

UCLA

UCLA Previously Published Works

Title

NCCN Guidelines Insights: Colorectal Cancer Screening, Version 2.2020.

Permalink

<https://escholarship.org/uc/item/8x53x221>

Journal

Journal of the National Comprehensive Cancer Network, 18(10)

ISSN

1540-1405

Authors

Provenzale, Dawn
Ness, Reid M
Llor, Xavier
[et al.](#)

Publication Date

2020

DOI

10.6004/jnccn.2020.0048

Peer reviewed



Published in final edited form as:

J Natl Compr Canc Netw. ; 18(10): 1312–1320. doi:10.6004/jnccn.2020.0048.

Colorectal Cancer Screening, Version 2.2020 Featured Updates to the NCCN Guidelines

Dawn Provenzale, MD, MS¹, Reid M. Ness, MD, MPH², Xavier Llor, MD, PhD³, Jennifer M. Weiss, MD, MS⁴, Benjamin Abbadessa, MD⁵, Gregory Cooper, MD⁶, Dayna S. Early, MD⁷, Mark Friedman, MD⁸, Francis M. Giardiello, MD, MBA⁹, Kathryn Glaser, MA, PhD¹⁰, Suryakanth Gurudu, MD¹¹, Amy L. Halverson, MD¹², Rachel Issaka, MD, MAS¹³, Rishi Jain, MD, MS¹⁴, Priyanka Kanth, MD, MS¹⁵, Trilokesh Kidambi, MD¹⁶, Audrey J. Lazenby, MD¹⁷, Lillias Maguire, MD¹⁸, Arnold J. Markowitz, MD¹⁹, Folasade P. May, MD, PhD²⁰, Robert J. Mayer, MD²¹, Shivan Mehta, MD, MBA, MS²², Swati Patel, MD, MS²³, Shajan Peter, MD²⁴, Peter P. Stanich, MD²⁵, Jonathan Terdiman, MD²⁶, Jennifer Keller, MSS²⁷, Mary A. Dwyer, MS, CGC²⁷, Ndiya Ogba, PhD²⁷

¹Duke Cancer Institute

NCCN: Continuing Education

Target Audience: This activity is designed to meet the educational needs of oncologists, nurses, pharmacists, and other healthcare professionals who manage patients with cancer.

Accreditation Statements

In support of improving patient care, National Comprehensive Cancer Network (NCCN) is jointly accredited by the Accreditation Council for Continuing Medical Education (ACCME), the Accreditation Council for Pharmacy Education (ACPE), and the American Nurses Credentialing Center (ANCC), to provide continuing education for the healthcare team.

Medicine (ACCME): NCCN designates this journal-based CME activity for a maximum of 1.0 *AMA PRA Category 1 Credit*[™]. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Nursing (ANCC): NCCN designates this educational activity for a maximum of 1.0 contact hour.

Pharmacy (ACPE): NCCN designates this knowledge-based continuing education activity for 1.0 contact hour (0.1 CEUs) of continuing education credit. UAN: JA4008196-0000-20-011-H01-P

All clinicians completing this activity will be issued a certificate of participation. To participate in this journal CE activity: (1) review the educational content; (2) take the posttest with a 66% minimum passing score and complete the evaluation at <https://education.nccn.org/node/88515>; and (3) view/print certificate.

Pharmacists: You must complete the posttest and evaluation within 30 days of the activity. Continuing pharmacy education credit is reported to the CPE Monitor once you have completed the posttest and evaluation and claimed your credits. Before completing these requirements, be sure your NCCN profile has been updated with your NAPB e-profile ID and date of birth. Your credit cannot be reported without this information. If you have any questions, please e-mail education@nccn.org.

Release date: October 10, 2020; Expiration date: October 10, 2021

Learning Objectives:

Upon completion of this activity, participants will be able to:

- Integrate into professional practice the updates to the NCCN Guidelines for Colorectal Cancer Screening
- Describe the rationale behind the decision-making process for developing the NCCN Guidelines for Colorectal Cancer Screening

Disclosure of Relevant Financial Relationships

The NCCN staff listed below discloses no relevant financial relationships:

Kerrin M. Rosenthal, MA; Kimberly Callan, MS; Genevieve Emberger Hartzman, MA; Erin Hesler; Kristina M. Gregory, RN, MSN, OCN; Rashmi Kumar, PhD; Karen Kanefield; and Kathy Smith.

Individuals Who Provided Content Development and/or Authorship Assistance:

Dawn Provenzale, MD, MS, Panel Chair, has disclosed that she has no relevant financial relationships.

Reid M. Ness, MD, MPH, Panel Vice Chair, has disclosed that he has no relevant financial relationships.

Xavier Llor, MD, PhD, Panel Member, has disclosed that he has no relevant financial relationships.

Jennifer M. Weiss, MD, MS, Panel Member, has disclosed that she has received honoraria from Medscape.

Jennifer Keller, MSS, Guidelines Layout Specialist, NCCN, has disclosed that she has no relevant financial relationships.

Mary A. Dwyer, MS, CGC, Director, Guidelines Operations, NCCN, has disclosed that she has no relevant financial relationships.

Ndiya Ogba, PhD, Oncology Scientist/Senior Medical Writer, NCCN, has disclosed that she has no relevant financial relationships.

To view all of the conflicts of interest for the NCCN Guidelines panel, go to [NCCN.org/disclosures/guidelinepanellisting.aspx](https://www.nccn.org/disclosures/guidelinepanellisting.aspx).

