Health Maintenance in Inflammatory Bowel Disease

Contents

Overview of Health Maintenance in IBD

IBD and Health Maintenance

- Health maintenance through preventive care is an important aspect of IBD management because patients often require lifelong care and are subject to complications from the disease itself as well as from the immunosuppressive therapies[1,2]
- Goals of preventive care include[2]
  - Reducing morbidity, hospitalization, and surgery
  - Improving disease-free remission and quality of life

Despite availability of treatments, patients with IBD do not receive adequate preventive services compared with the general population[1-3]

- Suggested reasons for such disparity include[2,3]
  - Patient perception of the gastroenterologist as their PCP, resulting in infrequent visits to PCPs
  - Provider focus on disease control rather than preventive measures
  - Lack of consensus regarding whether gastroenterologist or PCP should offer preventive service
- Gastroenterologists should[2]
  - Clarify with patients the limits of gastroenterologist responsibility for preventive health
  - Communicate with PCPs about the unique health maintenance needs of patients with IBD

IBD=inflammatory bowel disease; PCP=primary care physician.

1. Long MD. *Pract Gastroenterol*. 2020;44(2):32-37. **2.** Abegunde AT, et al. *World J Gastroenterol.* 2016;22(34):7625-7644. **3.** Selby L, et al. *Inflamm Bowel Dis.* 2008;14(2):253-258.

Categorization of Preventive Care Practices

- Preventive activities are typically categorized by 3 definitions[1,2]:

Primary prevention	Intervention before health effects occur ▪ Example measures may include vaccinations and altering risky behaviors (eg, poor eating habits, tobacco use)
Secondary prevention	Screening to identify diseases in the earliest stages, before the onset of signs and symptoms ▪ Includes cancer and other screenings
Tertiary prevention	Management of disease after diagnosis to slow or stop progression ▪ Examples may include management of IBD symptoms and mucosal inflammation

- Most prevention suggestions fall under primary or secondary efforts[1]

IBD=inflammatory bowel disease.

1. Centers for Disease Control and Prevention. https://www.cdc.gov/pictureofamerica/pdfs/Picture_of_America_Prevention.pdf. Accessed March 22, 2021. **2.** Long MD. *Pract Gastroenterol*. 2020;44(2):32-37.

Primary Preventive Care in Patients With IBD

- Vaccination
- Smoking cessation
- Nutrition

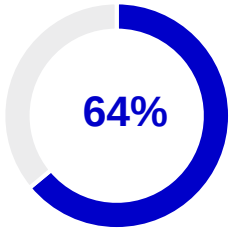
Patients With IBD and Vaccine-Preventable Infections

Patients With IBD Have an Increased Risk of Infections

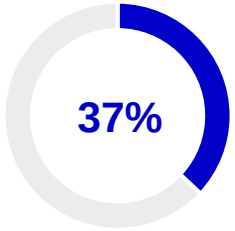
- Patients with IBD are often treated with long-term immunosuppressive therapies, which may increase their risk of infection[1]
- These infections include vaccine-preventable infections, such as pneumonia and herpes zoster, both of which occur more frequently in the IBD population than in the general population[2,3]

Yet Patients With IBD May Not Receive Adequate Preventative Treatment

- Many patients with IBD do not receive routine preventive care, resulting in low vaccination rates for many IBD patients[1,4]
- Gastroenterologists may often be the only clinicians that a patient with IBD will see[1]



% of gastroenterologists reported that providing vaccinations is the responsibility of primary care physicians[4,5]



% of family medicine practitioners reported being comfortable providing primary care to patients with IBD[4,6,a]

[a]Attendees of a family medicine regional review course in 2007 were surveyed to assess exposure to and comfort level with IBD patients.[6]

IBD=inflammatory bowel disease.

1. Farraye FA, et al. *Am J Gastroenterol*. 2017;112(2):241-258. ***2.*** Long MD, et al. *Am J Gastroenterol*. 2013;108(2):240-248. **3**. Long MD, et al. *Aliment Pharmacol Ther*. 2013;37(4):420-429. **4.** Reich JS, et al. *Dig Dis Sci*. 2016;61(8):2205-2216. **5.** Wasan SK, et al. *Inflamm Bowel Dis*. 2011;17(12):2536-2540. **6.** Selby L, et al. *Dig Dis Sci.* 2011;56(3):819-824.

Potential Strategies to Increase Vaccine Uptake in IBD Patients

- Education on the importance of vaccination for both gastroenterologists and patients[1-3]
- Incorporation of vaccination reminders and order panels into electronic medical records[3,4]
- Gastroenterologists could offer vaccinations in their own office or refer patients to their primary care provider or local pharmacy with explicit vaccination recommendations or prescription[5]
- Gastroenterologists ideally should be proactive in formulating a series of recommendations for vaccinations during the first office visit of a newly diagnosed patient with IBD to increase[5] vaccination rates[5]

IBD=inflammatory bowel disease.

1. Sapir T, et al. *Dig Dis Sci.* 2016;61(7):1862-1869. **2.** Reich JS, et al. *Gastroenterol Hepatol (N Y).* 2015;11(6):396-401. **3.** Farraye FA, et al. *Am J Gastroenterol*. 2017;112(2):241-258. **4.** Karr JR, et al. *Ochsner J.* 2016;16(1):90-95. **5.** Farraye FA. *Gastroenterol Hepatol.* 2017;13(7):431-434.

