Gastroenterology 2023;165:1280–1291

CLINICAL PRACTICE UPDATES

AGA Clinical Practice Update on Risk Stratification for Colorectal Cancer Screening and Post-Polypectomy Surveillance: Expert Review

Rachel B. Issaka,[1,2] Andrew T. Chan,[3] and Samir Gupta[4,5]

[1]Public Health Sciences and Clinical Research Divisions, Fred Hutchinson Cancer Center, Seattle, Washington; [2]Division of Gastroenterology, University of Washington School of Medicine, Seattle, Washington; [3]Clinical and Translational Epidemiology Unit, Division of Gastroenterology, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts; [4]Division of Gastroenterology, Department of Medicine, University of California San Diego, La Jolla, California; and [5]Section of Gastroenterology, Jennifer Moreno Department of Medical Affairs Medical Center, San Diego, California

DESCRIPTION: Since the early 2000s, there has been a rapid decline in colorectal cancer (CRC) mortality, due in large part to screening and removal of precancerous polyps. Despite these improvements, CRC remains the second leading cause of cancer deaths in the United States, with approximately 53,000 deaths projected in 2023. The aim of this American Gastroenterological Association (AGA) Clinical Practice Update Expert Review was to describe how individuals should be risk-stratified for CRC screening and post-polypectomy surveillance and to highlight opportunities for future research to fill gaps in the existing literature. **METHODS:** This Expert Review was commissioned and approved by the American Gastroenterological Association (AGA) Institute Clinical Practice Updates Committee (CPUC) and the AGA Governing Board to provide timely guidance on a topic of high clinical importance to the AGA membership, and underwent internal peer review by the CPUC and external peer review through standard procedures of *Gastroenterology*. These Best Practice Advice statements were drawn from a review of the published literature and from expert opinion. Because systematic reviews were not performed, these Best Practice Advice statements do not carry formal ratings regarding the quality of evidence or strength of the presented considerations. **BEST PRACTICE ADVICE 1:** All individuals with a first-degree relative (defined as a parent, sibling, or child) who was diagnosed with CRC, particularly before the age of 50 years, should be considered at increased risk for CRC. **BEST PRACTICE ADVICE 2:** All individuals without a personal history of CRC, inflammatory bowel disease, hereditary CRC syndromes, other CRC predisposing conditions, or a family history of CRC should be considered at average risk for CRC. **BEST PRACTICE ADVICE 3:** Individuals at average risk for CRC should initiate screening at age 45 years and individuals at increased risk for CRC due to having a first-degree relative with CRC should initiate screening 10 years before the age at diagnosis of the youngest affected relative or age 40 years, whichever is earlier. **BEST PRACTICE ADVICE 4:** Risk stratification for initiation of CRC screening should be based on an individual's age, a known or suspected predisposing hereditary CRC syndrome, and/or a family history of CRC. **BEST PRACTICE ADVICE 5:** The decision to continue CRC screening in individuals older than 75 years should be individualized, based on an assessment of risks, benefits, screening history, and comorbidities. **BEST PRACTICE ADVICE 6:** Screening options for individuals at average risk for CRC should include colonoscopy, fecal immunochemical test, flexible sigmoidoscopy plus fecal immunochemical test, multitarget stool DNA fecal immunochemical test, and computed tomography colonography, based on availability and individual preference. **BEST PRACTICE ADVICE 7:** Colonoscopy should be the screening strategy used for individuals at increased CRC risk. **BEST PRACTICE ADVICE 8:** The decision to continue post-polypectomy surveillance for individuals older than 75 years should be individualized, based on an assessment of risks, benefits, and comorbidities. **BEST PRACTICE ADVICE 9:** Risk-stratification tools for CRC screening and post-polypectomy surveillance that emerge from research should be examined for real-world effectiveness and cost-effectiveness in diverse populations (eg, by race, ethnicity, sex, and other sociodemographic factors associated with disparities in CRC outcomes) before widespread implementation.

Keywords: Colorectal Cancer; CRC; First-Degree Relative; Second-Degree Relative; Third-Degree Relative; Fecal Immunochemical Test; FIT.

CLINICAL PRACTICE UPDATE

BEST PRACTICE ADVICE STATEMENTS

The aim of this Clinical Practice Update from the Clinical Practice Update Committee of the American Gastroenterological Association was to describe how individuals should be risk-stratified for colorectal cancer (CRC) screening and post-polypectomy surveillance and to highlight opportunities for future research that fill gaps in the existing literature. The target health care audience is all gastroenterologists, primary care providers, and other members of the health care team involved in ensuring individuals are up to date with CRC screening or post-polypectomy surveillance. The target patient population is adults eligible for CRC screening and their families.

Abbreviations used in this paper: CRC, colorectal cancer; CT, computed tomography; FDR, first-degree relative; FIT, fecal immunochemical test; HR, hazard ratio; RCT, randomized controlled trial; RR, relative risk.

Most current article

0016-5085
https://doi.org/10.1053/j.gastro.2023.06.033

Best Practice Advice 1: All individuals with a first-degree relative (FDR) (defined as a parent, sibling, or child) who was diagnosed with CRC, particularly before the age of 50 years, should be considered at increased risk for CRC.

Best Practice Advice 2: All individuals without a personal history of CRC, inflammatory bowel disease, hereditary CRC syndromes, other CRC predisposing conditions, or a family history of CRC should be considered at average risk for CRC.

Most CRCs are sporadic and risk increases with older age.[1] Individuals without a personal or family history of colorectal neoplasia are considered at average risk for CRC. These individuals have an approximate 4% lifetime risk of being diagnosed with CRC,[2] thus screening is recommended for all average-risk adults. Approximately 20% of CRCs are associated with familial clustering and approximately 5% are due to predisposing hereditary CRC syndromes.[3,4] Hereditary CRC syndromes, such as Lynch syndrome and polyposis syndromes, confer increased CRC risk (covered elsewhere[5,6]), and even in the absence of an established hereditary syndrome, a family history of CRC increases an individual's risk of CRC. This risk differs by the degree of relation between an individual and relatives, the number of relatives diagnosed with CRC, the age of the individual, and the age of the relatives at the time of diagnosis.[7,8]

In meta-analyses published between 2001 and 2006, the pooled relative risk (RR) of developing CRC if at least 1 FDR was affected ranged from 2.24 (95% CI, 2.06–2.43)[9] to 2.26 (95% CI, 1.86–2.73).[10] A 2018 meta-analysis reported a pooled RR of 1.76 (95% CI, 1.57–1.97)[11] and a 2019 systematic review and meta-analysis by Roos et al[12] that stratified RR by study design, also reported a more modest overall risk estimate, particularly in cohort studies compared with case–control studies, than the prior meta-analyses. This may reflect how case–control studies may be more prone to recall bias than cohort studies, which tend to exaggerate association. However, notably in Roos et al,[12] results stratified by age of affected FDR showed that risk of CRC was substantially higher when the FDR was younger than age 50 years at diagnosis, regardless of study design, with an RR of 3.57 (95% CI, 1.07–11.85) in pooled case–control studies and 3.26 (95% CI, 2.82–3.77) in pooled cohort studies. In contrast, when the FDR was older than 50 years at diagnosis, the RR associated with family history was more modest in both (in pooled case-control studies: RR, 1.88; 95% CI, 1.66–2.13 and pooled cohort studies: 1.83; 95% CI, 1.55–2.16).[12]