- ²Vanderbilt-Ingram Cancer Center
- ³Yale Cancer Center/Smilow Cancer Hospital
- ⁴University of Wisconsin Carbone Cancer Center
- ⁵UC San Diego Moores Cancer Center
- ⁶Case Comprehensive Cancer Center/University Hospitals Seidman Cancer Center and Cleveland Clinic Taussig Cancer Institute
- ⁷Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine
- ⁸Moffitt Cancer Center
- ⁹The Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins
- ¹⁰Roswell Park Comprehensive Cancer Center
- ¹¹Mayo Clinic Cancer Center
- ¹²Robert H. Lurie Comprehensive Cancer Center of Northwestern University
- ¹³Fred Hutchinson Cancer Center/Seattle Cancer Care Alliance
- ¹⁴Fox Chase Cancer Center
- ¹⁵Huntsman Cancer Institute at the University of Utah
- ¹⁶City of Hope National Medical Center
- ¹⁷Fred & Pamela Buffett Cancer Center
- ¹⁸University of Michigan Rogel Cancer Center
- ¹⁹Memorial Sloan Kettering Cancer Center
- ²⁰UCLA Jonsson Comprehensive Cancer Center
- ²¹Dana-Farber/Brigham and Women's Cancer Center | Massachusetts General Hospital Cancer Center
- ²²Abramson Cancer Center at the University of Pennsylvania
- ²³University of Colorado Cancer Center
- ²⁴O'Neal Comprehensive Cancer Center at UAB
- ²⁵The Ohio State University Comprehensive Cancer Center - James Cancer Hospital and Solove Research Institute
- ²⁶UCSF Helen Diller Family Comprehensive Cancer Center
- ²⁷National Comprehensive Cancer Network.

Abstract

The NCCN Guidelines for Colorectal Cancer (CRC) Screening describe various colorectal screening modalities as well as recommended screening schedules for patients at average or

increased risk of developing sporadic CRC. They are intended to aid physicians with clinical decision-making regarding CRC screening for patients without defined genetic syndromes. These NCCN Guidelines Insights focus on select recent updates to the NCCN Guidelines, including a section on primary and secondary CRC prevention, and provide context for the panel's recommendations regarding the age to initiate screening in average risk individuals and follow-up for low-risk adenomas.

Overview

Colorectal cancer (CRC) is the fourth most frequently diagnosed cancer in the United States. In 2020, an estimated 104,610 new cases of colon cancer and 43,340 new cases of rectal cancer will be diagnosed in the United States,¹ and an estimated 53,200 people will die of these cancers.¹ Data suggest that approximately half of all CRC cases and deaths are attributable to modifiable risk factors, such as physical activity, smoking, and diet, and are thus potentially preventable.^{2,3} Screening of average-risk individuals may decrease CRC incidence through detection and removal of polyps, and can reduce CRC mortality by detecting cancer at an early, curable stage.⁴⁻⁶ Patients with localized CRC have a 90% relative 5-year survival rate, whereas rates for those with regional and distant disease are 71% and 14%, respectively, demonstrating that earlier diagnosis can have a large impact on survival.³

Importantly, the incidence of colon and rectal cancers is decreasing.^{7,8} In addition, mortality from CRC decreased by almost 35% from 1990 to 2007,⁹ and in 2017 was down from peak mortality rates by 53% in men and 57% in women.¹ These improvements in incidence and mortality from CRC over past years are thought, at least in part, to be a result of advances in cancer prevention, earlier diagnosis through screening, and better treatment modalities. In fact, modeling suggests that approximately 63% of CRC deaths can be attributed to a lack of adherence with current screening recommendations.¹⁰ According to data from the Centers for Disease Control and Prevention, the CRC screening rate among US adults aged 50 years has increased from approximately 38% in 2000 to 66% in 2018, but varies with age.^{3,11} The National Colorectal Cancer Roundtable goal to increase the US CRC screening rates to 80% in every community could prevent approximately 280,000 new CRC cases and 200,000 CRC deaths through 2030.^{12,13} Conversely, the incidence rates of colon and rectal cancers in adults aged <50 years have been increasing by approximately 2% per year since 2003.^{3,14} In general, most CRC cases in adolescent and young adult individuals appear to be sporadic.¹⁵ Causes for this increase in early-onset CRC are unknown and may be attributable to diet and other lifestyle factors.³

These NCCN Guidelines Insights focus on recent additions to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines), including a section on primary and secondary CRC prevention, and provide a summary of the panel's discussion of relevant data related to the age at which to initiate screening in average-risk individuals and the follow-up of low-risk adenomas after an initial colonoscopy, with concluding statements on specific changes made to the Guidelines.

Primary and Secondary CRC Prevention

Background

The panel discussed primary and secondary preventive measures that impact CRC risk due to increasing data on the impact of therapeutic and lifestyle interventions on CRC risk. During the 2020 update, the panel expanded the scope of the guidelines to cover primary and secondary CRC prevention based on the comments and data summarized in this section.

Physical Activity and Diet

A report from the Continuous Update Project (CUP) led by the World Cancer Research Fund International and the American Institute for Cancer Research recommends maintaining a healthy weight, being physically active (via recreation, occupation, and/or transportation), and eating a healthy diet, because these measures are strongly associated with decreased colon and/or rectal cancer risk.¹⁶ Other analyses have shown that adherence to guidelines promoting physical activity and a healthy diet are associated with reductions in the incidence of CRC.^{17,18} Initiating physical activity during adolescence also appears to lower the risk of developing colorectal adenomas later in life.¹⁹

In regard to diet and nutrition, the CUP report recommends obtaining nutrients from natural food sources over solely from dietary supplements.¹⁶ In limited studies, a low intake of vitamin D is associated with increased CRC risk.²⁰ Some studies suggest that a diet high in fruits and vegetables is associated with decreased CRC risk.^{21,22} In addition, some data suggest that a high body mass index (BMI) is associated with an increased risk for CRC recurrence and mortality, but the data are not consistent.^{23–25}

An international panel of experts formed a working group for the International Agency for Research on Cancer (IARC) and assessed >800 epidemiologic studies that investigated the association of cancer with the consumption of red and processed meats.²⁶ Based on their review of the data, the IARC working group determined that there is sufficient evidence supporting a procarcinogenic effect of processed meats on CRC, but consumption of red meat was determined to be “probably carcinogenic” based on limited evidence.²⁶ In contrast, the Nutritional Recommendations (NutriRECS) guidelines panel decided not to recommend a decrease in red meat or processed meat consumption due to insufficient evidence and the small magnitude of effect for most individuals, arguing that a consideration should be made for the impact on quality of life and burden of modifying diet habits.²⁷ Their recommendations reflect the need for further studies that examine the association between meat consumption and cancer outcomes.