2017 ACG Clinical Guidelines for Vaccinations in Patients With IBD

Patients with IBD can receive all inactive vaccines regardless of their level of immunosuppression[1]

Live vaccines should be used with caution in patients who are on high-level immunosuppression[1]

In general, adherence to age-appropriate vaccination schedules is recommended, with special considerations for patients receiving or initiating immunosuppressive therapies. Adults with IBD should receive vaccinations prior to receiving immunosuppressive therapies when possible.[2]

- All adult patients with IBD should undergo annual vaccination against influenza
  - Patients on immunosuppressive therapies and their household contacts should receive the non-live trivalent (IIV) influenza vaccine
- Adult patients with IBD receiving immunosuppressive therapy should receive pneumococcal vaccination with PCV13 and PPSV23 per national guidelines
- Adults with IBD aged >50 years should consider vaccination against HZ, including certain subgroups of immunosuppressed patients
- Adults with IBD should be vaccinated against varicella if naïve, ideally before initiation of immunosuppressive therapy
- Vaccination against Tdap, HAV, HBV, and HPV should be administered per the ACIP guidelines

ACG=American College of Gastroenterology; ACIP=Advisory Committee on Immunization Practice; HAV=hepatitis A virus; HBV=hepatitis B virus; HPV=human papillomavirus; HZ=herpes zoster; IBD=inflammatory bowel disease; IIV=inactivated influenza vaccine; PCV13=13-valent pneumococcal conjugate vaccine; PPSV23=23-valent pneumococcal polysaccharide vaccine; Tdap=tetanus, diphtheria, and pertussis.

1. Farraye FA. *Gastroenterol Hepatol.* 2017;13(7):431-434. **2.** Farraye FA, et al. *Am J Gastroenterol*. 2017;112(2):241-258.

Crohn's Disease and Smoking

Smoking is correlated with disease development, progression, and poor medical and surgical outcomes[1]

In patients with CD

- Smokers may be more likely to develop perianal disease, ileal disease, and stricturing or penetrating disease compared with nonsmokers[2]
- Smoking may be an independent predictor of the need for maintenance treatment and specifically for biologic therapy[3]
- Smoking cessation may reduce the likelihood of repeated surgeries for recurrent CD[4]

CD=Crohn's disease; UC=ulcerative colitis.

1. Farraye FA, et al. *Am J Gastroenterol.* 2017;112(2):241-258. **2.** Parkes GC, et al. *J Crohns Colitis.* 2014;8(8):717-725. **3.** Nunes T, et al. *Inflamm Bowel Dis.* 2013;19(1):23-29. **4.** Ryan WR, et al. *Am J Surg.* 2004;187(2):219-225.

Ulcerative Colitis and Smoking

Some research has suggested that active smoking may prevent or delay the development of UC; however, it remains unclear whether smoking has beneficial effects on the disease course or progression[1]

In patients with UC

- A meta-analysis of 13 studies (N=11,741) on smoking and UC found that current smoking had a protective effect on the development of UC compared with controls (OR: 0.58; 95% CI: 0.45-0.75), whereas former smoking had a negative impact on UC development (OR: 1.79; 95% CI: 1.37-2.34)[2]

  Note: This meta-analysis was limited by the lack of uniformity in smoking definitions and selection of only the non-Jewish white population, which may not be representative of other races

- A recent retrospective study from the UK using a clinical research database (N=6754[a]; 41,024 person-years) with patient data from 2005 to 2016 revealed that smokers had a similar risk of corticosteroid-requiring flares (OR: 1.16; 95% CI: 0.92-1.46), thiopurine use (HR: 0.84; 95% CI: 0.62-1.14), corticosteroid dependency (HR: 0.85; 95% CI: 0.60-1.11), hospitalization (HR: 0.92; 95% CI: 0.72-1.18), and colectomy (HR: 0.78; 95% CI: 0.50-1.21) compared with never-smokers; in addition, smoking cessation was not correlated with worse disease course in patients with UC[3]

  Note: There could be introduced bias due to lack of smoking-status data in 30% of patients in the 2 years before diagnosis, and smoking status did not consider alternative types of tobacco exposure or the use of transdermal nicotine patches. Additionally, corticosteroid use may be underestimated because prescription data in a hospital outpatient setting were not captured. Finally, results on surgery were not adjusted due to lack of disease-extent data

Given the known cardiac, pulmonary, and oncologic risks associated with smoking, the risks of smoking are considered to outweigh any benefit for patients with UC[1,4]

[a]878 patients were smokers and 2698 patients were never-smokers at diagnosis.
CI=confidence interval; HR=hazard ratio; OR=odds ratio; UC=ulcerative colitis.

1. Crohn's & Colitis UK. https://www.crohnsandcolitis.org.uk/about-crohns-and-colitis/publications/smoking-and-ibd. Accessed April 26, 2021. **2.** Mahid SS, et al. *Mayo Clin Proc.* 2006;81(11):1462-1471. **3.** Blackwell J, et al. *Aliment Pharmacol Ther.* 2019;50(5):556-567. **4.** Centers for Disease Control and Prevention. https://www.cdc.gov/tobacco/data_statistics/fact_sheets/health_effects/effects_cig_smoking/index.htm. Accessed March 22, 2021.

