Malignancy in Patients With Inflammatory Bowel Disease (IBD)

Pfizer Medical Affairs

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Risk of Cancer in IBD

Patients With IBD are at an Increased Risk of Intestinal Cancers

- Patients with IBD are at an increased risk of intestinal cancers, including colorectal cancer (CRC), small-bowel adenocarcinoma, intestinal lymphoma, and anal cancer[1]
  - According to a meta-analysis assessing the association between IBD and risk of gastrointestinal tract cancers[2]:
    - IBD was associated with an 80% increased risk of intestinal cancer compared with the reference population (OR [95% CI]: 1.80 [1.56-2.03])
    - IBD was not associated with a risk of gastric cancer (OR [95% CI]: 0.87 [0.62-1.13])

Note: Limitations of this study include the small number of studies available for the subgroup analysis, increasing the risk of bias; and lack of data on the age at IBD onset and duration of follow-up, which might have clinical significance.[2]

ORs of Overall Intestinal and Specific Cancers in Patients With CD and UC[2]

Cancer	OR (95% CI)	
	CD	UC
Intestinal cancer	1.90 (1.51-2.30)	1.44 (1.24-1.64)
Small-bowel cancer	9.82 (8.04-11.60)	1.21 (0.15-2.27)
CRC	1.47 (1.32-1.61)	1.51 (1.28-1.74)

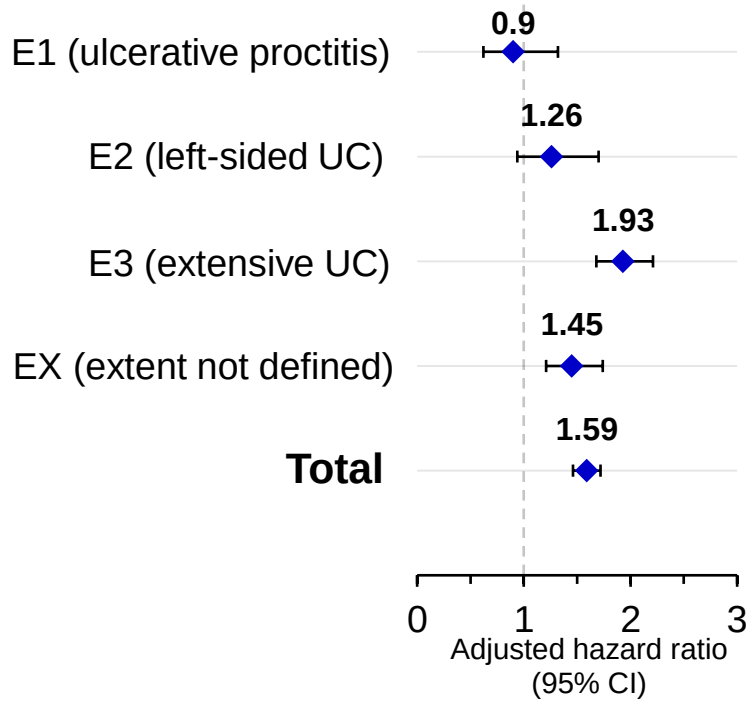
CD=Crohn's disease; CI=confidence interval; IBD=inflammatory bowel disease; OR=odds ratio; UC=ulcerative colitis.

1. Axelrad JE, et al. *World J Gastroenterol.* 2016;22(20):4794-4801. **2.** Wan Q, et al. *J Cancer Res Clin Oncol*. 2021;147(4):1077-1087.

Patients With IBD are at an Increased Risk of Intestinal Cancers *(cont'd)*

- Longer disease duration increases risk of CRC in IBD[1]
  - In a meta-analysis of population-based studies, estimated cumulative risks of CRC were 0.8%, 2.2%, and 4.5% after <10, 10 to 20, and >20 years since IBD diagnosis, respectively [2,a]
- Colitis-associated CRC is a leading cause of mortality and reason for colectomy in the IBD population[3]
  - In a cohort study of patients with UC (N=96,447) compared with matched individuals from the general population (N=949,207), patients with UC were found to be at an increased risk of dying from CRC[4,c]
    - In the UC cohort, 0.55 CRC deaths occurred per 1000 person-years, compared with 0.38 CRC deaths per 1000 person-years in reference individuals

Adjusted Hazard Ratios for Incident CRC Deaths Comparing Patients With Incident UC and Matched General Population (by Maximum Extent of Disease and Total)[4,b,c]



[a]Risks were censored for colectomy and ileal CD. Limitations of this meta-analysis included European origin of most studies and potential heterogeneity between study populations. For the cumulative risk calculation, 4 population-based studies were included.[2] [b]Hazard ratios are adjusted for sex, age at diagnosis, calendar year at diagnosis, and country. Follow-up of UC extent during follow-up started on the first date of the corresponding register entry. Extent of disease is presented according to Montreal classification.[4] [c]Limitations of this ex-US population-based study include absence of data on potential lifestyle risk factors and absence of data on mucosal or laboratory markers of disease activity or information on macroscopic endoscopy findings. Potential effects of drug treatment were not investigated, and populations were limited to Denmark and Sweden.[4] CD=Crohn's disease; CI=confidence interval; CRC=colorectal cancer; IBD=inflammatory bowel disease; N=number of patients; UC=ulcerative colitis.

1. Axelrad JE, Shah SC. *Therap Adv Gastroenterol.* 2020;13:1756284820920779. **2.** Lutgens MW, et al. *Inflamm Bowel Dis.* 2013;19(4):789-799. **3.** Shah SC, Itzkowitz SH. *Gastroenterology.* 2022;162(3):715-730. **4.** Olén O, et al. *Lancet.* 2020;395(10218):123-131.