These data were not incorporated in the most recent guidelines by the American College of Gastroenterology and the National Comprehensive Cancer Network (Table 1), but suggest a potential role for less intensive screening and perhaps increased use of noninvasive screening modalities for individuals with an FDR with CRC, particularly for those in whom cancer was diagnosed after the age of 50 years in the FDR. The rationale for our Best Practice Advice statement to consider more intensive screening for all individuals with an FDR with CRC, irrespective of the age at onset of the affected relative, is based on several factors. First, in clinical practice, most individuals do not know the exact age that their relatives were diagnosed with CRC and it is cumbersome to obtain this information. Thus, screening recommendations that rely on this information could be challenging to implement in real-world clinical settings. As discussed below, more data are needed to examine the yield of advanced neoplasia in adults between the ages of 40 and 50 years based on family history. In addition, the extent to which risk estimates have varied across meta-analyses due to variation in the time periods of the included studies is unclear. The natural history of CRC likely differs by time period based on variation in secular trends in the prevalence of screening, as well as other CRC risk factors (eg, intake of aspirin, body mass index, and dietary habits). For these reasons, we suggest continuing to consider any individual with a family history of CRC, irrespective of age of the family member, as high risk, warranting more intensive screening until additional data are available (Figure 1). Finally, we recognize that few studies have assessed an individual's risk of CRC when a second-degree relative or third-degree relative is affected. Emerging data, including a study by Taylor et al,[13] have suggested that the most important predictor of CRC was the number of affected FDRs, and having a single FDR in combination with a second-degree relative or third-degree relative could also increase an individual's risk for CRC by more than 2-fold.

As mentioned previously, few studies have examined the association between a family history of any adenomatous polyps and CRC risk.[14] In a population CRC screening program, among individuals with an abnormal fecal immunochemical test (FIT) result, the RR of CRC for individuals with an FDR with any adenomatous polyp was 4.36 (95% CI, 1.60–10.21) compared with individuals without FDR with any adenomas.[15] Another study found that individuals with an FDR with adenomas ≥1 cm were 2-fold more likely to be diagnosed with CRC or large adenomas (≥1 cm) compared with individuals without such family history (odds ratio, 2.27; 95% CI, 1.01–5.09).[16] In the National Polyp Study, FDR of individuals with any adenomas had an almost 2-fold increased risk for CRC compared with spouse controls (RR, 1.78; 95% CI, 1.18–2.67).[17] Finally, in a population-based study from Sweden, having an FDR with any type of colorectal polyp was associated with a 1.4-fold higher risk of CRC after adjusting for family history and other factors (odds ratio, 1.40; 95% CI, 1.35 to 1.45). However, study limitations include an unexpected association between family history of hyperplastic polyps and CRC risk, as well as potential bias in ascertainment of family history of polyps based on colonoscopy exposure in the population.[18] In terms of yield of colonoscopy among relatives of individuals with advanced adenoma, Ng et al[19] concluded in a prospective study that the prevalence of advanced adenomas was 11.5% among siblings of patients with advanced adenomas compared with 2.5% among siblings of individuals without advanced adenomas (odds ratio, 6.05; 95% CI, 2.74–13.36).

Taken together, these data showed how an individual's family history of CRC (particularly when an FDR is diagnosed before the age of 50 years) and/or any adenomas (particularly those ≥1 cm) are important in risk-based CRC

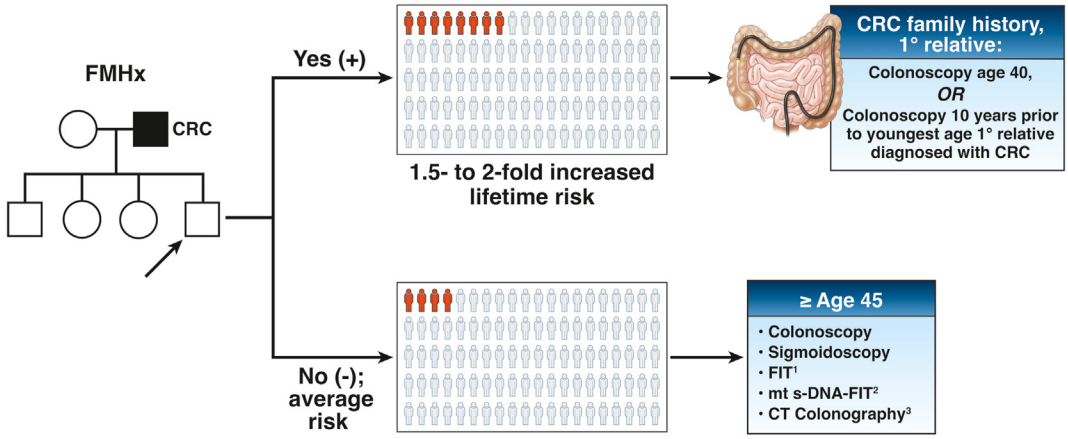
Table 1. Samples of Practice Guidelines Recommending Initiation of Colorectal Cancer Screening in Average-Risk Populations and Increased-Risk Groups Based on Family History of Colorectal Cancer

Variable	Criteria	Recommendation	Synthesis
Sample of practice guidelines recommending initiation of CRC screening in average-risk populations			
American Cancer Society, 2018[2]	Average-risk adults in good health with a life expectancy of more than 10 y	Begin screening at age 45 y with any test (qualified recommendation) Screen adults between ages 50 and 75 y with any test (strong recommendation)	In average-risk adults, all practice guidelines gave a strong recommendation to begin CRC screening at age 50 y with any test Most practice guidelines gave a weak or qualified recommendation to begin CRC screening in average-risk adults at age 45 y with any test Two practice guidelines (American College of Gastroenterology and USMSTF) recommended a tiered approach of screening tests to use, with tier 1 tests including a colonoscopy every 10 y or FIT every 1 y
American College of Gastroenterology, 2021[7]	Average-risk adults	Begin screening adults between ages 45 and 49 y (conditional recommendation) Screen adults between ages 50 and 75 y (strong recommendation) Colonoscopy every 10 y or FIT every 1 y as primary screening modalities (strong recommendation) Flexible sigmoidoscopy every 5–10 y, multitarget stool DNA test every 3 y, CT colonography every 5 y, or colon capsule every 5 y (conditional recommendation)	
American College of Physicians, 2019[96]	Average-risk adults in good health with a life expectancy of more than 10 y	Screen adults between ages of 50 and 75 y with any test	
National Comprehensive Cancer Network, 2022	Average-risk adults	Begin screening at age 45 y with any test	
USMSTF,[a] 2022[30]	Average-risk adults	Begin screening at age 45 y (weak recommendation)	
	Average-risk adults	Begin screening at age 50 y if no prior screening completed (strong recommendation)	
US Preventive Services Task Force, 2021[29]	Asymptomatic, average-risk adults	Screen adults between ages 50 and 75 y (Grade A) Begin screening adults between ages 45 and 49 y (Grade B) Selectively screen adults aged 76–85 y (Grade C)	

