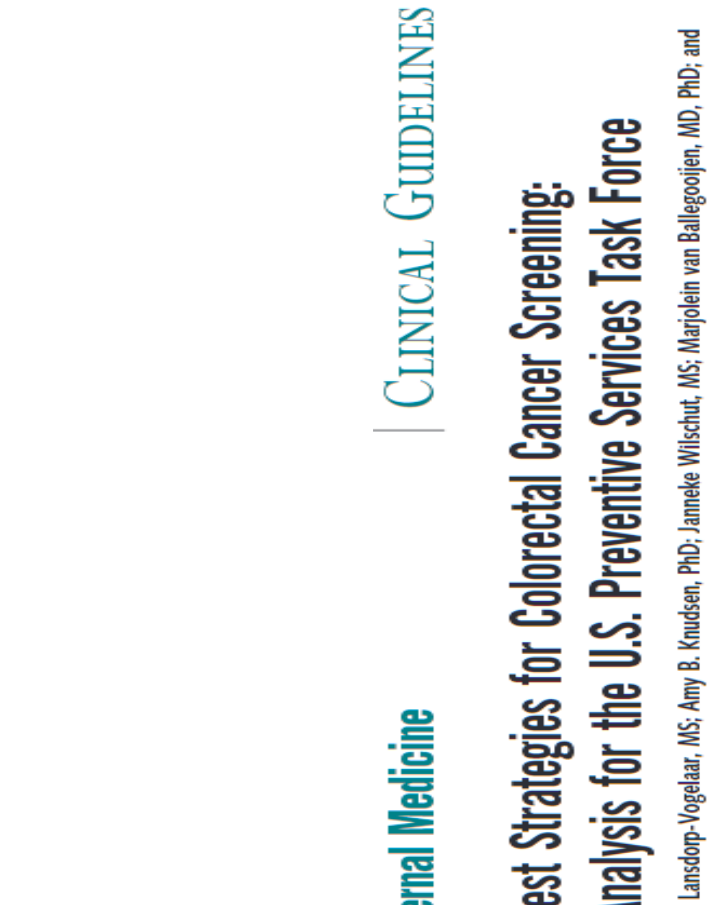

ernal Medicine | CLINICAL GUIDELINES

est Strategies for Colorectal Cancer Screening:
nalysis for the U.S. Preventive Services Task Force

Lansdorp-Vogelaar, MS; Amy B. Knudsen, PhD; Janneke Wilschut, MS; Marjolein van Ballegooijen, MD, PhD; and

2008: Age 50 to Begin Screening

Life-Years Gained per 1000 Persons vs. No Screening (SimCRC)

Colonoscopies per 1000 Persons

50–75, 5
50–85, 5
50–85, 10
50–75, 10
50–75, 20
60–75, 20
No screening

● Strategies starting at age 50 and 60 y
○ Strategies starting at age 40 y
— Frontier of efficient strategies (50, 60 y)
--- Frontier of efficient strategies (40, 50, 60 y)

Contrasting Colorectal Cancer Screening Guidelines Worldwide

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US Preventive Services Task Force | Modeling Study

