2021 NCCRT Annual Meeting – November 15-17

Thank you for joining!
The session will begin shortly.

Progress Update: Developments Following the NCCRT's Action Plan to Address the Rising Burden of Colorectal Cancer in Younger Adults

Wednesday, November 17, 2:00 PM

NCCRT Action Plan Progress for CRC in Younger Adults

Andrea Dwyer
BS
University of Colorado Cancer Center

Paul Schroy
MD, MPH
Boston University School of Medicine

Caitlin Murphy
PhD, MPH, CPH
UTHealth School of Public Health

Peter Liang
MD, MPH
NYU Grossman School of Medicine

Joshua Demb
PhD
University of California, San Diego

Progress Update: “Developments following the NCCRT’s Action Plan to Address the Rising Burden of Colorectal Cancer in Younger Adults”

Concurrent Session 4

November 16th, 3:00-4:00pm EST

"Progress Report: Developments following the NCCRT's Action Plan to Address the Rising Burden of Colorectal Cancer in Younger Adults"

Moderators:

Paul C. Schroy III, MD, MPH

Emeritus Professor of Medicine, BU School of Medicine

Co-Chair, NCCRT Family History and Early Age Onset Colorectal Cancer Strategic Priority Team

Andrea (Andi) Dwyer

The Colorado School of Public Health, University of Colorado Cancer Center

Scientific Advisor to Fight Colorectal Cancer

Early Onset CRC Summit 2017

"What we know, what we don't know, and what we need to know"

- The *National Colorectal Cancer Roundtable*, the *American Cancer Society*, and the *Colon Cancer Challenge Foundation* convened a strategic meeting on December 6, 2017, with a small group of key thought leaders and national stakeholders to focus on the concerning trend of early age onset colorectal cancer.

- Purpose: To assess how the NCCRT and its partners, including clinical practitioners, researchers, and advocacy organizations, can most effectively align to address the issue in both the short and long term.

Early Onset CRC Summit 2017

Objectives:

- Review *what we thought we knew about* current practices and research related to EAO CRC.
- To identify initiatives that could/should be done now based on *what we knew.*
- To define some of *what we need to know* about causation, natural history, prevention, screening and early diagnosis.
- Develop an action plan, including priorities, strategies, necessary resources and potential partners, to address these unanswered issues.

Early Onset CRC Summit 2017

Special Report

Colorectal Cancer

For reprint orders, please contact: reprints@futuremedicine.com

An action plan to address the rising burden of colorectal cancer in younger adults

Jan T Lowery*,[1], Thomas K Weber[1,2], Dennis J Ahnen[3], Paul C Schroy III[4], Caleb L Levell[5] & Robert A Smith[5]

[1]Center for Personalized Medicine, University of Colorado, Aurora, CO 80045, USA

[2]Northwell Health, Professor of Surgery, Donald & Barbara Zucker School of Medicine at Hofstra/Northwell, New York, NY 10028, USA

[3]Gastroenterology of the Rockies, University of Colorado School of Medicine & Director of Genetics Program, Aurora, CO 80045, USA

[4]Boston University School of Medicine, Section of Gastroenterology, Boston, MA 02118, USA

[5]American Cancer Society, Atlanta, GA 30303, USA

*Author for correspondence: jan.lowery@cuanschutz.edu

‡TK Weber is deceased

Colorectal Cancer 2020;9(Suppl): https://doi.org/10.2217/crc-2020-0004

Early Onset CRC Summit 2017

Action Plan Objectives

- Accelerate research to address unanswered questions about the causes of the increase of early onset CRC.
- Increase adoption of evidenced-based practices to identify and manage younger adults at risk for CRC.
- Solidify commitment from engaged partners that is essential for moving this plan into action.

"Developments following the NCCRT's Action Plan to Address the Rising Burden of Colorectal Cancer in Younger Adults"

Progress Update

- "What is the cause of the rising incidence of EAOCRC?"

  Presenter: Caitlin Murphy, PhD

- "What is the natural history of EAOCRC?

  Presenter: Peter Liang, MD

- "What are best practices for implementing current recommendations for identifying and managing EAOCRC?

  Presenter: Joshua Demb, PhD

What is the cause of the rising incidence of early-age-onset colorectal cancer?

Caitlin C. Murphy, PhD, MPH

National Colorectal Cancer Roundtable

November 17, 2021

UTHealth | School of Public Health
The University of Texas
Health Science Center at Houston

Unanswered questions at the Early-Onset Colorectal Cancer Summit in 2017

What is the role of known risk factors (e.g., obesity, family history)?

What is the role of novel risk factors?

Do risk factors differ by site (colon vs. rectum)?

Are there vulnerable times of exposure related to risk?

Is early-onset colorectal cancer different than colorectal cancer in older adults?

Unanswered questions at the Early-Onset Colorectal Cancer Summit in 2017

What is the role of known risk factors (e.g., obesity, family history)?

What is the role of novel risk factors?

Do risk factors differ by site (colon vs. rectum)?

Are there vulnerable times of exposure related to risk?

Is early-onset colorectal cancer different than colorectal cancer in older adults?

What is the role of known risk factors?

Known risk factors – or “usual suspects” – of colorectal cancer in older adults that may also increase risk in younger adults

What is the role of known risk factors?

Known risk factors – or “usual suspects” – of colorectal cancer in older adults that may also increase risk in younger adults

- Diet
- Processed meat
- Type 2 diabetes
- Obesity
- Family history
- IBD
- Aspirin/ NSAID use
- Sedentary lifestyle
- Smoking

What is the role of known risk factors?

Cancer Causes & Control (2021) 32:1063–1083
https://doi.org/10.1007/s10552-021-01456-8

ORIGINAL PAPER

Risk factors for early-onset colorectal cancer: a population-based case–control study in Ontario, Canada

Vicky C. Chang[1,2] · Michelle Cotterchio[1,2] · Prithwish De[1] · Jill Tinmouth[1,3,4]

JAMA Oncology | Original Investigation

Association of Obesity With Risk of Early-Onset Colorectal Cancer Among Women

Po-Hong Liu, MD, MPH; Kana Wu, MD, MPH, PhD; Kimmie Ng, MD, MPH; Ann G. Zauber, PhD; Long H. Nguyen, MD, MS; Mingyang Song, MD, ScD; Xiaosheng He, MD; Charles S. Fuchs, MD, MPH; Shuji Ogino, MD, PhD, MS; Walter C. Willett, MD, DrPH; Andrew T. Chan, MD, MPH; Edward L. Giovannucci, MD, ScD; Yin Cao, MPH, ScD

Gastroenterology 2021;161:1208–1217

OXFORD

JNCI Cancer Spectrum (2021) 5(3): pkab029

doi: 10.1093/jncics/pkab029
Article

Nongenetic Determinants of Risk for Early-Onset Colorectal Cancer

Alexi N. Archambault, MPH,[1] Yi Lin, MS,[2] Jihyoun Jeon, PhD, MS,[3] Tabitha A. Harrison, MPH,[2] D. Timothy Bishop, PhD, MSc,[4] Hermann Brenner, MD, MPH,[5,6,7] Graham Casey, PhD,[8] Andrew T. Chan, MD, MPH,[9,10,11,12,13,14] Jenny Chang-Claude, PhD,[15,16] Jane C. Figueiredo, PhD,[17,18] Steven Gallinger, MD, MSc,[19] Stephen B. Gruber, MD, PhD,[20] Marc J. Gunter, PhD,[21] Michael Hoffmeister, PhD,[5] Mark A. Jenkins, PhD,[22] Temitope O. Keku, PhD, MSPH, MSc,[23] Loïc Le Marchand, MD, PhD,[24] Li Li, MD, PhD,[25] Victor Moreno, PhD,[26,27,28,29] Polly A. Newcomb, PhD, MPH, Rish Pai, MD, PhD,[31] Patrick S. Parfrey, MD,[32] Gad Rennert, MD, PhD,[33,34,35] Lori C. Sakoda, PhD,[2,36] Robert S. Sandler, MD, MPH,[37] Martha L. Slattery, PhD,[38] Mingyang Song, ScD, MS,[9,11,39] Aung Ko Win, PhD, MPH,[22] Michael O. Woods, PhD,[40] Neil Murphy, PhD,[41] Peter T. Campbell, PhD, MSc,[42] Yu-Ru Su, PhD, MS,[43] Anne Zeleniuch-Jacquotte, MD, MS,[1] Peter S. Liang, MD, MPH,[44] Mengmeng Du, ScD,[45] Li Hsu, PhD,[2,46,1] Ulrike Peters, PhD, MPH,[2,47,1] Richard B. Hayes, PhD, MPH, DDS[1,*,1]

Original research

Metabolic syndrome, metabolic comorbid conditions and risk of early-onset colorectal cancer

Hanyu Chen,[1,2] Xiaobin Zheng, [1,3,4] Xiaoyu Zong, [1] Zitong Li,[1,5] Na Li,[1,6] Jinhee Hur, [7] Cassandra DL Fritz,[1,8] William Chapman Jr,[9] Katelin B Nickel,[10] Andrew Tipping,[10] Graham A Colditz,[1,11] Edward L Giovannucci, [7,12] Margaret A Olsen,[1,10] Ryan C Fields,[11,13] Yin Cao [1,8,11]

Clinical Gastroenterology and Hepatology 2020;18:2752–2759

Total Vitamin D Intake and Risks of Early-Onset Colorectal Cancer and Precursors

Hanseul Kim,[1] Marla Lipsyc-Sharf,[2] Xiaoyu Zong,[3] Xiaoyan Wang,[3] Jinhee Hur,[4] Mingyang Song,[1,4,5,6] Molin Wang,[1,7,8] Stephanie A. Smith-Warner,[1,4] Charles Fuchs,[9] Shuji Ogino,[1,10,11,12] Kana Wu,[4] Andrew T. Chan,[5,8,12,13] Yin Cao,[3,14,15,§] Kimmie Ng,[16,§] and Edward L. Giovannucci[1,4,8,§]

Risk Factors for Early-Onset Colorectal Cancer

Eric E. Low,[1,2,3,*] **Joshua Demb**,[2,4,*] Lin Liu,[3,4,5] Ashley Earles,[6] Ranier Bustamante,[3,4] Christina D. Williams,[7,8,9] Dawn Provenzale,[7,8,9] Tonya Kaltenbach,[10,11] Andrew J. Gawron,[12,13] Maria Elena Martinez,[4,5] and Samir Gupta[1,2,3,4]

Risk Factors Associated With Early-Onset Colorectal Cancer

Valerie Gausman,* David Dornblaser,* Sanya Anand,* Richard B. Hayes,‡ Kelli O'Connell,§ Mengmeng Du,§ and Peter S. Liang*,‖

CANCER EPIDEMIOLOGY, BIOMARKERS & PREVENTION | RESEARCH ARTICLE

Metabolic Risk Factors Associated with Early-Onset Colorectal Adenocarcinoma: A Case–Control Study at Kaiser Permanente Southern California

Andrew J. Schumacher[1], Qiaoling Chen[2], Vikram Attaluri[3], Elisabeth C. McLemore[3], and Chun R. Chao[2]

Risk Factors Associated With Young-Onset Colorectal Adenomas and Cancer: A Systematic Review and Meta-Analysis of Observational Research

Genevieve Breau, PhD[1] and Ursula Ellis, MLIS[2]

Clinical Gastroenterology and Hepatology 2021;■:■–■

Risk Factors for Early-Onset Colorectal Cancer: A Systematic Review and Meta-analysis

Dylan E. O'Sullivan,*,‡,§ R. Liam Sutherland,*,‡,§ Susanna Town,§ Kristian Chow,* Jeremy Fan,* Nauzer Forbes,*,§,‖ Steven J. Heitman,*,§,‖ Robert J. Hilsden,*,§,‖ and Darren R. Brenner*,‡,§

What is the role of known risk factors?