Table 1. Continued

Variable	Criteria	Recommendation	Synthesis
Sample of practice guidelines recommending initiation of CRC screening in increased-risk groups based on family history of CRC			
American College of Gastroenterology, 2021[7]	CRC or advanced adenoma in 1 FDR at age <60 y or CRC or advanced adenoma in 2 or more FDRs at any age	Colonoscopy at age 40 y or 10 y before earliest diagnosis of CRC, repeat every 5 y (conditional recommendation)	In adults with an increased risk of CRC based on a family history of CRC, all practice guidelines gave a strong recommendation to begin CRC screening at age 40 y or 10 y before earliest diagnosis of CRC with colonoscopy every 5 to 10 y In adults with a family history of advanced adenoma, most practice guidelines recommended to begin CRC screening at age 40 y or 10 y before earliest diagnosis of adenoma with any test
	CRC or advanced adenoma in single FDR diagnosed at 60 y or older	Begin screening at age 40 y or 10 y before earliest diagnosis of CRC with any test (conditional recommendation)	
Canadian Association of Gastroenterology, endorsed by American Gastroenterological Association, 2018[97]	CRC in 2 or more FDRs	Colonoscopy every 5 y at age 40 y or 10 y younger than age of diagnosis of earliest diagnosed FDR, whichever is earlier	
	CRC in 1 FDR	Colonoscopy every 5–10 y at age 40–50 y or 10 y younger than age of diagnosis of FDR, whichever is earlier FIT every 1–2 y is suggested as second-line option	
	1 or more FDR with documented advanced adenoma	No recommendation for a preferred test Colonoscopy or FIT are both options Colonoscopy every 5–10 y at age 40–50 y or 10 y younger than age of diagnosis of FDR, whichever is earlier FIT every 1–2 y is suggested as second-line option	
National Comprehensive Cancer Network, 2022	CRC 1 or more FDR with CRC at any age	Colonoscopy every 5 y or per colonoscopy findings beginning at age 40 y or 10 y before earliest diagnosis of CRC	
	CRC in second- and third-degree relatives at any age	Colonoscopy every 10 y or per colonoscopy findings beginning at age 45 y	
	Advanced adenoma in FDR at any age	Colonoscopy every 5–10 y or per colonoscopy findings beginning at age 40 y or at age of onset of adenoma in relative, whichever is first	
USMSTF, 2017[31]	CRC or advanced adenoma in 2 FDRs at any age or CRC or advanced adenoma in a single FDR younger than 60 y	Colonoscopy every 5 y beginning 10 y before age at FDR diagnosis or age 40 y	
	CRC or advanced adenoma in single FDR diagnosed a *t* 60 y or older	Begin screening at age 40 y with any test	

USMSTF, US Multi-Society Task Force on Colorectal Cancer.
[a]The USMSTF represents the American Gastroenterological Association, the American Society for Gastrointestinal Endoscopy, and the American College of Gastroenterology.



[1]Fecal Immunochemical Test (FIT)
[2]Multi-target stool DNA-FIT
[3]Computed Tomography (CT) Colonography

Figure 1. Recommended CRC screening test options based on family history (FMHx) of CRC.

screening recommendations. Yet, family CRC and adenoma history are not consistently collected or documented,[20] often lack the age at diagnosis of the affected individual, and the accuracy of details provided has been called into question.[21–23] This presents an opportunity to increase awareness of family history knowledge in the general population and to standardize how physicians and other health care professionals collect and document family history.[20]

Best Practice Advice 3: Individuals at average risk for CRC should initiate screening at age 45 years and individuals at increased risk for CRC due to having an FDR with CRC should initiate screening 10 years before the age at diagnosis of the youngest affected relative or age 40 years, whichever is earlier.

Best Practice Advice 4: Risk stratification for initiation of CRC screening should be based on an individual's age, a known or suspected predisposing hereditary CRC syndrome, and/or a family history of CRC.

In contrast to the declining incidence of CRC in people older than 50 years, the incidence of CRC in people younger than 50 years, also known as "early-onset CRC," has been increasing. It is estimated that over the next decade, early-onset CRC will account for 10% of colon cancers and 25% of rectal cancers.[24,25] Due to the absence of randomized controlled trials (RCTs) examining the effectiveness of lowering the age at CRC screening, recommendations to date have largely been supported by decision analytic models. Results of a microsimulation analysis that incorporated the recent increase in CRC incidence among younger individuals in the United States showed that starting a 10-yearly colonoscopy, annual FIT, or 5-yearly flexible sigmoidoscopy at the age of 45 years resulted in the most optimal balance of burden to benefit of screening.[26] Results of another modeling analysis showed that initiating screening colonoscopy at age 45 years instead of 50 years cost $33,900 per quality-adjusted life-year gained, and initiating FIT at 45 years instead of 50 years cost $7700 per quality-adjusted life-year gained.[27] A cohort study of US women also supported earlier initiation of endoscopy screening for CRC. Compared with no endoscopy, undergoing lower endoscopy was associated with a significantly lower risk of incident CRC when age at initiation was before age 45 years (hazard ratio [HR], 0.37; 95% CI, 0.26–0.53), 45–49 years (HR, 0.43; 95% CI, 0.29–0.62), 50–54 years (HR, 0.47; 95% CI, 0.35–0.62), and 55 years or older (HR, 0.46; 95% CI, 0.30–0.69).[28] Compared with no endoscopy, initiation of endoscopy before 50 years of age was also associated with a reduced risk of CRC diagnosed before 55 years of age (younger than 45 years: HR, 0.45; 95% CI, 0.29–0.70; 45–49 years: HR, 0.43; 95% CI, 0.24–0.76). Taken together, the US Multi-Society Task Force on Colorectal Cancer, the US Preventive Services Task Force, and the American Cancer Society recommend (with varying strength) initiating CRC screening in individuals at average risk for CRC at the age of 45 years, while acknowledging limited evidence.[29–32]

As discussed in Best Practice Advice statements 1 and 2, individuals with a family history of CRC and/or adenomas have an increased risk of CRC compared with individuals without such a history.[8,17] Empirical evidence on when to initiate screening in a population with a family history of CRC is limited. Results of a microsimulation analysis showed that screening people with 1 FDR affected with CRC every 3 years beginning at the age of 40 years was the most cost-effective.[33] An analysis conducted according to the age at diagnosis of affected relatives suggested that CRC screening should begin at age 30 years for those with 1 affected FDR diagnosed before age 45 years and at age 20 years for those with 2 affected FDRs before the age of 50 years or 1 affected FDR and 1 second-degree relative diagnosed before the age of 50 years.[34] Fewer data are available to inform screening strategies for individuals with a family history of polyps. An earlier-referenced observational study supported earlier screening for CRC in individuals with a family history of colorectal polyps by showing increased risk of CRC, particularly early-onset CRC, in those with an FDR diagnosed with a polyp at a younger age.[18]