Patients With IBD are at an Increased Risk of Extraintestinal Cancers

- Patients with IBD are also at an increased risk of extraintestinal cancers
  - According to a meta-analysis of 11 studies on CD and 12 studies on UC, overall risk was increased in patients with CD and UC by 43% and 15%, respectively
  - The increased risk was driven primarily by skin, hepatobiliary, and hematologic malignancies

Note: Limitations of this study include short follow-up time within each cohort (<10 years), risk of misclassification and insufficient coding in registry studies, national differences in treatment exposure, and deficient reporting of cancer risk factors. Only cancers occurring after the diagnosis of IBD were reported in the included studies.

Incidence Rate Ratios (IRRs) of Overall and Site-Specific Extraintestinal Cancers in Patients With CD and UC

Cancer	IRR (95% CI)	
	CD	UC
Extraintestinal cancers	1.43 (1.26-1.63)	1.15 (1.02-1.31)
Skin cancers	2.22 (1.41-3.48)	1.38 (1.12-1.71)
Hepatobiliary cancers	2.31 (1.25-4.28)	2.05 (1.52-2.76)
Hematologic malignancies	2.40 (1.81-3.18)	1.15 (0.96-1.39)

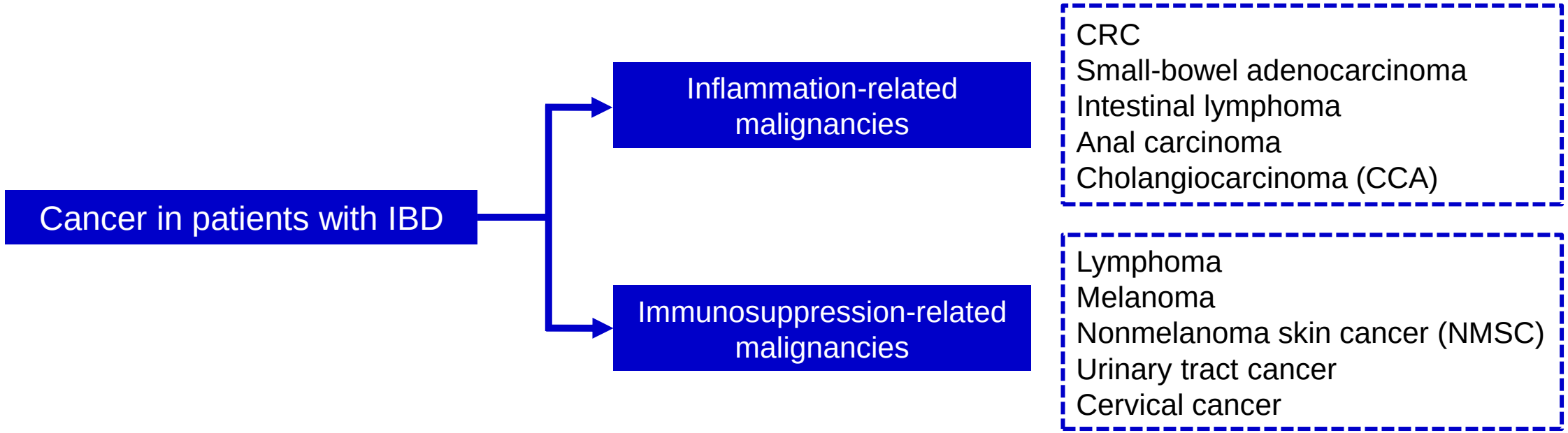
CD=Crohn's disease; CI=confidence interval; IBD=inflammatory bowel disease; UC=ulcerative colitis.

Lo B, et al. *Clin Gastroenterol Hepatol.* 2021;19(6):1117-1138.

Cancer Risk Factors in Patients With IBD

- **Chronic intestinal inflammation** is the primary risk factor for the development of gastrointestinal malignancy in patients with IBD[1]
- **Immunosuppressive drugs** might promote immunosuppression-related cancers[1,2]

Classification of Cancer in Patients With IBD[2]



CRC=colorectal cancer; IBD=inflammatory bowel disease.

1. Axelrad JE, et al. *World J Gastroenterol.* 2016;22(20):4794-4801. **2.** Greuter T, et al. *Digestion.* 2020;101(suppl 1):136-145.

Ongoing Challenges in the Treatment and Management of Cancer in Patients With IBD

IBD, Cancer Risk, and Age

- Older adult patients with IBD are at a higher risk of malignancy than younger patients[1]
  - With the aging of the patient population, the incidence of cancer is expected to increase[3,5]

Limited Data on Cancer Risks With IBD Therapies[4,5]

- There is increasing debate about the impact of IBD therapies on cancer development and progression; the data on safety, particularly in relation to cancer risks, are limited
- Patients with active cancers or a history of cancer in the preceding 5 to 10 years are excluded from randomized controlled trials or registration trials due to the unknown risk of cancer recurrence or progression
  - Patients who develop cancer while receiving newer therapies, such as biologics, are withdrawn from the studies

IBD=inflammatory bowel disease.

