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

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

Jan T Lowery, Thomas K Weber, Dennis J Ahnen, Paul C Schroy III, Caleb L Levell & Robert A Smith

1Center for Personalized Medicine, University of Colorado, Aurora, CO 80045, USA
2Northwell Health, Professor of Surgery, Donald & Barbara Zucker School of Medicine at Hofstra/Northwell, New York, NY 11028, USA
3Gastroenterology of the Rockies, University of Colorado School of Medicine & Director of Genetics Program, Aurora, CO 80045, USA
4Boston University School of Medicine, Section of Gastroenterology, Boston, MA 02118, USA
5American Cancer Society, Atlanta, GA 30303, USA
*Author for correspondence: jan.lowery@cureus.edu
1 TK Weber is deceased

Colorectal Cancer 2020;9(Suppl): https://doi.org/10.2217/crc-2020-0004
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.
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
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 (e.g., obesity, family history)?

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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?

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

Vicky C. Chang1,2, Michella Cottorchio1,2, Prithwish Do1, Jill Timmou1,3,4

Original research

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

Hanyu Chen1,2, Xiaohua Zheng1,3, Xiaoyu Zong2, Zitong Li2,1, Na Li2,1, Jinhee Hur2, Cassandra DL Fritz1,4, William Chapman1,4, Kaitlin B Nickel1, Andrew Tipping1, Graham A Colditz1,5, Edward L Giovannucci1,5, Margaret A Olsen1,8, Ryan C Fields1,11, Yim Cao1,8,11

Clinical Gastroenterology and Hepatology 2020;18:2752-2759

Risk Factors Associated With Early-Onset Colorectal Cancer

Valerie Gausman,1 David Dombiaser,2 Sanya Anand,1 Richard B. Hayes,2 Kelli O’Connell,2 Mengmeng Du1 and Peter S. Liang1

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 Qisaihao Chen2, Vakaram Attaluri3, Elisabeth C. McLemore1, and Chun R. Choe1

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

Hanseul Kim1, Maria Liptsy-Sharf2, Xiaoyu Zong2, Xiaoyan Wang3, Jinhee Hur2, Mingyang Song1,4,5, Molin Wang5,8, Stephanie A. Smith-Warner1, Charles Fuchs1, Shuji Ogino2,9,15,16, Kana Wu1, Andrew T. Chan1,11, Yin Cao1,8,11, Kimmie Ng6,8, and Edward L. Giovannucci1,5,8,11

Clinical Gastroenterology and Hepatology 2020;18:2752-2759

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

Genevieve Breau, PhD1,2,3 and Ursula Ellis, MLS1,5

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

Dylan E. O’Sullivan4,5,6, R. Liam Sutherland4,5,6, Susanna Town,7 Jeremy Fan,3 Nauzer Forbes,8,9 Steven J. Heitman,6,10 Robert J. Hilson,6,10 and Darren R. Brenner3,9

Nongenetic Determinants of Risk for Early-Onset Colorectal Cancer

Alessi N. Archambault3, MPH1, Yl Yi Lin, MS2, Joyburn Jenn1, PhD, MS1, Tabitha A. Harris1, MPH1,2, D. Timothy Babor1, PhD, MD3,4,5,6 Hermann Brenner7, MD, MPH4,5,6, Graham Casey, PhD, Andrew T. Chan, MD, MPH1,2,6,7,8,9,10,11 Junny Chang-Claude1, PhD,1,2,10,11 Jane C. Figueroa1, PhD,1,2,10,11 Steven Gallinger, MD, MSc1,2,10,11, Stephen B. Gruber1, PhD, MD, PhD2,10,11 Marc J. Gunter1, PhD, Michael Hoffmeister1, PhD, Mark A. Jenkins1, PhD, Tamirgo O. Kikuzuki, PhD, MPH4,5,6,7,8 Loic Le Marchand, MD, PhD2, Li Li, MD, PhD2,10,11 Victor Moreno1, PhD,1,2,10,11,12,13 Polly A. Newcomb, PhD, MPH1,2,10,11, Richard Poi1, MD, PhD, Patrick S. Partley, MD, GD Hennett1, MD, PhD,1,2,6,11,12 Lori C. Salo1, PhD,1,2,10,11,13,14 Robert S. Sandler, MD, MPH2,10,11, Martha L. Slattery1, PhD,1,2,10,11,13 Mingyang Song1,4,5, Li Xu, MD, PhD1,2,6,11,13,14,15 Aung Ko Win1, PhD, MPH1,2,10,11,13,14,15 Micahel O. Wood1, PhD,1,2,6,11,13,14,15 Neil Murphy1, PhD,1,2,6,11,13,14,15 Peter T. Campbell1, PhD, MSc1,2,6,11,13,14,15, Yu-Ru Su1, PhD, MS1, Anne Zeleniuch-Jacquotte1, MD, MS1, Peter S. Liang1, MD, MPH1,2, Mengmeng Dù, ScD6, Li Hui, PhD1,2,6,11,13,14,15,16 Ulrike Peters1, PhD, MPH,1,2,6,11,13,14,15,16 Richard B. Hayes1, PhD, MPH, DDS1,2,3
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
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- 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?

