

Ask the Experts: Revised CRC Screening



From the Editor

Lawrence S. Friedman, MD, FASGE

The Anton R. Fried, MD, Chair
Department of Medicine
Newton-Wellesley Hospital

Assistant Chief of Medicine
Massachusetts General Hospital

Professor of Medicine
Harvard Medical School

Professor of Medicine
Tufts University School of Medicine

Given the recently updated recommendations published in July *GIE: Gastrointestinal Endoscopy*, “Colorectal cancer screening: Recommendations for physicians and patients from the U.S. Multi-Society Task Force on Colorectal Cancer,” which note the rise of colorectal cancer in younger adults over the past few decades, we changed our usual format to bring you articles from three experts instead of one, along with a comment from Fight CRC, a CRC awareness and advocacy organization. We trust you will find these discussions informative.

Print a PDF

For a PDF of the complete Ask the Experts article, visit www.asge.org, log in, click on Education & Meetings, Publications and then *Ask the Expert*.

The information presented in Ask the Experts reflects the opinions of the authors and does not represent the position of ASGE. ASGE expressly disclaims any warranties or guarantees, expressed or implied, and is not liable for damages of any kind in connection with the material, information, or procedures set forth.



Douglas K. Rex, MD, FASGE

Director of Endoscopy
Indiana University
Medical Center

Distinguished Professor of
Medicine, Indiana University
School of Medicine

- How did the MSTF approach the under-50 trend for this new recommendation?
- What research was considered?
- What are the MSTF recommendations for a screening approach based on the limited information that we do have?

The revised Multi-Society Task Force (MSTF) on Colorectal Cancer recommendations are to begin screening before age 50 in two groups: African Americans and those who have a family history of a first-degree relative with colorectal cancer (CRC) or an advanced precancerous lesion.

Screening in average risk African-American persons is recommended to begin at age 45. Early screening (before age 50) in African Americans was first recommended by the American College of Gastroenterology more than a decade ago. The evidence supporting early screening in African Americans is considered very low quality, given the limited direct evidence. The rationale for the MSTF recommendation is that African Americans have a high incidence rate of cancer and an early mean age of onset. Mortality rates for CRC are even greater for African Americans than age-matched people of other racial backgrounds. An additional potential advantage of recommending African Americans for early screening may be improved awareness of CRC risk in this group, for whom screening rates are lower.

The MSTF also recommends early screening for persons who have a first-degree family member with a documented CRC or advanced precancerous lesion (conventional adenoma with advanced features defined as size ≥ 1 cm in diameter or having high-grade dysplasia or villous elements or a sessile serrated polyp ≥ 10 mm in size or with cytologic dysplasia) before age 60. This group is recommended to begin screening at age 40 or 10 years younger than the youngest affected relative, whichever comes first, and to undergo colonoscopy every five years when the exam is

Screening Recommendations

negative. The MSTF gives the same recommendation to persons with two first-degree relatives who have one of the diagnoses described above (at any age). Persons with a single first-degree relative with one of these diagnoses should begin screening at age 40 and use the average-risk screening options to select screening tests and intervals. Physicians are encouraged to obtain detailed family histories of colorectal neoplasia and update them regularly.

The MSTF does not recommend earlier screening outside these groups. The risk of CRC is rising disproportionately in persons under age 50, but absolute incidence rates remain low. Proposed etiologies for the rising cancer rates in young persons include obesity and alterations in the gut microbiome, but they remain unproven. Lynch syndrome underlies a minority of cancers in persons under 50 years of age. Colonoscopic screening in persons 40 to 49 years of age has a very low yield for advanced precancerous lesions and for cancers. The fecal immunochemical test (FIT) for blood seems attractive for persons under age 50 because it has good sensitivity, excellent specificity and low cost. However, data on the utility or effectiveness of FIT in persons under age 50 are limited. More data are needed on the yield of screening in persons under age 50 with known risk factors that are not usually factored into screening decisions, including long-term smoking, obesity and diabetes mellitus.