1. Khan N, et al. *Drugs Aging.* 2017;34(11):859-868. **2.** Xu F, et al. *MMWR Morb Mortal Wkly Rep.* 2021;70(19):698-701. **3.** Axelrad JE, et al. *World J Gastroenterol.* 2016;22(20):4794-4801. **4.** Sebastian S, Neilaj S. *Therap Adv Gastroenterol.* 2019;12:1756284818817293. 5. Axelrad JE, et al. *Clin Gastroenterol Hepatol* 2024;22:1365–1372

Ongoing Challenges in the Treatment and Management of Cancer in Patients With IBD *(cont'd)*

Challenges in IBD Management in Patients With Cancer

- Immunosuppression for IBD is suspended upon cancer diagnosis, which may cause a flare[1,2]
  - Historically, immunosuppression, including the use of biologics, was generally suspended both during and for 2 to 5 years after completion of cancer treatment[1-4] which can result in worsening IBD, increase risk of surgery in patients with severe IBD, and complicate cancer management[1,2]
  - The AGA guideline states that, despite limited data, in patients whose IBD activity needs to be controlled, it is recommended to consider using IBD therapy, including biologic agents, after collaboration between gastroenterologist and oncologist.[7]
- Cancer treatment may cause a relapse of IBD
  - Patients with inactive IBD who were diagnosed with breast or prostate cancer and receive hormone therapy (alone or in combination with cytotoxic therapy) have an increased risk for relapse of IBD, including IBD-related surgery, hospital admission, disease complication and/or escalation of IBD therapy[5]
  - Approximately 40% of patients with preexisting IBD experience relapse of their IBD or gastrointestinal immune-related adverse events when treated with immune checkpoint inhibitors[6]
  - Oncologists generally avoid administering pelvic irradiation in the setting of IBD, as the tolerance of pelvic irradiation in these patients is largely unknown[1]

IBD=inflammatory bowel disease.

1. Axelrad JE, et al. *World J Gastroenterol.* 2016;22(20):4794-4801. **2.** Sebastian S, Neilaj S. *Therap Adv Gastroenterol.* 2019;12:1756284818817293. **3.** Annese V, et al. *J Crohns Colitis.* 2015;9(11):945-965. **4.** Jauregui-Amezaga A, et al. *Ann Gastroenterol.* 2016;29(2):127-136. **5.** Axelrad JE, et al. *Clin Gastroenterol Hepatol.* 2020;18(4):872-880. **6.** Meserve J, et al. *Aliment Pharmacol Ther.* 2021;53(3):374-382. **7.** Axelrad JE, et al. *Clin Gastroenterol Hepatol.* 2024;22:1365-1372

Cancer Secondary to Chronic Intestinal Inflammation

Cancers Associated With Chronic Intestinal Inflammation

- Ongoing intestinal inflammation has been associated with the following cancers[1]:
  - CRC
  - Small-bowel adenocarcinoma
  - Intestinal lymphoma
  - Anal carcinoma
  - Cholangiocarcinoma (CCA)
- These cancers are potentially preventable with the use of immunosuppressive and biologic agents[1,2]
  - No increased risk of these cancers is observed in patients with IBD compared with age- and gender-matched individuals in the general population when the digestive organs are not chronically inflamed[2]

Standardized Incidence Ratios (SIRs) for Cancers Secondary to Intestinal Inflammation

Cancer type	SIR (95% CI)
CRC[3,a]	• Population-based studies: 1.7 (1.2-2.2) • Referral center studies: 6.9 (4.1-9.7)
Small-bowel adenocarcinoma[4,b]	• IBD overall: 4.0 (3.1-5.1) • CD: 8.3 (5.9-11.3) • UC: 2.0 (1.2-3.1)
Intestinal lymphoma[5,c]	• IBD overall: 17.51 (6.43-38.11)
Biliary tract cancers, including CCA[6,d]	• IBD overall: 5.2 (4.8-5.7) • PSC-IBD: 140 (123-159)

[a]Limitations of this meta-analysis include heterogeneity between included study populations and the fact that most studies included were from European centers.[3] [b]Limitations of this ex-US population-based study include potential misclassification between CD and UC, short follow-up time, and absence of information on disease activity and IBD treatment.[4] [c]Primary intestinal lymphoproliferative disorders. Limitations of this ex-US study included the fact that only patients enrolled in the French nationwide CESAME observational cohort were included, short follow-up time (<4 years), and inclusion of malignancies occurring before and during the follow-up time in the analyses.[5] [d]Limitations of this ex-US study included potential misclassifications of cancers, surveillance bias, lack of information about potential confounding variables, and restriction of analysis to the Nordic population.[6]

CD=Crohn's disease; CESAME=Cancers et Surrisque Associé aux Maladies Inflammatoires Intestinales en France; CI=confidence interval; CRC=colorectal cancer; IBD=inflammatory bowel disease; PSC=primary sclerosing cholangitis; UC=ulcerative colitis.

1. Axelrad JE, et al. *World J Gastroenterol.* 2016;22(20):4794-4801. **2.** Beaugerie L, Kirchgesner J. *Clin Gastroenterol Hepatol.* 2019;17(3):370-379. **3.** Lutgens MW, et al. *Inflamm Bowel Dis.* 2013;19(4):789-799. **4.** Yu J, et al. *Ann Oncol.* 2022;33(6):649-656. **5.** Sokol H, et al. *Inflamm Bowel Dis.* 2012;18(11):2063-2071. **6.** Yu J, et al. *United European Gastroenterol J.* 2022;10(2):212-224.

