FIGHT
COLORECTAL CANCER
Agenda

12:00-12:10p ET  Welcome and Introductions: Andrea Andi (Dwyer) and Elsa Weltzien

12:10- 12:45p ET  Dr. Samir Gupta: On-Time Screening based on Family History and Average Risk – Current Status and Potential Consequences

12:45-12:55p ET  Discussion with Dr. Whitney Jones: Implications for Clinical Practice – Messaging and Communication Strategies

12:55-1:05p ET  Addressing Specific Questions Posed before Webinar

1:05-1:50p ET  Discussion

1:50-2:00p ET  Close out and next steps: Andi Dwyer
Objectives

• Review available data on prevalence of on time screening for family history

• Explore potential consequences of suboptimal rates of on time screening

• Discuss potential messaging strategies for patients and providers to promote on-time screening for those with a family history and those at average risk
Presenter
Samir Gupta, MD
Gastroenterologist, Professor of Medicine, UC San Diego Health

Lead Discussant
Whitney Jones, MD
Gastroenterologist, Colon Cancer Prevention Project
On-Time Screening Based on Family History and Average Risk: Current Status and Potential Consequences

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Outline

• Prevalence and consequences of on-time screening
  • Average risk
  • Family history
• Future directions
• Summary of current opportunities
On Time: Importance

- Aspirational goal:
  - Offer every opportunity for timely detection and prevention of CRC
    - Asymptomatic individuals
      - Family history
      - Risk factors
    - Symptomatic individuals
  - Outcomes:
    - Optimize early detection and prevention
    - Improve incidence and mortality
- Its about avoiding missed opportunities!
<table>
<thead>
<tr>
<th>Age Category</th>
<th>Overall</th>
<th>50 to 54</th>
<th>55 to 64</th>
<th>65 to 75</th>
</tr>
</thead>
<tbody>
<tr>
<td>50 to 75</td>
<td>67%</td>
<td>48%</td>
<td>68%</td>
<td>71%</td>
</tr>
</tbody>
</table>

**Up-to-Date with CRC Screening, National Health Interview Survey 2018**

Slow uptake has taken on increased importance

- Incidence consistently rising birth to 49
- Decreasing trend has flipped to an increasing trend for age 50 to 64
- Age-specific incidence (# of cases) sharply increases after age 50
- Point: consequences of delayed uptake have become more acute

Uptake is particularly important for individuals with a family history

<table>
<thead>
<tr>
<th>&gt; 1 first degree relative with CRC at age:</th>
<th>Relative Risk (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50 y</td>
<td>3.31 (2.79–3.89)</td>
</tr>
<tr>
<td>&gt;50 y</td>
<td>2.02 (1.93–2.11)</td>
</tr>
<tr>
<td>&gt;60 y</td>
<td>1.99 (1.90–2.09)</td>
</tr>
</tbody>
</table>

![Graph showing the relative risk of CRC by number of first degree relatives with CRC](image)
Family history “left shifts” age-specific CRC risk

