Session Ten

Panel
Early-Age Onset Colorectal Cancer: What’s Experienced, What’s Known, and What’s Next?

11:15 AM to 12:30 PM
Panel
Early-Age Onset Colorectal Cancer: What’s Experienced, What’s Known, and What’s Next?

Moderator
Allison Rosen
MS

Suzy Reyes

Scott Kopetz
MD, PhD, FACP

Cassandra Fritz MD,
MPHS
Azucena (Suzy) Reyes

Suzy Reyes
Early-Age Onset Colorectal Cancer Survivor
Azucena (Suzy) Reyes
Cancer Survivor
1st Chemotherapy
1 down out of 12
11/16/2016
CHEMOTHERAPY #4 😮😮💊
Chemotherapy
#7 2/8/16
Chemotherapy
PY #9
3/21/16
Chemotherapy #11
4/19/16 😛
Final chemo ring the bell... then run like hell!!!
Thank You
Overview of Early-Onset Colorectal Cancer

Scott Kopetz, MD, PhD, FACP
Deputy Chair for Translational Research and Professor
Department of Gastrointestinal (GI) Medical Oncology, Division of Cancer Medicine
The University of Texas MD Anderson Cancer Center
Overview of Early-Onset Colorectal Cancer

Scott Kopetz, MD, PhD

Department of Gastrointestinal Medical Oncology
MD Anderson Cancer Center
Topics

01 EPIEMIOLOGY
The epidemiology of EOCRC globally and in the United States.

02 EXPOSOME
Exposures or risk factors potentially contributing to the rising risk of EOCRC.

03 GENETICS & EPIGENETICS
Molecular aspects of EOCRC.
US Incidence

50% Incidence of EOCRC
Incidence rate of EOCRC raised by more than 50% in both genders since 1994.

32% Incidence of LOCRC
Incidence rate of LOCRC declined by around 34% in both genders since 2000.

Siegel RL, et al. CA Cancer J Clin' 2020
Global Prevalence: Europe, North America & Oceania

EOCRC incidence increased in 19 countries. Nine of which had stable or declining trends in older adults.

Average annual per cent change (AAPC) in colorectal cancer incidence by age during the most recent 10 years of available data.

Siegel RL, et al. Gut’19
EOCRC Age Distribution

- **44%** of EOCRC cases are **45-49 years old**
EOCRC by Race/Ethnicity

Annual per cent change (APC)
Bold = p<0.05

NH White
APC, +2.0

Am Indian/ AK Native
APC, +2.2

NH Black
APC, +0.5

Asian/ Pacific Islander
APC, +0.4

Hispanic
APC, +2.8
40% of EOCRC cases are rectal cancer

40% of men; 35% of women

27% of men; 20% of women
EOCRC Clinical Diagnosis

- **Stage**: 71% Diagnosed at stage III or IV.
- **Diagnosis Time**: 67% Visited two physician at least before they get the diagnosis.
- **Family**: 80% Around 80% with young children
- **Diagnosis Period**: 41% Waited six months at least when they experienced symptoms before talking to a doctor.
AGENDA