Clinical Risk Factors for IBD-Associated Colorectal Neoplasia (CRN)

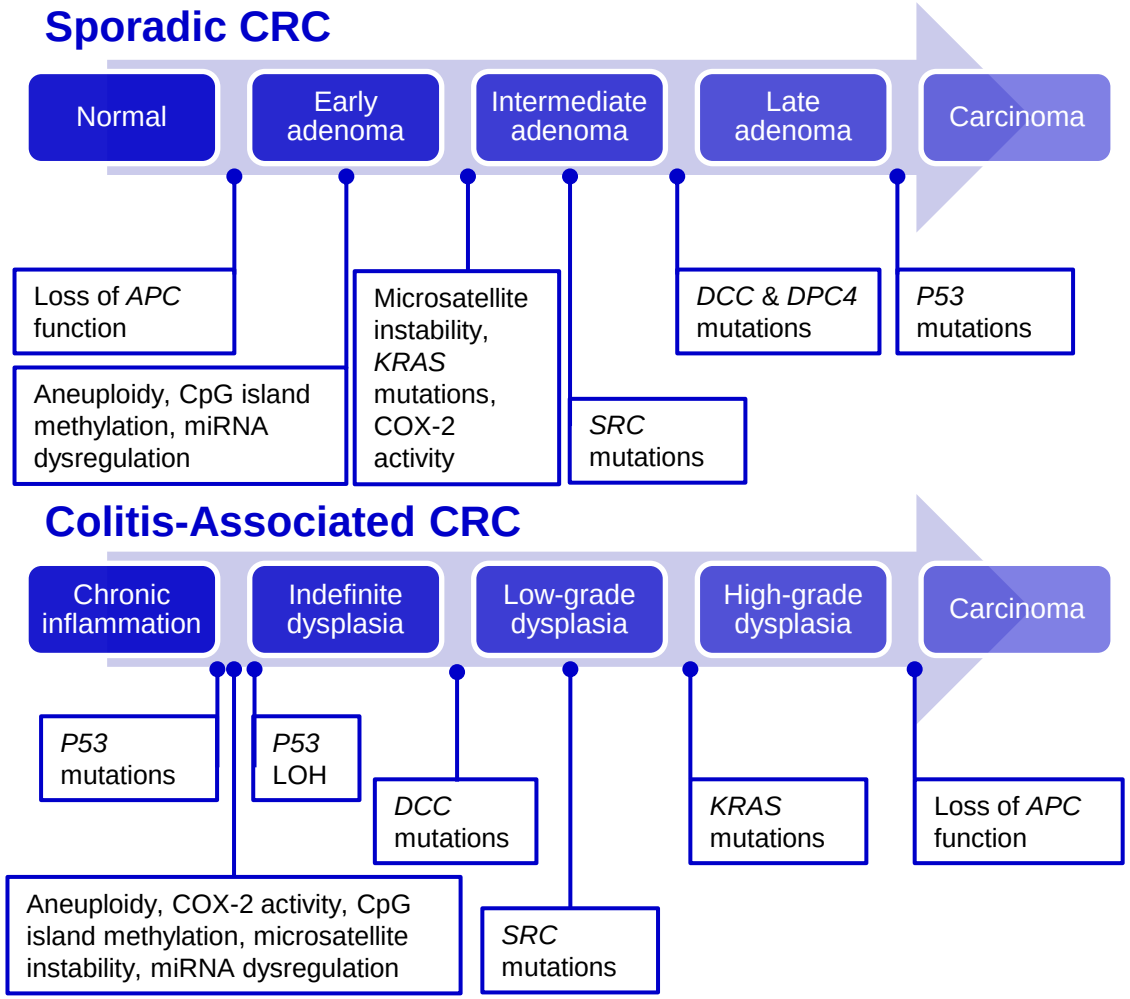
- Patients with IBD are at increased risk of developing CRN, including dysplasia and CRC, as a primary consequence of chronic colonic inflammation compounded by intermittent episodes of acute or subacute inflammation as part of the natural disease course
- Multiple factors modifying the risk of IBD-related CRN have been identified

Patient-specific factors	Disease-specific factors	Inflammatory complications
PSC	Age of IBD onset	Stricture (+/−)
Personal history of CRN	Disease duration	Shortened tubular colon
Family history of CRC in first-degree relative	Disease extent	Pseudopolyps[a]
Smoking	Cumulative inflammatory burden	
Male sex (+/−)	Disease severity (endoscopic and histologic)	

[a]Recent multicenter retrospective cohort studies that control for inflammation and other relevant confounders do not support an independent association of pseudopolyps with advanced CRN.
CRC=colorectal cancer; IBD=inflammatory bowel disease; PSC=primary sclerosing cholangitis.
Axelrad JE, Shah SC. *Therap Adv Gastroenterol.* 2020;13:1756284820920779.

Pathogenesis of Colitis-Associated CRC

- Colitis-associated CRC progresses through dysplastic precursor lesions, whereas sporadic CRC arises from adenoma (and sessile serrated polyp) precursors that progress through various stages until carcinoma
- In colitis-associated CRC, lesions
  - Tend to have a flatter morphology
  - Demonstrate reversal of the *APC* and *P53* sequence of molecular alterations, with *P53* changes occurring early, even before dysplasia
- The molecular alterations associated with both sporadic and colitis-associated carcinogenesis are influenced by environmental factors, including general and specific components of the microbiome



APC=adenomatous polyposis coli; COX-2=cyclooxygenase 2; CRC=colorectal cancer; DCC=deleted in colon cancer; DPC4=deleted in pancreatic cancer locus 4; KRAS=Kirsten rat sarcoma viral oncogene homolog; LOH=loss of heterozygosity; miRNA=microRNA; SRC=SRC proto-oncogene.