Family history-based recommendations

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRC or advanced adenoma in 2 first degree relatives at any age OR CRC or adenoma in a single first degree relative &lt; age 60 years</td>
<td>Colonoscopy every 5 years beginning 10 years prior to age of first degree relative diagnosis or age 40</td>
</tr>
<tr>
<td>CRC or adenoma in single first degree relative diagnosed age &gt;=60 OR CRC in 2 second degree relatives at any age</td>
<td>Begin screening at age 40 with any test</td>
</tr>
<tr>
<td>CRC or advanced adenoma in 2 first degree relatives at any age OR CRC or advanced adenoma in a single first degree relative &lt; age 60 years</td>
<td>Colonoscopy every 5 years beginning 10 years prior to age of first degree relative diagnosis or age 40</td>
</tr>
<tr>
<td>CRC or advanced adenoma in single first degree relative diagnosed age &gt;=60</td>
<td>Begin screening at age 40 with any test</td>
</tr>
<tr>
<td>CRC &gt;=1 first degree relative with CRC at any age</td>
<td>Colonoscopy at age 40 or 10 years before earliest diagnosis of CRC, repeat every 5 years</td>
</tr>
<tr>
<td>CRC in 2 or more first degree relatives</td>
<td>Colonoscopy every 5 years at age 40 or 10 years younger than age of diagnosis of earliest diagnosed first degree relative, whichever is earlier</td>
</tr>
<tr>
<td>CRC in 1 first degree relative</td>
<td>Colonoscopy every 5-10 years at age 40-50 years or 10 years younger than age of diagnosis of first degree relative, whichever is earlier. FIT every 1-2 years is suggested as 2nd line option</td>
</tr>
<tr>
<td>1 or more first degree relative with documented advanced adenoma</td>
<td>No recommendation for a preferred test. Colonoscopy or FIT are both options. Colonoscopy every 5-10 years at age 40-50 years or 10 years younger than age of diagnosis of first degree relative, whichever is earlier. FIT every 1-2 years is suggested as 2nd line option</td>
</tr>
</tbody>
</table>
Effectiveness of family-history based guidelines depends on uptake and performance

• What proportion of individuals with a family history are up-to-date?
• What is the sensitivity and specificity of family history-based guidelines for identifying individuals with CRC, and particularly early onset CRC?
Despite recommendations, proportion up-to-date probably low

- Aim: estimate colonoscopy exposure using US National Health Interview Survey data from 2005 and 2010
- Age 40 and older
- Survey included questions about whether a mother/father/sibling, or child had cancer, and type of cancer
Results

Key Finding
38.3% individuals age 40-49 reporting first degree relative with CRC were up to date with colonoscopy in 2010

Limitations and Strengths:
- No data below age 40
- Data from 2010
- Population-based estimate
**TABLE 3.** Sensitivity and Specificity of Family History-Based Criteria Issued by the ACS, NCCN, USMSTF, and CAN for Identifying Patients Aged 40 to 49 Years With Early-Onset CRC

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACS 2008&lt;sup&gt;a&lt;/sup&gt;</td>
<td>25%</td>
<td>90%</td>
</tr>
<tr>
<td>NCCN 2017</td>
<td>21%</td>
<td>92%</td>
</tr>
<tr>
<td>USMSTF 2017</td>
<td>21%</td>
<td>92%</td>
</tr>
<tr>
<td>CAN 2018</td>
<td>21%</td>
<td>92%</td>
</tr>
</tbody>
</table>

Abbreviations: ACS, American Cancer Society; CAN; Joint Canada/American Gastroenterological Association; CRC, colorectal cancer; NCCN, National Comprehensive Cancer Network; USMSTF, US Multi-Society Task Force on Colorectal Cancer.

<sup>a</sup>Joint recommendations by the ACS, USMSTF, and American College of Radiology in 2008.
Figure 1. Potential impact of family history-based guidelines on time of colorectal cancer (CRC) diagnosis. Of 2473 cases of CRC, approximately 25% met the criteria for early screening. Among 614 CRC cases meeting the criteria for early screening, approximately 98% could have been recommended to initiate screening at an age younger than the actual age at the time of diagnosis of CRC.
Limitations

• Focus on age 40-49
  • 72% of early onset in the age range

• Spectrum bias
  • Enrolled cases may have been more likely to have family history than those in general population
  • Bias towards estimating higher than true sensitivity, overestimating percent meeting criteria for early screening

• Mode of detection unknown

• No info on whether participants had been recommended early initiation based on guidelines
Bottom Line

• Of CRC cases age 40 to 49:
  • 1 in 4 met family history based early screening criteria
    • 3 in 4 did not
  • 98% meeting early criteria could have had CRC diagnosed earlier (or possibly prevented) if earlier screening had been implemented

• Implications:
  • Increase implementation of family history-based recommendations
  • Develop additional strategies for identifying individuals at risk for early onset, beyond family history
On-Time Screening Summary