01
EPIDEMIOLOGY
The epidemiology of EOCRC globally and in the United States.

02
EXPOSOME
Exposures or risk factors potentially contributing to the rising risk of EOCRC.

03
GENETICS & EPIGENETICS
Molecular aspects of EOCRC.

04
CONCLUSION
Remarks and recommendations.
## Specific External Environment

<table>
<thead>
<tr>
<th>Etiological factors</th>
<th>Level of evidence</th>
<th>Unit increase</th>
<th>RR (95% CI)</th>
<th>Temporal trend</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obesity</td>
<td>++</td>
<td>5 kg/m² in BMI</td>
<td>1.05 (1.03–1.07)</td>
<td></td>
</tr>
<tr>
<td>Western dietary pattern</td>
<td>++</td>
<td>Highest vs lowest</td>
<td>1.12 (1.01–1.24)</td>
<td>Poorest in 2000s then stable</td>
</tr>
<tr>
<td>Processed meat</td>
<td>++</td>
<td>50 g per day</td>
<td>1.16 (1.08–1.26)</td>
<td></td>
</tr>
<tr>
<td>Alcohol (as ethanol)</td>
<td>++</td>
<td>10 g per day</td>
<td>1.07 (1.05–1.09)</td>
<td>Peak in 1980s then down</td>
</tr>
<tr>
<td>Red meat</td>
<td>+</td>
<td>100 g per day</td>
<td>1.12 (1.00–1.25)</td>
<td>Peak in 1970s then down</td>
</tr>
<tr>
<td>Diabetes</td>
<td>+</td>
<td>Yes vs no</td>
<td>1.30 (1.20-1.40)</td>
<td></td>
</tr>
<tr>
<td>Smoking</td>
<td>+</td>
<td>Current vs never</td>
<td>1.15 (1.00–1.32)</td>
<td></td>
</tr>
<tr>
<td>Total physical activity</td>
<td>–</td>
<td>5 MET- hours per week</td>
<td>0.97 (0.94–0.99)</td>
<td></td>
</tr>
<tr>
<td>Aspirin</td>
<td>–</td>
<td>75-1200 mg per day</td>
<td>0.76 (0.63–0.94)</td>
<td></td>
</tr>
<tr>
<td>Total fiber</td>
<td>–</td>
<td>10 g per day</td>
<td>0.93 (0.87–1.00)</td>
<td></td>
</tr>
<tr>
<td>Whole grain</td>
<td>–</td>
<td>90 g per day</td>
<td>0.83 (0.79–0.89)</td>
<td></td>
</tr>
<tr>
<td>Total calcium</td>
<td>–</td>
<td>300 mg per day</td>
<td>0.92 (0.89–0.95)</td>
<td></td>
</tr>
</tbody>
</table>


Table by Yin Cao
Microbiome

**Early-life exposures**
- Mode of nutritional provision
  - Breastfeeding
  - Diet formula
  - Pre-probiotic supplement
- Mode of delivery
  - Caesarean
  - Vaginal
- Environment
  - Psychological and/or physical stress
- Family environment and pets
- Genetics
- Antibiotics
  - 2.7 courses by age 2 years
  - 10.9 courses by age 10 years
- Maternal infection, disease and/or medication
- Maternal nutrition
- Maternal stress

**Exposomal elements**
- Global westernization of diet
- Unhealthy cooking practices
- Red and processed meats
- Synthetic dyes
- MSG
- Titanium dioxide
- High-fructose corn syrup

**Microbiome development**

**EOCRC**
- Immunity and/or inflammation
- Obesity
- Diabetes

Table by Yin Cao
## Molecular Features: MD Anderson + AACR GENIE + Foundation Medicine

<table>
<thead>
<tr>
<th>Patient Information</th>
<th>MDACC Molecular Cohort</th>
<th>MDACC Tumor Registry Cohort</th>
<th>AACR Project GENIE Cohort</th>
<th>CMS Cohort</th>
</tr>
</thead>
<tbody>
<tr>
<td>MD Anderson</td>
<td>N=1877</td>
<td>N=32507</td>
<td>N=1868</td>
<td>Total N=626</td>
</tr>
<tr>
<td></td>
<td>Seen at MDACC from January 1, 2012 to September 1, 2016</td>
<td>Seen at MDACC from January 1, 1980 to present</td>
<td>Excluded patients from MDACC to prevent duplication of data</td>
<td>N=448 from TCGA N=178 from MDACC</td>
</tr>
</tbody>
</table>

| Clinical Data       | Baseline clinical and pathologic characteristics | Baseline clinical and pathologic characteristics | Limited clinical and pathologic characteristics | Limited clinical and pathologic characteristics |

| Molecular Data      | Mutational data available from 46- or 50-gene CLIA next-generation sequencing panel | Unavailable | Mutation data available from AACR Project GENIE database, which includes a mixture of next-generation sequencing platforms | RNA expression data. For TCGA patients, data were publicly available. For MDACC patients, data were obtained with Affymetrix RNA expression arrays. |

| Cancer Stage(s)     | Stage IV | Stages I-IV | Majority stage IV | Stages I-IV |

| Additional Data     | Comorbid predisposing condition information available for patients < 50 years | | Classification by CMS subtype | |