In the opportunistic setting, clinicians seeing patients under 50 years of age are bound to consider a lower threshold for colonic imaging in light of these new data on incidence rates. This consideration should be balanced against awareness of the huge population of young people with irritable bowel syndrome, who in many cases do not need colonoscopy. The MSTF found good evidence that bleeding symptoms, including hematochezia (in this case, blood in the toilet bowl rather than just on the paper), unexplained iron deficiency anemia and/or melena with a negative upper endoscopy, have substantial predictive value for CRC.

Other colorectal symptoms, including abdominal pain and altered bowel habits, in the absence of any evidence of bleeding, predict a risk of cancer similar to that in asymptomatic persons. Thus, the MSTF recommends that symptoms and lab results indicative of bleeding that is potentially of a colonic source can be used as a guide to direct the extent of imaging. Bleeding should be evaluated by colonoscopy in patients in the 40- to 49-year age group. For younger patients, colonoscopy is often the best course in patients with bleeding, although a more limited endoscopy (e.g. sigmoidoscopy or anoscopy) can be appropriate if it establishes a clear source of the bleeding. If more limited endoscopy is used, the bleeding source should be treated and the patient

followed until the bleeding resolves. The MSTF looks forward to additional evidence to guide best practices that can reduce the frequency of CRC and CRC deaths in young people.

Disclosures: Dr. Rex discloses relationships related to the content of this article with Olympus, Boston Scientific, EndoChoice, EndoAid, Medtronic and Colony Solutions.



Mark B. Pochapin, MD

Clinical Vice-Chair, Department of Medicine

Director, Division of Gastroenterology

Sholtz/Leeds Professor of Gastroenterology

NYU Langone Health

- **In general, what do we know, and what don't we know?**
- **What are the unique challenges for screening in this population?**
- **For GI endoscopists in practice, how does this uptick in younger CRC patients change our world?**

As noted in the updated U.S. Multi-Society recommendations for colorectal cancer (CRC) screening¹, the incidence of CRC in younger adults has been increasing over the past few decades²⁻³. Clearly, this is a public health concern, since individuals who are younger than age 50 and considered to be at average risk are not captured in our screening guidelines. Given these data, we must dedicate ourselves to determining why more young adults are developing CRC and what we can do to end this disturbing trend.

The causes for the increasing incidence are not yet clear. As researchers begin to probe the questions of etiology, clinicians must be vigilant in using the knowledge we do have to ensure appropriate screening and diagnosis in this younger population. It is important to recognize that while the incidence of CRC is rising in younger adults, the relative incidence in this age group remains low¹. Until we have a better understanding of the contributing factors, and which additional subgroups are at increased risk, we must commit to utilizing the recommendations and tools we currently have to their fullest potential and optimum efficacy.

First, we need to ensure that we document a detailed family history of cancers and polyps and recommend that those who are at high risk due to genetic syndromes (such as Lynch syndrome) or increased risk due to family history,

start screening at the appropriate age and continue at the appropriate intervals. It is critical to utilize the expertise of our colleagues and refer patients for genetic counseling and genetic testing, when indicated. It is also important that we recognize the increased risk for CRC in African Americans. Due to the higher incidence, earlier mean age at onset and increased mortality rate from colorectal cancer, individuals who are African American (but otherwise average risk), should start screening at age 45, per the new Multi-Society recommendations¹. Further, given the increasing incidence in persons age 50 to 54 years², it is important to encourage all average-risk persons who are not African American to begin screening promptly at age 50, rather than delaying to a later date.

Second, we must take a closer look at differential diagnosis in younger adults who present with symptoms. In my practice, I have heard too many stories from individuals in their 40s, 30s, and even 20s, telling me that they went to the doctor with gastrointestinal symptoms and were misdiagnosed with and treated for hemorrhoids or irritable bowel syndrome for years, only to be diagnosed later with inflammatory bowel disease or advanced CRC. We must ensure that CRC is part of the differential diagnosis in younger adults and take the appropriate steps to rule it out, just as we would in older patients. In my opinion, this means lowering our threshold for ordering a diagnostic colonoscopy in younger, symptomatic adults—especially when bleeding is present.