FREE

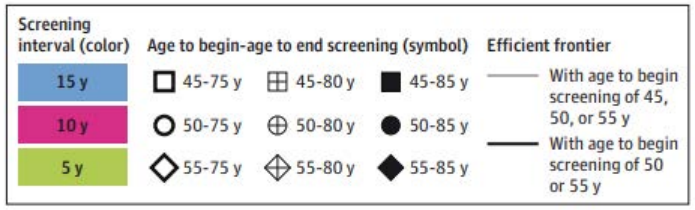
June 21, 2016

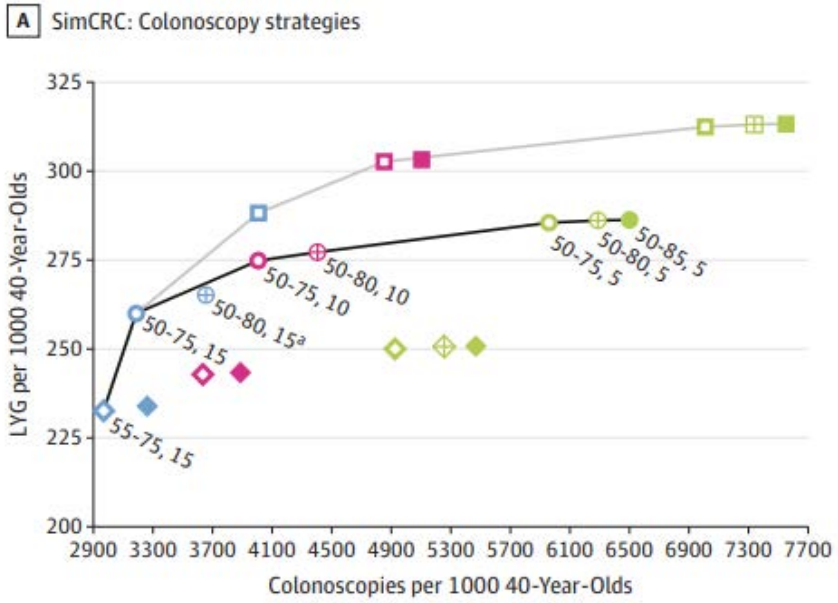
Estimation of Benefits, Burden, and Harms of Colorectal Cancer Screening Strategies

Modeling Study for the US Preventive Services Task Force

Amy B. Knudsen, PhD[1]; Ann G. Zauber, PhD[2]; Carolyn M. Rutter, PhD[3]; Steffie K. Naber, MSc[4]; V. Paul Doria-Rose, DVM, PhD[5]; Chester Pabiniak, MS[6]; Colden Johanson, BA[1,8]; Sara E. Fischer, MPH[2]; Iris Lansdorp-Vogelaar, PhD[4]; Karen M. Kuntz, ScD[7]

2016: Age 50 to Begin Screening





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Professor, Department of Public Health of Erasmus MC, Erasmus MC, Rotterdam, Netherlands

2018: Modeling to Inform First Guidelines to Begin Screening at Age 45

Original Article

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

Elisabeth F. P. Peterse, MSc[1]; Reinier G. S. Meester, PhD[1,2]; Rebecca L. Siegel, MPH[3]; Jennifer C. Chen, MPH[4]; Andrea Dwyer, BS[5,6]; Dennis J. Ahnen, PhD[7]; Robert A. Smith, PhD[8]; Ann G. Zauber, PhD[4]; and Iris Lansdorp-Vogelaar, PhD[1]

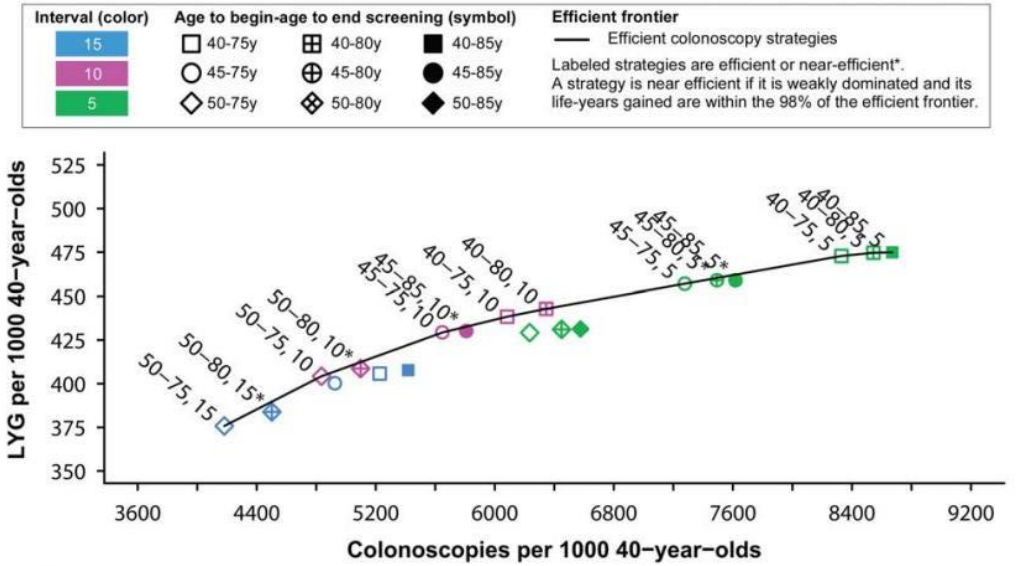

Figure 2. Lifetime number of colonoscopies and life-years gained (LYG) for colonoscopy screening strategies.

