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Colorectal Cancer Screening Starting at Age 45 Years—Ensuring Benefits Are Realized by All

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The latest recommendations from the US Preventive Services Task Force (USPSTF) represent a significant change in the scope of colorectal cancer (CRC) screening.^{1–3} For the first time, the USPSTF recommends initiating average-risk CRC screening at age 45 years, reduced from age 50 years in previous versions. This was a B statement, reflecting moderate certainty of moderate net benefit.^{1–3} The USPSTF continues to issue an A statement (reflecting high certainty of substantial net benefit) for screening adults aged 50 to 75 years.^{1–3} While other guidelines have recommended this younger age, the USPSTF guidelines directly inform insurance coverage and waiving of cost sharing as part of federal law. The new recommendation¹ is based on a systematic review by Lin et al,² recent epidemiology data from Siegel et al,⁴ and a modeling study by Knudsen et al,³ suggesting that the burden for CRC could be reduced at an acceptable burden of harms related to screening, which reflects both the established effectiveness of screening and the increase in incidence of early onset CRC (ie, diagnosis of CRC younger than age 50 years). In addition to the potential benefits of screening starting at age 45 years, an ancillary benefit could be an increase in screening rates among individuals aged 50 years and older.

Still, a number of concerns and questions have been raised about implementation of population-based CRC screening beginning at age 45 years. First, given that this recommendation¹ is based on a systematic review² and modeling study³ rather than randomized clinical trials of sufficient power among participants specifically younger than 50 years, it is dependent on a few assumptions, including 100% adherence, which is not experienced in routine practice. Moreover, if there is differential uptake by healthier individuals with low risk in the younger age range, the net benefits might not be fully realized.⁵ Second, a significant portion of early onset CRC occurs among individuals younger than age 45 years.⁴ It follows that population-based screening initiation at this age is only one step in addressing early onset CRC; symptoms and family history must continue

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to guide diagnostic or screening examinations among younger adults.⁶ Third, implementation of the revised recommendations¹⁻³ might exacerbate known racial/ethnic disparities in screening and outcomes, especially among Black, American Indian, and Alaska Native individuals, who already have worse CRC outcomes than other racial/ethnic groups.^{4,7,8} Implementation could reduce access among individuals who are medically underserved if capacity is not expanded, or it may simply result in improved outcomes among individuals with more advantages that are not shared by others, thus widening an existing gap. Reliance on colonoscopy for screening among individuals aged 45 to 49 years might crowd out approximately one-third of individuals aged 50 to 75 years whose CRC screening is not up-to-date, given limited endoscopy capacity in some communities.⁹ An estimated 10.7 million additional colonoscopies might be required as a result of this recommendation change.^{1-3,5}

To realize the benefits of expanding the screening-eligible population, a number of approaches could be considered. While much of CRC screening is offered opportunistically during office visits to a primary care clinician, proactive and population-based approaches at a system level potentially could help to ensure equity in CRC screening.¹⁰ This should include identification of eligible individuals using system-level analytics designed with algorithms that adhere to principles of equity,¹¹ providing direct outreach to people at home, reminders to clinicians about screening in the electronic health record, and providing navigation for those who need it.¹² For example, once health systems adopt the new recommendations,¹⁻³ in addition to embedding the screening age into EHR alerts to nudge clinicians,¹³ they could also use population-level outreach to send reminders and opportunities for testing directly to patients to reduce differential uptake by clinicians. The same population-based efforts should continue to increase screening rates among patients aged 50 to 75 years, a recommendation considered an A statement, as well as continuously working to improve equity across racial/ethnic groups and geographic locations.

To provide access for the newly enlarged screening population, greater promotion and use of alternatives to screening colonoscopy, such as stool-based testing for individuals with low risk, should be considered. Although a variety of screening test options are recommended by the USPSTF,¹⁻³ most screening in the United States is completed through screening colonoscopy. As the eligible age range expands, health care systems could take advantage of the opportunity to incorporate more stool-based testing for individuals at average risk, particularly for individuals aged 45 to 49 years. There are also opportunities to incorporate sequential or active choice of testing options to increase overall screening uptake and to increase uptake of stool-based screening options.¹⁴

While the new USPSTF recommendations¹⁻³ stand to benefit adults with average risk beginning at age 45 years, the importance of active CRC testing for symptomatic or high-risk adults younger than age 45 years must be emphasized. Nearly half of patients with early onset CRC are diagnosed before age 45 years, and these individuals continue to be ineligible for screening,⁴ as was the case for the actor Chadwick Boseman, who died from CRC at age 43 years. Symptoms of CRC, such as rectal bleeding, persistent change in bowel habits or abdominal discomfort, unexplained weight loss, and iron deficiency anemia, should be evaluated promptly with appropriate diagnostic tests. More than two-thirds of patients with

early onset CRC present with gastrointestinal symptoms without another identifiable risk factor.¹⁵ Furthermore, identification of individuals who would benefit from screening before age 45 years owing to strong family CRC history or an inherited cancer syndrome is critically important. Unfortunately, many of these individuals with high risk are being missed.¹⁶ Nearly one-quarter of patients with early onset CRC would have been eligible for earlier screening,⁶ highlighting the importance of family history–based risk stratification.

As the new recommendations^{1–3} are implemented into practice, it will be important to evaluate pragmatic experience with uptake, effectiveness, capacity, and access. A number of open questions about the new CRC screening recommendations remain to be answered. With adoption in clinical practice, the screening community can assess the effectiveness of screening strategies and screening modalities among individuals aged 45 to 49 years. Additionally, there will be an opportunity to think about how screening modalities may be optimized across all age groups to improve efficiency, effectiveness, and adherence in routine clinical settings. It will be useful to evaluate effective approaches to boost screening rates in the younger cohort, as well consider risk stratification for personalized screening based on personal and family history, lifestyle, and patient preferences and behavior.¹⁷

This is an important moment for CRC screening. As policy makers, health care systems, and clinicians respond by designing strategies that expand screening, we urge the thoughtful incorporation of practices to ensure equity in access and facilitate learning from implementation challenges and successes across populations. This is an opportunity to reduce the burden of CRC starting at age 45 years, but it is also a reminder to ensure the benefits are realized equitably.

Conflict of Interest Disclosures:

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