- Average risk, age >50
  - Major opportunity to reduce incidence and mortality by increasing pace of screening uptake age 50 to 54
  - Also highly relevant with shift to 45
- Family history
  - Substantial proportion of early onset cases may meet criteria for early initiation
  - Early initiation may have significant potential for early detection and proportion
  - Major opportunity to increase awareness and uptake
Missing pieces

- Strategies for on time, early detection and prevention for:
  - Asymptomatic individuals without a family history
  - People with symptoms under age 45
Future directions – on time, asymptomatic

- Genetic risk scores
- Diet, lifestyle, environmental, and constitutional factors
- Among those without a family history:
  - Combo of genetic, lifestyle, and other factors could result in recommendations for a wide range of risk-based screening initiation ages, from 41 to 74
- Genetic risk score alone identified individuals with up to 4.3 fold increased risk compared to those with low risk score
Current opportunities: on-time evaluation of symptoms

- Small single center case control study, younger vs older rectal cancer patients had longer median time from
  - Symptom onset to healthcare provider evaluation: 121 vs 21 days
  - Symptom onset to first course of treatment: 217 vs 58 days
- Single center retrospective study, younger vs older CRC patients had longer time from
  - Symptom onset to diagnosis: median 128 vs 79 days, with average 243 vs 154 days
  - First medical visit to diagnosis: median 31 vs 22 days, with average of 91 vs 67 days

Solutions for timely evaluation of symptoms

ID Signs & Symptoms
- Includes:
  - Rectal bleeding
  - Abdominal Pain
  - Weight Loss
  - Melena
  - Iron Deficiency Anemia
  - Constipation
  - Diarrhea

Triage to colonoscopy vs tx and f/u
- Strategies:
  - Clinical Guidelines
  - Symptom/Sign Severity
  - Clinical context

Close Clinical Loop
- Strategies:
  - Mandatory 30 day clinic f/u
  - Placeholder colonoscopy referral

Figure courtesy of Josh Demb, PhD
Credit to Jeff Lee, MD for “clinical loop”
Thank You!

- Acknowledgements
  - Grant Support:
    - NCI 1UG3CA233314-01A1
    - NCI Cancer Center Support Grant CA023100-32
  - Colon Cancer Family Registry
- Contact:
  - s1gupta@health.ucsd.edu
  - @samirguptaGI
Studies on delays in diagnosis

- Single center case control study 1997-2007 of young onset CRC cases <50 vs older onset cases. All rectal cancers. University of VT
- Excluded: 2nd opinion, personal hx of IBD, known hereditary syndrome, transplant
- Matched early onset cases to late onset cases 1:1 based on sex and dx date
- Chart review to identify: 1) time of first symptom; 2) time presentation to healthcare provider; 3) referral time; 4) diagnostic eval; 5) time of tx
## Results

### Table 1: Patient demographics

<table>
<thead>
<tr>
<th>Patient attribute</th>
<th>Under 50 y (n = 56)</th>
<th>Over 50 y (n = 56)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>45</td>
<td>64</td>
</tr>
<tr>
<td>Interquartile range</td>
<td>39–47</td>
<td>58–73</td>
</tr>
<tr>
<td>Male sex, n (%)</td>
<td>37 (66.1)</td>
<td>36 (64.3)</td>
</tr>
<tr>
<td>State, n (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vermont</td>
<td>45 (80.4)</td>
<td>40 (71.4)</td>
</tr>
<tr>
<td>New York</td>
<td>11 (19.6)</td>
<td>16 (28.6)</td>
</tr>
<tr>
<td>FmHx of CRC, n (%)</td>
<td>11 (19.6)</td>
<td>11 (19.6)</td>
</tr>
</tbody>
</table>

CRC = colon and rectal cancer; FmHx, family history.

