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

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Abstract

Description: Since the early 2000's, there has been a rapid decline in colorectal cancer (CRC) mortality in large part due 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 projected deaths in 2023. The purpose of this best practice advice article is to describe how individuals should be risk stratified for CRC screening and post-polypectomy surveillance and highlight opportunities for future research to fill gaps in the existing literature.

Methods: This expert review was commissioned and approved by the 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 (BPA) statements were drawn from a review of the published literature and from expert opinion. Since systematic reviews were not performed, these BPA statements do not carry formal ratings regarding the quality of evidence or strength of the presented considerations.

Introduction:

The purpose of this best practice advice article from the Clinical Practice Update Committee of the American Gastroenterological Association (AGA) is to describe how individuals

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should be risk stratified for colorectal cancer (CRC) screening and post-polypectomy surveillance and highlight opportunities for future research that fill gaps in the existing literature. The target healthcare audience is all gastroenterologists, primary care providers, and other members of the healthcare 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.

BPA 1:

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

BPA 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 relative(s), the number of relatives diagnosed with CRC, the age of the individual and the age of the relative(s) 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 one 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. 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.¹² This may reflect how case-control studies may be more prone to recall bias than cohort studies which tends to exaggerate association. However, notably in Roos et al., 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 a 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 age 50 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 (ACG) and the National Comprehensive Cancer Network (NCCN)

but suggest a potential role for less intensive screening and perhaps increased use of non-invasive screening modalities for individuals with an FDR with CRC, particularly for those for whom cancer was diagnosed after the age of 50 years in the FDR. The rationale for our BPA statement to consider more intensive screening for all individuals with an FDR with CRC, irrespective of the age of 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 are 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. Next, as discussed below, more data is needed to examine the yield of advanced neoplasia in adults between the ages of 40 and 50 years old based on family history. Additionally, 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 periods based on variation in secular trends in the prevalence of screening as well as other CRC risk factors (e.g intake of aspirin, body mass index, 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. Finally, we recognize that few studies have assessed an individual's risk of CRC when a second-degree relative (SDR) or third-degree relative (TDR) is affected. Emerging data, including a study by Taylor et al., suggest that the most important predictor of CRC was the number of affected FDRs and having a single FDR in combination with a SDR or TDR could also increase an individual's risk for CRC by more than two-fold.¹³

As previously mentioned, 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 to 10.21) compared to 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 to individuals without such family history (OR 2.27, 95% CI, 1.01–5.09).¹⁶ In the National Polyp Study, FDR of individuals with any adenomas had an almost two-fold increased risk for CRC compared to spouse controls (RR 1.78, 95% CI, 1.18 to 2.67).¹⁷ Finally, in a population-based study from Sweden, having a 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 (OR 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. 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 (OR 6.05, 95% CI, 2.74 –13.36).¹⁹

Taken together, these data show 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 screening recommendations. Yet, family

CRC and adenoma history are not consistently collected or documented,²⁰ often lack the age of diagnosis of the affected individual, and the accuracy of details provided have 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 professionals collect and document family history.²⁰

BPA 3:

Individuals at average risk for CRC should initiate screening at age 45 years while 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.

BPA 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 of age, the incidence of CRC in people younger than 50 years, also known as “early-onset CRC,” has been increasing. Over the next decade, early-onset CRC is estimated to 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 of CRC screening, recommendations to date have largely been supported by decision analytic models. A microsimulation analysis that incorporated the recent increase in CRC incidence among younger individuals in the U.S. 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 the benefit of screening.²⁶ Another modeling analysis showed that initiating screening colonoscopy at 45 years instead of 50 years cost \$33,900 per quality-adjusted life-year (QALY) gained, and initiating FIT at 45 years instead of 50 years cost \$7,700 per QALY gained.²⁷ A cohort study of U.S. 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 45 years (HR, 0.37; 95% CI, 0.26–0.53), 45 to 49 years (HR, 0.43; 95% CI, 0.29–0.62), 50 to 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 (<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 U.S. Multi-Society Task Force on Colorectal Cancer (USMSTF), the U.S. Preventive Services Task Force (USPSTF), and the American Cancer Society (with varying strength) recommend 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 BPA's 1–2, individuals with a family history of CRC and/or adenomas have an increased risk of CRC compared to 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. A microsimulation analysis showed that screening people with one FDR affected with CRC every 3 years beginning at the age of 40 years is the most cost-effective.³³ An analysis according to the age at diagnosis of affected relatives suggested that CRC screening should begin at age 30 years for those with one affected FDR diagnosed before 45 years and at age 20 years for those with two affected FDRs before the age of 50 or one affected FDR and one SDR diagnosed before the age of 50.³⁴ 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, the age of diagnosis of the affected relatives, as well as the 10-year cumulative incidence of CRC according to age within a specific source population (e.g., 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 prior the age of diagnosis of the youngest affected relative or at age 40.²⁸