Aspirin

The US Preventive Services Task Force (USPSTF) conducted systematic evidence reviews of trials that assessed the impact of aspirin on (1) total cancer mortality and incidence in persons eligible for primary prevention of cardiovascular disease (CVD), and (2) CRC mortality and incidence in persons at average CRC risk.²⁸ The 20 trials included in these systematic reviews compared the effects of oral aspirin versus placebo or no treatment in adults aged ≥40 years. In CVD primary and secondary prevention trials (4 trials; n=14,033),

20-year CRC mortality was decreased in persons who received aspirin therapy (relative risk [RR], 0.67; 95% CI, 0.52–0.86).²⁸ Based on 3 trials (n=47,464), aspirin also appeared to reduce CRC incidence beginning 10 to 19 years after initiation (RR, 0.60; 95% CI, 0.47–0.76).²⁸ Based on these data, the USPSTF recommends low-dose aspirin intake for primary prevention of CVD and CRC in adults aged 50 to 59 years who have 10% 10-year CVD risk, are not at increased risk for bleeding, have a life expectancy of at least 10 years, and are willing to take low-dose aspirin daily for at least 10 years.²⁹ A daily aspirin dose of 81 mg is suggested, although the optimal dose is not well-established.²⁹

An observational, population-based, retrospective cohort study examined the effect of aspirin on patients diagnosed with CRC from 2004 to 2011 in the Cancer Registry of Norway (n=23,162; 6,102 were exposed to aspirin after CRC diagnosis).³⁰ After a median follow-up of 3 years, the mortality rate from all causes was lower in patients who were exposed to aspirin (32.9%) versus those who were not exposed (42.3%).³⁰ In addition, aspirin exposure after CRC diagnosis was independently associated with improved CRC-specific survival (hazard ratio [HR], 0.85; 95% CI, 0.79–0.92) and overall survival (OS; HR, 0.95; 95% CI, 0.90–1.01).³⁰

Smoking

Cigarette smoking causes 480,000 deaths (including the effects of secondhand smoke) annually, accounting for 1 in 5 deaths in the United States.³¹ The Cancer Prevention Study II (CPS-II) examined the impact of cigarette smoking in relation to CRC mortality in a prospective cohort study of 1,184,657 adults (aged 30 years).³² Multivariate-adjusted CRC mortality rates were highest among smokers, intermediate in former smokers, and lowest in lifelong nonsmokers.³² The multivariate-adjusted RR for current smokers versus nonsmokers was 1.32 (95% CI, 1.16–1.49) among men, and 1.41 (95% CI, 1.26–1.58) among women.³² Increased risk of CRC was observed after 20 years of smoking for both men and women, compared with individuals who had never smoked.³² A subsequent study examined a subgroup of participants from the CPS-II study (n=184,187).³³ This prospective study assessed the association between cigarette smoking and risk of incident CRC during 13 years of follow-up in which individuals had initiated smoking an average of 44 years before enrollment.³³ The incidence of CRC was significantly higher in current (HR, 1.27; 95% CI, 1.06–1.52) and former smokers (HR, 1.23; 95% CI, 1.11–1.36) compared with lifelong nonsmokers.³³ Risk of CRC also decreased with longer time since cessation and earlier age at cessation.³³

Alcohol

Increased alcohol consumption is an established risk factor for several malignancies, including CRC, and is a potentially modifiable risk factor for cancer.^{34,35} A meta-analysis of 61 independent studies (27 cohort and 34 case-control studies) examined the association between alcohol intake (light, moderate, or high) and CRC risk.³⁶ Compared with nondrinkers or occasional drinkers, moderate drinking (>1 to 4 drinks/day, equivalent to 12.6–49.9 g of ethanol/day) and heavy drinking (>4 drinks/day, equivalent to >50 g of ethanol/day) were associated with increased risk for CRC, at 21% and 52%, respectively.³⁶

NCCN Recommendations

The panel discussed the importance of providing recommendations for primary and secondary prevention based on data from randomized controlled trials that impact CRC risk in adults. There was also consideration of the need to quantify or qualify the recommendations through the lens of varying levels of evidence. Based on these data, the panel added a new section to the CRC Screening Guidelines (see CSCR-PREV 1 of 2, page 1314). On this page, the panel also included reference to the NCCN Guidelines for Survivorship and the survivorship section of the NCCN Guidelines for Colon Cancer for further recommendations (see CSCR-PREV 1 of 2, page 1314) (to view the most recent version of those guidelines, visit [NCCN.org](https://www.nccn.org)).

Age to Initiate Screening in Average-Risk Individuals

Background

The NCCN Guidelines for CRC Screening currently recommend that screening for average-risk individuals begin at 50 years of age. However, epidemiologic reports have shown that the incidence of CRC is on the rise in adults aged <50 years,^{37–39} with a 22% increase from 2000 to 2013.⁴⁰ Based on some of these data and simulation models,^{41,42} in 2018 the American Cancer Society (ACS) recommended that adults aged 45 years with an average risk of CRC undergo regular screening with either a high-sensitivity stool-based test or a structural (visual) examination, depending on patient preference and test availability.⁴³ The ACS Guideline Development Group (GDG) noted that the recommendation to begin screening at age 45 years is a *qualified recommendation* based on the limited direct evidence of screening effectiveness in adults aged <50 years despite modeling evidence of its benefit.⁴³ The ACS GDG also noted that the recommendation for regular screening in adults aged 50 years is a *strong recommendation* based on abundant direct evidence from various clinical trials and observational studies.⁴³ The NCCN panel discussed whether the age of initiating screening in average-risk individuals should be lowered to 45 years.

On the one hand, the panel recognizes that for CRC, timely screening and early detection have significant impact on outcomes. In addition, there are multiple, affordable CRC screening options. However, the panel considered several issues in determining whether this change should be made. One set of issues focused on the biology of early-onset disease and the specific age to initiate screening. The ACS Guideline acknowledges certain assumptions within the microsimulation model inputs, including differences in underlying assumptions about the natural history of CRC and full adherence to all screening strategies.⁴³ It is unclear whether the cancer phenotype that occurs in younger individuals is similar to or different from CRC that develops in older adults.⁴⁴ In addition, there is a lack of data supporting efficacy of screening in younger adults because most landmark trials focused on adults aged >50 years.⁴⁴ Moreover, more than half of individuals with early-onset CRC are aged <45 years, and thus lowering the age of initiating screening to 45 years may not benefit these individuals.⁴⁴ Therefore, it is currently unclear whether screening at 45 years of age will be effective at preventing CRC-related mortality.