### Foundation Medicine

- 18,218 total patients
- 1,420 patients under the age of 40
- 3,248 between 40 and 49
- 13,550 age 50 and older
No significant difference in *KRAS, NRAS* mutations

Willauer et al Cancer ’19, Lieu CCR ‘19
### Table 1.

Significant alterations and alterations in genes of interest between cohorts using false discovery rate (FDR) in MSS colorectal cancer (CRC) and MSI-H colorectal cancer

<table>
<thead>
<tr>
<th>Gene</th>
<th>Rate observed in under 40 group (%)</th>
<th>Rate observed in 50 and over group (%)</th>
<th>FDR</th>
</tr>
</thead>
<tbody>
<tr>
<td>TP53</td>
<td>82.3</td>
<td>76.7</td>
<td>1.56E−05</td>
</tr>
<tr>
<td>APC</td>
<td>65.8</td>
<td>79.7</td>
<td>4.84E−26</td>
</tr>
<tr>
<td>KRAS</td>
<td>45.6</td>
<td>52.4</td>
<td>1.56E−05</td>
</tr>
<tr>
<td>PIK3CA</td>
<td>14.1</td>
<td>17.5</td>
<td>0.002959601</td>
</tr>
<tr>
<td>CTNNB1</td>
<td>4</td>
<td>2.7</td>
<td>0.013488987</td>
</tr>
<tr>
<td>BRAF</td>
<td>5.2</td>
<td>7.7</td>
<td>0.002067048</td>
</tr>
<tr>
<td>FAM123B</td>
<td>2</td>
<td>6.8</td>
<td>1.35E−12</td>
</tr>
<tr>
<td>NRAS</td>
<td>3.7</td>
<td>4.6</td>
<td>0.171847712</td>
</tr>
</tbody>
</table>
Consensus Molecular Subtypes Differences: Higher CMS1

**TABLE 1.** Baseline Characteristics of the MDACC Molecular Cohort Classified by Age

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>18-29 y</th>
<th>30-39 y</th>
<th>40-49 y</th>
<th>50-59 y</th>
<th>60-69 y</th>
<th>≥70 y</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients, No. (%)</td>
<td>46 (2)</td>
<td>177 (9)</td>
<td>411 (22)</td>
<td>605 (32)</td>
<td>454 (24)</td>
<td>184 (10)</td>
<td></td>
</tr>
<tr>
<td>MSI-H (n = 1525, 81% known), No. (%)</td>
<td>3 (7)</td>
<td>12 (8)</td>
<td>23 (3)</td>
<td>11 (2)</td>
<td>13 (4)</td>
<td>6 (4)</td>
<td>.038</td>
</tr>
</tbody>
</table>

High CMS1 despite low rates of MSI-H
Overall survival and progression-free survival from diagnosis of mCRC is worse for EOCRC patients

20,003 patients from 24 first line studies of mCRC (ARCAD database)

Lieu et al JCO '14
Are we overtreating Young Adults with Colon Cancer?
More intense treatments with unmatched survival gains

### Table 2. Likelihood of Receiving Postoperative Systemic Chemotherapy and Multiagent Regimens for Young Adults (Ages 18-49 Years at Diagnosis) vs Older Adults (Ages 65-75 Years at Diagnosis) With Colon Cancers