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 for 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 (IBD) with colonic involvement (i.e., ulcerative colitis & 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 CPU and are discussed elsewhere.^{35, 36}

BPA 5:

The decision to continue CRC screening in individuals over age 75 years should be individualized, based on an assessment of risks, benefits, prior screening history and comorbidities.

Risk-benefit assessment is important when making decisions for CRC screening in individuals over the age 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 the 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 over the age of 75 years to inform the optimal age to stop CRC screening. In a prospective cohort study in the U.S. 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 to 74 years and -0.14% (95% CI, -0.41% to 0.16%) in 75 to 79 years. The 30-day risk for the adverse event following colonoscopy was 5.6 and 10.3 events per 1000 in individuals 70 to 74 years and 75 to 79 years of age, respectively.³⁸ Another prospective cohort study among U.S. women showed 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, 0.46–0.78), 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 three or more comorbidities among cardiovascular disease (myocardial infarction or stroke), hypertension, hypercholesterolemia, and diabetes (HR [95% CI] of CRC incidence, 0.70 [0.44–1.10]; HR of CRC mortality, 1.17 [0.57–2.43]).³⁹

A microsimulation analysis evaluated the benefits and harms of biennial FIT according to individuals' prior screening history and comorbidities.⁴⁰ It showed 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

BPA 6:

Screening options for individuals at average risk for CRC should include colonoscopy, fecal immunochemical test (FIT), flexible sigmoidoscopy + FIT, multi-target stool DNA-FIT and CT colonography, based upon 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 primarily derived 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 to 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 to 0.93), the risk of CRC-related death did not differ between the two 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 to 0.83) and related mortality (RR, 0.50; 95% CI, 0.27 to 0.44) among those who completed a colonoscopy.

The superiority of colonoscopy in terms of sensitivity both for 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 + FIT, multi-target stool DNA-FIT are chosen based on availability of screening modalities and patients' 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 + FIT^{52–56} decrease CRC incidence and related mortality. Multi-target 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 6mm or larger. However empirical data on the impact of these tests on CRC incidence and mortality are limited. Among available options, the USPSTF recommends colonoscopy, annual FIT, multitarget stool DNA-FIT, sigmoidoscopy, and CT colonography as options, while the USMSTF 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 to FIT.

BPA 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 (family history, predisposing hereditary syndromes, IBD, etc.) 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. While relative sensitivity of colonoscopy vs. other tests is well established, few studies have compared 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 non-inferior for individuals with an FDR with CRC randomized to annual FIT over three rounds vs. one time colonoscopy. The per-protocol analysis noted a non-statistically 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 non-colonoscopy tests.⁶⁶

BPA 8:

The decision to continue post-polypectomy surveillance for individuals over age 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% to 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 also are 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 USMSTF 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 prior history of 1–2 adenomas <1cm 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 to time when reduced CRC risk would be realized should also be considered.⁷⁵ Exposure to colonoscopy, compared to 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 less than 5 years, based on a risk calculator (e.g., 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}

BPA 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 (e.g., by race, ethnicity, sex, and other sociodemographic factors associated with disparities in CRC outcomes) prior to wide-spread 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/ethnic populations is critical for models that include genetic factors, since

genetic discovery studies have largely focused on individuals with European ancestry, and because risk relevant genetic factors may vary according to individual's origin of genetic ancestry. While many studies differentiate individuals by race/ethnicity, which may capture some information about the likely presence of certain genetic variants, ancestry is a better predictor which 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 factors⁹¹ (colonoscopist adenoma detection rate, completeness of exam 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.

Conclusion:

In summary, most CRCs are sporadic and risk increases with older age. Screening is recommended for average-risk adults starting at age 45 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.

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Identify and disclose **ALL** conflict of interests (financial/non-financial) to the development of the clinical practice update.