Contrasting Colorectal Cancer Screening Guidelines Worldwide

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US Preventive Services Task Force | Modeling Study

FREE

May 18, 2021

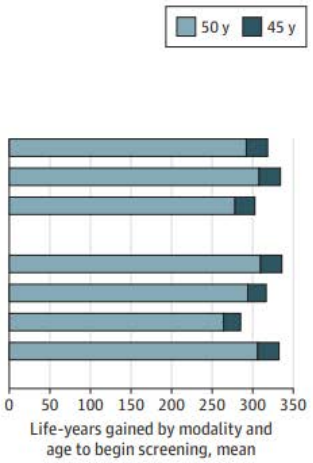
Colorectal Cancer Screening

An Updated Modeling Study for the US Preventive Services Task Force

Amy B. Knudsen, PhD[1,2]; Carolyn M. Rutter, PhD[3]; Elisabeth F. P. Peterse, PhD[4,5]; Anna P. Lietz, BA[1,6]; Claudia L. Seguin, BA[1]; Reinier G. S. Meester, PhD[4]; Leslie A. Perdue, MPH[7]; Jennifer S. Lin, MD[7]; Rebecca L. Siegel, MPH[8]; V. Paul Doria-Rose, DVM, PhD[9]; Eric J. Feuer, PhD[9]; Ann G. Zauber, PhD[10]; Karen M. Kuntz, ScD[11]; Iris Lansdorp-Vogelaar, PhD[4]

A Benefit: Estimated life-years gained per 1000 individuals screened[a]

Screening modality and frequency	Life-years gained if start screening at age 50 y				Additional life-years gained if start screening at age 45 y			
	SimCRC	CRC-SPIN	MISCAN	Mean	SimCRC	CRC-SPIN	MISCAN	Mean
Stool tests								
FIT every year	316	285	274	292	33	29	17	26
sDNA-FIT every year	330	301	290	307	33	30	16	26
sDNA-FIT every 3 y[b]	304	271	257	278	31	30	16	25
Direct visualization tests								
COL every 10 y	335	308	286	310	34	32	16	27
CTC every 5 y	325	287	268	293	31	26	14	24
SIG every 5 y	279	256	256	264	30	24	13	22
SIG every 10 y plus FIT every year	330	301	287	306	33	29	17	26



2021: USPSTF Recommend Screening at Age 45
Based on CISNET Modeling Work

Contrasting Colorectal Cancer Screening Guidelines Worldwide

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Can risk-stratification screening be used alleviate some of these concerns?