In those who present with symptoms or signs of gastrointestinal bleeding, it is not sufficient to make a diagnosis such as hemorrhoids, unless the bleeding source is clearly visualized (and then resolved). Nonspecific gastrointestinal symptoms—such as persistent change in bowel habits, change in stool shape (including ribbon-like stools) and abdominal pain—also require a thorough diagnostic work-up. While previous data indicate that persons with nonspecific gastrointestinal symptoms occurring without bleeding do not have an increased risk of CRC⁴⁻⁵, in some cases, endoscopic evaluation may be appropriate to rule out an inflammatory process or a neoplasm. Nonspecific gastrointestinal symptoms can be challenging; thus clinical expertise and judgment on an individual basis are warranted.

These measures—assuring that all patients undergo a thorough family history and are referred for genetic counseling when appropriate, starting CRC screening for African-American patients who are otherwise at average risk at age 45 and including CRC in the differential diagnosis of younger adults who present with gastrointestinal symptoms (particularly bleeding) in younger adults—do not represent the sole approach, but rather are essential parts of the strategy for preventing and detecting early cancers in younger people. Ultimately, more research is needed to evaluate the

etiology of this disease in our younger adult population. As these data become available, it is hoped that we can determine with greater clarity which individuals may benefit from screening or other interventions at a younger age.

References

1. Rex D, Boland CR, Dominitz JA, et al. Colorectal cancer screening: Recommendations for physicians and patients from the US Multi-Society Task Force on Colorectal Cancer. *Am J Gastroenterol*. Epub June 6, 2017.
2. Siegel RL, Fedewa SA, Anderson WF, et al. Colorectal cancer incidence patterns in the United States, 1974-2013. *JNCI J Natl Cancer Inst*. 2017;109(8).
3. Meyer J, Narang T, Schnoll-Sussman F, et al. Increasing incidence of rectal cancer in patients aged younger than 40 years. *Cancer*. 2010;116:4354-4359.
4. Lieberman DA, de Garmo PL, Fleischer DE, et al. Colonic neoplasia in patients with nonspecific GI symptoms. *Gastrointest Endosc*. 2000;51:647-651.
5. Rex DK, Mark D, Clarke B, et al. Flexible sigmoidoscopy plus air-contrast barium enema versus colonoscopy for evaluation of symptomatic patients without evidence of bleeding. *Gastrointest Endosc*. 1995;42:132-138.

Disclosure: Dr. Pochapin has no financial relationships pertaining to the content of this article.



Marcia Cruz-Correa, MD, PhD, FASGE

Professor of Medicine and Biochemistry

University of Puerto Rico Comprehensive Cancer San Juan, Puerto Rico

- **Do you know what sort of studies may be in the pipeline on this topic?**
- **What possible directions might future research take?**
- **Do we know how the biology of CRC is different in younger compared with older people?**

Recent epidemiologic studies have reported an increase in the incidence of sporadic colorectal cancer (CRC) in people younger than 50 years of age (early-onset CRC), despite a decrease in the incidence of CRC in older individuals (late-onset CRC)¹. Tumors from early-onset CRC patients are characteristically microsatellite stable, are located in the distal colon and have more advanced histologic features. Patients with early-onset CRC are often

diagnosed at a more advanced stage compared with those with late-onset CRC.

For example, early-onset CRC is more often complicated by metastasis either at presentation or during the disease course compared with CRC patients >50 years old². The presence of more advanced histologic features and clinical stage at diagnosis corresponds with the higher mortality rate seen in patients with early-onset CRC³⁻⁵. Furthermore, the population of CRC patients below the age of 50 years presents an epidemiologic challenge, because current guidelines for CRC screening target average-risk individuals ≥50 years old and advocate screening before the age of 50 for only select groups of people, such as African Americans (≥45 years old), individuals with a family history of CRC and persons at increased risk for CRC due to a genetic predisposition². There is evidence to suggest that the contribution of familial/hereditary cancer to early-onset CRC is small. For example, patients with early-onset CRC do not have a significantly increased frequency of CRC in their family history. Additionally, tumors from early-onset CRC demonstrate microsatellite stability in contrast to hereditary CRC tumors (Lynch Syndrome), which are microsatellite unstable.