Several recent, population-based studies conducted across a variety of settings:

- Integrated health system
- Nurses' Health Study
- Veterans Health Administration
- Case-control via cancer registry
- Pooled data from consortia
- Large medical centers

What is the role of known risk factors?

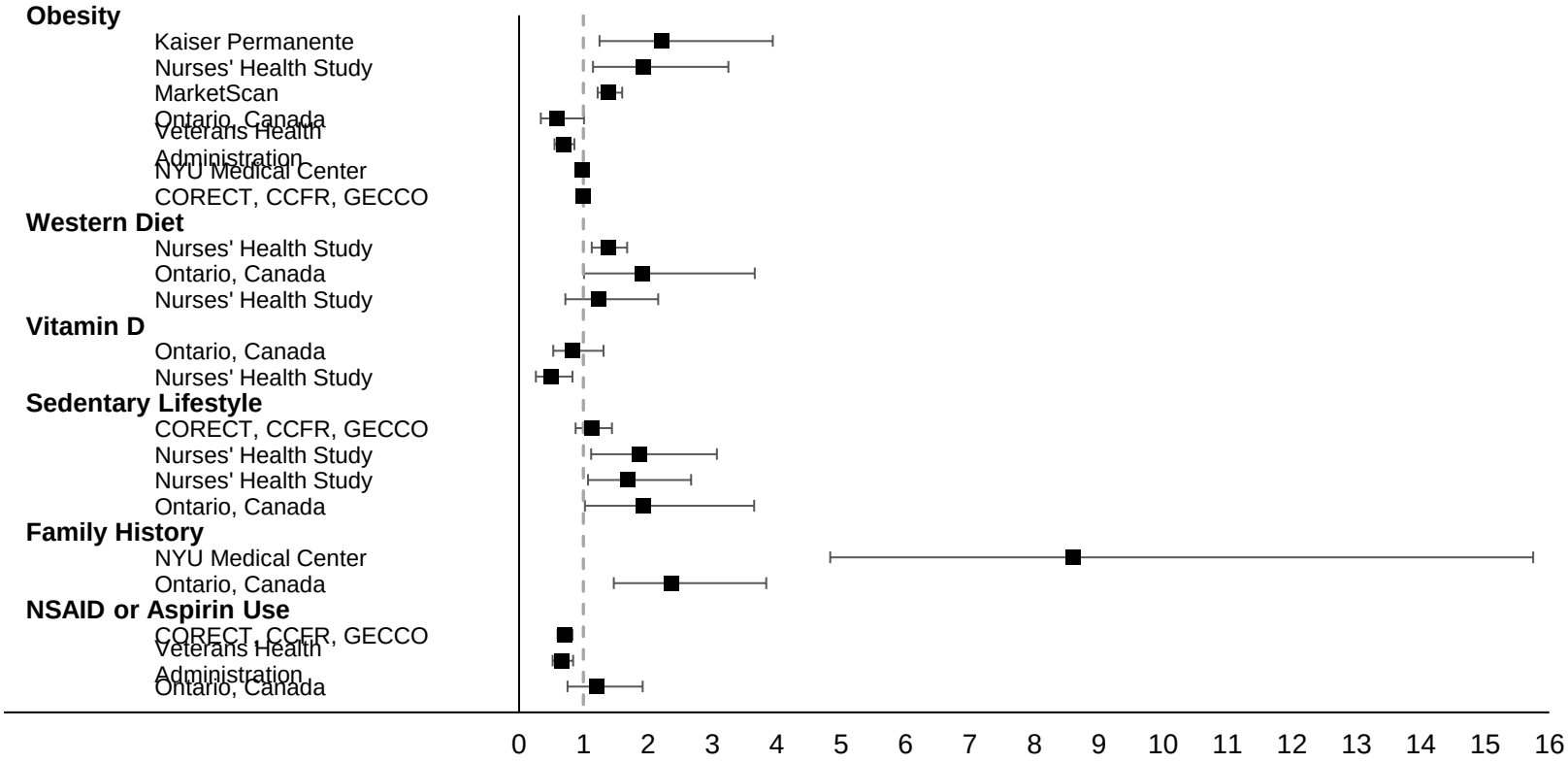
Several recent, population-based studies conducted across a variety of settings:

- Integrated health system
- Nurses' Health Study
- Veterans Health Administration
- Case-control via cancer registry
- Pooled data from consortia
- Large medical centers

Some caveats:

- Early-onset adenoma vs. CRC
- Timing of exposure assessment
- Different measures
- Population at risk

What is the role of known risk factors?



Gausman V et al. Clin Gastro Hepatol 2020; Nguyen LH et al. JNCI Cancer Spec 2019; Zheng X et al. JNCI Cancer Spect 2021; Low EE et al. Gastroenterology 2020; Chen H et al. Gut 2021; Yue Y et al. Ann Oncol 2021; Schumacher AJ et al. Cancer Epidemiol Biomarkers Prev 2021; Chang VC et al. Cancer Cause Control 2021

Archambault AN et al. JNCI Cancer Spect 2021; Kim H et al. Gastroenterology 2021; Liu P et al. JAMA Oncol 2019

Unanswered questions at the Early-Onset Colorectal Cancer Summit in 2017

What is the role of known risk factors (e.g., obesity, family history)?

What is the role of novel risk factors?

Do risk factors differ by site (colon vs. rectum)?

Are there vulnerable times of exposure related to risk?

Is early-onset colorectal cancer different than colorectal cancer in older adults?

What is the role of novel risk factors?

Novel risk factors – newly identified risk factors of early-onset colorectal cancer (and that may also be related to risk in older adults)

What is the role of novel risk factors?

Novel risk factors – newly identified risk factors of early-onset colorectal cancer (and that may also be related to risk in older adults)

- Antibiotic use
- Food additives
- Vaccines
- Gut microbiome
- Birth weight
- Pesticides
- HPV
- Helicobacter pylori
- Sleep patterns

What is the role of novel risk factors?

Novel risk factors – newly identified risk factors of early-onset colorectal cancer (and that may also be related to risk in older adults)

- **Antibiotic use**
- **Gut microbiome**
- HPV
- Food additives
- Birth weight
- Helicobacter pylori
- Vaccines
- Pesticides
- Sleep patterns

What is the role of novel risk factors? A closer look at dysbiosis-related factors

Several studies of antibiotic use conducted using national registries:

- UK (medical records)
- Sweden (GI biopsies)
- Netherlands (administrative claims)
- Sweden (cancer and population registries)
- UK (medical records)

What is the role of novel risk factors? A closer look at dysbiosis-related factors

Several studies of antibiotic use conducted using national registries:

- UK (medical records)
- Sweden (GI biopsies)
- Netherlands (administrative claims)
- Sweden (cancer and population registries)
- UK (medical records)

Same caveats apply:

- Polyp vs. adenoma vs. CRC
- Timing of exposure assessment
- Different measures
- Population at risk

What is the role of novel risk factors? A closer look at dysbiosis-related factors

Studies of antibiotic use	Measure	Effect size	95% CI
Sweden (GI biopsies)	≥6 dispensations	1.33	1.25, 1.43
Sweden (national registries)	Very high (>180 days)	1.17	1.05, 1.31
UK (medical records)	Use 10 years before dx	1.17	1.10, 1.23
UK (medical records)	>10 courses penicillin	1.20	1.11, 1.31
Netherlands (administrative claims)	High (≥8 rx)	1.26	1.11, 1.44
Nurses' Health Study	2+ months, age 20-39	1.36	1.03, 1.79

Cao Y et al. Gut 2018; Boursi B et al. Pharmacoepidemiol Drug Safety 2015; Vik DK et al. Dig Dis Sci 2016; Zhang J et al. Gut 2019; Lu SSM et al. J Natl Cancer Inst 2021; Song M et al. Clin Gastroenterol Hepatol 2021

Unanswered questions at the Early-Onset Colorectal Cancer Summit in 2017

What is the role of known risk factors (e.g., obesity, family history)?