The age to initiate screening according to family history of CRC could be optimized based on the number of affected family members, age at diagnosis of the affected relatives, as well as the 10-year cumulative incidence of CRC according to age within a specific source population (eg, country). However, in the absence of widely available risk calculators developed for such risk-adapted screenings, a simplified approach to consider is initiating screening approximately 10 years before the age of diagnosis of the youngest affected relative or at age 40 years.[28]

There is growing interest in tailoring individual screening recommendations to include race, smoking history, and other lifestyle factors in addition to the factors discussed above. Despite promising data, studies that validate findings to date across large diverse populations are still needed. Based on current evidence, risk stratification for initiation of CRC screening should be based on age, family history, or other CRC predisposing conditions. Other conditions that predispose to CRC include, but are not limited to, inflammatory bowel diseases with colonic involvement (ie, ulcerative colitis and Crohn's disease); hereditary CRC syndromes, including serrated polyposis syndrome, familial adenomatous polyposis, MYH-associated polyposis, and Lynch syndrome; primary sclerosing cholangitis; and many others. These populations are not considered in this Clinical Practice Update and are discussed elsewhere.[35,36]

Best Practice Advice 5: The decision to continue CRC screening in individuals older than 75 years should be individualized, based on an assessment of risks, benefits, screening history, and comorbidities.

Risk–benefit assessment is important when making decisions for CRC screening in individuals older than 75 years. Less intensive screening history, less severe comorbidities, and a greater number of risk factors for CRC are each associated with cost-effective screening.[37] Life expectancy and lag time in the progression of a polyp to CRC or CRC-related death also need to be compared to determine whether someone will benefit from the removal of polyps.

There have been no RCTs that have enrolled individuals older than 75 years to inform the optimal age to stop CRC screening. In a prospective cohort study in the United States that evaluated the risk and effectiveness of screening colonoscopy among Medicare beneficiaries without previous screening, the absolute reduction in 8-year risk of CRC was −0.42% (95% CI, −0.24% to −0.63%) in individuals aged 70–74 years and −0.14% (95% CI, −0.41% to 0.16%) in individuals aged 75–79 years. The 30-day risk for the adverse event after colonoscopy was 5.6 and 10.3 events per 1000 in individuals aged 70–74 years and 75–79 years, respectively.[38] Another prospective cohort study among US women reported reduced risks of CRC incidence (multivariable-adjusted HR, 0.61; 95% CI, 0.46 to 0.78) and CRC-related mortality (HR, 0.60; 95% CI, 0.46 to 0.78), regardless of screening history in individuals who underwent sigmoidoscopy or colonoscopy after 75 years of age.[39] However, the protective effect after 75 years of age was not observed in individuals with 3 or more comorbidities among cardiovascular disease (myocardial infarction or stroke), hypertension, hypercholesterolemia, and diabetes (HR of CRC incidence, 0.70; 95% CI, 0.44 to 1.10; HR of CRC mortality, 1.17; 95% CI, 0.57 to 2.43).[39]

A microsimulation analysis evaluated the benefits and harms of biennial FIT according to individuals' screening history and comorbidities.[40] It found that individuals who were previously unscreened and without comorbidities could undergo an initial screening through age 90 years (women) and age 80 years (men), with benefits outweighing risks. In contrast, those with a history of adherence to recommended screening guidelines and severe comorbidities should stop screening at age 66 years or younger.[40]

Best Practice Advice 6: Screening options for individuals at average risk for CRC should include colonoscopy, FIT, flexible sigmoidoscopy plus FIT, multitarget stool DNA-FIT, and computed tomography (CT) colonography, based on availability and individual preference.

Colonoscopy has a high sensitivity for cancer and precancerous lesions and enables screening and treatment simultaneously. Evidence on the effectiveness of colonoscopy screening in reducing CRC incidence and mortality is derived primarily from observational studies.[41,42] The Nordic-European Initiative on Colorectal Cancer (NORDICC), the only RCT of screening colonoscopy to date, included 84,584 participants aged 55–64 years and compared those who were invited to get a screening colonoscopy with those who underwent usual care.[43] Although the risk of CRC at 10 years was lower in participants who were invited to undergo colonoscopy (RR, 0.82; 95% CI, 0.70–0.93), the risk of CRC-related death did not differ between the 2 groups (RR, 0.90; 95% CI, 0.62–1.16). Notably, only 42% of individuals invited for colonoscopy completed the procedure, and there was a greater reduction in the risk of CRC (RR, 0.69; 95% CI, 0.55–0.83) and related mortality (RR, 0.50; 95% CI, 0.27–0.44) among those who completed a colonoscopy.

The superiority of colonoscopy in terms of sensitivity for both CRC and precancerous lesions is widely accepted, but compliance is lower than with alternative noninvasive methods.[44] As such, screening methods including FIT, flexible sigmoidoscopy plus FIT, and multitarget stool DNA-FIT are chosen based on availability of screening modalities and patient preferences. In rare circumstances, patients might also complete screening by CT colonography and colon capsule endoscopy. There is strong RCT-based evidence that sigmoidoscopy, and additional empirical evidence that FIT[45–51] and flexible sigmoidoscopy plus FIT[52–56] decrease CRC incidence and related mortality. Multitarget stool DNA-FIT, a stool-based test enhanced by molecular biomarkers for early CRC detection, has a higher sensitivity for detecting CRC (92%) and advanced precancerous lesions than conventional FIT (74%), albeit with a lower specificity.[57,58] However, a cost-effectiveness analysis showed that annual FIT is more effective and less costly than multitarget stool DNA-FIT.[59] Additional screening options that have been studied include CT colonography[60,61] and colon capsule endoscopy,[62,63] which demonstrate approximately 80% sensitivity for detecting polyps measuring ≥6 mm. However, empirical data on the impact of these tests on CRC incidence and mortality are limited. Among available

options, the US Preventive Services Task Force recommends colonoscopy, annual FIT, multitarget stool DNA-FIT, sigmoidoscopy, and CT colonography as options, and the US Multi-Society Task Force on Colorectal Cancer recommends these plus capsule endoscopy as an option.

Altogether, there are several choices of screening for CRC that have shown benefits in reducing the risk of CRC incidence and related death. Many guidelines do not recommend one screening method over the other and suggest decision making based on an individual's risk and preference.[7,29,31,32] In the future, we anticipate the completion of trials comparing the effectiveness of colonoscopy with that of FIT.

Best Practice Advice 7: Colonoscopy should be the screening strategy used for individuals at increased CRC risk.