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Abbreviations:

CRC	Colorectal Cancer
FDR	First-Degree Relative
SDR	Second-Degree Relative

TDR	Third-Degree Relative
FIT	Fecal Immunochemical Test

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Best Practice Advice (BPA) Statements:

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

BPA 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.

BPA 3: Individuals at average risk for CRC should initiate screening at age 45 years while 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.

BPA 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.

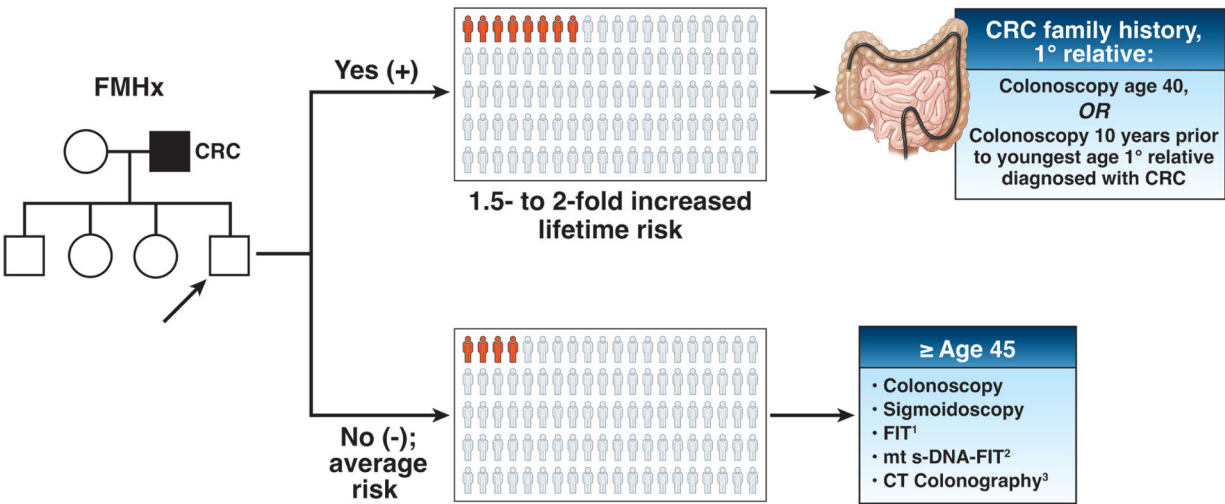
BPA 5: The decision to continue CRC screening in individuals over age 75 years should be individualized, based on an assessment of risks, benefits, prior screening history and comorbidities.

BPA 6: Screening options for individuals at average risk for CRC should include colonoscopy, fecal immunochemical test (FIT), flexible sigmoidoscopy + FIT, multi-target stool DNA-FIT and CT colonography, based upon availability and individual preference.

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

BPA 8: The decision to continue post-polypectomy surveillance for individuals over age 75 years should be individualized, based on an assessment of risks, benefits, and comorbidities.

BPA 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 (e.g., by race, ethnicity, sex, and other sociodemographic factors associated with disparities in CRC outcomes) prior to wide-spread implementation.



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

Figure 1:
Recommended colorectal cancer (CRC) screening test options based on family history of CRC

Table 1:

Samples of practice guidelines recommending initiation of colorectal cancer (CRC) screening in average-risk populations and high-risk groups based on family history of CRC