The other set of issues discussed centered around cost and the potential impact of lowering the age to initiate screening on existing infrastructure. A cost-effectiveness analysis determined that initiating a colonoscopy at age 45 years instead of 50 years in 1,000 persons averted 4 CRCs and 2 CRC deaths, gained 14 quality-adjusted life-years (QALYs), cost \$33,900/QALY gained, and required 758 additional colonoscopies.⁴⁵ In addition, the analysis found that the initiation of fecal immunohistochemical testing at age 45 years instead of 50 years cost \$7,700/QALY gained, suggesting that starting screening at age 45 years is likely to be costeffective.⁴⁵ Furthermore, the model noted that the additional 758 colonoscopies required to screen 1000 persons beginning at age 45 instead of 50 years could instead be used to initiate and sustain screening through age 75 years in 231 currently unscreened 55 year olds or 342 currently unscreened 65 year olds. These alternative allocations yielded substantially greater clinical benefits than initiating colonoscopy screening at age 45 years.⁴⁵ Allocating colonoscopies to improve follow-up rates after abnormal FIT results also yielded substantially greater benefits than initiating colonoscopy screening at age 45 years. The authors concluded that a greater benefit, at lower cost, could be achieved by increasing participation rates for unscreened older and higher-risk persons.⁴⁵

NCCN Recommendations

Considering that early detection via screening has a significant impact on CRC risk, the NCCN panel extensively discussed this issue. Some caveats with lowering the age of initiating screening include the limited direct evidence for its effectiveness and thus the potential to overwhelm current infrastructure at the national level without significantly decreasing the outcomes or preventing death due to CRC. Based on the panel's review of the data and discussion, the panel decided that additional data from longitudinal cohorts or population-based studies are needed to validate these analyses, given that the net benefits versus harms of beginning screening at an earlier age are uncertain. To acknowledge the complexity and significance of this issue, the panel included a new section in the guidelines aimed at aggressively addressing case findings in individuals aged <50 years (see CSCR-1, page 1315). If signs and symptoms of CRC occur in individuals aged <50 years, including iron-deficiency anemia, rectal bleeding, or a change in bowel habits,⁴⁶ the panel recommends prompt evaluation with a colonoscopy, or at least flexible sigmoidoscopy, if symptoms do not promptly respond to medical treatment (see CSCR-1, page 1315). As more data emerge, the panel will reassess this recommendation (see footnote "b" on CSCR-1, page 1315).

Follow-Up for Low-Risk Adenomas Post-Colonoscopy

Background

Adenomatous polyps are the most common neoplasm found during CRC screening, and removal of these cancer precursor lesions can decrease the incidence of CRC and CRC-related mortality.⁴⁷ For individuals with low-risk adenomas (<1 cm, 2 polyps), the panel recommends a repeat colonoscopy in 5 to 10 years. However, some data suggest that the risk of CRC postpolypectomy is similar between these patients and those without any polyps detected during colonoscopy.^{47,48} In addition, emerging data suggest that a 10-year follow-up may be safe for individuals with low-risk adenomas.^{49,50} During the 2020 update, the

panel discussed the data and potential benefits versus risks of changing the recommended follow-up for these individuals from 5 to 10 years to 10 years.

In 2012, the US Multi-Society Task Force (USMSTF) reviewed existing data and updated guidelines for colonoscopy surveillance after screening and polypectomy.⁴⁷ For most patients with low-risk adenomas (1–2 tubular adenomas <10 mm), evidence supported a surveillance interval of >5 years.⁴⁷ The USMSTF noted that the quality of bowel preparation may result in a less than optimal examination in some regions of the colon.⁴⁷ In addition, most studies reviewed had not subclassified patients with diminutive (1–5 mm) versus small (6–9 mm) polyps on screening examinations, and the USMSTF noted that such stratification may be helpful in future analyses.⁴⁷

Since then, emerging data suggest that the risk of CRC postpolypectomy is similar between individuals with low-risk or nonadvanced adenomas and those with no adenomas detected during colonoscopy. In a prospective cohort from the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, CRC incidence within 15 years of baseline colonoscopy adenoma findings was assessed in 15,935 participants.⁵¹ After a median follow-up of 13 years, CRC incidence rates per 10,000 person-years of observation were 20.0 (95% CI, 15.3–24.7) for advanced adenoma, 9.1 (95% CI, 6.7–11.5) for nonadvanced adenoma, and 7.5 (95% CI, 5.8–9.7) for no adenoma.⁵¹ No significant difference in CRC risk was seen between participants with nonadvanced adenoma and those with no adenoma (RR, 1.2; 95% CI, 0.8–1.7; $P=.30$).⁵¹

In a prospective study of 122,899 participants who underwent flexible sigmoidoscopy or colonoscopy, the study authors examined the association between findings from first endoscopy and CRC risk.⁴⁹ Adenomas were classified as advanced (≥10 mm, high-grade dysplasia, or tubulovillous or villous histology) or nonadvanced, and serrated polyps were categorized as large (≥10 mm) or small (<10 mm). After a median follow-up of 10 years, compared with participants with no polyps detected during initial endoscopy, the multivariate HR for incident CRC in individuals with advanced adenomas or large serrated polyps was 4.07 (95% CI, 2.89–5.72) and 3.35 (95% CI, 1.37–8.15), respectively.⁴⁹ In contrast, no significant increase in CRC risk was seen in patients with nonadvanced adenomas (HR, 1.21; 95% CI, 0.68–2.16; $P=.52$) or small serrated polyps (HR, 1.25; 95% CI, 0.76–2.08; $P=.38$).⁴⁹ An analysis of data from the Department of Veteran Affairs Cooperative Studies Program Study (n=3121) also determined that in a group of asymptomatic veterans who underwent colonoscopy, after a 10-year follow-up, individuals with 1 to 2 small adenomas at baseline did not have a higher risk of advanced neoplasia or CRC compared with those without adenomas.⁵⁰