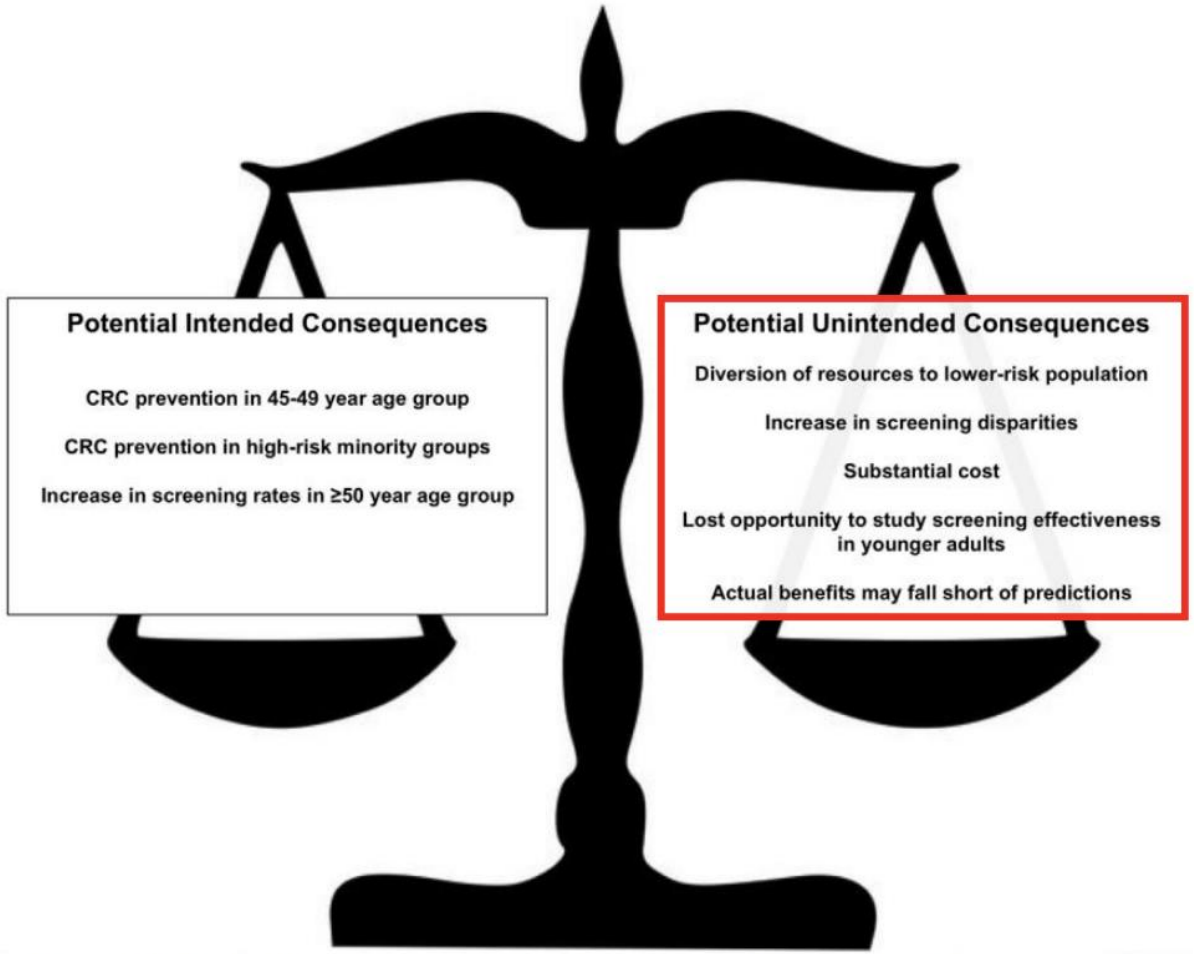

Figure 1. Potential consequences of recommending colorectal cancer (CRC) screening initiation at age 45 instead of age 50 years.

Liang et al, *Gastroenterology*, 2018

Contrasting Colorectal Cancer Screening Guidelines Worldwide

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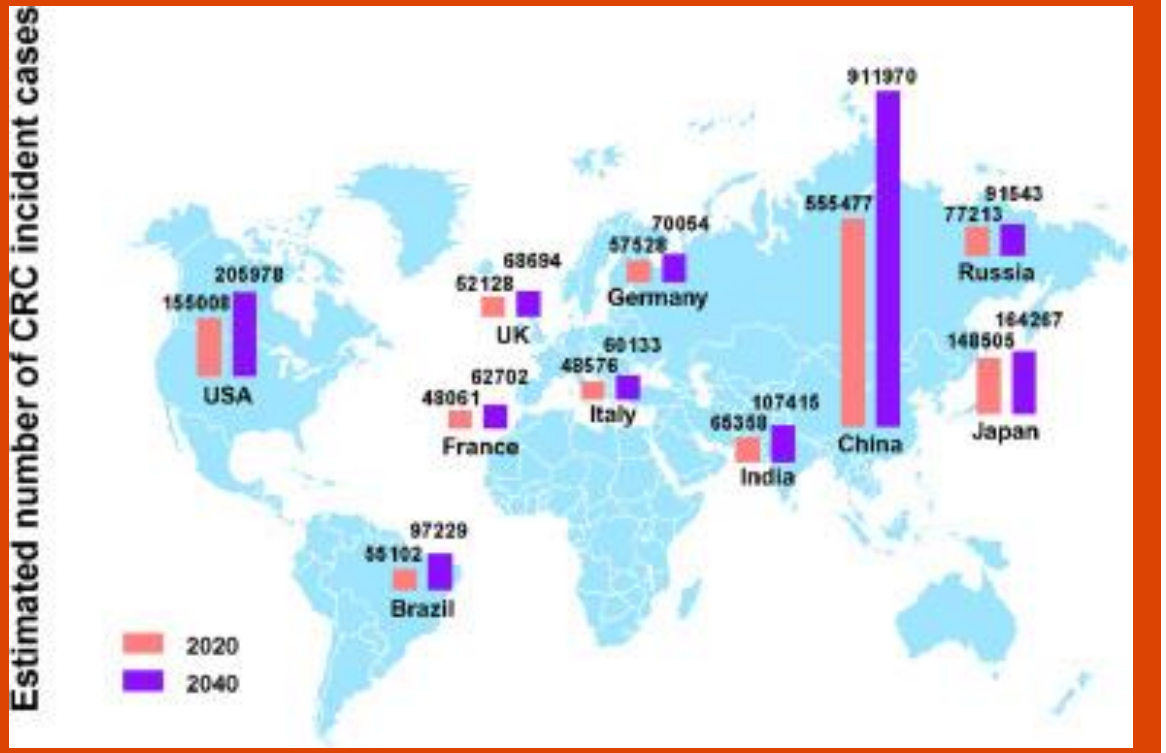
Professor, Department of Public Health of Erasmus MC, Erasmus MC, Rotterdam, Netherlands