<table>
<thead>
<tr>
<th>Patients Who Received Chemotherapy</th>
<th>Any Chemotherapy, No. (%)</th>
<th>Odds Ratio for Receiving Chemotherapy (95% CI)</th>
<th>Multiagent Regimens, No. (%)</th>
<th>Odds Ratio for Receiving Multiagent Regimen (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Stage I</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ages 65-75 y (n = 8991)</td>
<td>162 (1.8)</td>
<td>1 [Reference]</td>
<td>52 (43.0)</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Ages 18-49 y (n = 1926)</td>
<td>109 (5.7)</td>
<td>2.88 (2.21-3.77)</td>
<td>43 (48.3)</td>
<td>1.38 (0.71-2.68)</td>
</tr>
<tr>
<td><strong>Stage II Overall</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ages 65-75 y (n = 11011)</td>
<td>2748 (25.0)</td>
<td>1 [Reference]</td>
<td>773 (41.7)</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Ages 18-49 y (n = 3083)</td>
<td>1732 (56.2)</td>
<td>3.93 (3.58-4.31)</td>
<td>670 (54.9)</td>
<td>1.71 (1.48-1.97)</td>
</tr>
<tr>
<td><strong>Stage II Low Risk</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ages 65-75 y (n = 4822)</td>
<td>923 (19.1)</td>
<td>1 [Reference]</td>
<td>313 (39.6)</td>
<td>1 [Reference]</td>
</tr>
<tr>
<td>Ages 18-49 y (n = 1636)</td>
<td>826 (50.5)</td>
<td>4.22 (3.70-4.81)</td>
<td>388 (52.5)</td>
<td>1.67 (1.34-2.09)</td>
</tr>
</tbody>
</table>
What We Need to Do?

01 Etiology
unknown to the majority of ~80%

02 Risk Factor
No known major risk factor

03 Mechanism
No known differences in driver mechanisms

04 Evolution
Unknown in EOCRC

Multi-omics
Conclusion

- Early onset CRC is associated with unique clinical features and presentation
- Epidemiology suggests that this is not limited to US population, and that the impacts are across a diverse racial/ethnic groups.
- This rising incidence is in contrast to the gains being made in CRC prevention of screening age population
- Multiple etiologies have been proposed, but not yet clearly defined
- Molecular features are modestly different at the transcriptomic and mutational level, but do not provide clear clues yet
- Outcomes with treatment also vary, and yet overtreatment is a risk. Alignment of the treatments with the disease biology is needed
Thank You
Early-Onset Colorectal Cancer: Earlier Detection & Pathways to Prevention

Cassandra Fritz, MD, MPH
Assistant Professor of Medicine
Division of Gastroenterology
Washington University School of Medicine in St. Louis
Early-Onset Colorectal Cancer: Earlier Detection & Pathways to Prevention

Cassandra D.L Fritz, MD, MPHS
Assistant Professor of Medicine
Washington University in St. Louis

Department of Medicine
Division of Gastroenterology

No Financial Disclosures
Outline

• Pathway to detection of early-onset colorectal cancer

• Signs and symptoms & Diagnostic intervals

• Opportunities for improvement

• Primary prevention
5-year Relative Survival of Early-onset Colorectal Cancer (20-49 years of age) by Stage at Diagnosis
SEER 13, 1992-2013

- Morbidity and mortality are significant
- High mortality with later-stage disease
- Early-onset CRC is in the top 5 ranking cancers associated with high disability-adjusted life years (DALYs)

Cheng E. et al., JAMA Network Open. 2021
Zhao J. et al., BMJ Oncology 2023

Zaki T et al. CGH. 2023
From Symptoms to Detection

1. Patient notices symptoms
   - Patient needs to associate symptoms with CRC
   - Not be afraid to access care
   - Make an appointment (1-2 month delay)

2. Patient reports symptoms to healthcare provider
   - Provider has to associate concerning symptoms with CRC
   - Navigate other competing issues
   - Family history
   - 3-12 mo

3. Provider has to activate a diagnostic pathway
   - Close the loop on symptoms
   - Order a colonoscopy
   - 3-6 mo

4. Diagnosis of early-onset CRC
   - Receive a diagnosis of early-onset colorectal cancer
   - 1-2 mo
Objective: To identify signs & symptoms with early-onset CRC and report associated diagnostic intervals 3 months to 2 years before diagnosis.