Recommendations for Smoking Cessation in Patients With IBD

ACG recommendations[1-3]	**CD** • Patients who smoke should be counseled to quit (*strong recommendation*)[1] • Smoking should be avoided, and active smoking cessation programs should be encouraged (*strong recommendation*)[2] **UC** • No specific recommendations[3]
CCF recommendations[4]	• Screen all patients for smoking status at baseline, and refer current smokers for smoking cessation therapy
USPSTF recommendations[5,6] (general population)	• Screen all adults for tobacco use, advise to stop using tobacco, and provide behavioral interventions (and pharmacotherapy for nonpregnant adults) for smoking cessation[5] • Provide interventions (eg, education, brief counseling) to prevent initiation of tobacco use among school-age children and adolescents[6]

ACG=American College of Gastroenterology; CCF=Crohn's & Colitis Foundation; CD=Crohn's disease; IBD=inflammatory bowel disease; UC=ulcerative colitis; USPSTF=United States Preventive Services Task Force.

1. Farraye FA, et al. *Am J Gastroenterol.* 2017;112(2):241-258. **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.** Crohn's & Colitis Foundation. https://www.crohnscolitisfoundation.org/science-and-professionals/education-resources/health-maintenance-checklists. Accessed March 22, 2021. **5.** US Preventive Services Task Force. *JAMA.* 2021;325(3):265-279. **6.** US Preventive Services Task Force. *JAMA.* 2020;323(16):1590-1598.

Malnutrition in Patients With IBD

- Patients with IBD often suffer from malnutrition, and the reported prevalence of malnutrition ranges between 20% and 85%[1]
  - Malnutrition may be more prevalent in patients with CD, given its capacity to affect any part of the gastrointestinal tract—unlike UC, which is restricted to the colon[2,3]
- Malnutrition has many detrimental effects[4]
  - It is associated with deterioration in muscle, respiratory, and immune function
  - It may delay wound healing and recovery from illness
- Malnutrition is associated with poor outcomes in patients with IBD[2]
  - It is an independent risk factor for venous thromboembolism, nonelective surgery, and increased mortality in patients with IBD
  - It is also associated with a higher frequency of postoperative complications, longer hospital stays, decreased quality of life, and higher health costs

Malnutrition	CD	UC
Prevalence[5]	• 65%-75%	• 18%-62%
Presentation[1]	• May develop over a long period of time	• May present during a severe acute flare
Inflammation and potential impact on nutritional deficiencies[1-3]	• Inflammation is patchy and may occur throughout the small and large bowel • Ileal involvement may result in decreased nutrient absorption. Protein-energy and specific nutrient malnutrition is more common in patients with CD	• Continuous and uniform inflammation confined to the colon • Patients with UC may have less significant nutrient deficiencies, although severe diarrhea and blood loss can cause weight loss and anemia

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

1. Balestrieri P, et al. *Nutrients.* 2020;12(2):372. **2.** Bischoff SC, et al. *Clin Nutr*. 2020;39(3):632-653. **3.** Crohn's & Colitis Foundation. https://www.crohnscolitisfoundation.org/diet-and-nutrition/malnutrition-and-ibd. Accessed March 22, 2021. **4.** Nguyen GC, et al. *Inflamm Bowel Dis*. 2008;14(8):1105-1111. **5.** Lochs H. *E Spen Eur E J Clin Nutr Metab*. 2010;5(2):e100-e103.

Dietary Guidance From the International Organization for the Study of IBD (IOIBD)

- The IOIBD recently provided expert opinion on specific dietary components, food groups, and food additives that may be prudent to increase or decrease in the diet to control and prevent relapse of IBD
  - Recommendations specific to patients with CD and UC are included
  - Guidance is based on the best current evidence available
  - The recommendations are not meant to exclude the role of nutritional assessment for malnutrition and correction of deficiencies when needed
  - For patients with persistent symptoms despite resolution of inflammation and absence of strictures, the IOIBD suggested that a low-FODMAP or lactose-free diet may improve symptoms

Dietary Guidance for Patients With CD and UC

	CD recommendations	UC recommendations
Prudent to increase foods containing	• Vegetables • Fruits	• Omega 3 oils from fish and food
Prudent to decrease foods containing	• Saturated and trans fat • Emulsifiers • Carrageenans • Artificial sweeteners • Maltodextrins • Titanium dioxide	• Red meat, processed meats • Dairy fat, palm and coconut oil • Saturated and trans fat • Emulsifiers • Carrageenans • Artificial sweeteners • Maltodextrins • Titanium dioxide

CD=Crohn's disease; FODMAP=fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; IBD=inflammatory bowel disease; UC=ulcerative colitis.

Levine A, et al. *Clin Gastroenterol Hepatol*. 2020;18(6):1381-1392.

Assessment of Nutritional Status in Patients With IBD

Screening for malnutrition at time of diagnosis and on a regular basis thereafter[1]

- Dietetic evaluation including BMI and daily caloric intake and energy expenditure[2,3]
  - **BMI:** Measures ratio of weight (in kilograms) to the square of height (in meters)[3]
- Dual-energy X-ray absorptiometry (DEXA)[2]
  - **DEXA:** Assesses bone mineral density[2]
- Macronutrient and micronutrient assessments (eg, albumin)[1]
  - **Albumin:** Potential marker of malnutrition in quiescent disease; also influenced by other factors (eg, rate of synthesis by the liver and loss of protein from gut and/or kidney)[3]
    - Micronutrient assessment should be performed during times of inactive disease because the inflammatory response can alter micronutrient levels[4]

BMI=body mass index; IBD=inflammatory bowel disease.