NCCN Recommendations

Considering that the quality of colonoscopy has improved over the years, the NCCN panel considered the proposal that changing the interval to 10 years in these patients could allow for more screening, and in effect, improve overall care. However, the panel also discussed the possibility of missed lesions at baseline, which would cause unintended anxiety for patients who would need to wait 10 years for a follow-up. In addition, there were concerns that some of the data may not apply to the general population. Although the data trends may

suggest that a 10-year follow-up or a follow-up >5 years does not pose significant harms to the patient, the panel urged caution, which would allow for the consideration of more data, including those from randomized trials, and a gradual evolution of practice patterns to ensure appropriate and timely care for patients. The panel decided to leave the follow-up interval for these patients at 5 to 10 years and included a footnote to acknowledge the emerging data (see footnote “v” on CSCR-5, page 1316). If a shorter interval is being considered, the panel recommends a discussion between the physician and patient to individualize management based on an assessment of individual risk, age, family history, comorbidities, and results of prior colonoscopies (see footnote “v” on CSCR-5, page 1316). It is worth noting that in a recent update by the USMSTF, the recommended follow-up interval for patients with 1 to 2 tubular adenomas <10 mm completely removed at a high-quality examination is 7 to 10 years.⁵²

Conclusions

For effective CRC screening, several factors are important and should be considered, including age, first-degree relatives with CRC, high BMI, cigarette smoking, diet, use of some medications (eg, aspirin), and adherence.⁵³ During the 2020 update of the NCCN Guidelines for CRC Screening, the panel addressed some of these issues and added a new section to highlight the importance of primary and secondary preventive measures as an adjunct to CRC screening. Regarding the age at which to initiate screening for average-risk individuals, the panel decided that more data are needed to elucidate the benefits and burdens of lowering the age to begin screening to 45 years of age.^{53–55} However, the panel noted that emerging data are demonstrating increased CRC incidence in individuals <50 years, and provided some guidance on the management of aggressive case finding in these individuals. In terms of follow-up of low-risk adenomas after colonoscopy, the recommended surveillance time frame of 5 to 10 years was not changed, but the panel encouraged individualized management when a shorter interval is being considered. As more data emerge, they will continue to inform the panel’s recommendations in the NCCN Guidelines for CRC Screening.

Acknowledgments

This activity is supported by educational grants from AstraZeneca; Celgene Corporation; Coherus BioSciences; Genentech, a member of the Roche Group; and TESARO, a GSK Company. This activity is supported in part by an educational grant from Bayer Healthcare Pharmaceuticals. This activity is supported by an independent medical education grant from Bristol-Myers Squibb. This activity is supported by a medical education grant from Exelixis, Inc. This activity is supported by an independent educational grant from Merck & Co., Inc.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2020. *CA Cancer J Clin* 2020;70:7–30. [PubMed: 31912902]
2. Islami F, Goding Sauer A, Miller KD, et al. Proportion and number of cancer cases and deaths attributable to potentially modifiable risk factors in the United States. *CA Cancer J Clin* 2018;68:31–54. [PubMed: 29160902]
3. Siegel RL, Miller KD, Goding Sauer A, et al. Colorectal cancer statistics, 2020. *CA Cancer J Clin* 2020;70:145–164. [PubMed: 32133645]

4. Levin B, Lieberman DA, McFarland B, et al. Screening and surveillance for the early detection of colorectal cancer and adenomatous polyps, 2008: a joint guideline from the American Cancer Society, the US Multi-Society Task Force on Colorectal Cancer, and the American College of Radiology. *CA Cancer J Clin* 2008;58:130–160. [PubMed: 18322143]
5. Rex DK, Johnson DA, Anderson JC, et al. American College of Gastroenterology guidelines for colorectal cancer screening 2009 [corrected]. *Am J Gastroenterol* 2009;104:739–750. [PubMed: 19240699]
6. U.S. Preventive Services Task Force. Screening for colorectal cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2008;149:627–637. [PubMed: 18838716]
7. Ehemann C, Henley SJ, Ballard-Barbash R, et al. Annual Report to the Nation on the status of cancer, 1975–2008, featuring cancers associated with excess weight and lack of sufficient physical activity. *Cancer* 2012; 118:2338–2366. [PubMed: 22460733]
8. Cheng L, Eng C, Nieman LZ, et al. Trends in colorectal cancer incidence by anatomic site and disease stage in the United States from 1976 to 2005. *Am J Clin Oncol* 2011;34:573–580. [PubMed: 21217399]
9. Siegel R, Ward E, Brawley O, et al. Cancer statistics, 2011: the impact of eliminating socioeconomic and racial disparities on premature cancer deaths. *CA Cancer J Clin* 2011;61:212–236. [PubMed: 21685461]
10. Meester RG, Doubeni CA, Lansdorp-Vogelaar I, et al. Colorectal cancer deaths attributable to nonuse of screening in the United States. *Ann Epidemiol* 2015;25:208–213.e1.
11. Centers for Disease Control and Prevention. Cancer screening – United States, 2010. *MMWR Morb Mortal Wkly Rep* 2012;61:41–45. [PubMed: 22278157]
12. Meester RG, Doubeni CA, Zauber AG, et al. Public health impact of achieving 80% colorectal cancer screening rates in the United States by 2018. *Cancer* 2015;121:2281–2285. [PubMed: 25763558]
13. The National Colorectal Cancer Roundtable. What We Do: 80% in Every Community. Accessed July 29, 2020. Available at: <https://nccrt.org/80-in-every-community/>
14. Siegel RL, Miller KD, Jemal A. Cancer Statistics, 2017. *CA Cancer J Clin* 2017;67:7–30. [PubMed: 28055103]
15. Levine O, Zbuk K. Colorectal cancer in adolescents and young adults: defining a growing threat. *Pediatr Blood Cancer* 2019;66:e27941.
16. World Cancer Research Fund/American Institute for Cancer Research. Diet, Nutrition, Physical Activity and Cancer: a Global Perspective. Accessed March 19, 2020. Available at: <https://www.wcrf.org/dietandcancer>
17. Kohler LN, Harris RB, Oren E, et al. Adherence to nutrition and physical activity cancer prevention guidelines and development of colorectal adenoma. *Nutrients* 2018;10:1098.
18. Solans M, Chan DSM, Mitrou P, et al. A systematic review and meta-analysis of the 2007 WCRF/AICR score in relation to cancer-related health outcomes. *Ann Oncol* 2020;31:352–368. [PubMed: 32067678]
19. Rezende LFM, Lee DH, Keum N, et al. Physical activity during adolescence and risk of colorectal adenoma later in life: results from the Nurses' Health Study II. *Br J Cancer* 2019;121:86–94. [PubMed: 31114018]
20. International Agency for research on Cancer. Vitamin D and Cancer. IARC Working Group Report Volume 5. Lyon, France: IARC; 2008. Accessed March 24, 2020. Available at: <https://publications.iarc.fr/Book-And-Report-Series/Iarc-Working-Group-Reports/Vitamin-D-And-Cancer-2008>
21. Koushik A, Hunter DJ, Spiegelman D, et al. Fruits, vegetables, and colon cancer risk in a pooled analysis of 14 cohort studies. *J Natl Cancer Inst* 2007;99:1471–1483. [PubMed: 17895473]
22. Michels KB, Giovannucci Edward, Joshipura KJ, et al. Prospective study of fruit and vegetable consumption and incidence of colon and rectal cancers. *J Natl Cancer Inst* 2000;92:1740–1752. [PubMed: 11058617]
23. Karahalios A, English DR, Simpson JA. Weight change and risk of colorectal cancer: a systematic review and meta-analysis. *Am J Epidemiol* 2015;181:832–845. [PubMed: 25888582]