Methods
• MarketScan commercial database including adults aged 18 to 49 years.
• Required at least 2 years of continuous enrollment prior to the index date (pathology diagnosis of CRC).
• Nested case-control study of 5075 incident early-onset CRC and 22378 matched controls.
• Multivariable logistic regressions
• Examined the median diagnostic intervals based on associated signs and symptoms.
Early signs/symptoms for Early-Onset CRC
Claims data, nested case-control, 2005-2016

4 Red-Flag Signs and Symptoms, 3mo to 2 years prior to index date

<table>
<thead>
<tr>
<th>Sign/Symptom</th>
<th>No. of red-flag signs/symptoms</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal pain</td>
<td>0</td>
<td>1 (reference)</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>1</td>
<td>1.94 (1.76 to 2.14)</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2</td>
<td>3.59 (2.89 to 4.44)</td>
</tr>
<tr>
<td>Iron deficiency anemia</td>
<td>≥3</td>
<td>6.52 (3.78 to 11.23)</td>
</tr>
<tr>
<td>Per each additional sign/symptom</td>
<td></td>
<td>1.91 (1.78 to 2.05)</td>
</tr>
</tbody>
</table>

P_trend < 0.001

Fritz CDL & Otegbeye et al, JNCI 2023
Number of Red-flag Signs/Symptoms and Risk of Early-Onset Colorectal Cancer
3-month time intervals prior to the index date
Claims data, cases only, 2005-2016

Fritz CDL & Otegbeye et al, JNCI 2023
### Duration of Signs and Symptoms in Young Adults

Claims data, cases-only, 2005-2016

<table>
<thead>
<tr>
<th>Signs/Symptoms</th>
<th>Time to Diagnosis, mo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any signs/symptoms*</td>
<td></td>
</tr>
<tr>
<td>1 sign/symptom* (n=792)</td>
<td>8.7 (4.8 to 15.9)</td>
</tr>
<tr>
<td>Abdominal pain (54%)</td>
<td>11.7</td>
</tr>
<tr>
<td>Rectal bleeding (31%)</td>
<td>10.4</td>
</tr>
<tr>
<td>Diarrhea (6.8%)</td>
<td>10.3</td>
</tr>
<tr>
<td>Iron deficiency anemia (7.8%)</td>
<td></td>
</tr>
<tr>
<td>2 signs/symptoms* (n=159)</td>
<td>5.8 (4.0 to 9.9)</td>
</tr>
<tr>
<td>Abdominal pain/Rectal bleeding (36%)</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain/Diarrhea (31%)</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain/Iron deficiency anemia (14%)</td>
<td>7.8</td>
</tr>
<tr>
<td>Rectal bleeding/Iron deficiency anemia (11%)</td>
<td></td>
</tr>
<tr>
<td>Other (9%)</td>
<td></td>
</tr>
<tr>
<td>≥3 signs/symptoms* (n=32)</td>
<td>4.8 (3.8 to 7.2)</td>
</tr>
<tr>
<td>Abdominal pain/Rectal bleeding/Diarrhea (56%)</td>
<td></td>
</tr>
<tr>
<td>Abdominal pain/Rectal bleeding/Iron deficiency anemia (28%)</td>
<td></td>
</tr>
<tr>
<td>Other (16%)</td>
<td></td>
</tr>
</tbody>
</table>

- *Early onset CRC cases reported their first symptom > 3 months prior to diagnosis: 19%*
- *Early onset CRC cases reported their first symptom < 3 months: 50%*
Current Prevention Approach

Lowered CRC screening age to 45 years

~50% of early-onset CRC cases are diagnosed <45 years

Screening in younger individuals has had slow uptake

Wolf AMD et al, CA Cancer J Clin 2018
Davidson KW. JAMA 2021

Ladabaum U, et al. CGH 2022
Estimating the Screening-Eligible Population Size, Ages 45–74, at Average Risk to Develop CRC in the United States

~20 million people aged 45-49 years + 27 million 50-74 years

60% increase in the “average-risk” screening pool size

Do we have the resources?

