Prioritizing Actionable Steps to Decrease the Incidence of Early Age Colorectal Cancer

Early age onset colorectal cancer (EAO CRC) is an undeniable health priority that must be addressed on an international scale; data has indicated that those who were born in the 1990s have twice the risk of colon cancer and 4 times the risk of rectal cancer than adults born in the 1950s.[1] In 2018, the American Cancer Society (ACS) lowered their screening guidelines to age 45 from 50 based on modeling studies conducted, as the rates of CRC among 45-year-olds are comparable with those among 50-year-olds in 1993.[2]

Current strategies for medical management and screening for those under age 50 exist for those who are at increased or high risk. Within this population, screening rates are <40% for those that are 40–49 years old, and even lower for those who are <40.[3] Based on a study published in July 2019, on average 294 days passed between initial symptoms and diagnosis for young patients with CRC, suggesting the need for greater awareness in the patient and provider community.[4]

As a national advocacy organization, Fight Colorectal Cancer (Fight CRC) is actively tracking trends in CRC diagnoses and prevention. Fight CRC has identified EAO as a priority area to take action to help advance initiatives addressing this trend. In February of 2019, Fight CRC hosted a working meeting to explore research strategies to address the etiology of EAO, which was published in *Gastroenterology* in August of 2019 (https://www.gastrojournal.org/article/S0016-5085(19)40882-2/fulltext).[5] Part of the call to action from this meeting was a request for Fight CRC to convene an EAO working group of professionals to meet frequently to progress the agenda (independent calls/gathering and at large professional meetings). Since the initial February meeting, Fight CRC has engaged the policy and funding community regarding research initiatives and the outcomes of the meeting have spurred interest in furthering research support. However, how and where to place priority to reduce EAO incidence is a big question.

The questions is, "If every priority is equal, what should the research, medical, and advocacy communities prioritize to address EAO CRC with what we know and what we do not know, and what are the opportunities to move this work ahead?"

To address these different factors, members of Fight CRC's Health Promotion team, with support from staff at the University of Colorado Cancer Center facilitated 4 nominal group technique (NGT) sessions in the summer of 2019 with members of the Early Age Onset Working Group. The NGT was selected over a traditional focus group method as a way to elicit equal involvement from participants. The NGT, as explained by the Centers for Disease Control and Prevention, is an efficient method used to prioritize topics and to have weighted feedback from the group.[6] The sessions were conducted online via Zoom technology to give opportunity for international participation.

The Question

Participants were asked the following question: What do you think are the most important approaches to addressing the increase in the incidence of EAO CRC in the United States and internationally?

The Process

Four NGT sessions were held between June and August of 2019. The NGT process began with an introduction and question presentation. Next, a silent idea generation ensued wherein participants wrote down as many statements as possible in response to the question. After this, a round robin occurred where each participant in turn, shared one statement from their list. Each statement was written down on a shared screen. Duplicate ideas were not repeated. This process continued until all participants exhausted their list. Each statement was read aloud by the facilitator to determine if there were any questions or comments, or if 2 statements were close enough in meaning to be combined. Next, participants selected their top 5 statements in no particular order. Finally, participants ranked their priority ideas, from most important to least important, assigning a number from 1 to 5, following a dedicated approach explained by the NGT.

Each NGT session was assessed individually, with every statement added to a tracking document. Each statement's total score, which resulted from the ranking within the NGT process, was divided by the total number of people in the group, providing the average of each total score. Using these averages, the data were sorted into descending order, identifying the top-ranked statements in each group. For each question, statements were condensed into themes. Themes were developed by thorough examination of statements and topic areas which arose during NGT discussions.

In total, 29 people participated in the NGT process, with an equal distribution among the 4 groups. There was a diverse mix of medical and scientific professionals, with about one-half of the group comprising medical gastroenterologists, epidemiologists, and oncologists, and a smaller representation of primary care physicians, microbiologists, and biostatisticians. Participants were affiliated with the Veteran's Administration, NCI, ACS, academic cancer centers and hospitals, and private practice medical institutions.

The Results

The primary themes of the NGT sessions fell into 7 primary themes: etiology/biology, genetics/family history, establishing cohorts, evaluation of screening in younger adults, education, microbiome and risk factors. The rating and ranking of each of the specific themes in each NGT group and the

Themes coded by color						
Etiology and biology	Genetics and family history	Establishing cohorts	Evaluation of screening in younger adults	Education	Microbiome	Risk factors

Rank	Group A	Group B	Group C	Group D
1–Top priority	Evaluation of screening in younger adults	Etiology and biology	Etiology and biology	Establishing cohorts and robust data from cohort
2	Education initiatives	Establishing cohorts and robust data from cohort	Education initiatives	Microbiome focus
3	Establishing cohorts and robust data from cohort	Risk factors	Genetics and family history	Risk factors
4	Etiology and biology	Evaluation of screening in younger adults	Evaluation of screening in younger adults	Education initiatives
5	Genetics and family history	Risk factors	Microbiome focus	Etiology and biology

Figure 1. Outcomes of the early age onset colorectal cancer nominal group process.

specific action and detail related to that theme (Figure 1).