1. Bischoff SC, et al. *Clin Nutr*. 2020;39(3):632-653. **2.** Balestrieri P, et al. *Nutrients.* 2020;12(2):372. **3.** Halmos EP, Gibson PR. *Nat Rev Gastroenterol Hepatol*. 2015;12(3):133-146. **4.** Nazarenkov N, et al. *Gastroenterol Hepatol*. 2019;15(3):133-144.

Secondary Preventive Care in Patients With IBD

- Cancer screening
- Osteoporosis screening
- Ocular health screening
- Oral health screening
- Anxiety and depression screening

Pfizer

Colorectal Cancer in Patients With IBD

- Patients with IBD are at increased risk of developing CRC[1,2]
  - Reported risk factors include age at diagnosis, duration of disease, extent of colonic involvement, presence of primary sclerosing cholangitis, family history of CRC, and severity of ongoing colonic inflammation
- Genetic and environmental factors are thought to contribute to the pathogenesis of CRC in IBD[3]
  - Genetic instability, epigenetic alteration, immune response, oxidative stress, and intestinal microbiota have been implicated
- The increased risk of CRC relative to the general population appears to be decreasing, which may be associated with improved control of inflammation and effective surveillance[4]

Recognizing risk factors, identifying high-risk patients, and implementing appropriate surveillance are key to managing IBD-related CRC[5]

CRC=colorectal cancer; IBD=inflammatory bowel disease.

1. Lichtenstein GR, et al. *Am J Gastroenterol.* 2018;113(4):481-517. **2.** Rubin DT, et al. *Am J Gastroenterol.* 2019;114(3):384-413. **3.** Kim ER, et al. *World J Gastroenterol.* 2014;20(29):9872-9881. **4.** Andersen NN, Jess T. *World J Gastroenterol.* 2013;19(43):7561-7568. **5.** Keller DS, et al. *Tech Coloproctol.* 2019;23(1):3-13.

Guideline Recommendations for CRC Screening and Surveillance

	Population	Frequency and screening method
ACG recommendations[1-3]	General population • Average-risk individuals: between ages 50 and 75 years • 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
AGA recommendations[4] (general population)	• Age ≥50 years (≥45 years in African American individuals suggested)	• 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
USPSTF recommendations[5] (general population)	• Average-risk individuals: age ≥50 years • Decision to screen between ages 76 and 85 years to be individualized • Screening in adults beyond age 86 years is not recommended	The USPSTF found no head-to-head studies showing that any of the screening strategies are more effective than others; suggested tests and frequencies include the following: • Stool-based tests: annual gFOBT, annual FIT, FIT-DNA every 1 or 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

ACG=American College of Gastroenterology; AGA=American Gastroenterological Association; CD=Crohn's disease; CRC=colorectal cancer; CT=computerized tomography; FIT=fecal immunochemical test; gFOBT=guaiac focal occult blood test; PSC=primary sclerosing cholangitis; UC=ulcerative colitis; USPSTF=United States Preventive Services Task Force.

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.** US Preventive Services Task Force. *JAMA.* 2016;315(23):2564-2575.

Risk of Skin Cancer in Patients With IBD

- IBD may confer an increased risk of melanoma[1,2]
  - A systematic review and meta-analysis including 12 studies (N=172,837[a]) showed that IBD was associated with a 37% increase in risk of melanoma (RR: 1.37; 95% CI: 1.10-1.70) and stratified by CD (RR: 1.51; 95% CI: 1.14-1.98) and UC (RR: 1.23; 95% CI: 1.01-1.50)[2]

    Note: This analysis was limited by the potential for misclassification bias, unadjusted health care use/heath care contact in patients with IBD in the included studies, and limited information on melanoma outcomes in patients with IBD
- Immunomodulator or immunosuppressive therapy has been shown to increase the risk of melanoma and NMSC in patients with IBD[1,3,4]
- However, patients with IBD appear to have suboptimal rates of skin cancer screening[5]

Given the increased risk of skin cancer, emphasis on patient education, prevention, and screening merits attention[5]

[a]Included 92,208 patients with CD, 79,360 with UC, and 1269 unclassified.
CD=Crohn's disease; CI=confidence interval; IBD=inflammatory bowel disease; NMSC=nonmelanoma skin cancer; RR=relative risk; UC=ulcerative colitis.

1. Farraye FA, et al. *Am J Gastroenterol*. 2017;112(2):241-258. **2.** Singh S, et al. *Clin Gastroenterol Hepatol.* 2014;12(2):210-218. **3.** Long MD, et al. *Gastroenterology.* 2012;143(2):390-399. **4.** Hagen JW, Pugliano-Mauro MA. *Dermatol Surg.* 2018;44(4):469-480. **5.** Anderson A, et al. *Dig Dis Sci.* 2018;63(10):2729-2739.

Preventive Measures and Screening Recommendations for Skin Cancer

Suggested primary preventive measures include the following[1-4]:

- Monthly skin self-examination
- Sun protection (such as sunglasses, protective clothing, and sunscreen)
- Avoidance of tanning beds

Guideline Recommendations for Skin Cancer Screening

ACG recommendations[4]	• All patients with IBD should undergo screening for melanoma independent of the use of biologic therapy • Patients with IBD on immunomodulators (6-mercaptopurine or azathioprine) should undergo screening for NMSC while on medication, particularly over 50 years of age • Refer patients who are starting or receiving immunosuppressive therapies to a dermatologist for skin evaluation • Maintain skin surveillance strategies even after stopping thiopurine therapy
USPSTF recommendations[5] (general population)	• Behavioral counseling of young adults, adolescents, children, and parents of young children about minimizing exposure to ultraviolet radiation for persons aged 6 months to 24 years with fair skin types

ACG=American College of Gastroenterology; IBD=inflammatory bowel disease; NMSC=nonmelanoma skin cancer; USPSTF=United States Preventive Services Task Force.