Sample of practice guidelines recommending initiation of CRC screening in average-risk populations			Synthesis
American Cancer Society, 2018 ²	Average-risk adults in good health with a life expectancy of more than 10 years	Begin screening at age 45 with any test (qualified recommendation) Screen adults between ages 50 and 75 years with any test (strong recommendation)	In average-risk adults, all practice guidelines gave a strong recommendation to begin CRC screening at age 50 with any test. Most practice guidelines gave a weak or qualified recommendation to begin CRC screening in average-risk adults at age 45 with any test. Two practice guidelines (ACG and USMSTF) recommended a tiered approach to use of screening tests with Tier 1 tests including a colonoscopy every 10 years or fecal immunochemical test every 1 year.
American College of Gastroenterology, 2021 ⁷	Average-risk adults	Begin screening adults between ages 45 and 49 years (conditional recommendation) Screen adults between ages 50 and 75 years (strong recommendation) Colonoscopy every 10 years or fecal immunochemical test every 1 year as primary screening modalities (strong recommendation) Flexible sigmoidoscopy every 5 to 10 years, multitarget stool DNA test every 3 years, CT colonography every 5 years, or colon capsule every 5 years (conditional recommendation)	
American College of Physicians, 2019 ⁹⁶	Average-risk adults in good health with a life expectancy of more than 10 years	Screen adults between ages 50 and 75 years with any test	
National Comprehensive Cancer Network, 2022	Average-risk adults	Begin screening at age 45 with any test	
US Multi-Society Task Force on Colorectal Cancer (USMSTF ⁹), 2022 ³⁰	Average-risk adults	Begin screening at age 45 (weak recommendation)	
	Average-risk adults	Begin screening at age 50 if no prior screening completed (strong recommendation)	
U.S. Preventive Services Task Force (USPSTF), 2021 ²⁹	Asymptomatic, average-risk adults	Screen adults between ages 50 and 75 years (Grade A) Begin screening adults between ages 45 and 49 years (Grade B) Selectively screen adults ages 76 to 85 years (Grade C)	
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 first-degree relative at age <60 years or CRC or advanced adenoma in ≥ 2 first-degree relative at any age	Colonoscopy at age 40 or 10 years before earliest diagnosis of CRC, repeat every 5 years (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 or 10 years before earliest diagnosis of CRC with colonoscopy every 5 to 10 years. In adults with a family history of advanced adenoma, most practice guidelines recommended to begin CRC screening at age 40 or 10 years before earliest diagnosis of adenoma with any test.
	CRC or advanced adenoma in single first degree relative diagnosed age ≥ 60 years	Begin screening at age 40 or 10 years 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 first degree relatives	Colonoscopy every 5 years at age 40 or 10 years younger than age of diagnosis of earliest diagnosed first degree relative, whichever is earlier	
	CRC in 1 first degree relative	Colonoscopy every 5–10 years at age 40/50 years or 10 years younger than age of diagnosis of first degree relative, whichever is earlier. FIT every 1–2 years is suggested as 2 nd line option	
	1 or more first degree relative with documented advanced adenoma	No recommendation for a preferred test. Colonoscopy or FIT are both options. Colonoscopy every 5–10 years at age 40–50 years or 10 years younger than age of diagnosis of first degree relative, whichever is earlier. FIT every 1–2 years is suggested as 2 nd line option	
National Comprehensive Cancer Network, 2022	CRC ≥ 1 first degree relative with CRC at any age	Colonoscopy every 5 years or per colonoscopy findings beginning at age 40 or 10 years before earliest diagnosis of CRC	
	CRC in second- and third-degree relatives at any age	Colonoscopy every 10 years or per colonoscopy findings beginning at age 45	
	Advanced adenoma in first degree relative at any age	Colonoscopy every 5 to 10 years or per colonoscopy findings beginning at age 40 or at age of onset of adenoma in relative, whichever is first	
USMSTF 2017 ³¹	CRC or advanced adenoma in 2 first degree relatives at any age OR CRC or advanced adenoma in a single first degree relative < age 60 years	Colonoscopy every 5 years beginning 10 years prior to age of first-degree relative diagnosis or age 40	
	CRC or advanced adenoma in single first degree relative diagnosed age ≥ 60 years	Begin screening at age 40 with any test	

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USMSTF, US Multi-Society Task Force on Colorectal Cancer, represents the American Gastroenterological Association (AGA), the American Society for Gastrointestinal Endoscopy (ASGE), and the American College of Gastroenterology (ACG)

Table 2:

Research priorities to improve risk stratification for colorectal cancer (CRC) screening and post-polypectomy surveillance

Evaluate interventions that increase awareness about family history knowledge in the general population and standardize how health professionals collect and document family history, and implement family history-based guidelines for screening.
Compare effectiveness of colonoscopy to other tests for screening individuals at increased-risk for CRC based on family history or other risk factors.
Conduct studies with individuals over the age of 75 years 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 (e.g., by ancestry, race, ethnicity, other sociodemographic factors).
Determine best practices and implementation challenges (e.g., acceptability and feasibility) of riskstratification models in clinical practice across multiple stakeholder groups (e.g., patients, providers, healthcare systems)
Evaluate clinical utility and cost-effectiveness of risk prediction models in different populations (e.g., 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.