The most prominent themes across NGT groups to addressing the rise in incidence of EAO CRC in the United States and internationally included:

1. Understanding the etiology of EAO CRC.
2. Education to medical providers about EAO CRC.
3. Establishing international cohorts.

Next Steps and Considerations

Fight CRC is using the themes and specific recommendations to consider the course of the Workgroup in the next year and to further address the needs of professionals and experts to create an organized and dedicated approach to advancing EAO CRC with a common voice. Fight CRC assessed the activities of the workgroup members at the outset of the workgroup establishment in February of 2019, but will continue to assess what is happening in the primary domains and assess gaps. At the time of this commentary in September 2019, these are specific areas of dedicated interest, broad reaching progress, and key opportunities that have developed to advance the work for the 3 prominent themes.

Understanding the Etiology of EAO CRC

Collaborations and Resources. To build on current and established cohorts, studies and existing resources, Fight CRC is now cataloging and organizing specific information and details about studies, cohorts, and established and completed research to help build on and inform the future direction of research. The convening of the EAO workgroup will also be used to help advance shared and collaborative research initiatives in the future. Working with Get Your Rear In Gear, Fight CRC is currently supporting a biobank effort to address EAO CRC at Mayo Clinic.

Prioritizing the Research Question(s). At the February Fight CRC EAO meeting, the agenda focused upon the priorities of study for etiology; Figure 2 summarizes these key questions and considerations.

Funding. Throughout the convening of the EAO Workgroup, Fight CRC has worked closely with the NCI, Department of Defense, and ACS to understand the current and future portfolio of funding to address study of etiology of disease. NCI has provided updates about funding mechanisms to address biology and etiology in 2019 and 2020. The Department of Defense has engaged in the discussion and shared their vision and passion for research with specific cohorts available for research and exploring potential funding mechanisms. The ACS has allowed for EAO research in their current funding mechanism.

Policy and Legislation. Fight CRC secured report language in the FY20 Labor, Health and Human Services appropriations bill directing NCI to focus additional resources on the etiology of EAO CRC. The inclusion of this language shows that there is strong support in congress for advancing research in this area. Fight CRC has also routinely advocated for medical research funding within the Department of Defense.

Challenges. Funding is the key impediment. The more funding that is made available through the National Institutes of Health and nonprofit entities, societies, and foundations, the more work that can be done in this area.

Education to Medical Providers About EAO CRC

Collaborations and Resources. The Centers for Disease Control and Prevention have now actively engaged with the Fight CRC EAO working group and have shared that through their established Colorectal Cancer Control Program and several public health initiatives working with the primary care and public health community, EAO CRC is a priority. The National Colorectal Roundtable and the ACS are supporting practice change in primary care work to explore better opportunities for symptom management. Initiated by Bowel UK, The Never Too Young Coalition also now in the United States is also now working on provider and patient awareness in the United States. Recent publications and findings from the National Colorectal Roundtable Early Age Onset

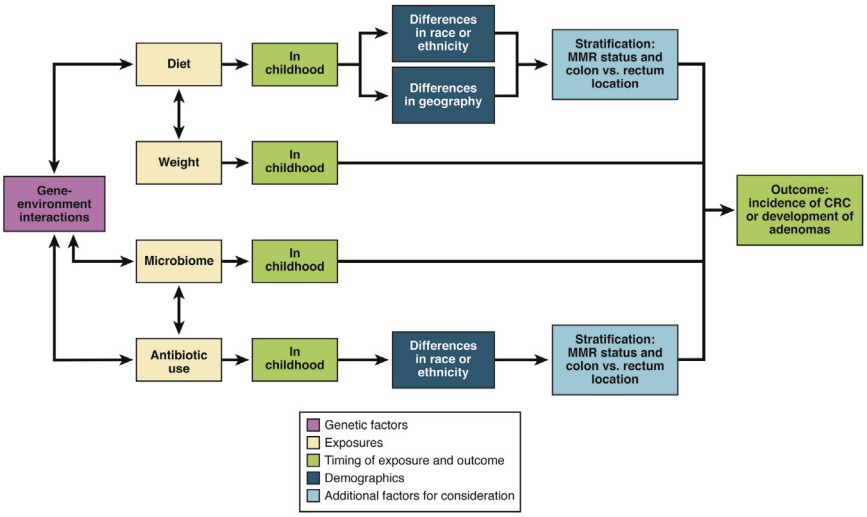

Figure 2. Early age onset colorectal cancer incidence or adenoma development, timing of exposures, and stratification of risk factor examination.

meeting suggest messaging as early as 40 years old about the importance of screening may have a significant impact to on-time screening.