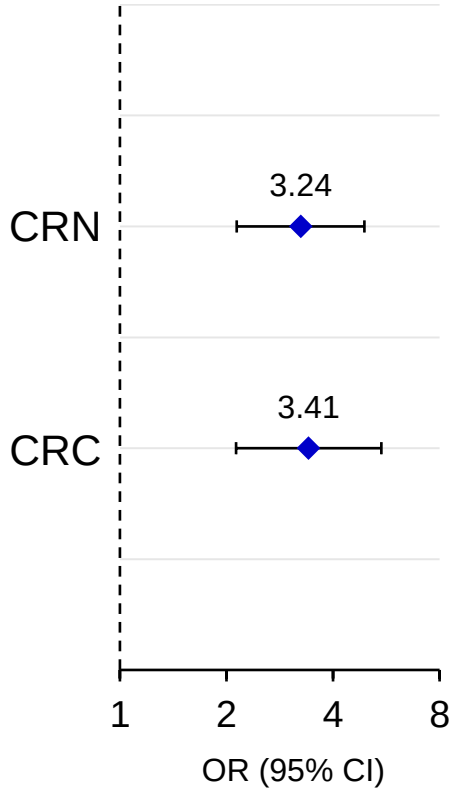
Shah SC, Itzkowitz SH. *Gastroenterology.* 2022;162(3):715-730.

Impact of Primary Sclerosing Cholangitis (PSC) on CRC in IBD

- PSC is a chronic cholestatic liver disease characterized by intrahepatic and/or extrahepatic bile duct injury, leading to stricturing, cholestasis, and biliary cirrhosis with progressive liver dysfunction[1]
- Approximately 70% of patients with PSC have underlying IBD, most frequently UC, with mild and occasionally asymptomatic disease course, increased incidence of extensive colitis, pancolitis, rectal sparing, and backwash ileitis[2,3]
- PSC occurs in 3% to 8% of patients with UC and 1% to 3% of patients with CD[4]
- PSC is a risk factor for IBD-CRC[4]
  - Patients with IBD-PSC, especially UC-PSC, have a markedly higher risk for the development of CRN than patients with IBD alone[5]

    Note: This meta-analysis did not include unpublished studies and included both prospective and retrospective studies, which may have contributed toward some bias and heterogeneity in the analysis.
  - Screening colonoscopy at the time of UC diagnosis and annual surveillance thereafter is recommended in patients with UC-PSC[6]

Odds of CRN and CRC in Patients With PSC-IBD Compared With Patients With IBD Alone[5]



CD=Crohn's disease; CI=confidence interval; CRC=colorectal cancer; CRN=colorectal neoplasia; IBD=inflammatory bowel disease; OR=odds ratio; UC=ulcerative colitis.

1. Dyson JK, et al. *Lancet.* 2018;391(10139):2547-2559. **2.** de Vries AB, et al. *World J Gastroenterol.* 2015;21(6):1956-1971. **3.** Palmela C, et al. *Gut Liver.* 2018;12(1):17-29. **4.** Stidham RW, Higgins PDR. *Clin Colon Rectal Surg.* 2018;31(3):168-178. **5.** Zheng HH, Jiang XL. *Eur J Gastroenterol Hepatol.* 2016;28(4):383-390. **6.** Rubin DT, et al. *Am J Gastroenterol.* 2019;114(3):384-413.

Cholangiocarcinoma (CCA) and Association With PSC

- CCA constitutes a diverse group of malignancies emerging in the biliary tree[1]
- CCA is the most common malignancy in patients with PSC and carries a high rate of mortality[2]
  - In patients with PSC, CCA occurs at a rate nearly 10 to 1000 times higher than in the general population
  - When PSC-associated CCA is diagnosed, most tumors are unresectable, and no effective medications are available
- The risk of CCA is approximately 2 to 4 times as high in patients with IBD as in the general population, although the absolute risk is low[3]
  - Most of the increased CCA risk in patients with IBD is seen in patients with associated PSC
- Prolonged duration of IBD is associated with an increased risk of CCA in patients with PSC-IBD[4]
  - This risk is not modified by colectomy

IBD=inflammatory bowel disease; PSC=primary sclerosing cholangitis.

1. Banales JM, et al. *Nat Rev Gastroenterol Hepatol.* 2020;17(9):557-588**. 2.** Song J, et al. *Clin Rev Allergy Immunol.* 2020;58(1):134-149. **3.** Beaugerie L, Itzkowitz SH. *N Engl J Med.* 2015;372(15):1441-1452. **4.** Gulamhusein AF, et al. *Am J Gastroenterol.* 2016;111(5):705-711.

Cancer Secondary to Immunosuppression in IBD

Overview of Cancers Secondary to Immunosuppression

- Both conventional immunosuppressive agents and biologics have been linked to various cancer subtypes, including[1]
  - Lymphoma
  - Skin cancer (melanoma and NMSC)
  - Urinary tract cancer
  - Cervical cancer
- Immunosuppressive agents may cause tumor formation by[1]
  - Altering DNA
  - Impairing immune control of chronic infection by mutagenic viruses such as EBV and HPV
  - Reducing immunosurveillance of cancer or dysplastic cells

Increased Cancer Risks With Existing IBD Therapies

Drug class/ combination	Potential risk of cancer in patients with IBD compared with unexposed patients
Thiopurines	Increased risk of lymphoma,[2,3] NMSC,[4] and urinary tract cancer[5,6]
Anti-TNF	Increased risk of lymphoma[2,3] and melanoma[4]
Combination of thiopurine and anti-TNF	Increased risk of lymphoma[2,3,a]
Anti–interleukin 12/23	Limited data available,[711]
Anti-integrin	Limited data available[8,11]
Janus kinase inhibitors	Increased risk of malignancies (excluding NMSC) compared with anti-TNF treatment[9,b,11]
S1P receptor modulators	Limited data available[10,11]