Established dietary and lifestyle factors associated with CRC include excess body weight, high consumption of processed meat and alcohol, low levels of physical activity, low fiber consumption and cigarette smoking⁶⁻⁹. There are increasing trends (by birth cohort) for some of these risk factors, such as excess body fat, occurring⁸ in parallel with the rise in early-onset CRC incidence. It is possible, therefore, that the interaction between dietary factors, obesity and other factors, such as the gut microbiome and an individual's genetic profile, may contribute significantly to early-onset CRC^{10,11}.

Research to explore the contribution of lifestyle exposures, metabolic risk factors and epigenetic/genetic factors among persons with early-onset CRC is ongoing. For instance, a recent study demonstrated an association between a Western-type diet, a predominantly genotoxic-inflammatory gut microbiome and colonic mucosal proliferation¹²; in fact, dietary exposures can modify the gut microbiome and colonic mucosal biomarkers within several weeks of dietary exposure. These findings are consistent with the one-generation increase in CRC risk that has been observed among Japanese immigrants to the United States and that is attributed to diet¹³.

Based on the observed CRC risk among young individuals, several groups are advocating modification of current CRC screening guidelines to start before the age of 50. The Cancer Intervention and Surveillance Modeling Network (CISNET) researchers recently reported that beginning screening at age 45 years is “more effective and provided (in a modeling study) a more favorable balance between

life-years gained and screening burden than starting at age 50 years”¹⁴.

In addition, until additional scientific discoveries on the etiology and modifiable/non-modifiable risk factors for early-onset CRC are available, we need to consider developing alternative, targeted screening strategies for select high-risk cohorts. For example, since nearly one-third of rectal cancer patients are younger than age 55 years¹, initiation of screening before age 50 years with methods that examine the distal colorectum or with noninvasive stool testing could be considered. This approach has been started by the Puerto Rico (PR) Department of Health due to the high burden of early-onset CRC. In March 2015, the PR Department of Health issued an administrative order recommending coverage for CRC screening with fecal-based testing starting at age 40.

This modified CRC screening program is expected to decrease the burden of disease among young individuals. In addition, efforts to educate the population about the role of healthier living, obesity and early evaluation of CRC symptoms regardless of age should be coordinated across all stakeholders to mitigate premature morbidity and mortality from this disease.

See pg. 8 for Dr. Cruz-Correa's references.

Disclosure: Dr. Cruz-Correa has no financial relationships pertaining to the content of this article.



Anjelica (Anjee) Davis

President

Fight Colorectal Cancer

Springfield, Mo.

Fight Colorectal Cancer (Fight CRC) is a patient advocacy organization, whose mission is to see victory over colon and rectal cancers—the #2 cause of cancer deaths in the U.S. Fight CRC focuses its efforts on advocacy, research, education and awareness. Visit <https://fightcolorectalcancer.org/> for more information.

The Multi-Society Task Force (MSTF) informs us on the use and role of new screening options for colorectal cancer, such as the new stool DNA and assay tests. Having that guidance enhances our ability to provide coverage for patients and clear options for the 23 million unscreened in


the U.S. We appreciated that the MSTF included language in this new guideline regarding family history. As we see mounting evidence supporting a rise in CRC frequency in persons under age 50, we hope to see more evidence that will help experts to stratify younger patients for risk.

As an organization, Fight CRC educates and promotes all the screening options for those age 50 and over. Our policy efforts rely on the guidance provided by the MSTF, which is why we hope that the task force will continue to address early detection efforts for those under age 50 in future updates. In the meantime, we will continue to vigilantly monitor and fight for access to screening options and funding for research.