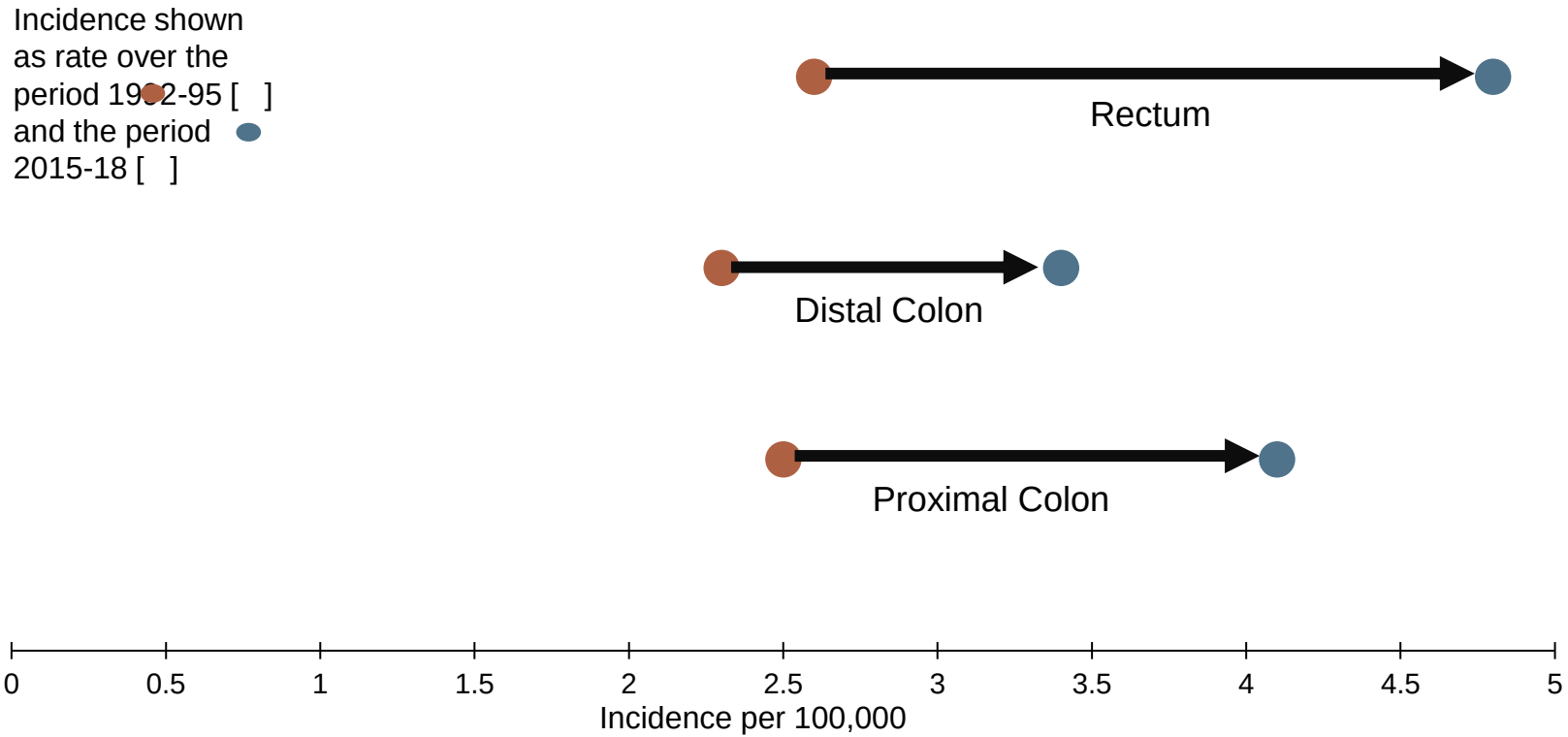
What is the role of novel risk factors?

Do risk factors differ by site (colon vs. rectum)?

Are there vulnerable times of exposure related to risk?

Is early-onset colorectal cancer different than colorectal cancer in older adults?

Notable increases in incidence rates of early-onset rectal cancer



SEER 13 Incidence, 1992-2018, Age 18-49 years

Across recent studies, differential association with colon vs. rectal cancer

Some examples:

- Low fiber intake more strongly associated with rectal vs. colon cancer (CORECT, CCFR, GECCO)
- Obesity associated with colon vs. rectal cancer (Kaiser Permanente)
- Metabolic syndrome associated with colon vs. rectal cancer (MarketScan)
- Antibiotics increased risk of colon but decreased risk of rectal cancer (Sweden, UK)

Across recent studies, differential association with colon vs. rectal cancer

Some examples:

- Low fiber intake more strongly associated with rectal vs. colon cancer (CORECT, CCFR, GECCO)
- Obesity associated with colon vs. rectal cancer (Kaiser Permanente)
- Metabolic syndrome associated with colon vs. rectal cancer (MarketScan)
- Antibiotics increased risk of colon but decreased risk of rectal cancer (Sweden, UK)

This phenomenon has also been well-described in colorectal cancer in older adults:

- Demb J, et al. BMJ Open Gastroenterol 2019; 6(10):e000313
- Murphy N, et al. Clin Gastroenterol Hepatol 2019; 17:1323-1331

Unanswered questions at the Early-Onset Colorectal Cancer Summit in 2017

What is the role of known risk factors (e.g., obesity, family history)?

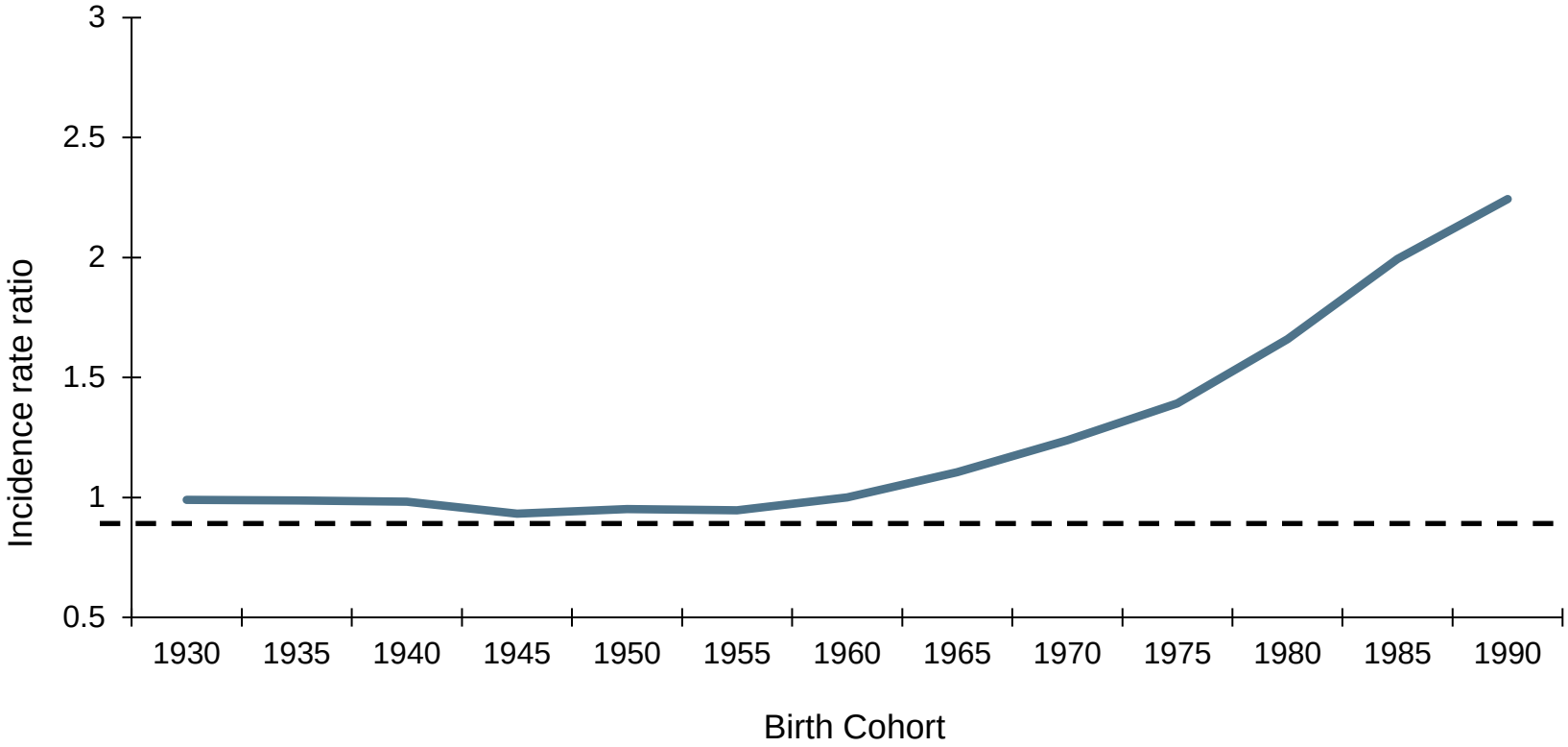
What is the role of novel risk factors?

Do risk factors differ by site (colon vs. rectum)?

Are there vulnerable times of exposure related to risk?

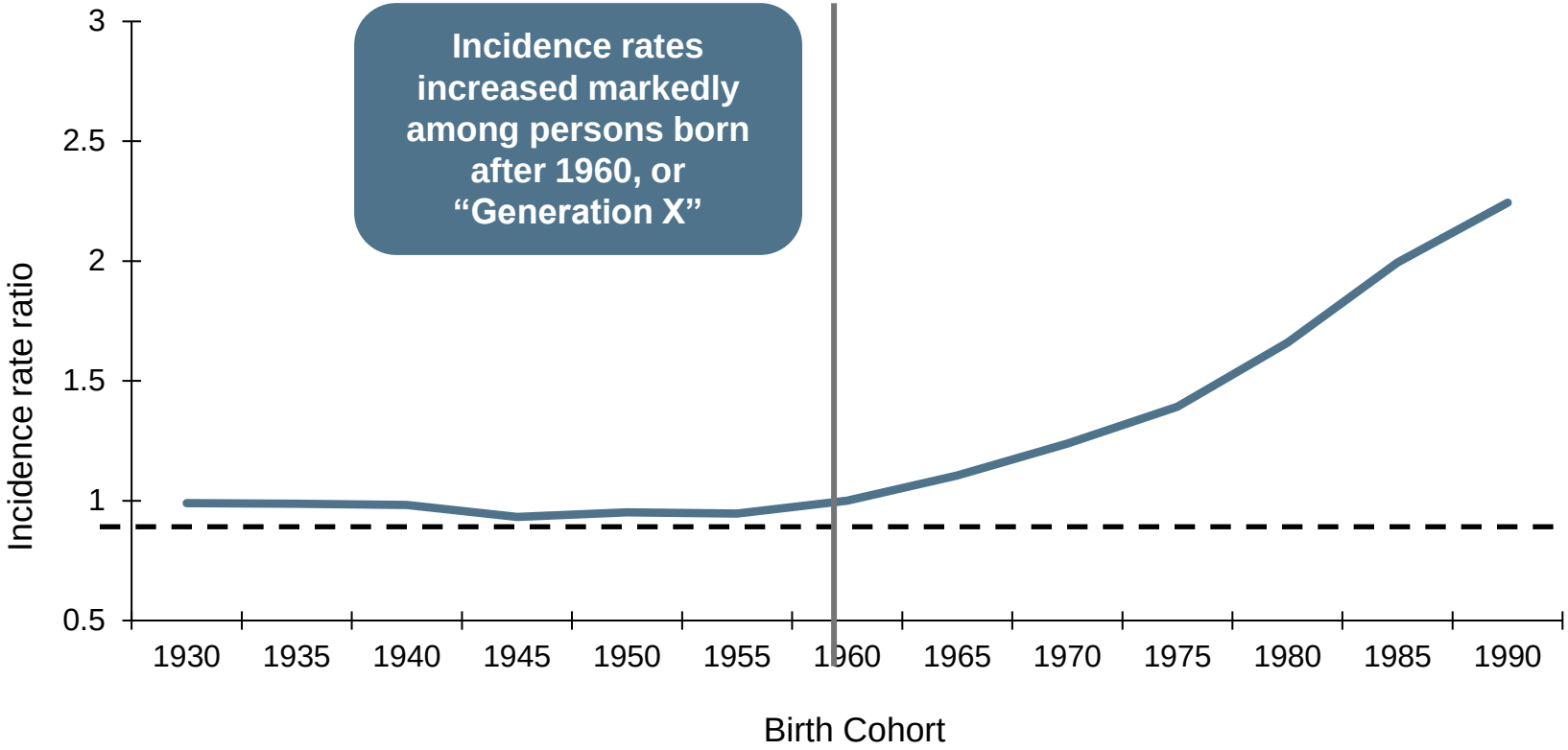
Is early-onset colorectal cancer different than colorectal cancer in older adults?