- Four main components to making screening recommendations:
  - Who needs to be screened?
  - What are the appropriate intervals?
  - Which screening method?
  - What is the appropriate age?
- Screening guidelines for average-risk individuals vary by country, ranging from as early as 40-years old to as late as 60-years old.
- The global rise in EAO-CRC suggests that there may be a need to review global screening guidelines; however, there are significant challenges and implications to consider.



Yue et al. Trans Onc. 2021.

Research in Implementation and Risk and Family History and Risk Stratification

Understanding colorectal cancer risk can help prevent disease in the future.

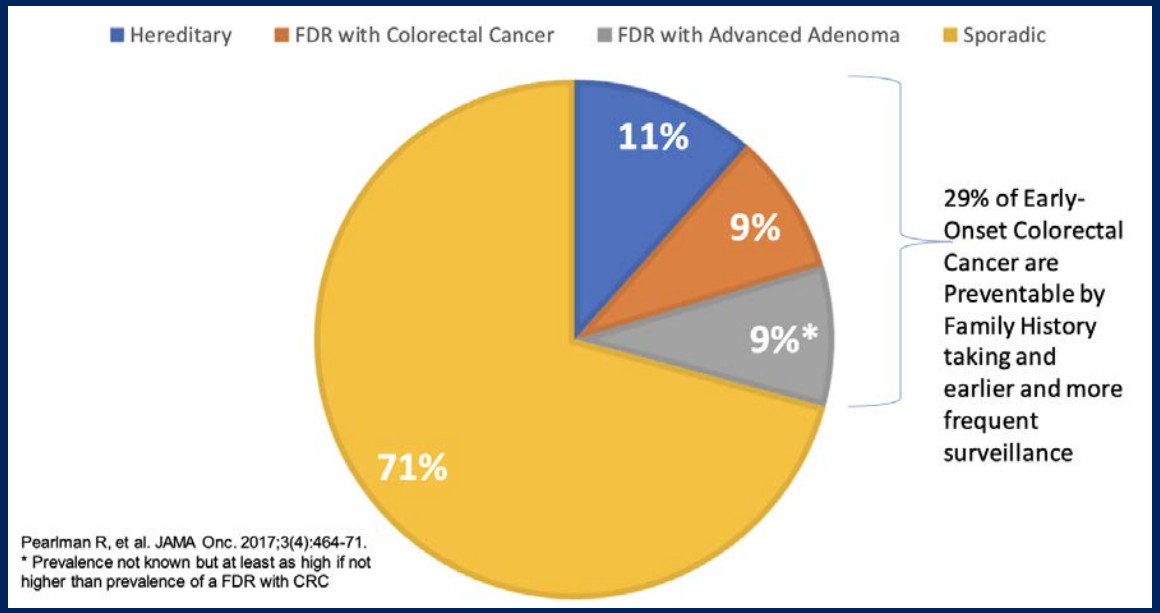
José Perea García, MD, PhD, MSc.
SPEAKER

Chief Department of Surgery in Vithas Arturo Soria University Hospital, Professor of Surgery for the European University of Madrid, Principal Investigator in the Institute of Biomedical Research of Salamanca

Heather Hampel, MS, CGC
SPEAKER

Professor in the Department of Medical Oncology and Therapeutics Research and Associate Director of the Division of Cancer Genomics at City of Hope National Cancer Center

- A substantial portion of EAO-CRC diagnoses in patients with a family history of CRC or a hereditary cancer syndrome could be preventable if:
  - High-risk screening guidelines were followed
  - Average-risk screening was initiated at 45 years old.
- Critical need to develop and implement a method for collecting family history.