Obesity
- Kaiser Permanente
- Nurses’ Health Study
- MarketScan
- Ontario, Canada
- Veterans Health Administration
- NYU Medical Center
- CORECT, CCFR, GECCO

Western Diet
- Nurses’ Health Study
- Ontario, Canada
- Nurses’ Health Study

Vitamin D
- Ontario, Canada
- Nurses’ Health Study

Sedentary Lifestyle
- CORECT, CCFR, GECCO
- Nurses’ Health Study
- Nurses’ Health Study
- Ontario, Canada

Family History
- NYU Medical Center
- Ontario, Canada

NSAID or Aspirin Use
- CORECT, CCFR, GECCO
- Veterans Health Administration
- Ontario, Canada
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
- Gut microbiome
- HPV
- Food additives
- Birth weight
- Helicobacter pylori
- Vaccines
- Pesticides
- 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
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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)
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- UK (medical records)
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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

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

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

Incidence shown as rate over the period 1992-95 and the period 2015-18.

- Rectum
- Distal Colon
- Proximal Colon

Incidence per 100,000

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:

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This phenomenon has also been well-described in 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?
Increasing incidence rates across generations – a birth cohort effect
Increasing incidence rates across generations – a birth cohort effect

Incidence rates increased markedly among persons born after 1960, or “Generation X”
Increasing incidence rates across generations – a birth cohort effect

Incidence rates increased markedly among persons born after 1960, or “Generation X”

→ Exposures in early life may be important risk factors
Are there vulnerable times of exposure related to risk?

*In utero* exposures in 18,751 mother-child dyads

<table>
<thead>
<tr>
<th>Exposure</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal obesity</td>
<td>2.51</td>
<td>1.05, 6.02</td>
</tr>
<tr>
<td>Pregnancy weight gain</td>
<td>4.78</td>
<td>1.45, 15.74</td>
</tr>
<tr>
<td>Synthetic hormones</td>
<td>5.51</td>
<td>1.73, 17.59</td>
</tr>
<tr>
<td>Sulfonamide antibiotics</td>
<td>5.40</td>
<td>2.15, 13.58</td>
</tr>
<tr>
<td>Anti-nauseants</td>
<td>3.29</td>
<td>1.63, 6.63</td>
</tr>
</tbody>
</table>
**Are there vulnerable times of exposure related to risk?**

<table>
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<tr>
<th>In utero exposures in 18,751 mother-child dyads</th>
<th>Early life exposures in the Nurses’ Health Study</th>
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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!

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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
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

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

*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)

Kolb et al, *Gastroenterology* 2021

Difference NOT statistically significant
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

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

*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

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).

<table>
<thead>
<tr>
<th>Age</th>
<th>Prevalence</th>
<th>Prevalence Ratio (95% CI)</th>
<th>Absolute/relative difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>50-54</td>
<td>4.8%</td>
<td>REF</td>
<td></td>
</tr>
<tr>
<td>45-49 (avg risk)</td>
<td>3.8%</td>
<td>0.79 (0.76-0.81)</td>
<td>-1.0% / -21%</td>
</tr>
</tbody>
</table>

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

## Summary of studies

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

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!

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

1. Faster work-up of signs or symptoms in EAOCRC cases
About 35% of EAOCRC cases have family history of CRC, polyps or other genetic factors. (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)
IMPROVING FAMILY HISTORY ASCERTAINMENT

• More consistent family history capture in primary care
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RISK ASSESSMENT AND SCREENING TOOLKIT

To detect familial, hereditary, and early onset colorectal cancer

NCCRT, ACS and The Jackson Laboratory
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• Integration into the electronic health record to trigger follow-up
• Ensuring feasibility in diverse healthcare settings
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THREE KEY ISSUES

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

• 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”
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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

RED FLAG SIGNS/SYMPOTOMS 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.
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  - 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