Dr. Cruz-Correa's Article References

1. Rebecca L. Siegel, Stacey A. Fedewa, William F. Anderson, et al. Colorectal Cancer Incidence Patterns in the United States, 1974–2013. *JNCI J Natl Cancer Inst* (2017) 109(8).
2. Dominic, O.G., et al. American College of Gastroenterology Guidelines for Colorectal Cancer Screening 2008. *The American Journal of Gastroenterology*, 2009. 104(10): 2626–7; author reply 2628–9.
3. Boardman, L.A. et al. Higher frequency of diploidy in young-onset microsatellite-stable colorectal cancer. *Clinical Cancer Research: An Official Journal of the American Association for Cancer Research*, 2007. 13(8):2323–8.4.
4. Chan, T.L., et al. Early-onset colorectal cancer with stable microsatellite DNA and near-diploid chromosomes. *Oncogene*, 2001. 20(35):4871–6.
5. Chang, D.T., et al. Clinicopathologic and molecular features of sporadic early-onset colorectal adenocarcinoma: an adenocarcinoma with frequent signet ring cell differentiation, rectal and sigmoid involvement, and adverse morphologic features. *Modern Pathology: An Official Journal of the United States and Canadian Academy of Pathology, Inc*, 2012. 25(8):1128–39.
6. Huxley RR, Ansary-Moghaddam A, Clifton P, Czernichow S, Parr CL, Woodward M. The impact of dietary and lifestyle risk factors on risk of colorectal cancer: A quantitative overview of the epidemiological evidence. *Int J Cancer*. 2009;125(1):171–180.
7. Aune D, Chan DS, Lau R, et al. Dietary fibre, whole grains, and risk of colorectal cancer: systematic review and dose-response meta-analysis of prospective studies. *BMJ*. 2011;343:d6617.
8. Lee JM, Pilli S, Gebremariam A, et al. Getting heavier, younger: Trajectories of obesity over the life course. *Int J Obes (Lond)*. 2010;34(4):614–623.
9. French SA, Story M, Jeffery RW. Environmental influences on eating and physical activity. *Annu Rev Public Health*. 2001;22:309–335.
10. Brownson RC, Boehmer TK, Luke DA. Declining rates of

physical activity in the United States: What are the contributors? *Annu Rev Public Health*. 2005;26:421–443.

11. Nielsen SJ, Popkin BM. Patterns and trends in food portion sizes, 1977–1998. *JAMA*. 2003;289(4):450–3.
12. O’Keefe SJ, Li JV, Lahti L, et al. Fat, fibre and cancer risk in African Americans and rural Africans. *Nat Commun*. 2015;6:6342.
13. Marchand LL. Combined influence of genetic and dietary factors on colorectal cancer incidence in Japanese Americans. *J Natl Cancer Inst Monogr*. 1999. <http://www.ncbi.nlm.nih.gov/pubmed/10854493>(26):101–5.
14. Knudsen AB, Zauber AG, Rutter CM, et al. Estimation of benefits, burden, and harms of colorectal cancer screening Strategies: Modeling study for the US Preventive Services Task Force. *JAMA*. 2016;315(23):2595–2609. 

Resources

- “Colorectal cancer screening: Recommendations for physicians and patients from the U.S. Multi-Society Task Force on Colorectal Cancer,” published in the July issue of *GIE: Gastrointestinal Endoscopy* at www.giejournal.org.
- Visit www.asge.org and www.screen4coloncancer.org for physician and patient resources.
- Display the downloadable “Prep-Scope-Live” poster and bookmarks.
- Post a link to the www.screen4coloncancer.org patient education website on your practice website; share e-cards from the site on social media.
- Follow ASGE on Facebook and Twitter, and share our NCR CAM messages, graphics and videos.
- Share and comment on the National Colorectal Cancer Roundtable blog at <http://nccrt.org/80-by-2018-blog/>.
- Use the new public service ads featuring businesswoman and Honorary ASGE Foundation Trustee Kathy Ireland, which were broadcast during March for National Colorectal Cancer Awareness Month.