1. Abegunde AT, et al. *World J Gastroenterol.* 2016;22(34):7625-7644. **2.** Long MD. *Pract Gastroenterol*. 2020;44(2):32-37. **3.** Reich JS, et al. *Dig Dis Sci.* 2016;61(8):2205-2216. **4.** Farraye FA, et al. *Am J Gastroenterol*. 2017;112(2):241-258. **5.** US Preventive Services Task Force. *JAMA.* 2018;319(11):1134-1142.

Cervical Cancer in Women With IBD

- It remains unclear whether IBD alone increases the risk of cervical dysplasia, but an elevated risk is associated with the use of immunosuppressants[1,2]
- Women with IBD, particularly immunosuppressed patients, appear to have less frequent screening compared with the general population[1,3]
  - Reported factors associated with reduced testing include Medicaid insurance, CD diagnosis, and use of immunosuppressants[1]

Recommendations for Cervical Cancer Screening in Immunosuppressed Women

ACG recommendations[1]	• Women with IBD on immunosuppressive therapy should undergo annual cervical cancer screening
CCF recommendations[4]	• All women with IBD who are being treated with systemic immunosuppression[a] should undergo cervical cancer screening by cytology annually (if cytology alone) or every 2 years (if HPV negative)
ASCCP recommendations[5] (immunosuppressed population)	• Screening should begin within 1 year of first insertional sexual activity and continue throughout a patient's lifetime: annually for 3 years, then every 3 years (cytology only) until age 30 years, and then either continuing with cytology alone or cotesting every 3 years after age 30 years

[a]Systemic immunosuppression refers to current treatment with prednisone (>20 mg/day for more than 14 days), azathioprine (>2.5 mg/kg/day), mercaptopurine (>1.5 mg/kg/day), methotrexate (>0.4 mg/kg/week), cyclosporine, tacrolimus, infliximab, adalimumab, golimumab, certolizumab, ustekinumab, or tofacitinib.[5]

ACG=American College of Gastroenterology; ASCCP=American Society for Colposcopy and Cervical Pathology; CCF=Crohn's & Colitis Foundation; CD=Crohn's disease; HPV=human papillomavirus; IBD=inflammatory bowel disease.

1. Farraye FA, et al. *Am J Gastroenterol*. 2017;112(2):241-258. **2.** Allegretti JR, et al. *Inflamm Bowel Dis.* 2015;21(5):1089-1097. **3.** Long MD, et al. *Clin Gastroenterol Hepatol.* 2009;7(5):549-553. **4.** Crohn's & Colitis Foundation. https://www.crohnscolitisfoundation.org/science-and-professionals/education-resources/health-maintenance-checklists. Accessed March 22, 2021. **5.** Perkins RB, et al. *J Low Genit Tract Dis.* 2020;24(2):102-131.

Osteoporosis in Patients With IBD

- Although the precise prevalence is unknown, it has been estimated that between 14% and 42% of patients with IBD may have osteoporosis[1]
- Patients with IBD are at an increased risk for loss of bone mass[1,2]
- The pathogenesis of bone loss is multifactorial and not thoroughly understood; however, chronic steroid use, chronic inflammation, calcium and vitamin D deficiency, and malnutrition are considered strong risk factors[1,2]

Examples of Risk Factors for Osteoporosis in IBD[3]

- Increasing age
- Corticosteroid use
- Malnutrition
- Low BMI
- Malabsorption of vitamin D, vitamin K, and calcium
- Immobilization
- Prior fragility fracture
- Hypogonadism
- Smoking

BMI=body mass index; IBD=inflammatory bowel disease.

1. Mir FA, Kane SV. *Curr Gastroenterol Rep.* 2018;20(5):23. **2.** Farraye FA, et al. *Am J Gastroenterol*. 2017;112(2):241-258. **3.** Ali T, et al. *Am J Med.* 2009;122(7):599-604.

Preventive Measures and Screening Recommendations for Osteoporosis

Suggested preventive measures include the following[1,2]:

- Adequate intake of calcium and vitamin D
- Regular weight-bearing exercise
- Smoking cessation
- Avoidance of excess alcohol
- Minimizing use of corticosteroids
- Correction of hypogonadism

ACG recommendations[3]	• Patients with conventional risk factors for abnormal BMD should undergo screening for osteoporosis with BMD testing at the time of diagnosis and periodically after diagnosis • Patients with IBD should be screened based on established guidelines for the general population • DEXA screening is recommended in all patients starting OCS therapy and specifically in those who have used OCS for >3 months in a dosage ≥7.5 mg/day of prednisone or equivalent in the absence of baseline BMD measurement
AGA recommendations[1]	• Postmenopausal women, men aged >50 years, and patients with prolonged corticosteroid use (>3 months consecutive or recurrent courses), low-trauma fracture, or hypogonadism should undergo DEXA screening

NOP recommendations[4] (general population)	• BMD testing should be performed in
	  • Women aged ≥65 years and men aged ≥70 years
	  • People with a bone fracture after 50 years of age
	  • Women of menopausal age or postmenopausal aged <65 years with risk factors
	  • Men between ages 50 and 69 years with risk factors
	• Peripheral tests including pDEXA, QUS, and pQCT are recommended to help identify patients who are most likely to benefit from further bone density testing; for diagnosis of osteoporosis, central DEXA is recommended

USPSTF recommendations[5] (general population)	• Women aged ≥65 years and postmenopausal women aged <65 years who are at increased risk of osteoporosis should undergo screening for osteoporosis

ACG=American College of Gastroenterology; AGA=American Gastroenterological Association; BMD=bone mineral density; DEXA=dual-energy X-ray absorptiometry; IBD=inflammatory bowel disease; NOP=National Osteoporosis Foundation; OCS=oral corticosteroids; pQCT=peripheral quantitative computed tomography; QUS=quantitative ultrasound; USPSTF=United States Preventive Services Task Force.