Research in Implementation and Risk and Family History and Risk Stratification

José Perea García, MD, PhD, MSc.
SPEAKER

Heather Hampel, MS, CGC
SPEAKER

What proportion of EAOCRC is preventable?

- Study aim:
  - Determine proportion of EAOCRC cases potentially prevented if high-risk screening guidelines were followed and if average-risk screening was started at age 45
- Study population:
  - Prospective cohort of people newly diagnosed w EAOCRC in Ohio.
- Protocol:
  - All provided family history and received germline multigene panels.

Stanich et al., Gastro. 2021.

Research in Implementation and Risk and Family History and Risk Stratification

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SPEAKER

What proportion of EAOCRC is preventable?

713 Patients with EAOCRC

- 566 (79.4%) No FH, No hereditary syndrome
  - **Sporadic EAOCRC**
  - **234 (41.3%)** would have been diagnosed earlier if screened appropriately at age 45
- 64 (9.0%) + FH, No hereditary syndrome
- 33 (4.6%) + FH + hereditary syndrome

97 (13.6%) had **family history of CRC**

Of these, if guidelines followed:
80 (82.5%) would have been diagnosed earlier
65 (67.0%) had potentially preventable CRC

- 50 (7.0%) No FH + hereditary syndrome

83 (11.6%) had **at least 1 hereditary syndrome**

Of these, if guidelines followed:
81 (97.6%) would have been diagnosed earlier
74 (89.2%) had potentially preventable CRC

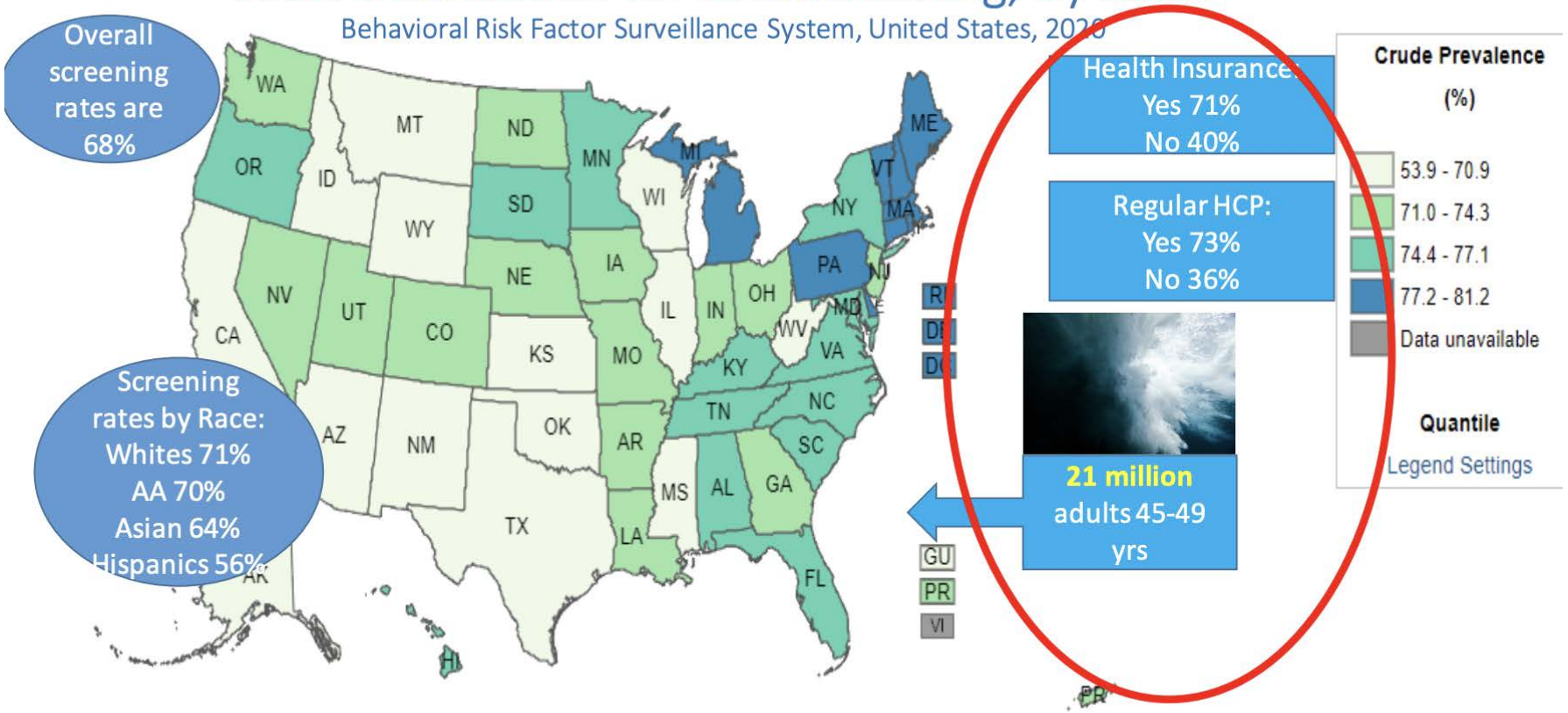
Stanich et al., Gastro. 2021.