### Table 2: Initial symptom documented at the time of 1st physician visit

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Under 50 y, total (%)</th>
<th>Over 50 y, total (%)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rectal bleeding</td>
<td>34 (61)</td>
<td>38 (68)</td>
<td>.52</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>4 (7)</td>
<td>2 (4)</td>
<td>.68</td>
</tr>
<tr>
<td>Rectal pain</td>
<td>2 (4)</td>
<td>0 (0)</td>
<td>.49</td>
</tr>
<tr>
<td>Change in bowel habits</td>
<td>8 (14)</td>
<td>6 (11)</td>
<td>.78</td>
</tr>
<tr>
<td>Not documented</td>
<td>8 (14)</td>
<td>10 (18)</td>
<td>.79</td>
</tr>
</tbody>
</table>
**results**

- Interval from symptom onset to initial presentation to healthcare 121 days early onset vs 21 days late onset
- Time from presentation to referral 10 days vs 7 days
- Time from symptom onset to treatment 217 vs 58 days
- No major differences in types of symptoms or stage at presentation
- Limitations:
  - Very small case control
  - Single center
  - Unclear if patients received primary care at U Vt or other place
  - Focus only on rectal cancer
- Bottom line: A small single center case control study of individuals with rectal cancer found delay between first symptom onset and treatment for younger vs older rectal cancer patients, with intervals of 121 vs 21 days between symptom onset to healthcare provider evaluation and 217 vs 58 days from symptom onset to first course of treatment.
Chen, Ladabaum et al CGH 2017

- Single center retrospective study compared clinical features and presentation for early vs late onset CRC, 2008-2014
- Inclusion: all under 50 plus random sample of those over 50
- Evaluated time to diagnosis from symptom onset through workup.
- Compared to older patients, younger patients:
  - Had more office visits prior to diagnosis
  - Longer time from symptom onset to diagnosis: median 79 days for older vs 128 days for younger, average 154 vs 243 days
  - Longer time from first symptom to first medical visit: median 30 days for older vs 60 days for younger, with average 87 vs 152 days
  - Longer time from first medical visit to diagnosis: median 22 days for older vs 31 days for younger, with average 67 vs 91 days
• Limitations:
  • Single institution
  • Sampling strategy not completely clear
  • Patients may not have received primary care at Stanford – unclear if duration well captured

• Bottom line: In a single institution study comparing 253 early vs 232 late onset CRC patients, early onset cases had longer time from symptom onset to diagnosis (median 128 vs 79 days for younger vs older, with average 154 vs 152 day), and longer time from first medical visit to diagnosis (median 31 vs 22 days ofr younger vs older, with average of 91 vs 67 days)
The faces of colorectal cancer are changing.....
..........we must adapt our approach!
A complementary, not competitive, messaging strategy

Lead time messaging
On-time screening

Whitney F Jones, MD
coloncancerpreventionproject.org
Upstream Health Strategies, LLC

Fight CRC EAO work group
November 3, 2020
% Eligible Actually Screened

Goal
> 80% High Risk
ID + screen (Cscope)
> 90% Normal Risk screened at age 45

Current
< 1 in 4 high risk screened on time
~ 10% screened at 45
~ 50% screened at 50

80% Persistent Compliance
Critical questions for potential study

• Is on-time screening time important?
  • Too hard to measure?
  • Not critical?
  • We can’t do family history well?
• Opportunities for CRC prevention if 80% achieved on time
  • disparities, high risk, normal risk
• How to screen those not engaged with health system?
• Best way to inform around sporadic EAO CRC?
• Do we believe in genetics>? Why do we use so little?
The odds are NOT in your favor (until you are 55)

How many must we reach?

Figure 2. Time trends of colorectal cancer screening rates among adults aged 50 to 75 years by age. Adapted from National Center for Health Statistics. 2015 National Health Interview Survey (NHIS) Public Use Data File. Division of Health Interview Statistics, National Center for Health Statistics, National Institutes of Health; 2016.
What we **don’t** have to do

- Develop new guidelines
- Redefine elevated risk groups
- Deal with 50 vs 45 vs states
- Study if guidelines work
- Invent Cancer Family History
- Figure out if marketing works
- Develop new testing options
Under age 50 CRC: Timeline considerations

• Optimistic we find out **why** within 10 yrs.
  • so we can, if able, counteract the cause

• Millions of people are at risk now and WILL be impacted for the next 40 yrs. even if we figure this out in the next 10 yrs.

