

# Editorials

## *Controversies in Family Medicine*

# Should Routine Screening for Colorectal Cancer Start at 45 Years of Age?

### **Yes: Lowering the Starting Age Is a Settled Issue**

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The American Academy of Family Physicians (AAFP) recently issued an updated colorectal cancer screening guideline that disagrees with the U.S. Preventive Services Task Force (USPSTF) recommendation to begin screening average-risk individuals at 45 years of age. AAFP continues to recommend that screening begin at 50 years of age.<sup>1</sup> This places AAFP at odds with the USPSTF, the American Cancer Society, the National Comprehensive Cancer Network, and the American College of Gastroenterology, which cite similar factors in support of lowering the age to initiate screening.<sup>2-5</sup>

First, and most importantly, the incidence of colorectal cancer and related mortality in individuals younger than 50 years have been increasing for several decades.<sup>6,7</sup> The incidence of colorectal cancer in 45-year-olds today is 30 per 100,000, which is almost identical to the risk in 50-year-olds in 1979 when colorectal cancer screening was first recommended.<sup>2</sup> A recent study derived from the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) program found a dramatic 46% increase in colorectal cancer incidence at age 50 compared with age 49, evidence that many previously undiagnosed cancers are found when screening starts at 50 years of age.<sup>8</sup> Of all U.S. deaths from colorectal cancer in the United

States, 10% occur in individuals diagnosed between 45 and 49 years of age and 13% occur in individuals diagnosed between 50 and 54 years of age.<sup>9</sup> Without intervention, colorectal cancer is projected to become the leading cause of cancer-related deaths in individuals younger than 50 years by 2030.<sup>9</sup>

Second, Stanford's Laudabaum Colon Cancer Screening model and all three models that comprise the Cancer Intervention and Surveillance Modeling Network for colorectal cancer (CISNET-CRC) conclude that beginning screening at 45 years of age is the most efficient strategy based on life-years gained and number of additional colonoscopies needed.<sup>10-12</sup> The independent models that comprise CISNET-CRC are the same models that the USPSTF relied on for their 2016 recommendation to begin screening at 50 years of age. These three models use different assumptions and approaches, and all are validated by real-world evidence, with analyses updated based on current incidence of disease.

Third, evidence indicates that the pathology and polyp-to-cancer sequence in those 45 to 49 years of age are the same as in older individuals. A recent study of the New Hampshire Colonoscopy Registry found a 20% prevalence of polyps in both the 45- to 49-year-old and 50- to 54-year-old populations.<sup>13</sup>

The following is a brief critique of each objection raised in the AAFP statement that disagrees with the USPSTF recommendation to lower the age of screening onset:

- Randomized trials of screening in those 45 to 49 years of age have not been conducted.

The starting age of 50 was originally selected based on the risk of cancer in those patients at that time. Guideline groups have reassessed the optimal starting age based on current data and high-quality models. Conducting a randomized trial comparing different starting ages is a poor use of resources, would take more than a decade to complete, and is not feasible because screening is already shifting to starting at 45 years.

This is one in a series of pro/con editorials discussing controversial issues in family medicine.

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A collection of Editorials: Controversies in Family Medicine published in *AFP* is available at <https://www.aafp.org/afp/pro-con>.

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- The increase in the risk of colorectal cancer in younger individuals may be overestimated or may not be sustained.

SEER data show that the birth cohort effect associated with higher colorectal cancer risk in younger people began decades ago and is continuing.

- The natural history of colorectal cancer may be different in individuals younger than 50 years, which may render screening ineffective.

There is no evidence that colorectal cancers are biologically different or less amenable to screening in patients 45 to 49 years of age compared with those 50 years and older. In Austria, opportunistic colorectal cancer screening with fecal immunochemical testing is offered starting at 40 years of age. Unlike the trends seen in other high-resource nations, colorectal cancer incidence in Austria is increasing up to 39 years of age but declining starting at 40 years of age.<sup>14</sup>

- Models were based on the unrealistic assumption of 100% adherence to screening and follow-up.

The models assume 100% adherence to estimate risk and benefits in the population that participates in screening, recognizing that there is no benefit in people who decide not to be screened. In 2018, actual adherence to colorectal cancer screening in the United States was approximately 68.8% in people 50 years and older and 79.3% in those 65 years and older.<sup>15</sup>

In 2011, the Institute of Medicine published a report on how to write trustworthy clinical guidelines.<sup>16</sup> The USPSTF and the American Cancer Society closely adhere to this process, which includes an independent evidence review; incorporation of all available data, including modeling if applicable; a period of public comment; and a system to grade the quality of evidence. The AAFP did not follow these steps.