Increasing incidence rates across generations – a birth cohort effect



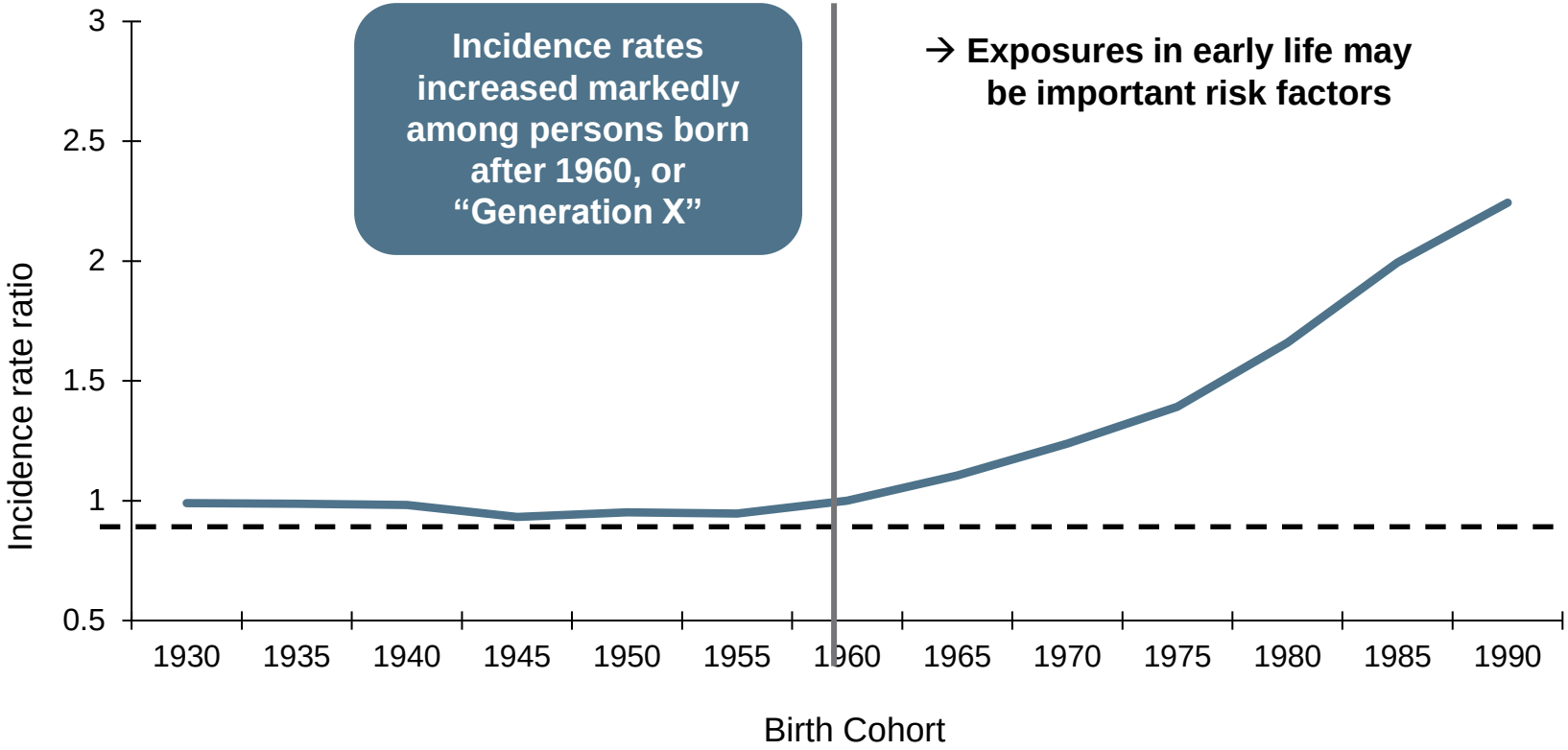
Murphy CC, et al. Gastroenterology 2018; 155(6):1716-19

Increasing incidence rates across generations – a birth cohort effect



Murphy CC, et al. Gastroenterology 2018; 155(6):1716-19

Increasing incidence rates across generations – a birth cohort effect



Murphy CC, et al. Gastroenterology 2018; 155(6):1716-19

Are there vulnerable times of exposure related to risk?

In utero exposures in 18,751 mother-child dyads

	HR	95% CI
Maternal obesity	2.51	1.05, 6.02
Pregnancy weight gain	4.78	1.45, 15.74
Synthetic hormones	5.51	1.73, 17.59
Sulfonamide antibiotics	5.40	2.15, 13.58
Anti-nauseants	3.29	1.63, 6.63

Murphy CC et al. Gut 2021; Murphy CC et al. Am J Obst Gynecol 2021

Are there vulnerable times of exposure related to risk?

In utero exposures in 18,751 mother-child dyads

	HR	95% CI
Maternal obesity	2.51	1.05, 6.02
Pregnancy weight gain	4.78	1.45, 15.74
Synthetic hormones	5.51	1.73, 17.59
Sulfonamide antibiotics	5.40	2.15, 13.58
Anti-nauseants	3.29	1.63, 6.63

Early life exposures in the Nurses' Health Study

	RR	95% CI
BMI at age 18	1.63	1.01, 2.61
Weight gain since age 18	1.09	1.02, 1.16
Antibiotics at age 20-29	1.36	1.03, 1.79
Sugar-sweetened beverages in adolescence	3.41	1.08, 10.80

Liu P et al. JAMA Oncol 2019; Cao Y et al. Gut 2018; Hur J et al. Gut 2021

Unanswered questions at the Early-Onset Colorectal Cancer Summit in 2017

What is the role of known risk factors (e.g., obesity, family history)?

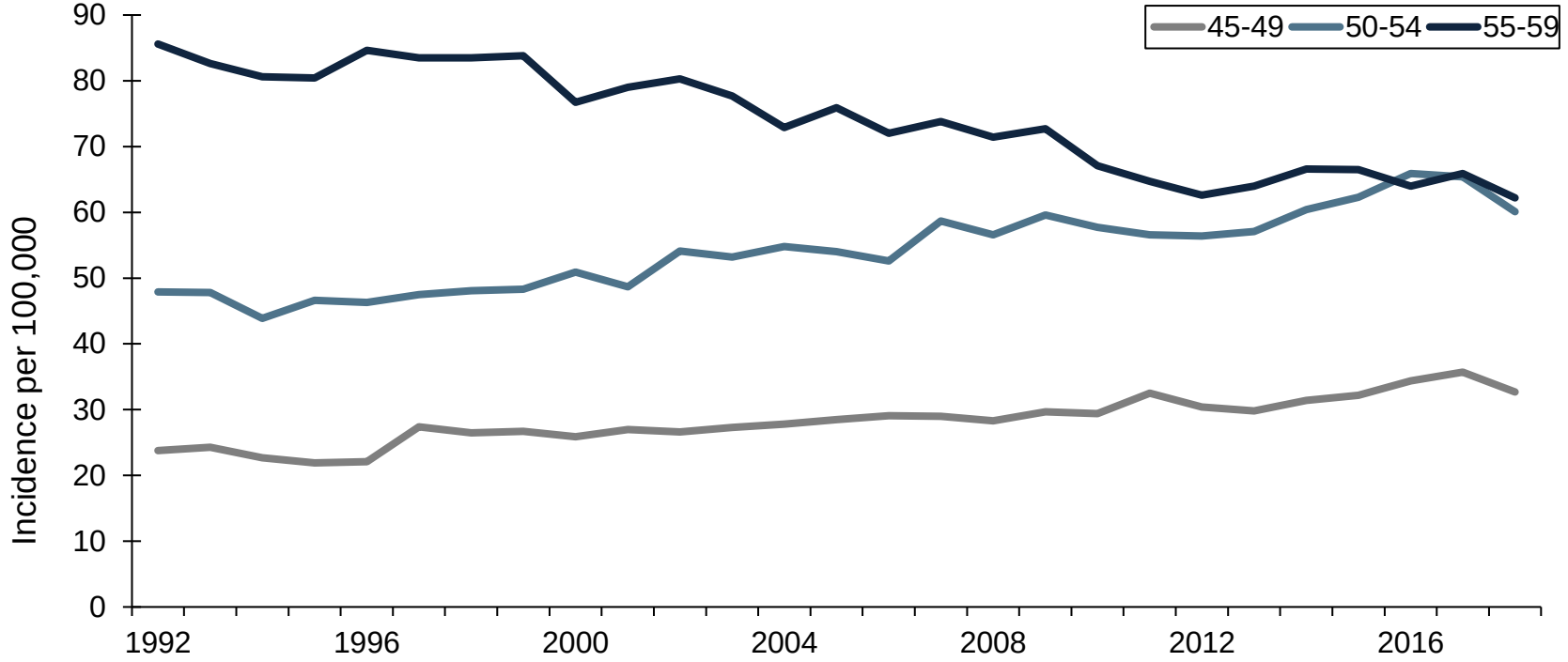
What is the role of novel risk factors?

Do risk factors differ by site (colon vs. rectum)?

Are there vulnerable times of exposure related to risk?