1. Bernstein CN, et al. *Gastroenterology.* 2003;124(3):795-841. **2.** Abegunde AT, et al. *World J Gastroenterol.* 2016;22(34):7625-7644. **3.** Farraye FA, et al. *Am J Gastroenterol*. 2017;112(2):241-258. **4.** National Osteoporosis Foundation. https://www.nof.org/patients/diagnosis-information/bone-density-examtesting/. Accessed March 22, 2021. **5.** US Preventive Services Task Force. *JAMA.* 2018;319(24):2521-2531.

Ocular Manifestations in Patients With IBD

- Ocular manifestations have been reported to occur in 0.3% to 13% of patients with IBD and often occur with concomitant musculoskeletal manifestations[1,2]
  - Ocular manifestations may be more common in patients with CD than in those with UC[1]
  - Episcleritis is the most common ocular manifestation in IBD, followed by uveitis[1,2]

Episcleritis[2]

Episcleritis[1-3]	Uveitis[1-3]	Scleritis[1-3]
▪ Occurs in ~2%-5% of patients ▪ Usually painful, with acute hyperemia but no photophobia, blurring of vision, or vision loss ▪ Treatment includes controlling intestinal flare and symptom management with lubricant eye drops, cold compresses, or topical steroids	▪ Occurs in ~0.5%-3.5% of patients ▪ Usually painful, with headache, photophobia, blurring of vision, or vision loss ▪ Treatment includes topical and/or systemic steroids or immunomodulatory therapies	▪ Occurs in <1% of patients ▪ Usually painful, with tenderness, edema, visual impairment, or visual loss ▪ Treatment includes controlling intestinal flare with systemic steroids or immunomodulatory therapies and NSAIDs
▪ Parallels IBD activity	▪ Does not parallel IBD activity	▪ Parallels IBD activity

CD=Crohn's disease; IBD=inflammatory bowel disease; NSAID=nonsteroidal anti-inflammatory drug; UC=ulcerative colitis.

1. Troncoso LL, et al. *World J Gastroenterol.* 2017;23(32):5836-5848. **2.** Vavricka SR, et al. *Inflamm Bowel Dis*. 2015;21(8):1982-1992. **3.** Mady R. *ScientificWorldJournal.* 2015;2015:438402.

Screening for Ocular Diseases in Patients With IBD

Annual ophthalmologic evaluation should be considered in patients with IBD, especially those receiving immunosuppressive therapy[1]

- Because asymptomatic inflammation of ocular tissues may occur, a routine ophthalmologic follow-up should be considered in all patients, preferably before changes in IBD therapy, because some drugs may cause ocular adverse effects[2]
- Ocular pain or vision impairment may be indicative of uveitis or scleritis; to prevent potentially permanent vision loss, evaluation by an ophthalmologist is warranted[3,4]
- Patient awareness of possible ocular involvement in IBD is important to improve understanding of the disease and health outcomes and to prompt early diagnosis and treatment[2]

IBD=inflammatory bowel disease.

1. Abegunde AT, et al. *World J Gastroenterol.* 2016;22(34):7625-7644. **2.** Troncoso LL, et al. *World J Gastroenterol.* 2017;23(32):5836-5848. **3.** Jansen FM, et al. *United European Gastroenterol J.* 2020;8(9):1031-1044. **4.** Harbord M, et al. *J Crohns Colitis.* 2016;10(3):239-254.

Oral Manifestations in Patients With IBD

- Oral manifestations can occur in patients with IBD and may have some correlation with disease activity[1-3]
  - Presentation of oral lesions may be more severe with flare; however, up to 30% of patients may continue to experience oral manifestations despite IBD disease control[2]
  - In ~5%-10% of patients, oral lesions may present earlier than gastrointestinal symptoms[2]
  - Oral aphthous ulcers have been estimated to occur at a frequency of ~4%-5% in patients with IBD and occur more frequently in patients with CD compared with UC and among males[1,2]
- Dental manifestations, such as periodontitis, may also be related to IBD disease activity[1]

Spectrum of Oral Manifestations in IBD[1,a]

Crohn's Disease → **Ulcerative Colitis**

Highly specific	Highly suspicious	Nonspecific oral lesions (IBD and non-IBD)	Highly specific
• Metastatic CD of the face • Orofacial • Granulomatous cheilitis: subacute involvement of the area of the mouth, mostly focal granulomatous inflammation of the lower lip	• Taglike lesions • Cobblestoning • Mucogingivitis • Lip swelling and vertical fissuring • Deep linear oral ulcers	• Malabsorption related • Medication related • Other	• Pyostomatitis vegetans: erythematous and thickened oral mucosa with multiple pustules and superficial erosions

[a]Index of suspicion for IBD (UC or CD) is increased with the increasing intensity of the color.
CD=Crohn's disease; IBD=inflammatory bowel disease; UC=ulcerative colitis.