[a]Greater risk than for each treatment alone. [b]Data from a randomized, postauthorization, noninferiority trial evaluating the safety and efficacy of pan-JAK inhibitor compared with a TNF inhibitor in patients with rheumatoid arthritis who were 50 years or older and had at least one additional cardiovascular risk factor.[9]

EBV=Epstein-Barr virus; HPV=human papillomavirus; IBD=inflammatory bowel disease; JAK=Janus kinase; NMSC=nonmelanoma skin cancer; S1P=sphingosine-1-phosphate; TNF=tumor necrosis factor.

1. Greuter T, et al. *Digestion.* 2020;101(suppl 1):136-145. **2.** Lemaitre M, *JAMA.* 2017;318(17):1679–1686. **3.** Chupin A, et al. *Aliment Pharmacol Ther.* 2020;52(8):1289-1297. **4.** Long MD, et al. *Gastroenterology.* 2012;143(2):390-399. **5.** Bourrier A, al. *Aliment Pharmacol Ther.* 2016;43(2):252-261. **6.** Pasternak B, et al. *Am J Epidemiol.* 2013;177(11):1296-1305. **7.** Sandborn WJ, et al. *Inflamm Bowel Dis.* 2021;27(7):994-1007. **8.** Card T, et al. *Aliment Pharmacol Ther.* 2020;51(1):149-157. **9.** Ytterberg SR, et al. *N Engl J Med.* 2022;386(4):316-326. **10.** Sandborn WJ, et al. *J Crohns Colitis.* 2021;15(7):1120-1129. **11.** Axelrad JE, et al. *Clin Gastroenterol Hepatol.* 2024;22:1365-1372

Risk of Cancer Recurrence With Immunosuppression in IBD

IBD Management in Patients With Cancer

- Oncologists and gastroenterologists generally suspend immunosuppression for IBD after a diagnosis of cancer, both while patients are undergoing cancer treatment and during remission from cancer[1]
  - This approach may worsen IBD and complicate appropriate cancer management

Immunosuppression in Patients With IBD and a History of Cancer

- Given the risks of immunomodulator- and biologic-associated malignancy, patients with a history of cancer were excluded from clinical trials of TNF antagonists[1]
- Data within the transplant literature indicate that immunosuppression increases the risk of new and recurrent malignancies in patients with a history of cancer[1]
- In an ongoing prospective analysis of the SAPPHIRE registry of patients with IBD and a recent history of cancer[a] (N=267), exposure to immunosuppressive IBD therapies conferred no increased risk of new or recurrent cancer compared with individuals who did not receive immunosuppressive IBD therapies[2]

Note: Limitations of this study include small sample size and short follow-up time (up to 5 years; the study is ongoing).

IBD=inflammatory bowel disease; N=number of patients; SAPPHIRE=Safety of Immunosuppression in a Prospective Cohort of Inflammatory Bowel Disease Patients With a History of Cancer; TNF=tumor necrosis factor.

[a]Defined as histologically confirmed first cancer within the last 5 years.[2]

1. Axelrad JE, et al. *World J Gastroenterol.* 2016;22(20):4794-4801. **2.** Axelrad J, et al. Poster presented at: Digestive Disease Week; May 21-24, 2022; San Diego, CA. Poster Tu1437.

Cancer Surveillance and Guideline Recommendations in IBD

Strategies for the Prevention and Early Detection of CRC in Patients With IBD

- Although there may be an overlap between disease- and therapy-related cancers, the general strategy for prevention of cancer in patients with IBD should include[1]
  - Understanding the risk factors for these malignancies
  - Educating patients about the recommended screening and surveillance practices
  - Incorporating general screening recommendations into routine IBD care
- An individualized screening and surveillance strategy for CRC should be developed for each patient that considers modifiable and nonmodifiable risk factors[1]
- Because CRC risk in IBD is primarily driven by inflammation, optimal disease control with medical therapy is imperative to minimizing an individual's lifetime risk of developing CRC[2]
- However, optimized medical therapy alone is not an appropriate prevention method for CRC and does not replace the need for screening and early surveillance[3]

CRC=colorectal cancer; IBD=inflammatory bowel disease.

1. Cleveland NK, Rubin DT. *Pract Gastroenterol.* 2021;45(8):12-28. **2.** Murthy SK, et al. *Gastroenterology.* 2021;161(3):1043-1051. **3.** Rubin DT, et al. *Am J Gastroenterol.* 2019;114(3):384-413.