24. Lauby-Secretan B, Scoccianti C, Loomis D, et al. Body fatness and cancer—viewpoint of the IARC Working Group. *N Engl J Med* 2016;375: 794–798. [PubMed: 27557308]
25. Ligibel JA, Alfano CM, Courneya KS, et al. American Society of Clinical Oncology position statement on obesity and cancer. *J Clin Oncol* 2014; 32:3568–3574. [PubMed: 25273035]
26. Bouvard V, Loomis D, Guyton KZ, et al. Carcinogenicity of consumption of red and processed meat. *Lancet Oncol* 2015;16:1599–1600. [PubMed: 26514947]
27. Johnston BC, Zeraatkar D, Han MA, et al. Unprocessed red meat and processed meat consumption: dietary guideline recommendations from the Nutritional Recommendations (NutriRECS) Consortium. *Ann Intern Med* 2019;171:756–764. [PubMed: 31569235]
28. Chubak J, Whitlock EP, Williams SB, et al. Aspirin for the prevention of cancer incidence and mortality: systematic evidence reviews for the U.S. Preventive Services Task Force. *Ann Intern Med* 2016;164:814–825. [PubMed: 27064482]
29. U.S. Preventive Services Task Force. Final Recommendation Statement: Aspirin Use to Prevent Cardiovascular Disease and Colorectal Cancer: Preventive Medication. Accessed March 23, 2020. Available at: <https://www.uspreventiveservicestaskforce.org/Page/Document/RecommendationStatementFinal/aspirin-to-prevent-cardiovascular-disease-and-cancer>
30. Bains SJ, Mahic M, Myklebust TA, et al. Aspirin as secondary prevention in patients with colorectal cancer: an unselected population-based study. *J Clin Oncol* 2016;34:2501–2508. [PubMed: 27247217]
31. U.S. Department of Health and Human Services. 2014 Surgeon General’s Report: The Health Consequences of Smoking—50 Years of Progress. Accessed March 20, 2020. Available at: https://www.cdc.gov/tobacco/data_statistics/sgr/50th-anniversary/index.htm
32. Chao A, Thun MJ, Jacobs EJ, et al. Cigarette smoking and colorectal cancer mortality in the Cancer Prevention Study II. *J Natl Cancer Inst* 2000; 92:1888–1896. [PubMed: 11106680]
33. Hannan LM, Jacobs EJ, Thun MJ. The association between cigarette smoking and risk of colorectal cancer in a large prospective cohort from the United States. *Cancer Epidemiol Biomarkers Prev* 2009;18:3362–3367. [PubMed: 19959683]
34. LoConte NK, Brewster AM, Kaur JS, et al. Alcohol and Cancer: A Statement of the American Society of Clinical Oncology. *J Clin Oncol* 2018;36:83–93. [PubMed: 29112463]
35. LoConte NK, Gershenwald JE, Thomson CA, et al. Lifestyle modifications and policy implications for primary and secondary cancer prevention: diet, exercise, sun safety, and alcohol reduction. *Am Soc Clin Oncol Educ Book* 2018;38:88–100. [PubMed: 30231343]
36. Fedirko V, Tramacere I, Bagnardi V, et al. Alcohol drinking and colorectal cancer risk: an overall and dose-response meta-analysis of published studies. *Ann Oncol* 2011;22:1958–1972. [PubMed: 21307158]
37. Bailey CE, Hu CY, You YN, et al. Increasing disparities in the age-related incidences of colon and rectal cancers in the United States, 1975–2010. *JAMA Surg* 2014;150:17–22.
38. Siegel RL, Jemal A, Ward EM. Increase in incidence of colorectal cancer among young men and women in the United States. *Cancer Epidemiol Biomarkers Prev* 2009;18:1695–1698. [PubMed: 19505901]
39. Vuik FE, Nieuwenburg SA, Bardou M, et al. Increasing incidence of colorectal cancer in young adults in Europe over the last 25 years. *Gut* 2019; 68:1820–1826. [PubMed: 31097539]
40. Siegel RL, Miller KD, Fedewa SA, et al. Colorectal cancer statistics, 2017. *CA Cancer J Clin* 2017;67:177–193. [PubMed: 28248415]
41. Meester RGS, Peterse EFP, Knudsen AB, et al. Optimizing colorectal cancer screening by race and sex: microsimulation analysis II to inform the American Cancer Society colorectal cancer screening guideline. *Cancer* 2018;124:2974–2985. [PubMed: 29846942]
42. 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. [PubMed: 29846933]
43. 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. [PubMed: 29846947]