1. Katsanos KH, et al. *Aliment Pharmacol Ther.* 2015;42(1):40-60. **2.** Lankarani KB, et al. *World J Gastroenterol*. 2013;19(46):8571-8579. **3.** Vavricka SR, et al. *Inflamm Bowel Dis*. 2015;21(8):1982-1992. **4.** Papageorgiou SN, et al. *J Clin Periodontol.* 2017;44(4):382-393.

Screening for Oral Diseases in Patients With IBD

Because oral manifestations may precede gastrointestinal symptoms, dentists may play an important role in the early diagnosis of IBD[1,2]

Patients with oral lesions should receive a workup for IBD[3]

- Endoscopy may be indicated in patients with specific oral lesions and concomitant gastrointestinal symptoms and should be considered in patients with relapsing or persistent oral lesions[4]
- Gingival biopsy may be helpful for early diagnosis of underlying CD[4]

Routine dental care by a dental professional should be considered for patients with IBD[5,6]

- Patients with gingivitis and periodontitis should have dental follow-ups at least 3 times annually[5]
- Prescriptions for NSAIDs should be avoided to prevent disease flares[6]

CD=Crohn's disease; IBD=inflammatory bowel disease; NSAID=nonsteroidal anti-inflammatory drug.

1. Lankarani KB, et al. *World Gastroenterol*. 2013;19(46):8571-8579. **2.** Pereira MS, Munerato MC. *Clin Med Res.* 2016;14(1):46-52. **3.** Ribaldone DG, et al. *Medicines (Basel).* 2020;7(6):33. **4.** Katsanos KH, et al. *Aliment Pharmacol Ther.* 2015;42(1):40-60. **5.** Krasteva A, et al. *Biotechnol Biotechnol Equip.* 2014;25(2):2305-2309. **6.** Franch AM, et al. *J Clin Exp Dent.* 2010;2(4):e191-e195.

Anxiety and Depression in Patients With IBD

- Reported prevalence of anxiety and depression is approximately 2 times higher in patients with IBD than in the general population (anxiety: 19.1% vs 9.6%; depression: 21.2% vs 13.4%)[1,2]
- Despite the implications of these mental disorders on IBD disease course, anxiety and depression may still be underdiagnosed in patients with IBD[3]
- Evidence suggests that anxiety and depression may share common etiologic factors with IBD, and the risk of these psychiatric disorders may be influenced by the inflammation and activation of cell-mediated immunity[4]
- When left untreated, mental disorders can worsen IBD disease course and lead to more-severe symptoms, more-frequent flares, higher hospitalization rates, and poor treatment compliance[1,3]

IBD=inflammatory bowel disease.

1. Mikocka-Walus A, et al. *Inflamm Bowel Dis.* 2016;22(3):752-762. **2.** Farraye FA, et al. *Am J Gastroenterol*. 2017;112(2):241-258. **3.** Lewis K, et al. *Inflamm Bowel Dis.* 2019;25(10):1674-1680. **4.** Marrie RA, et al. *Epidemiol Psychiatr Sci.* 2019;28(3):333-342.

Screening for Anxiety and Depression

- The 2017 ACG guideline on preventive care in IBD recommends screening for anxiety and depression in patients with IBD[1]

Characteristics of Depression and Anxiety Screening Questionnaires

Scale	Description	Number of items[2]	Total score[2,a]
Patient Health Questionnaire-9 (PHQ-9)	• May be used for confirmatory depression testing[3]	9	0-27
Patient Health Questionnaire-2 (PHQ-2)	• Truncated version of PHQ-9; may be used to screen for depression[3]	2	0-6
Hospital Anxiety and Depression Scale (HADS)	• Most common method used to measure anxiety and depression[4]	Depression: 7 Anxiety: 7	0-21
Patient-Reported Outcomes Measurement Information System (PROMIS)	• Measures patient-reported outcomes including pain, fatigue, physical functioning, emotional distress, and social role participation[5]	Depression: 8 Anxiety: 8	Depression: 38.2-81.3 Anxiety: 37.1-83.1
Generalized Anxiety Disorder 7-item scale (GAD-7)	• Used as a measure for anxiety in general[6]	7	0-21
Overall Anxiety Severity and Impairment Scale (OASIS)	• Assesses frequency of anxiety, intensity of anxiety symptoms, behavioral avoidance, and functional impairment associated with anxiety[7]	5	0-20

[a]Higher scores indicate more pronounced symptoms.
ACG=American College of Gastroenterology; IBD=inflammatory bowel disease.

1. Farraye FA, et al. *Am J Gastroenterol.* 2017;112(2):241-258. **2.** Bernstein CN, et al. *Inflamm Bowel Dis.* 2018;24(9):1867-1875. **3.** Abegunde AT, et al. *World J Gastroenterol.* 2016;22(34):7625-7644. **4.** Neuendorf R, et al. *J Psychosom Res*. 2016;87:70-80. **5.** National Institutes of Health. https://commonfund.nih.gov/promis/index. Accessed April 15, 2021. **6.** Johnson SU, et al. *Front Psychol.* 2019;10:1713. **7.** Campbell-Sills L, et al. *J Affect Disord.* 2009;112(1-3):92-101.