• When we find out why, how skilled are we at communicating people in their 20s, 30s, 40s?
  • Avoid something, take something, take action earlier

• **45** coming soon for all - are we ready to take full advantage?

• Covid-19 lessons – if we know, why are we STILL not acting, albeit imperfectly. How will we be judged?
Working the problem backwards

~ 100 million are at risk

- When do we want to behavior to occur?
- How many messages does it take to get a screening done?
- Realistically, how frequently can the message be delivered?
- High risk ID + compliance = more frequency to average risk
- Allows more shared decision making for average risk
- Where do people NOT get their messages? Provider, health network, insurer, media (traditional or digital). Low health literacy, men?

- HUGE potential to **better addresses health equity + disparities**

- How will we communicate as we solve EAO CRC etiology puzzle?
Marketing essentials

Triad

Message

Advocacy leaders
ACS, NCCRT,

Timing

Frequency

Targets

Patients

Advocacy leaders
ACS, NCCRT,

Insurers
Health Systems

Providers:
Primary, GYN, GI, ONC,

One “perfect” message @ time VS Multiple good/great messages with lead time
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.
Timeline of EAO-CRC and average risk CRC Messaging
Complementary not competitive

Early Message Package
- ID + evaluate symptoms
- Family history + test
- Lifestyle modification

On Time Message Package
- On time date
- On time options

Current Message Package

21yr
35-40yr
45/50-75
Needs implementation....STAT!

- High risk messaging to age 35-40
- Average risk message to 40-45
- Implementation of family history collection as a benchmark
- Education to all around the signs and sx of CRC sporadic. Reduce delays
- Making appointment in advance for your screenings
- Data mining → Pt scheduling
- Covid-19 plan to increase screenings
Still Lots left to do.

- Logistics
- Informatics
- Marketing
  - On-time screening: Gen X Y Z
  - Providers, consumers
  - Granular behavior 35-45/H/L risk
  - Health disparities

- Continuous process improvements
  - Modeling: flatten the curve
  - Benchmarking 40/45
  - Health disparities

- Etiology EAO
Big Hairy Audacious PLAN (BHAP)

Today, NOW, we have data, guidelines, screening tools, great messages 80% on time for every risk group 80% in every community

- **Reset target demographic** messages as a national plan
  - Morph ACS, NCCRT partners to message with lead time in mind
  - Start messaging at least 5 yrs before Family Hx screen needed (40)
  - Achieve message frequency required (deliverable)
  - Hard stops @ age 35, 40 and 45. USPSTF now on board (milestone)
  - *Potential to impact 75% EAO CRC NOW, with what we already have*

- **Fund clinical research for on-time screen impact**

- **Elevate Cancer FHx in EHR space (CRC, AA, + other relevant)**
  - Advocate to venders to do so. Position statement with FU report cards –
  - Collaborate with primary care, payers, GI/GYN/Onc + EHR vendors
  - Benchmark ala colonoscopy quality improvement process
End of presentation

• Remaining slides for information only.
Opposing trends within ages 50-59 years

**Colon**

- 55-59 years
- 50-54 years

**Rectum**

- 55-59 years
- 50-54 years
• FDR CRC low rates of on/near time screening
• 2010 – screening rates 40-49 38% vs >50 69.7%
• Only 39% asked by PCP about Fhx CRC (much less AA)
• 46% with CRC in FDR thought screening = 50 yo

Conclusions
  – Pt lack awareness (providers lack awareness too?)
  – Pt lack MD recommendations
Clues in our own writings........ HRSA DOC.

We are messaging too late!