Guideline Recommendations for CRC Screening and Surveillance

	Population	Frequency and screening method
American College of Gastroenterology recommendations[1-3]	General population • Average-risk individuals: age 50-75 years recommended, age 45-49 years suggested • Decision to screen beyond age 75 years to be individualized	• Colonoscopy every 10 years and annual FIT • Alternative tests: flexible sigmoidoscopy every 5-10 years, multitarget stool DNA test every 3 years, CT colonography every 5 years, capsule colonoscopy every 5 years
	• CD patients	• Surveillance colonoscopy in CD patients with ≥30% of colon involved and a disease duration of ≥8 years
	• UC patients	• UC extending beyond rectum: colonoscopy 8 years after diagnosis and every 1-3 years thereafter • UC + PSC: colonoscopy at time of diagnosis and surveillance annually thereafter
US Multi-Society Task Force on Colorectal Cancer recommendations[4,5] (general population)	• Age ≥45 years	• Tier 1: colonoscopy every 10 years and annual FIT • Tier 2: CT colonography every 5 years, FIT–fecal DNA test every 3 years, flexible sigmoidoscopy every 10 years (or every 5 years) • Tier 3: capsule colonoscopy every 5 years
US Preventive Services Task Force recommendations[6] (general population)	• Age 50-75 years: substantial net benefit • Age 45-49 years: moderate net benefit • Decision to screen between ages 76 and 85 years to be individualized	Several recommended screening tests are available. Clinicians and patients may consider a variety of factors in deciding which test may be best for each person. Suggested tests and frequencies include the following: • Stool-based tests: annual HSgFOBT, annual FIT, FIT-DNA every 1 to 3 years • Direct visualization tests: colonoscopy every 10 years, CT colonography every 5 years, flexible sigmoidoscopy every 5 years, flexible sigmoidoscopy every 10 years + annual FIT

CD=Crohn's disease; CRC=colorectal cancer; CT=computed tomography; FIT=fecal immunochemical test; HSgFOBT=high-sensitivity guaiac fecal occult blood test; PSC=primary sclerosing cholangitis; UC=ulcerative colitis.

1. Shaukat A, et al. *Am J Gastroenterol.* 2021;116(3):458-479. **2.** Lichtenstein GR, et al. *Am J Gastroenterol.* 2018;113(4):481-517. **3.** Rubin DT, et al. *Am J Gastroenterol.* 2019;114(3):384-413. **4.** Rex DK, et al. *Am J Gastroenterol*. 2017;112(7):1016-1030. 5. Patel SG, et al. *Gastroenterology.* 2022;162(1):285-299. **6.** US Preventive Services Task Force. *JAMA.* 2021;325(19):1965–1977.

Endoscopic Surveillance and Management of Colorectal Dysplasia in IBD

- According to the 2021 AGA Clinical Practice Update on Endoscopic Surveillance and Management of Colorectal Dysplasia in IBD, precancerous colorectal lesions in IBD should be described as polypoid (≥2.5 mm tall), nonpolypoid (<2.5 mm), or invisible (detected on nontargeted biopsy), using a modified Paris classification[a]

Updated Lesion Description in IBD

Updated terminology	Paris endoscopic classification of superficial neoplastic lesions		Invisible dysplasia
	• Polypoid	• Nonpolypoid	Dysplasia not seen by the endoscopist within presently or previously inflamed mucosa
	• Pedunculated • Sessile	• Flat elevated • Flat • Flat depressed	

- In addition to Paris classification, report lesion size, morphology, border clarity, ulceration, location, if within area of colitis, completeness of resection, and any special techniques used to visualize

[a]The older terms *dysplasia-associated lesion or mass*, *adenoma-like mass*, and *flat dysplasia* (when referring to dysplasia detected in nontargeted biopsies) should be abandoned.
AGA=American Gastroenterological Association; IBD=inflammatory bowel disease.
Murthy SK, et al. *Gastroenterology.* 2021;161(3):1043-1051.

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Endoscopic Surveillance and Management of Colorectal Dysplasia in IBD *(cont'd)*

Best Practice Advice According to the 2021 AGA Clinical Practice Update on Endoscopic Surveillance and Management of Colorectal Dysplasia in IBD

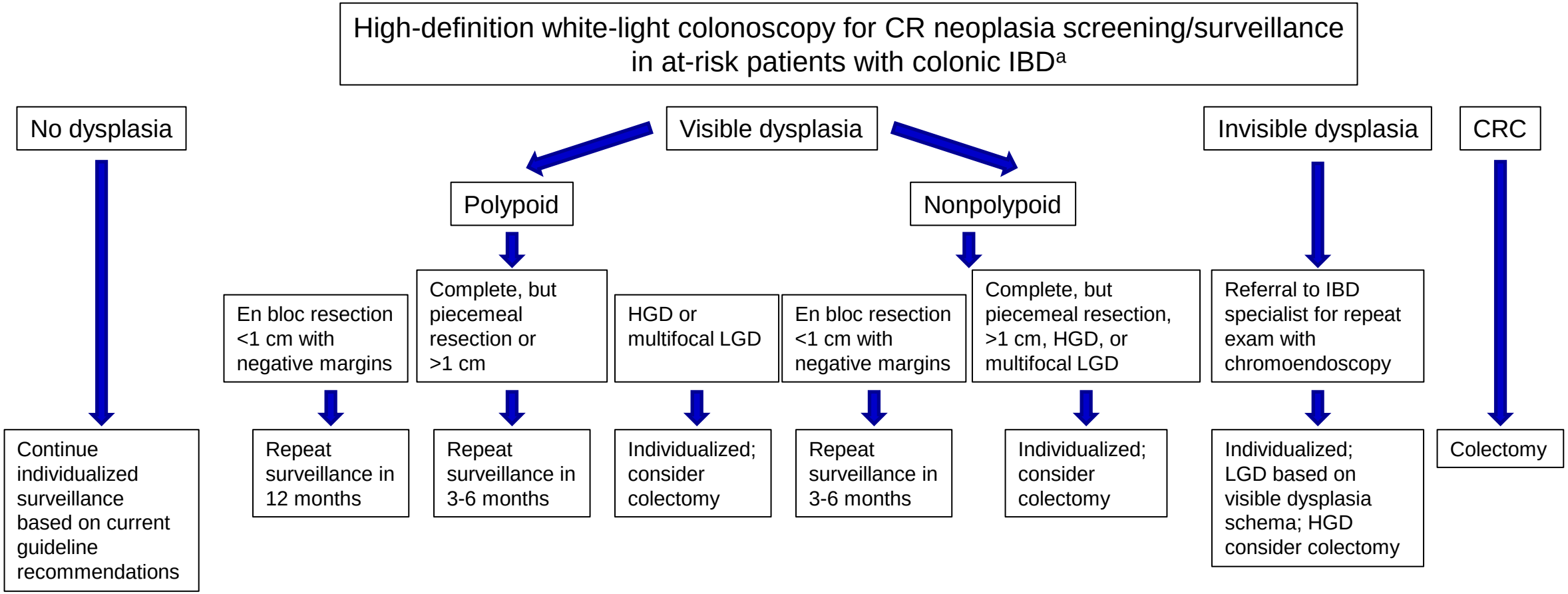
When to start screening	Fundamentals for dysplasia detection	Enhanced dysplasia-detection techniques
• 8-10 years after disease onset in all patients to stage histologic activity and extent and guide future surveillance • At diagnosis in PSC	• High-definition colonoscope • Quiescent disease • Washing and careful inspection of fully visible mucosa • Targeted biopsies of suspicious mucosal abnormalities or sites of prior dysplasia	• Dye-spray chromoendoscopy • Virtual chromoendoscopy • Nontargeted biopsies of nonsuspicious areas