Colonoscopy is the recommended strategy for individuals at increased CRC risk based on its high sensitivity for polyps and CRC, and favorable balance of risks vs benefits.[64] Groups at increased risk for CRC (eg, family history, predisposing hereditary syndromes, and inflammatory bowel diseases) might have more neoplasia detected by the most sensitive test. In contrast, because of higher observed prevalence of advanced polyps and CRC, use of less sensitive tests for screening might result in more missed neoplasia. Although relative sensitivity of colonoscopy vs other tests is well established, few studies have compared the effectiveness of colonoscopy vs other tests for screening individuals at increased risk. In an intention-to-screen analysis, yield for advanced neoplasia was found to be noninferior for individuals with an FDR with CRC randomized to annual FIT over 3 rounds vs 1-time colonoscopy. The per-protocol analysis noted a nonstatistically significant 1.5-fold increased chance of advanced neoplasia detection in the colonoscopy group.[65] Pending additional studies, colonoscopy remains the primary recommended screening strategy for individuals at increased risk based on family history. For individuals unwilling or unable to complete colonoscopy, alternative screening with FIT or another modality may be considered, as some patients with a family history may prefer noncolonoscopy tests.[66]

Best Practice Advice 8: The decision to continue post-polypectomy surveillance for individuals older than 75 years should be individualized, based on an assessment of risks, benefits, and comorbidities.

Surveillance colonoscopy is routinely recommended post polypectomy, with the goal of reducing risk for incident and fatal CRC.[67] However, for some adults 75 years and older ("older adults") risks of surveillance colonoscopy might outweigh the benefits. Harms associated with colonoscopy increase dramatically with age, with 3.8%–6.8% of older adults experiencing an emergency visit or hospitalization within 30 days of colonoscopy.[68–70] Older vs younger adults have a 1.5- to 3.7-fold increase in post-colonoscopy complications[71–73] and older adults are also less likely to live long enough to benefit from surveillance colonoscopy, due to competing, non-CRC mortality risks. As a result of sparse evidence regarding the benefit of post-polypectomy surveillance for older adults, recommendations for surveillance colonoscopy are not well defined. In 2020, the US Multi-Society Task Force on Colorectal Cancer did not offer specific recommendations for or against surveillance for older adults, but noted, ". . . more research is needed to determine whether the potential cancer prevention and early detection benefits of surveillance outweigh immediate procedure-related risks for individuals older than age 75 . . .."[67] While awaiting new evidence on the risk–benefit profile of surveillance for older adults, a pragmatic approach should consider the potential risks, benefits, and comorbidities. Clinicians should recognize and share with patients that risks for colonoscopy increase with age and consider neoplasia risk based on prior polyp findings. Accumulating evidence notes that individuals with a history of 1–2 adenomas <1 cm in size have a small (1.3-fold) increased risk for incident CRC, and no significant increased risk for fatal CRC.[74]

The concept of "lag time to benefit," defined as the time between surveillance colonoscopy and when reduced CRC risk would be realized, should also be considered.[75] Exposure to colonoscopy, compared with no exposure, requires at least 5 years to result in subsequent reduced risk for incident and fatal CRC.[43,76,77] For an older adult with life expectancy estimated to be fewer than 5 years, based on a risk calculator (eg, www.eprognosis.org) that takes into account age, sex, comorbidity, and frailty measures, lag time to benefit is likely too long for surveillance colonoscopy to be beneficial.[78] Patients and clinicians may find it difficult to de-implement cancer screening and surveillance.[79–81] Along with shared decision making with risks and benefits, using language such as, "this test would not help you live longer" and emphasizing that other health problems should take priority, may be one approach to communicate the message that surveillance is unlikely to be beneficial.[82,83]

Best Practice Advice 9: Risk-stratification tools for CRC screening and post-polypectomy surveillance that emerge from research should be examined for real-world effectiveness and cost-effectiveness in diverse populations (eg, by race, ethnicity, sex, and other sociodemographic factors associated with disparities in CRC outcomes) before widespread implementation.

Risk stratification models, incorporating demographic factors, lifestyle behaviors, and genetic factors have shown promise for identifying individuals at higher vs lower CRC risk.[84–87] These models have been proposed as strategies to inform age to initiate CRC screening, selection of CRC screening strategies, and time intervals for surveillance colonoscopy.[34] Absence of prospective studies showing impact; a lack of research on how best to incorporate models guiding screening initiation age and strategy selection (some of which require genetic analyses) into usual practice; and absence of validation within diverse populations, with diversity defined by race, ethnicity, and sociodemographic factors, are the main limitations to incorporation into clinical practice. Validation within diverse racial and ethnic populations is critical for models that include genetic factors, because genetic discovery studies have focused largely on individuals with European ancestry, and because risk-relevant genetic factors may vary

Table 2. Research Priorities to Improve Risk Stratification for Colorectal Cancer Screening and Post-Polypectomy Surveillance

Research priority
Evaluate interventions that increase awareness about family history knowledge in the general population and standardize how health care professionals collect and document family history, and implement family history–based guidelines for screening
Compare effectiveness of colonoscopy with other tests for screening individuals at increased risk for CRC based on family history or other risk factors
Conduct studies with individuals older than 75 y to inform when to stop screening and post-polypectomy surveillance
Validate risk-stratification models for screening and post-polypectomy surveillance that include race, smoking history, and other lifestyle factors
Validate risk-stratification models across large diverse populations (eg, by ancestry, race, ethnicity, and other sociodemographic factors)
Determine best practices and implementation challenges (eg, acceptability and feasibility) of risk-stratification models in clinical practice across multiple stakeholder groups (eg, patients, providers, and health care systems)
Evaluate clinical utility and cost-effectiveness of risk-prediction models in different populations (eg, average-risk vs high-risk, opportunistic vs population-based screening)
Leverage artificial intelligence to incorporate factors that contribute to post-polypectomy surveillance risk, including colonoscopy quality factors, genetics, and colon age
Conduct studies that evaluate the association between family history of colorectal polyps and CRC risk, and utility of earlier screening based on family history of polyps and type of polyps

according to individual's origin of genetic ancestry. Although many studies differentiate individuals by race and ethnicity, which may capture some information about the likely presence of certain genetic variants, ancestry is a better predictor and should be captured in validation studies.[88]

With respect to post-polypectomy surveillance models, encouraging results for model performance have been seen, but performance does not appear sufficiently superior for risk stratification based on current guidelines that only consider polyp findings.[89–93] Future research taking into account factors that contribute to risk, including colonoscopy quality factors[91] (eg, colonoscopist adenoma detection rate, completeness of examination, and polypectomy), genetic factors,[94] assessment of biologic factors, and advances in artificial intelligence analytics may help improve prediction, but require further study.[95] Prospective studies demonstrating clinical utility, as well as cost-effectiveness analyses, are also needed to help understand the best use of risk prediction models for informing CRC screening and post-polypectomy surveillance decisions.

