



45 is the New 50: Demographic Trends in Colorectal Cancer Drive Recent US Screening Guideline Changes

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This ASO Perspective discusses recent changes in clinical practice guidelines for colorectal cancer screening in the USA and reviews rationale, early findings, and implications for providers, systems, and patients. Between 2018 and 2022, the American Cancer Society, US Preventative Services Task Force, US Multisociety Task Force, and National Comprehensive Cancer Network all recommended lowering the recommended age of first screening for colorectal cancer from 50 to 45 years for average-risk patients, regardless of ethnicity. Modeling analyses and early data suggest improved prevention and early detection of colorectal cancer with this change, along with a cost-effective profile. We recommend adhering to these guidelines, spreading awareness, and implementation of system improvements to support equal access to screening.

Screening for colorectal cancer (CRC) by all methods has been demonstrated to decrease CRC incidence and mortality.¹ With increasing awareness and availability, the rate of screening for CRC among adults aged 50–74 years in the USA has steadily risen to around 70% in 2020 according to CDC Behavioral Risk Factor Surveillance System Survey Data.² In the USA, CRC screening undoubtedly saves lives and should be widely available.

As of August 2022, all major guideline-setting organizations in the USA have now aligned their overall recommendations for CRC screening around the following principles:

- Average-risk patients, regardless of ethnicity, should begin screening at age 45 years.
- Recommended screening modalities include the following: fecal immunochemical test annually; high-sensitivity, guaiac-based fecal occult blood test annually; multitarget stool DNA test every 3 years; colonoscopy every 10 years; computed tomography colonography every 5 years; or flexible sigmoidoscopy every 5 years.
- Positive fecal tests or colonography should be followed up with a colonoscopy. Colonoscopy is the gold-standard screening tool for CRC, and the only screening modality that provides both early detection and CRC prevention.
- Screening should end at age 75–85 years, based on individual patient factors.
- These guidelines do not change recommendations for high-risk patients, who have a personal or family history of polyps, cancer, inflammatory bowel disease, or high-risk colorectal cancer genetic syndromes. These guidelines apply for screening only, not diagnostic testing for specific presenting symptoms.
- Germline multigene panel genetic testing is now recommended for all CRC patients under the age of 50 years and can be considered for all CRC patients regardless of age.

The striking update in these recommendations is the earlier recommended age of first screening. Despite increased uptake of screening in patients over the age of 50 years, alarming demographic trends of early-occurring CRC have driven a reevaluation of screening practices by the major guideline-setting societies in the past decade. These trends included increasing rates of CRC in people aged 20–49 years and increased CRC deaths in young people (< 50 years) despite overall decreased deaths.³ In 2018, the American Cancer Society (ACS) became the first

major society in the USA to begin recommending earlier screening starting at age 45 years. The ACS based their qualified recommendations on a review of commissioned data and modeling analyses from the US Preventative Services Task Force (USPSTF) 2016 guideline update. This analysis demonstrated a likely similar CRC incidence rate in the 45–49-year age group when compared with patients aged 50–54 years (after taking into account lead time associated with screening uptake), and a reasonable harm reduction for younger patients.⁴

The ACS was the lone society officially recommending earlier screening at age 45 years until May 2021, when the USPSTF followed suit after careful review of the data and models.⁵ After a period of uncertainty for patients, the decision by the USPSTF to recommend earlier screening provided important leverage for patients and physicians arguing the importance of preventative care with health insurance companies. The US Multisociety Task Force on Colorectal Cancer, representing the American College of Gastroenterology, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy, updated its colorectal cancer screening recommendations in January 2022, and the National Comprehensive Cancer Network (NCCN) made the update in August 2022, finally bringing all of the major society recommendations into concordance.^{6,7}

The earliest data suggest that the predicted preventative benefit of lowering the age of first screening may be realized soon. In a single healthcare system review of 7990 screening colonoscopies published earlier this year, study authors found an increase from 3.5 to 11.6% in the proportion of first-time screening colonoscopies performed in patients aged 45–49 years.⁸ Supporting the earlier modeling predictions, a similar adenoma detection rate (ADR) was noted in the 45–49-year age group when compared with patients aged 50–54 years and 55–59 years. Despite a concern that ADR would fall in the younger age group due to a self-selective, highly motivated, and highly informed but low-risk population participating in earlier screening, ADR was actually noted to increase numerically (from 22 to 34%, though this finding was not statistically significant). Notably, the authors comment that quality improvement measures, including audit and feedback, may be central to improved ADR—and therefore CRC prevention—for all patients.

Major changes in clinical practice guidelines and recommendations always require thoughtful consideration of all associated implications. In the case of lowering the age of first screening, many of these considerations will revolve around systems and patients. How will we equip the healthcare system in the USA to take on the burden of an additional population utilizing the screening tool? How will we make sure all patients have equal access to the

process regardless of socioeconomic status, insurance, and education level? How can we best design quality improvement initiatives to maximize the cost effectiveness of the expanded screening? Future tasks must include studying and managing these implications, adapting systems to improve access and quality, and raising awareness and uptake in communities.

Finally, ongoing population research is focused on discerning patient and environmental factors underlying the trend of increased early-onset CRC. Some modifiable factors, such as obesity and sedentary behavior, have already been linked to early-onset CRC in women.^{9,10} Researchers are also examining tumor-specific factors, including histological features, gene mutations, and consensus molecular subtypes that may be linked to early-onset CRC and differentiable from traditional CRC models.¹¹ Data from recently published prospective studies demonstrated a higher prevalence of relevant inherited gene mutations than previously thought, many of which would have been missed without multigene panel testing.^{12–14} A significant proportion (over 10%, and up to 30% with high-penetrance variants) of patients undergoing multigene panel testing in these studies had modifications made in their cancer treatments on the basis of genetic testing findings. In addition, studies on multigene panel testing in patients with CRC under the age of 50 found that multigene panel testing identified relevant mutations in one third of patients who did not meet requirements for recommending genetic testing.¹⁵ These findings led the NCCN to revise its screening guidelines additionally: as of July 2022, germline multigene panel genetic testing is now recommended for all patients with colorectal cancer under the age of 50, and should no longer be restricted to those with evidence of mismatch repair deficiency in their tumor or suggestive family history for patients over the age of 50.

In summary, although there have been alarming trends in early-onset CRC in the past decade, early screening and genetic testing are effective modalities for prevention, early detection, and directing individualized and effective treatment. Future work in the US healthcare system will need to focus on access to cancer care for all. The bottom line: tell your family, friends, patients, colleagues, and community to get screened for CRC starting at age 45 years.

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