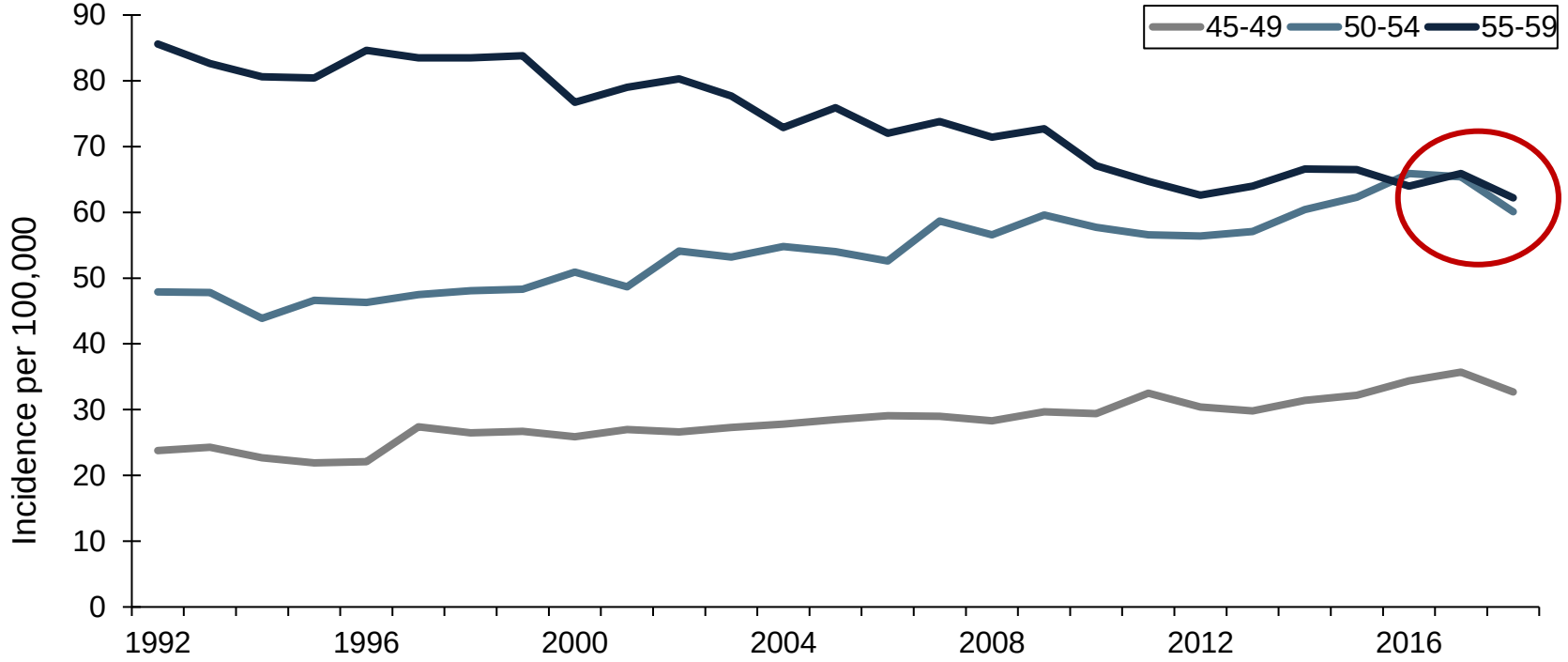
Is early-onset colorectal cancer different than colorectal cancer in older adults?

Parallel increases in incidence rates at age 50-54 years



Adapted from: Zaki T, et al. Gastroenterology 2021; in press

Parallel increases in incidence rates at age 50-54 years



Adapted from: Zaki T, et al. Gastroenterology 2021; in press

Where do we go from here?

Many (if not all) of the known risk factors of colorectal cancer in older adults are risk factors of early-onset colorectal cancer

At the same time, these risk factors cannot explain all of the increase in incidence rates, and they never explained much of the variation in older adults

Let's think outside the box and be creative, for example:

- Environmental chemicals

Thank you!

Caitlin C. Murphy, PhD, MPH
UTHealth School of Public Health
caitlin.c.murphy@uth.tmc.edu
(713) 500-9105

@caitlincmurphy

NYU Langone Health

NCCRT Annual Meeting

Nov 17, 2021

What is the natural history of early-onset colorectal cancer?

Peter S. Liang, MD MPH
Departments of Medicine and Population Health, NYU Langone Health
VA New York Harbor Health Care System
NYC Health + Hospitals Bellevue

@petersliang

Disclosures

Research support: Epigenomics, Freenome

Consulting: Guardant Health

2017 NCCRT summit research priorities

What is the natural history of EOCRC?

What is the prevalence of adenomas in younger adults?

What is rate of progression from adenoma to carcinoma in younger adults?

What is the screening regimen that will optimize reduction in incidence and mortality of EOCRC?

Lowery et al, *Colorectal Cancer* 2020

Key questions

1. What is the prevalence of advanced precancerous polyps (advanced neoplasia/AN) in average-risk adults younger than 50?

2. How does the prevalence of AN in younger age groups compare to older age groups?

3. How does family history influence AN prevalence in younger adults?

1) New Hampshire Colonoscopy Registry (NHCR)

- Population-based, statewide endoscopy registry started in 2004
- Patients complete questionnaire on demographics, health behavior, and family/personal history of colorectal neoplasia
- Pathology results are obtained directly from pathology lab and entered by study staff

Butterly et al, *Am J Gastroenterol* 2021

NHCR study on colorectal neoplasia

Study period: 2004-2018

Population: 1st exam, excludes those with first-degree relatives (FDR) with CRC

- Age <50: includes *average-risk equivalent* person with low-risk indications: abdominal pain, constipation
- Age ≥50: screening only

Family history: **15.1%** of age 45-49 vs. **4.0%** of age 50-54 had non-FDR with CRC

Butterly et al, *Am J Gastroenterol* 2021

NHCR study: similar prevalence of AN* in age 45-49 vs. 50-54

	< 40 % (95% CI) (n = 2,449)	40–44 % (95% CI) (n = 1,288)	45–49 % (95% CI) (n = 1,869)	50–54 % (95% CI) (n = 21,482)
Total advanced colorectal neoplasia	1.1% (0.8–1.7) (n = 28)	3.0% (2.2–4.0) (n = 38)	3.7% (3.0–4.7) (n = 70)	3.6% (3.4–3.9) (n = 783)
AA	1.1% (0.8–1.6) (n = 27)	2.8% (2.0–3.9) (n = 36)	3.3% (2.6–4.2) (n = 61)	3.6% (3.3–3.8) (n = 765)
CRC	0.0% (0.0–0.02) (n = 1)	0.2% (0.0–0.6) (n = 2)	0.5% (0.3–0.9) (n = 9)	0.1% (0.1–0.1) (n = 18)
Any colorectal neoplasia	6.5% (5.6–7.5) (n = 159)	14.9% (13.1–17.0) (n = 192)	17.5% (15.9–19.3) (n = 327)	22.1% (21.6–22.7) (n = 4,754)
CSSP	3.0% (2.4–3.7) (n = 73)	5.1% (4.1–6.5) (n = 66)	5.9% (4.9–7.0) (n = 110)	6.1% (5.8–6.5) (1,320)

*AN: advanced adenoma (≥10 mm, villous, or high-grade dysplasia) or CRC

Butterly et al, *Am J Gastroenterol* 2021

2) Meta-analysis of 17 studies

Study period: 1995-2017 (10/17 studies ended in 2011 or earlier)

Population: Average-risk individuals age <50 (9 countries)

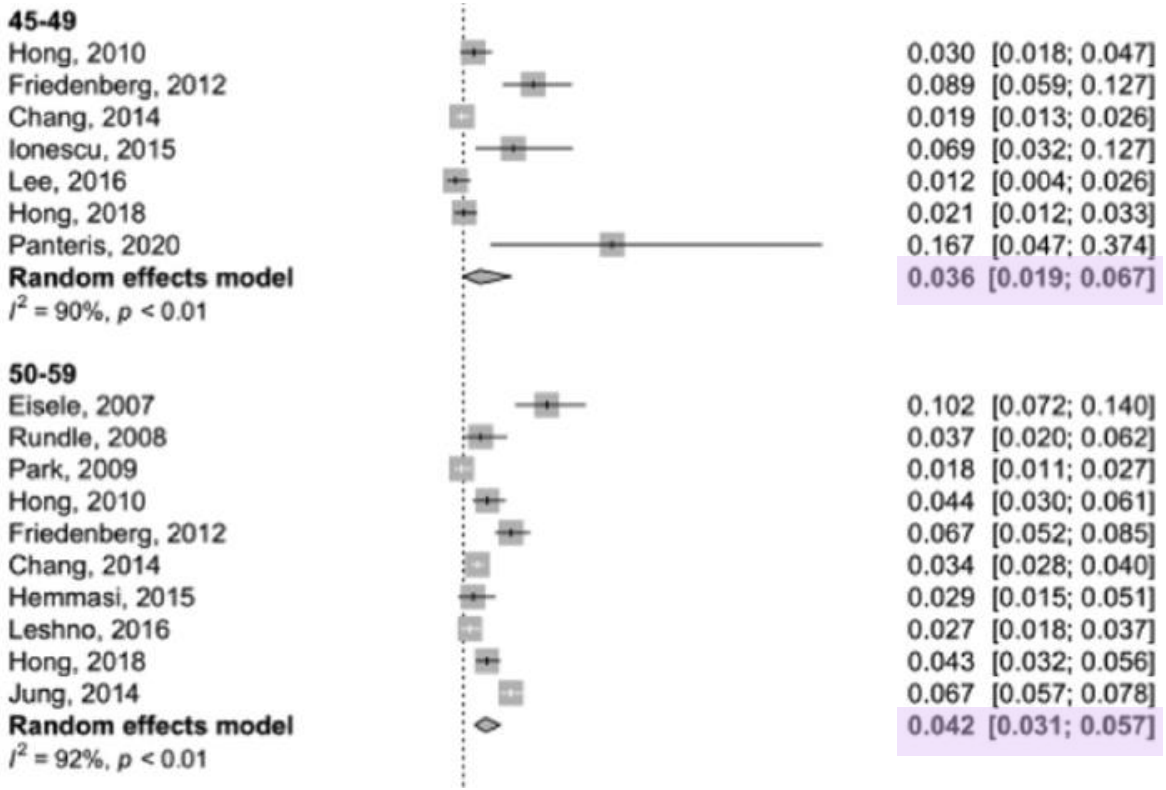
-5 US studies include employee-sponsored screening (2), routine screening for Black individuals (2), national endoscopic registry (1)