Potentially, if we leverage stool-based testing

Screening for CRC in the U.S.: Time trend by type of test

Preferred CRC Screening Tests Among 1,000 Unscreened Americans

<table>
<thead>
<tr>
<th>Test Type</th>
<th>40-49 yo</th>
<th>≥50 yo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multitarget stool DNA test every 3 years</td>
<td>34.6%</td>
<td>37.3%</td>
</tr>
<tr>
<td>Colon video capsule every 5 years</td>
<td>28.2%</td>
<td>22.9%</td>
</tr>
<tr>
<td>Colonoscopy every 10 years</td>
<td>13.7%</td>
<td>13.6%</td>
</tr>
<tr>
<td>FIT every year</td>
<td>12.2%</td>
<td>18.7%</td>
</tr>
<tr>
<td>Colon CT scan every 5 years</td>
<td>11.3%</td>
<td>7.6%</td>
</tr>
</tbody>
</table>

US MSTF Five Recommended Tests

US MSTF Tier 1 Tests

Clinical Gastroenterology and Hepatology

Shapiro JA, et al. Cancer Epidemiol Biomarkers 2021
Makaroff KE et al. CGH 2022
Screening: No difference between colonoscopy vs. FIT for additional early-onset CRC cases averted

<table>
<thead>
<tr>
<th>Screening modality and frequency</th>
<th>Mean CRC cases averted if start screening</th>
<th>Additional CRC cases averted if start screening at age 45 y</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stool tests</td>
<td>At age 50 y</td>
<td>At age 45 y</td>
</tr>
<tr>
<td>FIT every year</td>
<td>47</td>
<td>50</td>
</tr>
<tr>
<td>HsFOBT every year</td>
<td>39</td>
<td>42</td>
</tr>
<tr>
<td>sDNA-FIT every year</td>
<td>54</td>
<td>57</td>
</tr>
<tr>
<td>sDNA-FIT every 3 y</td>
<td>44</td>
<td>47</td>
</tr>
<tr>
<td>Direct visualization tests</td>
<td>At age 50 y</td>
<td>At age 45 y</td>
</tr>
<tr>
<td>COL every 10 y</td>
<td>58</td>
<td>61</td>
</tr>
<tr>
<td>CT colonography every 5 y</td>
<td>53</td>
<td>55</td>
</tr>
<tr>
<td>Flexible SIG every 5 y</td>
<td>49</td>
<td>51</td>
</tr>
<tr>
<td>Flexible SIG every 10 y plus FIT every year</td>
<td>54</td>
<td>57</td>
</tr>
</tbody>
</table>

Knudsen AB. JAMA. 2021
Opportunity to leverage FIT for diagnostic pathways?

- Likely yes but we don’t have the data for early-onset CRC population

Guideline from British Society of Gastroenterology: Using FIT in patients with signs and symptoms of suspected CRC

Table 1: Number needed to scope (NNS) to detect one cancer and number of missed cancers (NMC) per 1000 faecal immunochemical tests (FTTs) at various thresholds of FIT

- Referral on urgent pathway for colorectal cancer investigation
- Referral on either a routine or urgent pathway
- Reassurance / Non-referral / Management in primary care

Monahan KJ et al., Gut 2022
Primary Prevention

Mitigation of risk factors

Chemopreventative agents
Methods: Study population

Nurses’ Health Study II (NHSII): N=116,429 | age 25-42 in 1989

NSAID/aspirin every two years.