Conclusions

In summary, most CRCs are sporadic and risk increases with older age. Screening is recommended for average-risk adults starting at age 45 years with several available tests. For individuals with a family history of CRC, screening is recommended 10 years before the age at diagnosis of the youngest affected relative or age 40 years with colonoscopy. Based on current evidence, risk stratification for initiating CRC screening or surveillance should be based on age, family history, predisposing hereditary CRC syndromes, prior screening, or other CRC predisposing conditions. Future studies might lead to the incorporation of other factors in risk stratification for CRC screening and surveillance (Table 2).

References

1. Rim SH, Seeff L, Ahmed F, et al. Colorectal cancer incidence in the United States, 1999-2004: an updated analysis of data from the National Program of Cancer Registries and the Surveillance, Epidemiology, and End Results Program. Cancer 2009;115:1967–1976.
2. American Cancer Society. Colorectal Cancer Facts & Figures 2020-2022. Available at: https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/colorectal-cancer-facts-and-figures/colorectal-cancer-facts-and-figures-2020-2022.pdf. Accessed December 1, 2022.
3. Burt R, Neklason DW. Genetic testing for inherited colon cancer. Gastroenterology 2005;128:1696–1716.
4. Kastrinos F, Syngal S. Inherited colorectal cancer syndromes. Cancer J 2011;17:405–415.
5. Rubenstein JH, Enns R, Heidelbaugh J, et al. American Gastroenterological Association Institute Guideline on the Diagnosis and Management of Lynch Syndrome. Gastroenterology 2015;149:777–782; quiz e16–e17.
6. Syngal S, Brand RE, Church JM, et al. ACG clinical guideline: genetic testing and management of hereditary gastrointestinal cancer syndromes. Am J Gastroenterol 2015;110:223–262; quiz 263.
7. Shaukat A, Kahi CJ, Burke CA, et al. ACG Clinical Guidelines: Colorectal Cancer Screening 2021. Am J Gastroenterol 2021;116:458–479.
8. Fuchs CS, Giovannucci EL, Colditz GA, et al. A prospective study of family history and the risk of colorectal cancer. N Engl J Med 1994;331:1669–1674.

9. Butterworth AS, Higgins JP, Pharoah P. Relative and absolute risk of colorectal cancer for individuals with a family history: a meta-analysis. Eur J Cancer 2006; 42:216–227.
10. Baglietto L, Jenkins MA, Severi G, et al. Measures of familial aggregation depend on definition of family history: meta-analysis for colorectal cancer. J Clin Epidemiol 2006;59:114–124.
11. Wong MCS, Chan CH, Lin J, et al. Lower relative contribution of positive family history to colorectal cancer risk with increasing age: a systematic review and meta-analysis of 9.28 million individuals. Am J Gastroenterol 2018;113:1819–1827.
12. Roos VH, Mangas-Sanjuan C, Rodriguez-Girondo M, et al. Effects of family history on relative and absolute risks for colorectal cancer: a systematic review and meta-analysis. Clin Gastroenterol Hepatol 2019; 17:2657–2667.e9.
13. Taylor DP, Burt RW, Williams MS, et al. Population-based family history-specific risks for colorectal cancer: a constellation approach. Gastroenterology 2010; 138:877–885.
14. Imperiale TF, Ransohoff DF. Risk for colorectal cancer in persons with a family history of adenomatous polyps: a systematic review. Ann Intern Med 2012;156:703–709.
15. Nakama H, Zhang B, Fukazawa K, et al. Family history of colorectal adenomatous polyps as a risk factor for colorectal cancer. Eur J Cancer 2000;36:2111–2114.
16. Cottet V, Pariente A, Nalet B, et al. Colonoscopic screening of first-degree relatives of patients with large adenomas: increased risk of colorectal tumors. Gastroenterology 2007;133:1086–1092.
17. Winawer SJ, Zauber AG, Gerdes H, et al. Risk of colorectal cancer in the families of patients with adenomatous polyps. National Polyp Study Workgroup. N Engl J Med 1996;334:82–87.
18. Song M, Emilsson L, Roelstraete B, et al. Risk of colorectal cancer in first degree relatives of patients with colorectal polyps: nationwide case-control study in Sweden. BMJ 2021;373:n877.
19. Ng SC, Lau JY, Chan FK, et al. Risk of advanced adenomas in siblings of individuals with advanced adenomas: a cross-sectional study. Gastroenterology 2016; 150:608–616; quiz e16–e17.
20. Gupta S, Bharti B, Ahnen DJ, et al. Potential impact of family history-based screening guidelines on the detection of early-onset colorectal cancer. Cancer 2020; 126:3013–3020.
21. Murff HJ, Greevy RA, Syngal S. The comprehensiveness of family cancer history assessments in primary care. Community Genet 2007;10:174–180.
22. Mitchell RJ, Brewster D, Campbell H, et al. Accuracy of reporting of family history of colorectal cancer. Gut 2004; 53:291–295.
23. Mitchell RJ, Campbell H, Farrington SM, et al. Prevalence of family history of colorectal cancer in the general population. Br J Surg 2005;92:1161–1164.
24. Araghi M, Soerjomataram I, Bardot A, et al. Changes in colorectal cancer incidence in seven high-income countries: a population-based study. Lancet Gastroenterol Hepatol 2019;4:511–518.
25. REACCT Collaborative, Zaborowski AM, Abdile A, et al. Characteristics of early-onset vs late-onset colorectal cancer: a review. JAMA Surg 2021;156:865–874.
26. 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; 124:2964–2973.
27. 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; 157:137–148.
28. Ma W, Wang M, Wang K, et al. Age at initiation of lower gastrointestinal endoscopy and colorectal cancer risk among US women. JAMA Oncol 2022;8:986–993.
29. US Preventive Services Task Force, Davidson KW, Barry MJ, et al. Screening for colorectal cancer: US Preventive Services Task Force Recommendation Statement. JAMA 2021;325:1965–1977.
30. Patel SG, May FP, Anderson JC, et al. Updates on age to start and stop colorectal cancer screening: recommendations from the U.S. Multi-Society Task Force on Colorectal Cancer. Am J Gastroenterol 2022;117:57–69.
31. 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. Gastroenterology 2017;153:307–323.
32. 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;68:250–281.
33. Naber SK, Kuntz KM, Henrikson NB, et al. Cost effectiveness of age-specific screening intervals for people with family histories of colorectal cancer. Gastroenterology 2018;154:105–116.e20.
34. Tian Y, Kharazmi E, Brenner H, et al. Calculating the starting age for screening in relatives of patients with colorectal cancer based on data from large nationwide data sets. Gastroenterology 2020;159:159–168.e3.
35. Eaden JA, Mayberry JF. Guidelines for screening and surveillance of asymptomatic colorectal cancer in patients with inflammatory bowel disease. Gut 2002; 51(Suppl 5):V10–V12.
36. Hampel H. Population screening for hereditary colorectal cancer. Surg Oncol Clin N Am 2018;27:319–325.
37. van Hees F, Saini SD, Lansdorp-Vogelaar I, et al. Personalizing colonoscopy screening for elderly individuals based on screening history, cancer risk, and comorbidity status could increase cost effectiveness. Gastroenterology 2015;149:1425–1437.
38. Garcia-Albeniz X, Hsu J, Bretthauer M, et al. Effectiveness of screening colonoscopy to prevent colorectal cancer among medicare beneficiaries aged 70 to 79 years: a prospective observational study. Ann Intern Med 2017;166:18–26.