Family history: excluded

Kolb et al, *Gastroenterology* 2021

Meta-analysis: 3.6% AN prevalence in age 45-49 (n=7) vs. 4.2% in age 50-59 (n=10)

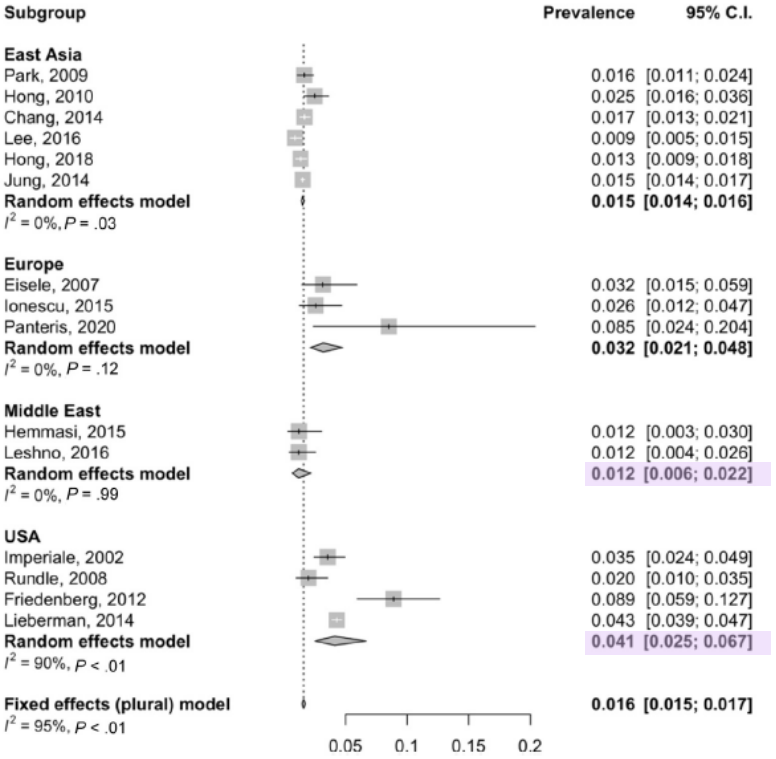
Only US study



Difference **NOT** statistically significant

Kolb et al, *Gastroenterology* 2021

AN prevalence varied significantly by region*



* All age<50 years

Kolb et al, *Gastroenterology* 2021

3) Large community practice in Minneapolis

Study period: 2015-2019

Population: Average-risk individuals age 45-75

Family history: excluded

Shaukat et al, *Gastroenterology* 2021

AN* prevalence was similar in age 45-49 vs. 50-54

	45-49 year old n=4841	50-54 year old n=58,914	
Overall ADR	28.4% (27.1%, 29.6%)	31.1% (30.7%, 31.4%)	P<0.001
ADR in men	34.8% (32.9, 36.8)	38.3% (37.7, 38.9)	P<0.001
ADR in women	22.6% (21.0, 22.4)	24.4% (23.9, 24.9)	P=0.001
APC	0.44 (0.41, 0.46)	0.49 (0.48, 0.49)	P<0.001
AN detection rate	3.28% (2.58, 3.97)	3.43% (3.23, 3.64)	P=.68
CRC detected	3	32	P=0.91

*AN = adenoma or SSL ≥ 10 mm, adenoma with villous histology or HGD, TSA, ≥5 adenomas/SSLs (excludes CRC)

Shaukat et al, *Gastroenterology* 2021

4) National endoscopic registry: GIQuIC

GIQuIC **GI Qu**ality **I**mprovement **C**onsortium

12,244,085 million colonoscopies (2010-2020)

5,678 endoscopists, 795 sites, 50 states/territories

Internal audit showed colonoscopy indication was **98.7%** accurate compared to medical record

GIQuIC study: design

Study period: 2010-2020

Population: Average-risk individuals age 18-49 undergoing screening, all individuals age 18-85+ undergoing screening

Family history: +/- individuals with CRC or advanced adenoma in FDR younger than age 60

Primary outcome: Prevalence of advanced neoplasia (adenoma/SSL ≥10 mm or with advanced histology, TSA, CRC)

GIQuIC study: flowchart

2010-2020: **3,928,727** screening colonoscopies

↓

Age <50: **211,020** (5.4%)

↓

Age <50 + no FDR aged <60 with CRC/advanced adenoma (average-risk): **129,736** (3.3%)

↓

Age 45-49, average-risk: **92,752** (2.4%)

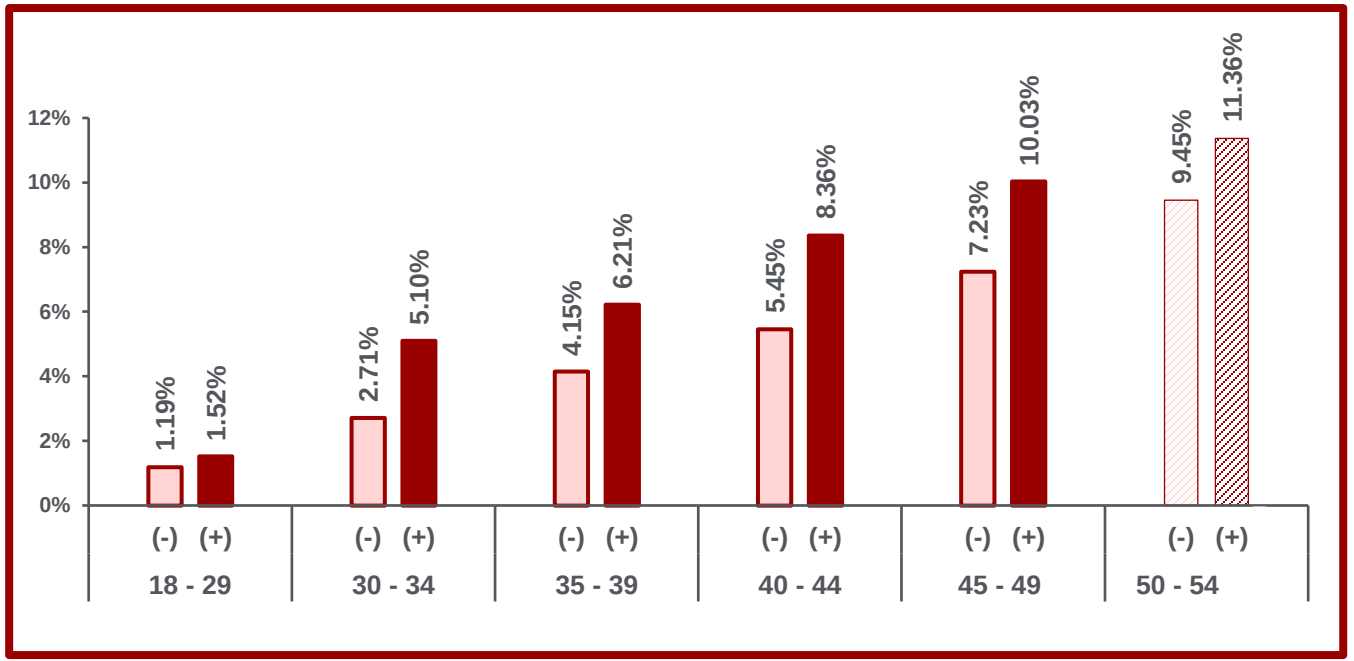
Funding: ReMission Foundation

Compared to age 50-54, AN (excluding serrated lesions) prevalence was 1.0% lower in age 45-49 (21% relative reduction)

Age	Prevalence	Prevalence Ratio (95% CI)	Absolute/relative difference
50-54	4.8%	REF	
45-49 (avg risk)	3.8%	0.79 (0.76-0.81)	-1.0% / -21%

Liang et al, unpublished

5) GIQuIC subset study: AN prevalence higher in age 45-49 with family history than age 50-54 without family history



Mohapatra et al, *Gastroenterology* 2021;160 (suppl):S-181

Summary of studies

Study	Population	Age 45-49 AN, %	Age 50-54 AN, %	Absolute / relative difference, 45-49 vs. 50-54
Butterly	New Hampshire (96% White)	3.7 (n=70)	3.6 (n=783)	+0.1% / +3%
Kolb	7 studies (1 in US)	3.6 (n<185)	Age 50-59: 4.2 (n=?)	-0.6 / -14%
Shaukat	Minneapolis (6 ASCs)	3.3 (n~159)	3.4 (n~2021)	-0.1 / -4%
GIQuIC	US (64% White, 21% Black)	3.8 (n=3480)	4.8 (n=63,132)	-1.0% / **-21%**

AN (advanced neoplasia): advanced adenoma (≥10 mm, villous, or high-grade dysplasia) or CRC. For Shaukat et al., AN excludes CRC but includes advanced serrated lesions and ≥5 adenomas/SSLs

Summary

- AN prevalence in average-risk individuals age 45-49 is 3.3-3.8% based on available data
- AN prevalence is lower in age 45-49 vs. age 50-54
- These figures likely overestimate the true values because of 1) higher proportion of individuals with family history or 2) particular definitions for AN and average-risk
- Family history increases AN risk

Future directions

1) Standardize definitions for AN, average-risk, and family history to improve data comparability
2) Update AN/adenoma prevalence in age 45-49 as greater number/proportion of average-risk individuals enter this screening pool (2018-)
3) Study progression of adenoma to CRC in younger people: are current surveillance intervals optimal?

Thank you!