44. Stoffel EM, Murphy CC. Epidemiology and mechanisms of the increasing incidence of colon and rectal cancers in young adults. *Gastroenterology* 2020;158:341–353. [PubMed: 31394082]
45. 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. [PubMed: 30930021]
46. Astin M, Griffin T, Neal RD, et al. The diagnostic value of symptoms for colorectal cancer in primary care: a systematic review. *Br J Gen Pract* 2011; 61:e231–243. [PubMed: 21619747]
47. Lieberman DA, Rex DK, Winawer SJ, et al. Guidelines for colonoscopy surveillance after screening and polypectomy: a consensus update by the US Multi-Society Task Force on Colorectal Cancer. *Gastroenterology* 2012;143:844–857. [PubMed: 22763141]
48. Cottet V, Jooste V, Fournel I, et al. Long-term risk of colorectal cancer after adenoma removal: a population-based cohort study. *Gut* 2012;61: 1180–1186. [PubMed: 22110052]
49. He X, Hang D, Wu K, et al. Long-term risk of colorectal cancer after removal of conventional adenomas and serrated polyps. *Gastroenterology* 2020;158:852–861.e4.
50. Lieberman D, Sullivan BA, Hauser ER, et al. Baseline colonoscopy findings associated with 10-year outcomes in a screening cohort undergoing colonoscopy surveillance. *Gastroenterology* 2020;158: 862–874.e8.
51. Click B, Pinsky PF, Hickey T, et al. Association of colonoscopy adenoma findings with long-term colorectal cancer incidence. *JAMA* 2018;319: 2021–2031. [PubMed: 29800214]
52. 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. *Am J Gastroenterol* 2020; 115:415–434. [PubMed: 32039982]
53. Imperiale TF, Kahi CJ, Rex DK. Lowering the starting age for colorectal cancer screening to 45 years: who will come...and should they? *Clin Gastroenterol Hepatol* 2018;16:1541–1544. [PubMed: 30114484]
54. Bretthauer M, Kalager M, Weinberg DS. From colorectal cancer screening guidelines to headlines: beware! *Ann Intern Med* 2018;169: 405–406. [PubMed: 29987330]
55. Liang PS, Allison J, Ladabaum U, et al. Potential intended and unintended consequences of recommending initiation of colorectal cancer screening at age 45 years. *Gastroenterology* 2018;155:950–954. [PubMed: 30138614]

NCCN CATEGORIES OF EVIDENCE AND CONSENSUS

Category 1: Based upon high-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2A: Based upon lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

Category 2B: Based upon lower-level evidence, there is NCCN consensus that the intervention is appropriate.

Category 3: Based upon any level of evidence, there is major NCCN disagreement that the intervention is appropriate.

All recommendations are category 2A unless otherwise noted.

Clinical trials: NCCN believes that the best management of any patient with cancer is in a clinical trial. Participation in clinical trials is especially encouraged.

PLEASE NOTE

The NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) are a statement of evidence and consensus of the authors regarding their views of currently accepted approaches to treatment. **The NCCN Guidelines Insights highlight important changes in the NCCN Guidelines recommendations from previous versions. Colored markings in the algorithm show changes and the discussion aims to further the understanding of these changes by summarizing salient portions of the panel’s discussion, including the literature reviewed.**

The NCCN Guidelines Insights do not represent the full NCCN Guidelines; further, the National Comprehensive Cancer Network® (NCCN®) makes no representations or warranties of any kind regarding their content, use, or application of the NCCN Guidelines and NCCN Guidelines Insights and disclaims any responsibility for their application or use in any way.

The complete and most recent version of these NCCN Guidelines is available free of charge at NCCN.org.

© National Comprehensive Cancer Network, Inc. 2020. All rights reserved. The NCCN Guidelines and the illustrations herein may not be reproduced in any form without the express written permission of NCCN.

PRIMARY AND SECONDARY PREVENTION OF COLORECTAL CANCER

Certain lifestyle modifications are associated with a reduced risk of colorectal cancer (CRC) and can be an important adjunct to screening for CRC prevention. For risk assessment for average risk individuals, see CSCR-1.

Lifestyle/dietary factors associated with reduced CRC risk/recurrence:

- **Physical activity:** Regular physical activity (ie, occupational, recreational, transportation) has been associated with decreased CRC risk.¹
- **Fruits and vegetables:** A diet high in fruits and vegetables has been associated with decreased CRC risk in some studies.^{2,3}
- In general, nutrients should be obtained from natural food sources rather than solely from dietary supplements.¹
- Smoking cessation counseling is strongly recommended.

Aspirin:

- There is substantial evidence about the protective effect of aspirin for CRC development when taken for at least 5–10 years.^{4,5}
 - ◊ This led to the recommendation by the U.S. Preventive Services Task Force to endorse low-dose aspirin (81 mg) intake for individuals ages 50–59 with a $\geq 10\%$ 10-year cardiovascular risk for the purposes of lowering both cardiovascular and CRC risk.
 - ◊ The decision to offer aspirin should take into consideration risk of bleeding, life expectancy, and long-term compliance.⁶ The optimal dose has not been well established.
 - ◊ Regarding secondary prevention, aspirin use has been associated with improved CRC-specific survival and overall survival.⁷

Lifestyle/dietary factors associated with increased CRC risk:

- **Smoking:** Long-term cigarette smoking is associated with CRC risk, after controlling for screening, multiple risk factors, and mortality.^{8,9} Risk reduction is seen with early smoking cessation.⁹
- **Red meat and processed meat:** Long-term consumption is associated with increased CRC risk.^{1,10}
- **Alcohol:** Alcohol consumption is associated with increased CRC risk.^{1,11,12}
- **Obesity:** Obesity is consistently associated with an increased risk for CRC.^{1,13,14,15}
- **Poor vitamin D:** In limited studies, low intake of vitamin D has been associated with increased CRC risk.¹⁶

Please also see relevant sections in:

- NCCN Guidelines for Colon Cancer - Principles of Survivorship
- NCCN Guidelines for Survivorship

Version 2.2020 © National Comprehensive Cancer Network, Inc. 2020. All rights reserved.
The NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN.

CSCR-PREV
1 OF 2

RISK ASSESSMENT FOR COLORECTAL CANCER

Average risk:^a

- Age ≥50 y^b
 - Consider aggressive case findings in patients <50 years (see below)
- No history of adenoma or sessile serrated polyp (SSP)^c or CRC
- No history of inflammatory bowel disease (IBD)
- Negative family history for CRC or confirmed advanced adenoma (ie, high-grade dysplasia, ≥1 cm, villous or tubulovillous histology) or an advanced SSP^d (≥1 cm, any dysplasia)

→ See Average-Risk Screening and Evaluation (CSCR-3)

Increased risk:

- Personal history
 - Adenoma or SSP^c → See Follow-up of Clinical Findings: Polyp Found at Colonoscopy (CSCR-5)
 - CRC → See Increased Risk Based on Personal History of Colorectal Cancer (CSCR-7)
 - IBD (ulcerative colitis, Crohn’s disease) → See Increased Risk Screening Based on Personal History of Inflammatory Bowel Disease (CSCR-8)
- Positive family history → See Increased Risk Based on Positive Family History (CSCR-11)

Aggressive case findings in patients <50 years:

- The incidence of CRC in individuals <50 years has increased 22% between 2003 and 2013 (Siegel RL, et al. CA Cancer J Clin 2017;67:177-193). The majority of CRCs in these younger individuals appears to be sporadic. (Levine O, et al. Pediatr Blood Cancer 2019;66:e27941).
- Presently available data do not justify lowering the age of initiation screening in average-risk individuals.^b
- Signs and symptoms of CRC such as iron deficiency anemia, rectal bleeding, or a change in bowel habits presenting in individuals <50 years warrant prompt evaluation with a colonoscopy or at least with flexible sigmoidoscopy.
 - If symptoms do not respond promptly to medical treatment, a colonoscopy is indicated.