- “..the group seeks to achieve 80 percent screening in patients over age 50 nationwide.
  (STILL FOCUSED ON 50, NOT A WORD ABOUT THE 20-25% NEEDING SCREEN @ AGE 40 OR SOONER)

- But the goal so far has only been reached among Americans age 65 and older.
  (IS THE MESSAGE DIFFERENT FOR > 65’s, 70’s? , DO WE NOT HAVE GREAT MESSAGE YET?. DID THEY JUST HEAR IT MORE TIMES TO REACH THAT COMPLIANCE LEVEL?) And those gains have effectively been muted by poor adherence among those in their fifties. (WE ARE REALLY MOST POOR AT LANDING THE PLANE ON TIME WITH THE HIGHEST RISK [SCREEN AT AGE 40] EVEN MORE SO THAN AGE 50/45 AND WE BLAME IT ON THE BEHAVIOR OF THE TARGETS, NOT OURSELVES.....WOW.)

- Deaths from colorectal cancer among people younger than age 55 increased one percent per year from 2007 and 2016. (NOW 1 IN 5 CASES AND GROWING. WILL WE REVIEW OR ACT ON DATA? WE KNOW ENOUGH, HAVE GREAT GUIDELINES, ENOUGH TOOLS ...READY NOW.) Screening prevalence in that cohort, in particular "is quite low," said Stacey Fedewa of the American Cancer Society – even though more than eight out of 10 of those patients are estimated to have some sort of health insurance. (80% UNSCREENED HAVE INSURANCE @ NO COST TO SCREEN. HALF OR MORE NEVER HEAR THE MESSAGE AT 50. MEN >> WOMEN.)

- Mew Rattanawatkul of HRSA's Bureau of Primary Health Care noted that HRSA health centers certified as patient-centered medical homes are bucking the trend, but the national average for colorectal cancer screening among the population as a whole was still only about 42 percent.” MAYBE HARD TO REACH POPULATIONS WITH HEALTH EQUITY ISSUES NEED EVEN MORE AND EARLIER + MORE FREQUENT MESSAGING TO HELP OVERCOME THEIR BARRIERS?
“What gets measured gets managed”
- Drucker

“No not everything that can be counted counts, and not everything that counts can be counted.”
- Einstein
Where and what: Let’s be crystal clear!
Study must not preempt action.

**Needs Study**
- Logistics based screening delivery
- Marketing on-time screening: Gen X Y Z
- More granular information on behavior around age 40 for high risk and age 45 for average risk.
- Benchmarking 40/45
- Delivering on data mining> Informatics
- Modeling: flatten the curve
- How and via which route do we communicate about CRC to 35-45 yo?
- Study ongoing implementation efforts for continuous improvement. “Mark Twain”
- Etiology of EAO
- Lead time messaging effects on health disparities

**Needs implementation**
- High risk messaging to age 35-40
- Average risk message to 40-45
- Implementation of family history collection as a benchmark
- Education to all around the signs and sx of CRC sporadic. Reduce delays
- Making appointment in advance for your screenings
- Data mining → Pt scheduling
- Covid 19 plan to maintain screenings
What we **DO** have to do.

- Pivot to an on-time vs sometime screen paradigm
- Expand thinking into the logistics of how to achieve on-time
- Lead time messaging enough? Doubtful
- Develop/”mine” data: insurers, health systems, Medicaid
- Embrace new screening options
- Go all in on 45!!!
- Re prioritize high risk at 40
- Quit blaming our targets
- Benchmark Cancer Family History

Professional, Ethical, Moral, obligation
The faces of colorectal cancer are changing.....

..........we must adapt our approach!
A complementary, not competitive, messaging strategy

Lead time messaging
On-time screening

Whitney F Jones, MD
coloncancerpreventionproject.org
Upstream Health Strategies, LLC

EO-FHx NCCRT taskforce
October 27, 2020
Discussion
Next EAO Workgroup webinar:

**Updated Date!** January 12, 2020 (Tuesday, 12pm ET).

3rd Annual EAO CRC International Symposium – 2021

- **Goal:** Engage the global community about current efforts and needs from the perspectives of researchers/medical community and patients/advocates to elevate EAO CRC as an issue and patient care and needs as the top priority.
- **Date:** To be announced
- **Location:** Virtual
LETS KEEP UP THE EFFORTS.