Lower endoscopy every two years

A sub-cohort of 32,058 women in NHS II with a lower endoscopy before age 50 between 1991-2015

• Excluded patients with CRC, inflammatory bowel disease, or missing medication info.
# Regular use (2+ times/week) of aspirin or NSAIDs and risk of early-onset adenoma, NHSII, 1991-2015

<table>
<thead>
<tr>
<th></th>
<th>No Regular Use (n=27795)</th>
<th>Regular Use (n=18732)</th>
<th>Multivariable OR (95% CI)</th>
<th>P het.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Adenoma</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>777</td>
<td>470</td>
<td>0.84 (0.75-0.95)</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Malignant potential</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>High-risk</td>
<td>185</td>
<td>105</td>
<td>0.77 (0.60-0.98)</td>
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<tr>
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<td>245</td>
<td>0.83 (0.70-0.98)</td>
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<td><strong>Histology</strong></td>
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<tr>
<td>Villous</td>
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<td>76</td>
<td>0.67 (0.51-0.89)</td>
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<tr>
<td>Tubular</td>
<td>620</td>
<td>394</td>
<td>0.89 (0.78-1.01)</td>
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<tr>
<td><strong>Size</strong></td>
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<tr>
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<td>0.80 (0.68-0.93)</td>
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DO NOT POST

Fritz et al., unpublished
Regular use (2+times/week) of aspirin or NSAIDs and risk of early-onset adenoma, NHSII, 1991-2015

First endoscopy

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<th>Regular use N=11890</th>
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<td>0.77 (0.59-1.00)</td>
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<tr>
<td>Low-risk</td>
<td>314</td>
<td>187</td>
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<tr>
<td>Villous</td>
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<td>Tubular</td>
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<td>0.89 (0.77-1.04)</td>
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<tr>
<td>Large</td>
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<td>71</td>
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<tr>
<td>Small</td>
<td>360</td>
<td>205</td>
<td>0.77 (0.64-0.92)</td>
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</tbody>
</table>

Fritz et al., unpublished
Chemoprevention for early-onset CRC

Regular aspirin/NSAID use (2+ times/week) was associated with a lower risk of early-onset adenomas, especially those with advanced histology.

Evaluate aspirin/NSAIDs as promising agents for chemoprevention of early-onset CRC:
- Gender, racial/ethnic diversity
- Dose and duration for young adults
- Precision-based strategies
Moving the needle on early-onset CRC

• Increased inclusion of minority populations into research and dissemination and implementation strategies

• Consider risk prediction models that incorporate family history, social vulnerability, risk factors, and genetics

• Change the conversation
  • Increase awareness of early-onset CRC & associated signs and symptoms
  • Targeting resources
  • System-level and population-level interventions
Conclusions

- Increase awareness in general public and among frontline providers about signs & symptoms
- Encourage patients to access care
- Close the loop on symptoms if no resolution -> dx pathway
- Decrease delay in diagnostic interval
- Potential to utilize FIT as a risk stratifying step within the diagnostic pathway
- Urgent endoscopy referral
Conclusions

- Increase awareness in the general public and among front-line providers about symptoms
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- Potential to utilize FIT as a risk stratifying step within the diagnostic pathway
- Urgent endoscopy referral
Acknowledgements

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Twitter: @yincaoScD

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Participants, Staff, and CRC investigators of NHSII

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T32 DK007130
T32 CA009621
P30 DK052574- WashU DDRCC

Contact
cfritz@wustl.edu  @cfritzMD
Thank You

nccrt.org  @NCCRTnews  #80inEveryCommunity
Table Talk Questions

1. What can our organizations do to take what we’ve learned about lead time messaging and EAO CRC signs and symptoms to make an impact in our communities?

2. What are some success stories from organizations that have specifically targeted EAO CRC awareness and processes that lead to timely diagnosis?