Peter.Liang@nyulangone.org

@petersliang

https://med.nyu.edu/lianglab/

UC San Diego

Three Key Issues in Identifying EAOCRC

Joshua Demb, PhD, MPH

THREE KEY ISSUES

1. Improving family history documentation

1. Increasing screening uptake in high-risk adults ages <50

1. Faster work-up of signs or symptoms in EAOCRC cases

THREE KEY ISSUES

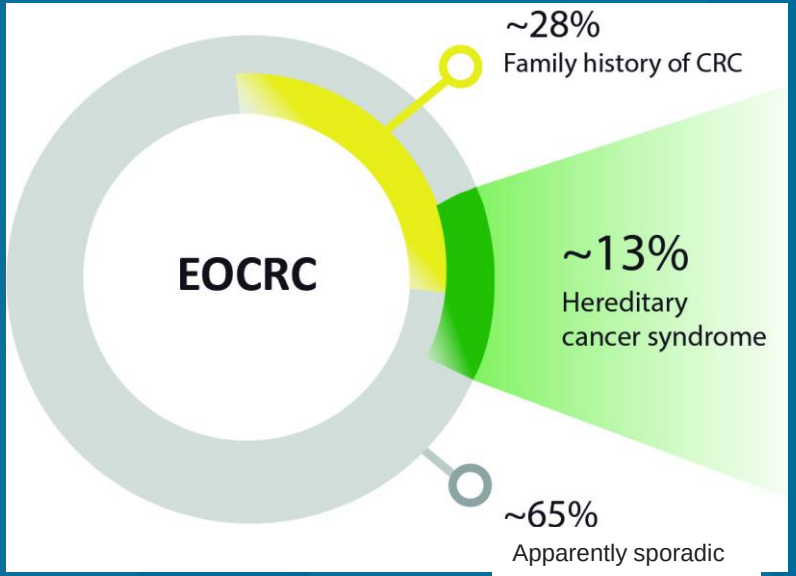
1. Improving family history documentation

1. Increasing screening uptake in high-risk adults ages <50

1. Faster work-up of signs or symptoms in EAOCRC cases

35% OF EAOCRC CASES HAVE FAMILY HISTORY, BUT FAMILY HISTORY CAPTURE IS LOW

- About 35% of EAOCRC cases have family history of CRC, polyps or other genetic factors. (Alvarez et al. *Cells.* Feb 2021)

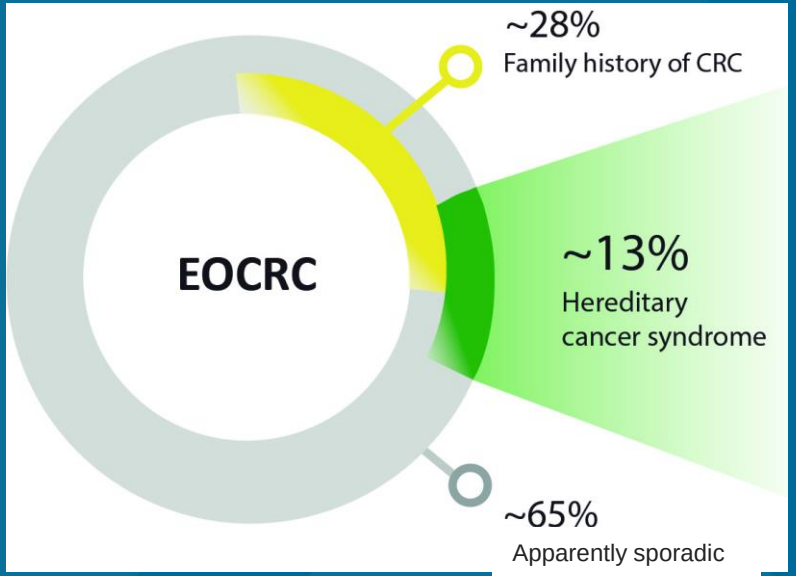


Alvarez et al. *Cells.* Feb 2021

35% OF EAOCRC CASES HAVE FAMILY HISTORY, BUT FAMILY HISTORY CAPTURE IS LOW

- About 35% of EAOCRC cases have family history of CRC, polyps or other genetic factors.
  (Alvarez et al. *Cells.* Feb 2021)

- Prior research showed only 39-54% capture of family history among patients ages <50.
  (Fletcher et al. *J Gen Int Med*. Apr 2007; Foo et al. *Colorectal Dis.* Jun 2009)
- Barriers include:
  - Limited patient knowledge of polyp/CRC family history (Elias et al. *Gastrointest Endosc.* 2012)
  - Physicians may lack time and knowledge to assess risk.
    (Fletcher et al. *J Gen Int Med.* Apr 2007; Solomon et al. *BMC Fam Prac.* 2016)



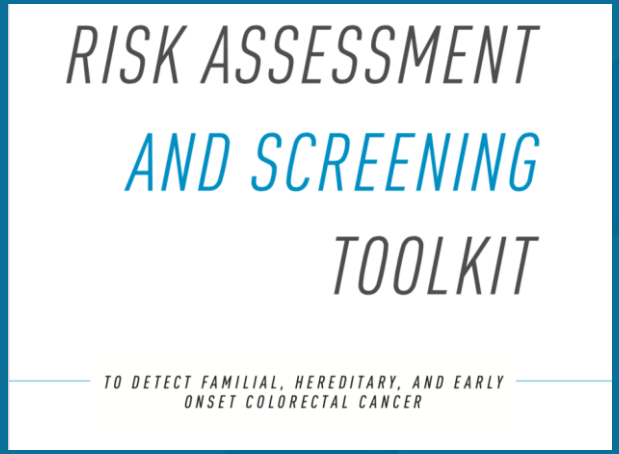
Alvarez et al. *Cells.* Feb 2021

IMPROVING FAMILY HISTORY ASCERTAINMENT

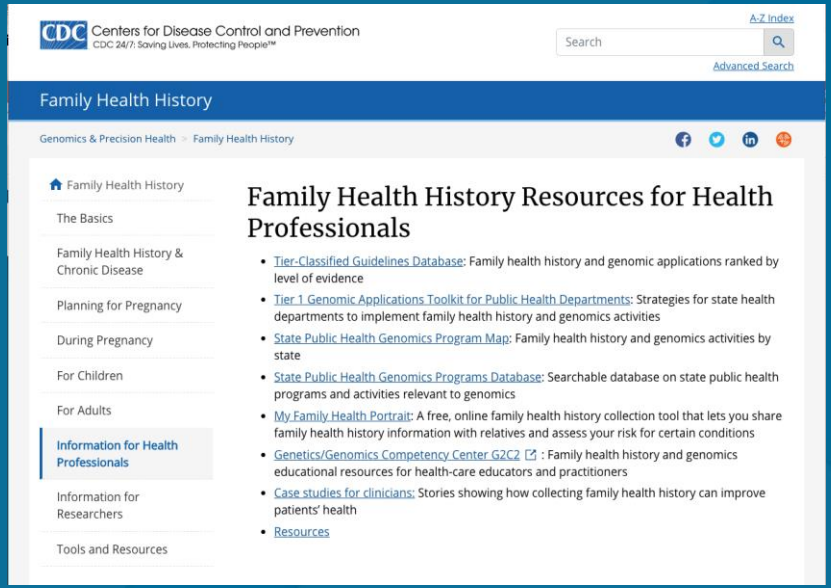
- More consistent family history capture in primary care

IMPROVING FAMILY HISTORY ASCERTAINMENT

- More consistent family history capture in primary care



NCCRT, ACS and The Jackson Laboratory



IMPROVING FAMILY HISTORY ASCERTAINMENT

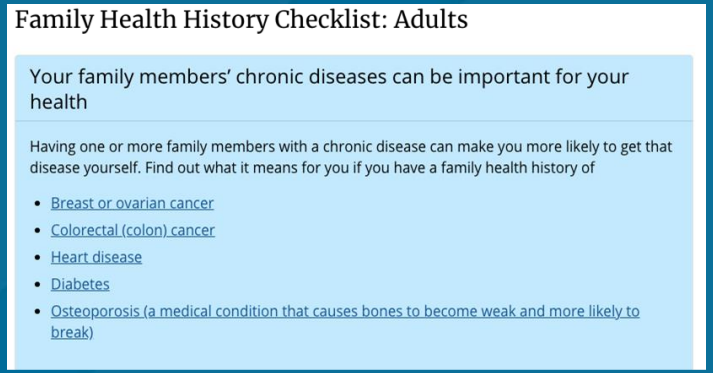
- More consistent family history capture in primary care
  - Integration into the electronic health record to trigger follow-up
  - Ensuring feasibility in diverse healthcare settings

IMPROVING FAMILY HISTORY ASCERTAINMENT

- More consistent family history capture in primary care
  - Integration into the electronic health record to trigger follow-up
  - Ensuring feasibility in diverse healthcare settings
- Educate patients about family history and CRC risk, provide resources to simplify at-home capture

IMPROVING FAMILY HISTORY ASCERTAINMENT

- More consistent family history capture in primary care
  - Integration into the electronic health record to trigger follow-up
  - Ensuring feasibility in diverse healthcare settings
- Educate patients about family history and CRC risk, provide resources to simplify at-home capture



Family Health History Checklist: Adults

Your family members' chronic diseases can be important for your health

Having one or more family members with a chronic disease can make you more likely to get that disease yourself. Find out what it means for you if you have a family health history of

- Breast or ovarian cancer
- Colorectal (colon) cancer
- Heart disease
- Diabetes
- Osteoporosis (a medical condition that causes bones to become weak and more likely to break)

Centers for Disease Control and Prevention

My Family Health Portrait

A tool from the Surgeon General

Get Help

Using My Family Health Portrait you can:

- Enter your family health history.
- Learn about your risk for conditions that can run in families.
- Print your family health history to share with family or your health care provider.
- Save your family health history so you can update it over time.

Talking with your health care provider about your family health history can help you stay healthy!

Learn more about My Family Health Portrait

Note: You must use the "Use a Saved History" button to open the family history file you created.

Create a Family Health History | Use a Saved History

U.S. Surgeon General

THREE KEY ISSUES

1. Improving family history documentation

1. Increasing screening uptake in high-risk adults ages <50

1. Faster work-up of signs or symptoms in EAOCRC cases

VERY LOW SCREENING UPTAKE IN HIGH-RISK ADULTS AGES <50

- High-risk Screening (Family History): Age 40 or 10 years younger than diagnosis of first degree relative.