^a See Discussion for further information on age of screening in African Americans.

^b The panel has reviewed the recent data for beginning screening of average-risk individuals at age <50 years. Based on those data, the panel continues to endorse screening of average-risk individuals at age 50 years. The panel will continue to review this strategy and monitor data as they emerge.

^c The terms sessile serrated polyp (SSP) and sessile serrated adenoma are synonymous; SSPs are a type of serrated polyp that are not dysplastic but they can develop foci of dysplasia and are then termed SSP with dysplasia (SSP-d). These guidelines will use “SSP” for SSPs without dysplasia and “SSP-d” for SSPs with dysplasia. In general SSPs are managed like tubular adenomas and SSP-d with any grade dysplasia are managed like high-risk adenomas but may need even more frequent surveillance. Classification systems for serrated lesions are evolving, and a recent proposal by WHO suggests using the term sessile serrated lesion (WHO Classification of Tumours Editorial Board. Digestive System Tumours: IARC Lyon, France; 2019:162-169).

^d Advanced SSPs are generally considered to have a comparable cancer risk and are managed similarly to advanced adenomas.

Version 2.2020 © National Comprehensive Cancer Network, Inc. 2020. All rights reserved.
 The NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN.

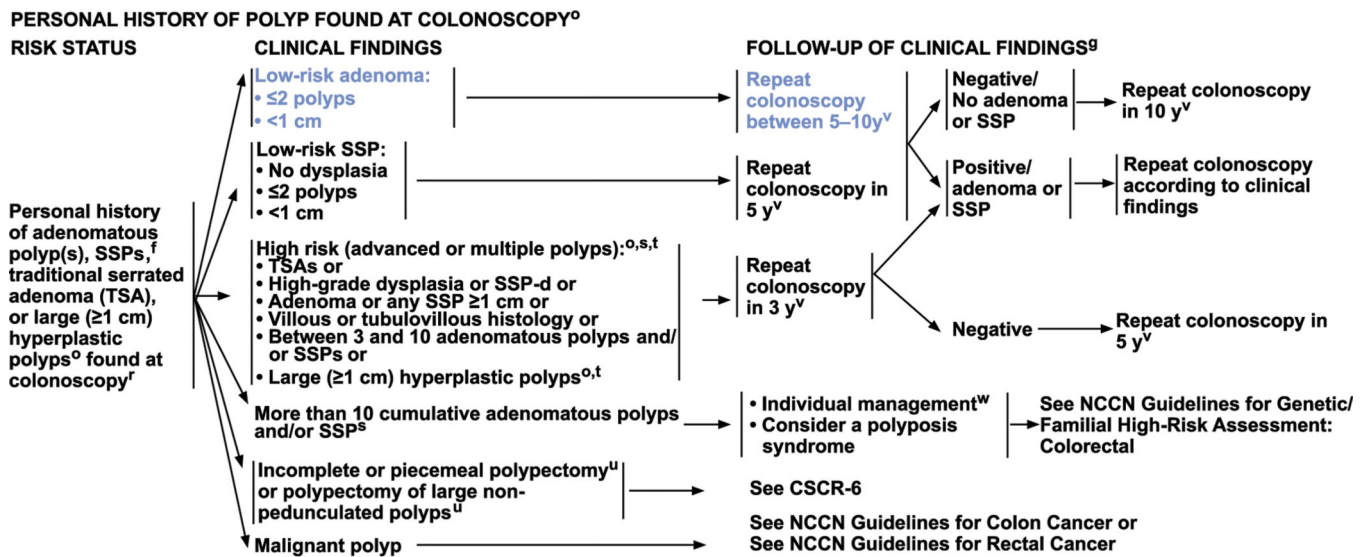
CSCR-1

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript



^f For details on classification, see footnote c on CSCR-1.

^g See Screening Modality and Schedule (CSCR-A).

^o There are limited data to support whether individuals with hyperplastic polyps ≥1 cm in size represent an increased risk group. Several analyses suggest that many of the larger polyps classified as hyperplastic in the past were re-classified as SSPs when reviewed by experts. For this reason, it is reasonable to follow patients with hyperplastic polyps ≥1 cm in size similarly to patients with SSPs, particularly if they have not been reviewed by an expert gastrointestinal pathologist.

^s Surveillance colonoscopy is recommended in adults aged 50–75 years with a history of adenomas. Surveillance of individuals between ages 76–85 years should be individualized and include a discussion of risks and benefits of continued colonoscopy based on comorbidity status, estimated life expectancy, and findings on the last or the most recent colonoscopy.

^t Ten or fewer polyps in the setting of a strong family history or younger age (<40 years) may sometimes be associated with an inherited polyposis syndrome.

^u Surveillance intervals assume complete resection, adequate bowel preparation, and complete examination.

^v Consider a referral to a center of expertise for large polyp management. For sessile polyps or LSL ≥20 mm size, recommend endoscopic tattoo placement for future lesion identification.

^w Available data suggest that individuals with low-risk adenomas or SSPs may not have an increased risk of metachronous advanced colorectal neoplasia compared to the general population (Cottet V, et al. Gut 2012;61:1180-1186; He X, et al. Gastroenterol 2019; 158(4):852-861). Any recommendation for a shorter interval should include a discussion with the individual based on an assessment of individual risk, including age, family history, comorbidity, and the results of previous colonoscopies.

^x If genetic testing is negative or if evaluation is not performed, repeat colonoscopy within 3 years.

Version 2.2020 © National Comprehensive Cancer Network, Inc. 2020. All rights reserved. The NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN.

CSCR-5