The four independent models discussed earlier concur that it is necessary to initiate colorectal cancer screening at 45 years of age in response to the concerning increase in colorectal cancer incidence in patients younger than 50 years and the increase in mortality that now extends through 60 years of age. The number of quality-adjusted life-years lost in younger patients with advanced colorectal cancer is substantially higher than in older individuals, and failing to initiate colorectal cancer screening at 45 years of age will result in thousands of preventable deaths.

The issue of what age to start screening for colorectal cancer has been settled. The National Committee for Quality Assurance has already initiated the process of changing its colorectal cancer screening Healthcare Effectiveness Data and Information Set quality measure to start at 45 years of age.<sup>17</sup> Family physicians should institute this vital change in preventive care without delay.

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## References

1. American Academy of Family Physicians. Clinical preventive service recommendation. Colorectal cancer screening, adults. Accessed September 30, 2021. <https://www.aafp.org/family-physician/patient-care/clinical-recommendations/all-clinical-recommendations/colorectal-cancer-adults.html>
2. Wolf AMD, Fontham ETH, Church TR, et al. Colorectal cancer screening for average-risk adults: 2018 guideline update from the American Cancer Society. *CA Cancer J Clin*. 2018;68(4):250-281.
3. Rex DK, Boland CR, Dominitz JA, et al. Colorectal cancer screening: recommendations for physicians and patients from the U.S. multi-society task force on colorectal cancer. *Am J Gastroenterol*. 2017;112(7):1016-1030.
4. Davidson KW, Barry MJ, Mangione CM, et al. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement [published correction appears in *JAMA*. 2021;326(8):773]. *JAMA*. 2021;325(19):1965-1977.
5. Benson AB, Venook AP, Al-Hawary MM, et al. Colon cancer, version 2.2021, NCCN clinical practice guidelines in oncology. *J Natl Compr Canc Netw*. 2021;19(3):329-359.
6. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin*. 2020;70(1):7-30.
7. Siegel RL, Jakubowski CD, Fedewa SA, et al. Colorectal cancer in the young: epidemiology, prevention, management. *Am Soc Clin Oncol Educ Book*. 2020;40:1-14.
8. Abualkhair WH, Zhou M, Ahnen D, et al. Trends in incidence of early-onset colorectal cancer in the United States among those approaching screening age [published correction appears in *JAMA Netw Open*. 2020;3(2):e201038]. *JAMA Netw Open*. 2020;3(1):e1920407.
9. Rahib L, Wehner MR, Matrisian LM, et al. Estimated projection of US cancer incidence and death to 2040. *JAMA Netw Open*. 2021;4(4):e214708.
10. Ladabaum U, Mannalithara A, Meester RGS, et al. Cost-effectiveness and national effects of initiating colorectal cancer screening for average-risk persons at age 45 years instead of 50 years. *Gastroenterology*. 2019;157(1):137-148.
11. Cancer Intervention and Surveillance Modeling Network. National Cancer Institute. Accessed November 2, 2021. <https://cisnet.cancer.gov>
12. Peterse EFP, Meester RGS, Siegel RL, et al. The impact of the rising colorectal cancer incidence in young adults on the optimal age to start screening: microsimulation analysis I to inform the American Cancer Society colorectal cancer screening guideline. *Cancer*. 2018;124(14):2964-2973.
13. Butterly LF, Siegel RL, Fedewa S, et al. Colonoscopy outcomes in average-risk screening equivalent young adults: data from the New Hampshire colonoscopy registry. *Am J Gastroenterol*. 2021;116(1):171-179.
14. Siegel RL, Torre LA, Soerjomataram I, et al. Global patterns and trends in colorectal cancer incidence in young adults. *Gut*. 2019;68(12):2179-2185.
15. Use of colorectal cancer screening tests. Centers for Disease Control and Prevention. Accessed November 2, 2021. <https://www.cdc.gov/cancer/colorectal/statistics/use-screening-tests-BRFSS.htm>
16. Institute of Medicine. *Clinical Practice Guidelines We Can Trust*. The National Academies Press; 2011.
17. HEDIS® ad hoc public comment period now open. NCQA Blog, October 1, 2021. Accessed September 30, 2021. <https://blog.ncqa.org/hedis-ad-hoc-public-comment-period-now-open> ■