- 2010 NHIS data: 38.3% screening uptake in adults ages 40-49 with family history of CRC. (Tsai et al. *Prev Chronic Dis.* 2015)

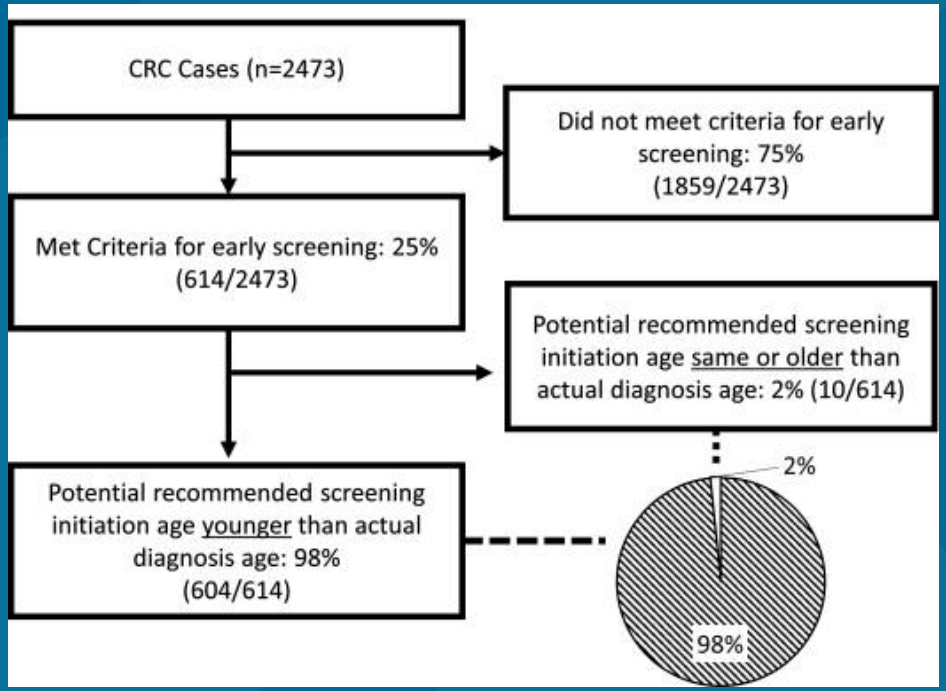
TABLE 1. Age to Initiate CRC Screening Based on Risk Category

Risk Category	Family History	Age to Initiate Screening	Recommended Test
Relative With CRC	Cancer in an FDR	Age 40 or 10 years younger than age of diagnosis of FDR[f,g]	Colonoscopy every 5 years
	Cancer in ≥ 2 SDRs	Age 40[f]	
FDR With Advanced Colorectal Polyp	Advanced adenoma in 1 FDR < 60 years or in 2 FDRs	Age 40 or 10 years younger than age of diagnosis of FDR[f]	Colonoscopy every 5 years
	Advanced adenoma in 1 FDR ≥ 60 years	Age 40[f]	Colonoscopy every 10 years or FIT annually
	Confirmed advanced polyp in 1 FDR (any age)	Age 40 or at age of diagnosis of advanced adenoma in FDR[g]	Colonoscopy every 5–10 years

Abbreviations: CRC, colorectal cancer; FDR, first-degree relative; FIT, fecal immunochemical testing; SDR, second-degree relative.
[a]U.S. Preventive Services Task Force.
[b]Canadian Task Force on Preventive Health Care.
[c]European Council.
[d]American Academy of Family Physicians.
[e]American College of Physicians.
[f]U.S. Multi-Society Task Force of Colorectal Cancer, which represents the American College of Gastroenterology, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy.
[g]National Comprehensive Cancer Network.
[h]American Cancer Society.

EARLIER FH-RELATED SCREENING UPTAKE COULD IMPROVE OUTCOMES

- Study found 614 of 2,473 EAOCRC cases (25%) met family history guidelines
  - 98% of these cases were eligible for earlier CRC screening
  - Earlier work-up could have prevented CRC or improved stage at detection and overall prognosis.



Gupta et al. *Cancer. Apr* 2020

INCREASING SCREENING UPTAKE IN HIGH-RISK ADULTS AGES <50

Commentary

Improving On-Time Colorectal Cancer Screening Through Lead Time Messaging

Whitney F. Jones, MD[1]; Dennis J. Ahnen, MD[2,3]; and Paul C. Schroy III, MD, MPH[4]

- Lead-time messaging: “[P]roviding additional lead time for the delivery of accurate, relevant, and actionable information regarding CRC risk and risk-based screening options”

Jones et al. *Cancer. Jan* 2020

INCREASING SCREENING UPTAKE IN HIGH-RISK ADULTS AGES <50

Commentary

Improving On-Time Colorectal Cancer Screening Through Lead Time Messaging

Whitney F. Jones, MD[1]; Dennis J. Ahnen, MD[2,3]; and Paul C. Schroy III, MD, MPH[4]

- Lead-time messaging: "[P]roviding additional lead time for the delivery of accurate, relevant, and actionable information regarding CRC risk and risk-based screening options"

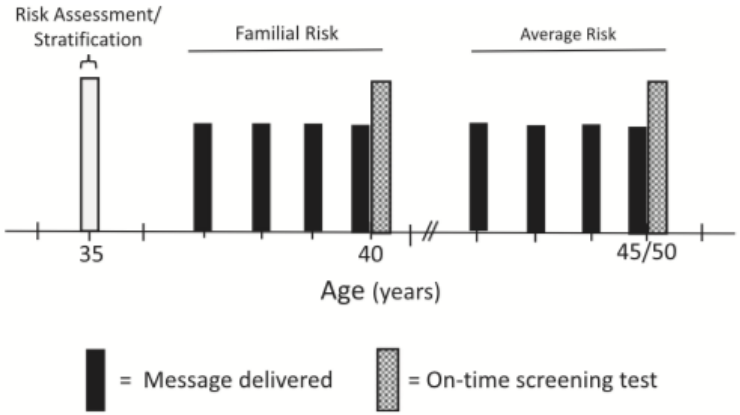


Figure 3. Lead time messaging paradigm to increase on-time colorectal cancer screening. Initial familial risk assessment and stratification should begin by age 35 years at the latest. Individuals at increased risk due to a family history of colorectal cancer or advanced adenomas should initiate screening at age 40 years versus age 45/50 years for those of average risk. Lead time messaging regarding the importance of on-time screening, primary prevention, and screening options should begin approximately 3 years before the age of initiation and be repeated annually.

Jones et al. *Cancer. Jan* 2020

THREE KEY ISSUES

1. Improving family history documentation

1. Increasing screening uptake in high-risk adults ages <50

1. Faster work-up of signs or symptoms in EAOCRC cases

MANY EAOCRC CASES ARE DIAGNOSED WITH SYMPTOMS

- About 70-95% of EAOCRC cases present with ”red-flag” signs or symptoms
- Common signs/symptoms include:
  - Rectal bleeding
  - Abdominal Pain
  - Change in bowel habits
  - Unexplained weight loss
  - Anemia

Myers et al. *World J Gastroenterol.* 2013; Read et al. *Clin Colon and Rectal Surg.* 2020; Silva et al. *Curr Probl Cancer*. 2019; Demb et al. *Gut*. 2020.

RED FLAG SIGNS/SYMPTOMS HIGHLIGHT SCREENING/WORK-UP DELAYS

- Study found iron deficiency anemia and hematochezia associated with 10-fold increased EAOCRC risk, with increased absolute risk among adults ages 40-49. (Demb et al. *Gut*. 2020)
  - Diagnostic colonoscopy receipt among patients with IDA (17%) and Hematochezia (46%) was low.

RED FLAG SIGNS/SYMPTOMS HIGHLIGHT SCREENING/WORK-UP DELAYS

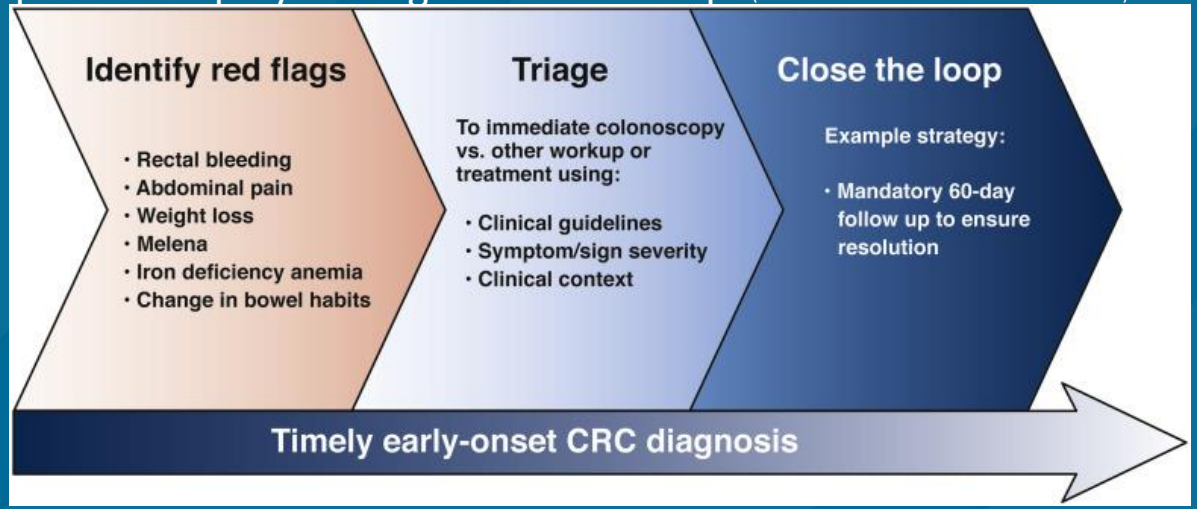
- Study found iron deficiency anemia and hematochezia associated with 10-fold increased EAOCRC risk, with increased absolute risk among adults ages 40-49. (Demb et al. *Gut*. 2020)
  - Diagnostic colonoscopy receipt among patients with IDA (17%) and Hematochezia (46%) was low.
- Diagnostic Delay: Average 6-month time to diagnosis from symptom presentation (Mauri et al. *Mol Oncol*. 2019)

RED FLAG SIGNS/SYMPTOMS HIGHLIGHT SCREENING/WORK-UP DELAYS

- Study found iron deficiency anemia and hematochezia associated with 10-fold increased EAOCRC risk, with increased absolute risk among adults ages 40-49. (Demb et al. *Gut*. 2020)
  - Diagnostic colonoscopy receipt among patients with IDA (17%) and Hematochezia (46%) was low.
- Diagnostic Delay: Average 6-month time to diagnosis from symptom presentation (Mauri et al. *Mol Oncol*. 2019)
- Multilevel Potential Causes of Delayed Diagnosis (Scott et al. *Am J Surg*. 2016)
  - Patients have low risk perception and awareness, or lack of primary care or health insurance.
  - Providers might dismiss symptoms or misattribute symptoms to more benign conditions.

CLOSING THE CLINICAL LOOP ON EAOCRC RED FLAG SIGNS/SYMPTOMS

- Identify most concerning red flag signs/symptoms for EAOCRC, and their association with EAOCRC risk.
- Ensuring rapid work-up by closing the clinical loop: (Burnett-Hartman et al. *Gastroentrol.* 2021)



- Partner with primary care groups to increase awareness of red flag signs/symptoms

SUMMARY

- Improving risk assessment completion and quality can expand access to more timely screening uptake
- Taking a proactive approach to risk assessment and screening messaging can prevent lapses in screening adherence among high-risk adults
- Identifying and triaging adults with red flag signs or symptoms can hasten work-up and mitigate worse EAOCRC outcomes

Questions & Answers