Prioritizing the Research Question(s). There is a current exploration with the NCI and other agencies to consider the dissemination and implementation study of clinical symptom management and collection and use of family history.

Funding. Resources for health promotion, awareness/media campaigns, and practice change will be imperative. Funding to ensure EAO CRC is included in accreditation and quality measures for primary and specialty care must also be considered.

Legislation and Advocacy. Fight CRC and international advocacy organizations are actively engaging and using the survivor voice to share their stories about missed and delayed diagnoses in addition to distributing patient education resources to policymakers and the medical community to raise awareness about EAO CRC. This year Fight CRC is launching a state advocacy program to help build the necessary infrastructure at the state level to effect meaningful policy change. A key focus of this program will be working to ensure that states follow ACS screening guidelines to begin screening at age 45 for those with average risk. States such as Maine and Kentucky have successfully ensured ACS guidelines are the priority guidelines, moving screening age from 50 to 45 years old. Currently, Colorado and California are initiating legislation and policy to ensure that ACS guidelines are recognized and implemented.

Challenges. At this time, there is not a full-scale approach or campaign reaching primary care health systems nationally or internationally to implement strategies to ensure on time screening, patient awareness, and implementation of screening guidelines for increase and high-risk individuals.

Establishing International Cohorts

Collaborations and Resources. The Colon Cancer Challenge has hosted conferences that attract international attention to help heighten awareness of colorectal cancer and support discussion to build the research initiatives. Dr Jose Perea from Spain has created opportunities to expand the conversation with forums in Madrid. At the February 1, 2019, meeting, Fight CRC also engaged researchers from 4 countries and are now collaborating with Dr Perea to cohost an international conference in Spain in 2020.

Prioritizing the Research Question. To establish the cohorts, the primary data elements must be examined to ensure common data gathering and standardization.

Funding. Conversations about an international funding mechanism with a variety of funders will be an integral discussion and focal point to establish international cohorts.

Legislation and Advocacy.- Engaging with global advocacy partners such as Europa Colon, Bowel UK, and Bowel Cancer Australia and working more closely with all continents will be imperative to ensure that there is proper and adequate funding mechanisms established along with government support.

Challenges. Accessing information about existing studies, cohorts, data elements, and a common means to collect data is a pivotal consideration in establishment of an international consortium.

Closing Thoughts and Next Steps

Participants expressed the value and satisfaction of applying the NGT process, stating that the NGT was "very effective in generating ideas from all participants" and also noted by comments such as, "I was impressed with the consistency of the aims and also the variability of approaches to address the issues."

Dr Dennis Ahnen, who has advised in the Fight CRC initiatives made a keen observation in the final review of the NGT process and final outcomes which will be used as a guiding principal in the work:

> *Regarding the study and etiology of disease, this is certainly a noble goal for the future; it will take years to do things like examine the role of changes in microbiome from early use of antibiotics. Which doesn't mean it shouldn't be done, this type of study must be done. But there will be little immediate impact on EAO CRC burden based on that work. It isn't clear what we would do clinically with the causation information to have an impact. For example, in the present time- we know that obesity is a risk factor for EOA CRC but what have we done about it?*

There is information that is vital now and should [be done] now to have an impact: such as, promote ACS screening guidelines, promote symptom recognition, and better collection and use of family history of both CRC and advanced adenomas. We need to spend more time thinking through the public health implementation and implementation science of the things we know now. If we can't do that now, it is unlikely that we will be able to do it for any other risk factors that we identify.

Based on Dr Ahnen's perspective and nearly 50 additional experts in the field and from the convening over the last 6 months, Fight CRC is dedicated to devoting resources to the themes and strategies noted, with a sense of urgency of helping inform the future by taking action immediately.

Fight CRC urges the primary care, GI teams, and the research and advocacy community to consider their current medical practices, public health initiatives, research perspectives, funding mechanisms and advocacy efforts to consider the findings from the EAO NGT process to inform the work and decrease the incidence of EAO CRC.

To learn more about the Fight CRC EAO Working Group, visit fightcrc.org.

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0016-5085/$36.00
https://doi.org/10.1053/j.gastro.2019.10.051