Population Identification Using Stool-based Screening and Emerging Technologies and Research Opportunities for EAO and Beyond

Aasma Shaukat, MD, MPH
SPEAKER
Professor of Medicine, NYU

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

Behavioral Risk Factor Surveillance System, United States, 2020



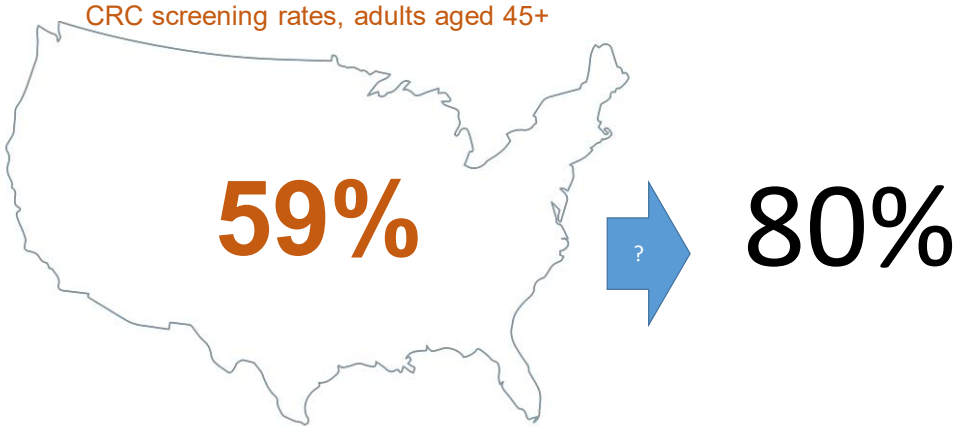
Joseph DA, et al. MMWR Morb Mortal Wkly Rep 2020;69:253–259.

Population Identification Using Stool-based Screening and Emerging Technologies and Research Opportunities for EAO and Beyond

Aasma Shaukat, MD, MPH
SPEAKER
Professor of Medicine, NYU

- Currently, the national average for meeting screening guidelines (starting at age 45) is 59%; however, the NCCRT goal is 80%.
- There are significant disparities in population adherence to CRC screening guidelines across the United States.
- Screening outreach has evolved:
  - Organized screening programs
  - Patient navigation
  - Offering choice of screening tests
  - Emergence of new test options:
    - Emerging stool-based tests
    - Blood-based screening
    - Challenges that remain

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



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

Recurring Themes

- There are significant disparities across each nation in the adherence to CRC screening guidelines.
- Identifying factors that are associated with the lack of screening in communities will provide an avenue for intervention.

- All stakeholders (industry, advocacy organizations, survivors, caregivers, researchers) must be involved in collaboration at an international level.
- Needs to include:
  - infrastructure development
  - multidisciplinary approaches
  - data sharing

- Future interventions will likely be tailored to individuals based on their exposures, microbiomes, epigenetic age, and risk.

Main Takeaway Questions

Asking the right questions and following-up with actionable items is key to advancing CRC research.

- What do we need to consider when evaluating screening guidelines (domestically and globally)?
- How do we accurately collect family history?
- How do we achieve “80%” in every country, state, and neighborhood?
- Where do stool- and blood-based screening methods fit into screening guidelines?
- How do we integrate the microbiome/exposome/etc. to screening and risk stratification strategies?