39. Ma W, Wang K, Nguyen LH, et al. Association of screening lower endoscopy with colorectal cancer incidence and mortality in adults older than 75 years. JAMA Oncol 2021;7:985–992.
40. Cenin DR, Tinmouth J, Naber SK, et al. Calculation of stop ages for colorectal cancer screening based on comorbidities and screening history. Clin Gastroenterol Hepatol 2021;19:547–555.
41. Guo F, Chen C, Holleczek B, et al. Strong reduction of colorectal cancer incidence and mortality after screening colonoscopy: prospective cohort study from Germany. Am J Gastroenterol 2021;116:967–975.
42. Nishihara R, Wu K, Lochhead P, et al. Long-term colorectal-cancer incidence and mortality after lower endoscopy. N Engl J Med 2013;369:10951105.
43. Bretthauer M, Loberg M, Wieszczy P, et al. Effect of colonoscopy screening on risks of colorectal cancer and related death. N Engl J Med 2022;387:1547–1556.
44. Hassan C, Giorgi Rossi P, Camilloni L, et al. Meta-analysis: adherence to colorectal cancer screening and the detection rate for advanced neoplasia, according to the type of screening test. Aliment Pharmacol Ther 2012; 36:929–940.
45. Breekveldt ECH, Lansdorp-Vogelaar I, Toes-Zoutendijk E, et al. Colorectal cancer incidence, mortality, tumour characteristics, and treatment before and after introduction of the faecal immunochemical testing-based screening programme in the Netherlands: a population-based study. Lancet Gastroenterol Hepatol 2022;7:60–68.
46. Chiu HM, Chen SL, Yen AM, et al. Effectiveness of fecal immunochemical testing in reducing colorectal cancer mortality from the One Million Taiwanese Screening Program. Cancer 2015;121:3221–3229.
47. Lindholm E, Brevinge H, Haglind E. Survival benefit in a randomized clinical trial of faecal occult blood screening for colorectal cancer. Br J Surg 2008;95:1029–1036.
48. Mandel JS, Bond JH, Church TR, et al. Reducing mortality from colorectal cancer by screening for fecal occult blood. Minnesota Colon Cancer Control Study. N Engl J Med 1993;328:1365–1371.
49. Quintero E, Castells A, Bujanda L, et al. Colonoscopy versus fecal immunochemical testing in colorectal-cancer screening. N Engl J Med 2012;366:697–706.
50. Shaukat A, Mongin SJ, Geisser MS, et al. Long-term mortality after screening for colorectal cancer. N Engl J Med 2013;369:1106–1114.
51. van Rossum LG, van Rijn AF, Laheij RJ, et al. Random comparison of guaiac and immunochemical fecal occult blood tests for colorectal cancer in a screening population. Gastroenterology 2008;135:82–90.
52. Atkin W, Wooldrage K, Parkin DM, et al. Long term effects of once-only flexible sigmoidoscopy screening after 17 years of follow-up: the UK Flexible Sigmoidoscopy Screening randomised controlled trial. Lancet 2017; 389:1299–1311.
53. Holme O, Loberg M, Kalager M, et al. Long-term effectiveness of sigmoidoscopy screening on colorectal cancer incidence and mortality in women and men: a randomized trial. Ann Intern Med 2018;168:775–782.
54. Lin JS, Perdue LA, Henrikson NB, et al. Screening for colorectal cancer: updated evidence report and systematic review for the US Preventive Services Task Force. JAMA 2021;325:1978–1998.
55. Miller EA, Pinsky PF, Schoen RE, et al. Effect of flexible sigmoidoscopy screening on colorectal cancer incidence and mortality: long-term follow-up of the randomised US PLCO cancer screening trial. Lancet Gastroenterol Hepatol 2019;4:101–110.
56. Segnan N, Armaroli P, Bonelli L, et al. Once-only sigmoidoscopy in colorectal cancer screening: follow-up findings of the Italian Randomized Controlled Trial–SCORE. J Natl Cancer Inst 2011; 103:1310–1322.
57. Imperiale TF, Ransohoff DF, Itzkowitz SH, et al. Multitarget stool DNA testing for colorectal-cancer screening. N Engl J Med 2014;370:1287–1297.
58. Bosch LJW, Melotte V, Mongera S, et al. Multitarget stool DNA Test performance in an average-risk colorectal cancer screening population. Am J Gastroenterol 2019;114:1909–1918.
59. Ladabaum U, Mannalithara A. Comparative effectiveness and cost effectiveness of a multitarget stool DNA test to screen for colorectal neoplasia. Gastroenterology 2016; 151:427–439.e6.
60. Johnson CD, Chen MH, Toledano AY, et al. Accuracy of CT colonography for detection of large adenomas and cancers. N Engl J Med 2008;359:1207–1217.
61. Pickhardt PJ, Choi JR, Hwang I, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. N Engl J Med 2003; 349:2191–2200.
62. Rex DK, Adler SN, Aisenberg J, et al. Accuracy of capsule colonoscopy in detecting colorectal polyps in a screening population. Gastroenterology 2015;148:948–957.e2.
63. Rondonotti E, Borghi C, Mandelli G, et al. Accuracy of capsule colonoscopy and computed tomographic colonography in individuals with positive results from the fecal occult blood test. Clin Gastroenterol Hepatol 2014; 12:1303–1310.
64. Gupta S. Screening for colorectal cancer. Hematol Oncol Clin North Am 2022;36:393–414.
65. Quintero E, Carrillo M, Gimeno-Garcia AZ, et al. Equivalency of fecal immunochemical tests and colonoscopy in familial colorectal cancer screening. Gastroenterology 2014;147:1021–1030.e1; quiz e16–e17.
66. Schroy PC Iii, Glick JT, Robinson PA, et al. Screening preferences of patients at familial risk of colorectal cancer. Dig Dis Sci 2007;52:2788–2795.
67. Gupta S, Lieberman D, Anderson JC, et al. Recommendations for follow-up after colonoscopy and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology 2020;158:1131–1153.e5.
68. Causada-Calo N, Bishay K, Albashir S, et al. Association between age and complications after outpatient colonoscopy. JAMA Netw Open 2020;3:e208958.
69. Day LW, Walter LC, Velayos F. Colorectal cancer screening and surveillance in the elderly patient. Am J Gastroenterol 2011;106:1197–1206; quiz 1207.