Types of biopsies to obtain				
Targeted		Nontargeted		Staging
Biopsies of suspicious or subtle mucosal abnormalities to rule out dysplasia	+	Biopsies of nonsuspicious areas to rule out invisible dysplasia	OR	Biopsies of macroscopically inflamed and uninflamed areas to assess histologic disease activity and extent

AGA=American Gastroenterological Association; IBD=inflammatory bowel disease; PSC=primary sclerosing cholangitis.

Murthy SK, et al. *Gastroenterology.* 2021;161(3):1043-1051.

Management of Patients With Colonic IBD Undergoing Surveillance for CRN



[a]For patients with concomitant PSC, there is a lower threshold for colectomy given the significantly higher rates of CRC and progression from LGD to advanced neoplasia compared with patients with colonic IBD and no PSC.

CRC=colorectal cancer; CRN=colorectal neoplasia; HGD=high-grade dysplasia; IBD=inflammatory bowel disease; LGD=low-grade dysplasia; PSC=primary sclerosing cholangitis.

Axelrad JE, Shah SC. *Therap Adv Gastroenterol.* 2020;13:1756284820920779.

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Preventive Measures and Screening Recommendations for Skin and Cervical Cancer in Patients With IBD

- Patients with IBD have unique health maintenance needs, which can be comanaged by the gastroenterologist and primary care provider[1,2]

Skin Cancer in Patients With IBD

- Screening for melanoma independent of the use of biologic therapy is recommended[2]
- Screening for NMSC is recommended for patients treated with immunomodulators (6-mercaptopurine or azathioprine), particularly for those over the age of 50 years[2]
- Skin surveillance strategies should be maintained even after stopping thiopurine therapy[2]
- Other risk factors to be considered include fair skin, prior or current high amounts of ultraviolet radiation exposure, and personal or family history of skin cancer[3]
- Primary prevention and protection by sun avoidance and sun protection with sunscreens is recommended[3]

Cervical Cancer in Women With IBD[2]

- Annual cervical cancer screening is recommended for women receiving immunosuppressive therapy

IBD=inflammatory bowel disease; NMSC=nonmelanoma skin cancer.

1. Abegunde AT, et al. *World J Gastroenterol.* 2016;22(34):7625-7644. **2.** Farraye FA, et al. *Am J Gastroenterol*. 2017;112(2):241-258. **3.** Cleveland NK, Rubin DT. *Pract Gastroenterol.* 2021;45(8):12-28.

Summary

- Patients with IBD are at an increased risk of intestinal and extraintestinal cancers due to chronic intestinal inflammation and the use of immunosuppressive drugs
- Colitis-associated CRC remains a leading cause of mortality and reason for colectomy in the IBD population
- The general strategy for prevention of cancer in patients with IBD includes understanding malignancy risk factors and incorporating general screening recommendations into routine IBD care
  - Optimal control of IBD with medical therapy, along with individualized screening and early surveillance that considers modifiable and nonmodifiable risk factors, is recommended

CRC=colorectal cancer; IBD=inflammatory bowel disease.

Resources and References

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Resources

- American Gastroenterological Association
  - AGA Clinical Practice Update on Endoscopic Surveillance and Management of Colorectal Dysplasia in Inflammatory Bowel Diseases
- American College of Gastroenterology
  - ACG Clinical Guidelines: Colorectal Cancer Screening 2021
  - ACG Clinical Guideline: Management of Crohn's Disease in Adults
  - ACG Clinical Guideline: Ulcerative Colitis in Adults
  - ACG Clinical Guideline: Preventive Care in Inflammatory Bowel Disease
- US Multi-Society Task Force on Colorectal Cancer
  - Colorectal Cancer Screening: Recommendations for Physicians and Patients From the U.S. Multi-Society Task Force on Colorectal Cancer
  - Updates on Age to Start and Stop Colorectal Cancer Screening: Recommendations From the U.S. Multi-Society Task Force on Colorectal Cancer
- US Preventive Services Task Force
  - Screening for Colorectal Cancer: US Preventive Services Task Force Recommendation Statement

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