70. Tran AH, Man Ngor EW, Wu BU. Surveillance colonoscopy in elderly patients: a retrospective cohort study. JAMA Intern Med 2014;174:1675–1682.
71. Ko CW, Riffle S, Michaels L, et al. Serious complications within 30 days of screening and surveillance colonoscopy are uncommon. Clin Gastroenterol Hepatol 2010; 8:166–173.
72. Rutter CM, Johnson E, Miglioretti DL, et al. Adverse events after screening and follow-up colonoscopy. Cancer Causes Control 2012;23:289–296.
73. Wang L, Mannalithara A, Singh G, et al. Low rates of gastrointestinal and non-gastrointestinal complications for screening or surveillance colonoscopies in a population-based study. Gastroenterology 2018; 154:540–555.e8.
74. Duvvuri A, Chandrasekar VT, Srinivasan S, et al. Risk of colorectal cancer and cancer related mortality after detection of low-risk or high-risk adenomas, compared with no adenoma, at index colonoscopy: a systematic review and meta-analysis. Gastroenterology 2021; 160:1986–1996.e3.
75. Lee SJ, Leipzig RM, Walter LC. Incorporating lag time to benefit into prevention decisions for older adults. JAMA 2013;310:2609–2610.
76. Lee SJ, Boscardin WJ, Stijacic-Cenzer I, et al. Time lag to benefit after screening for breast and colorectal cancer: meta-analysis of survival data from the United States, Sweden, United Kingdom, and Denmark. BMJ 2013;346:e8441.
77. Juul FE, Cross AJ, Schoen RE, et al. 15-Year benefits of sigmoidoscopy screening on colorectal cancer incidence and mortality: a pooled analysis of randomized trials. Ann Intern Med 2022;175:1525–1533.
78. May FP, Gupta S. When should screening stop for elderly individuals at average and increased risk for colorectal cancer? Clin Gastroenterol Hepatol 2018; 16:178–180.e1.
79. Enns JP, Pollack CE, Boyd CM, et al. Discontinuing cancer screening for older adults: a comparison of clinician decision-making for breast, colorectal, and prostate cancer screenings. J Gen Intern Med 2022; 37:1122–1128.
80. Issaka RB, Inadomi JM. Low-value colorectal cancer screening: too much of a good thing? JAMA Netw Open 2018;1:e185445.
81. Piper MS, Maratt JK, Zikmund-Fisher BJ, et al. Patient attitudes toward individualized recommendations to stop low-value colorectal cancer screening. JAMA Netw Open 2018;1:e185461.
82. Schoenborn NL, Boyd CM, Lee SJ, et al. Communicating about stopping cancer screening: comparing clinicians' and older adults' perspectives. Gerontologist 2019; 59:S67–S76.
83. Schoenborn NL, Lee K, Pollack CE, et al. Older adults' views and communication preferences about cancer screening cessation. JAMA Intern Med 2017; 177:1121–1128.
84. Usher-Smith JA, Walter FM, Emery JD, et al. Risk prediction models for colorectal cancer: a systematic review. Cancer Prev Res (Phila) 2016;9:13–26.
85. Sassano M, Mariani M, Quaranta G, et al. Polygenic risk prediction models for colorectal cancer: a systematic review. BMC Cancer 2022;22:65.
86. McGeoch L, Saunders CL, Griffin SJ, et al. Risk prediction models for colorectal cancer incorporating common genetic variants: a systematic review. Cancer Epidemiol Biomarkers Prev 2019;28:1580–1593.
87. Demb J, Gupta S. Realizing the promise of personalized colorectal cancer screening in practice. J Natl Cancer Inst 2021;113:1120–1122.
88. Borrell LN, Elhawary JR, Fuentes-Afflick E, et al. Race and genetic ancestry in medicine - a time for reckoning with racism. N Engl J Med 2021;384:474–480.
89. van Heijningen EM, Lansdorp-Vogelaar I, Kuipers EJ, et al. Features of adenoma and colonoscopy associated with recurrent colorectal neoplasia based on a large community-based study. Gastroenterology 2013;144:1410–1418.
90. Lee JY, Park HW, Kim MJ, et al. Prediction of the risk of a metachronous advanced colorectal neoplasm using a novel scoring system. Dig Dis Sci 2016;61:3016–3025.
91. Wieszczy P, Kaminski MF, Franczyk R, et al. Colorectal cancer incidence and mortality after removal of adenomas during screening colonoscopies. Gastroenterology 2020;158:875–883.e5.
92. Liu L, Messer K, Baron JA, et al. A prognostic model for advanced colorectal neoplasia recurrence. Cancer Causes Control 2016;27:1175–1185.
93. Gupta S, Earles A, Bustamante R, et al. Adenoma detection rate and clinical characteristics influence advanced neoplasia risk after colorectal polypectomy. Clin Gastroenterol Hepatol 2023;21:1924–1936.e9.
94. Guo F, Edelmann D, Cardoso R, et al. Polygenic risk score for defining personalized surveillance intervals after adenoma detection and removal at colonoscopy. Clin Gastroenterol Hepatol 2023;21:210–219.e11.
95. Gupta S, Thrift AP. Polygenic risk scores for follow up after colonoscopy and polypectomy: another tool for risk stratification and planning surveillance? Clin Gastroenterol Hepatol 2023;21:29–32.
96. Qaseem A, Crandall CJ, Mustafa RA, et al. Screening for colorectal cancer in asymptomatic average-risk adults: a guidance statement from the American College of Physicians. Ann Intern Med 2019;171:643–654.
97. Leddin D, Lieberman DA, Tse F, et al. Clinical Practice Guideline on screening for colorectal cancer in individuals with a family history of nonhereditary colorectal cancer or adenoma: the Canadian Association of Gastroenterology Banff Consensus. Gastroenterology 2018;155:1325–1347.e3.

Received April 26, 2023. Accepted June 30, 2023.

Correspondence
Address correspondence to: Rachel Issaka, MD, MAS, Public Health Sciences and Clinical Research Divisions, Fred Hutchinson Cancer Center, 1100 Fairview Avenue North, M/S: M3-B232, Seattle, Washington 98109. e-mail: rissaka@fredhutch.org.

Author Contributions
Rachel B. Issaka: Drafting of the manuscript and critical revision of the manuscript and approved final version. Andrew T. Chan: Drafting of the manuscript and critical revision of the manuscript and approved final version. Samir Gupta: Drafting of the manuscript and critical revision of the manuscript and approved final version.

Conflicts of interest
The authors disclose the following: Rachel B. Issaka has received consulting fees from Guardant Health, Inc. Andrew T. Chan has received consulting fees from Boehringer Ingelheim and Pfizer Inc. He has also received research funding from Pfizer Inc, Freenome, and Zoe Ltd. Samir Gupta has received research support from Epigenomics and Freenome. He has also received consulting fees from Guardant Health, Inc, Intervenn Biosciences, Geneoscopy, CellMax Life, and Universal Diagnostics.

Funding
Rachel B. Issaka was supported by grant K08CA241296 from the National Cancer Institute of the National Institutes of Health. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The funder had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.