Special Considerations for Health Maintenance

- Elderly patients
- Pediatric patients

Health Maintenance in the Elderly

- Incidence of IBD reaches a first peak between ages 20 and 39 years and a second peak between ages 50 and 70 years; ~10%-15% of patients diagnosed with IBD are aged >60 years[1]
  - Older patients with IBD are more susceptible to complications or worse outcomes (eg, infections, hospitalizations, malignancy, bone disease, psychological disorders, VTE, polypharmacy)[2,3]
- Suggestions in the management of IBD in the elderly include
  - Administering higher initial vaccination doses, particularly before initiating immunosuppressive therapy, and booster doses because older patients may have suboptimal serological responses[1,2]
  - Offering cancer screening to patients with life expectancy >10 years and who can tolerate cancer treatment[2]

Health Maintenance Issues for Older Patients With IBD[2]

Health issue	Monitoring
Bone health	Screen at-risk patients for decreased BMD
Mental health	Assess psychological status at regular visits
Nutritional status	Record weight change and inquire regarding food intake during regular visits
Smoking cessation	Assess at regular visits
VTE	Assess for thromboembolism, particularly during flares and hospitalizations
Ocular health	Conduct annual ophthalmologic exams
Oral health	Conduct annual or biannual dental exams

BMD=bone mineral density; IBD=inflammatory bowel disease; VTE=venous thromboembolism.

1. Nimmons D, Limdi JK. *World J Gastrointest Pharmacol Ther.* 2016;7(1):51-65. **2.** Shrestha MP, et al. *Ann Gastroenterol.* 2017;30(3):273-286. **3.** Gisbert JP, Chaparro M. *Aliment Pharmacol Ther.* 2014;39(5):459-477.

Health Maintenance in Pediatric Patients

- ~25% of patients with IBD are younger than 20 years at diagnosis, with the peak onset in adolescence[1]
- Clinical presentation of IBD in pediatric patients may be variable and initially include growth failure, malnutrition, and EIMs[1,2]
  - Growth failure and malnutrition occur in ~65%-85% of pediatric patients with CD and may precede gastrointestinal symptoms[2]
  - Because oral lesions occur more frequently in children than in adults, physical examination may include assessment of oral aphthous ulcers[1,3]
- Cognitive behavioral therapy should be considered for patients with anxiety or depressive symptoms[1]

CD=Crohn's disease; EIM=extraintestinal manifestation; IBD=inflammatory bowel disease.

1. Rosen MJ, et al. *JAMA Pediatr.* 2015;169(11):1053-1060. **2.** Gasparetto M, Guariso G. *World J Gastroenterol.* 2014;20(37):13219-13233. **3.** Lankarini KB, et al. *World Gastroenterol*. 2013;19(46):8571-8579.

Health Maintenance in Pediatric Patients (cont'd)

The Crohn's & Colitis Foundation provides a technical guide for pediatric health maintenance, which includes immunizations, cancer prevention, and bone, eye, skin, and mental health[1]

Health Maintenance Checklist for Pediatric IBD Patients[2]

Vaccines Outside of Routine Age Schedule	Which Patients	How Often
Pneumococcal disease	All with altered immunocompetence[a] The plan for immunization should be discussed with the patient's pediatric gastroenterologist.	• If aged > 6 yrs and not previously received PCV13, give this first (wait 8 weeks before giving PPSV23) • If aged > 2 yrs, give 1st dose PPSV23, then second dose 5 years later

Cancer Prevention	Which Patients	How Often
Full Skin Screen	All on chronic immunosuppression[a]	Annual
Colonoscopy	All with colonic disease for > 8 years	Every 1–3 years

Other Screenings	Which Patients	How Often
Nutritional evaluation	All	Height, weight, labs and BMI at each visit
Smoking status	All	Annual
Depression check	All	Annual
DEXA Scan	All	At time of diagnosis and periodically (every 5 years) after diagnosis based on DEXA findings
PPD or IGRA	Prior to anti-TNF or anti-IL-12/23	Once (repeat if potential TB exposure or in a high-risk region)
Serologies: HepBsAg, HepBsAb, HepA IgM	Prior to anti-TNF or anti-IL-12/23	Once (repeat if potential exposure or in a high-risk region)

Source: Crohn's & Colitis Foundation: Pediatric Health Maintenance Technical Guide and Healthcare Maintenance Checklist, updated 2020.

BMI=body mass index; DEXA=dual-energy X-ray absorptiometry; HepA IgM=hepatitis A immunoglobulin M; HepBsAb=hepatitis B surface antibody; HepBsAg=hepatitis B surface antigen; IBD=inflammatory bowel disease; IGRA=interferon gamma release assay; IL=interleukin; PCV13=13-valent pneumococcal conjugate vaccine; PPD=purified protein derivative; PPSV23=23-valent pneumococcal polysaccharide vaccine; TB=tuberculosis; TNF=tumor necrosis factor.

1. Crohn's & Colitis Foundation. https://www.crohnscolitisfoundation.org/sites/default/files/2021-01/Health%20Maintenance%20Technical%20Guide%20for%20Pediatric%20Patients.pdf. Accessed March 22, 2021.
2. Crohn's & Colitis Foundation. https://www.crohnscolitisfoundation.org/sites/default/files/2019-07/Health%20Maintenance%20Checklist%20Pediatric%202019-ESA-P55-19.pdf. Accessed March 22, 2021.

Summary

- Health maintenance through preventive care is important in managing IBD because patients often require lifelong care and are subject to complications
- Patients with IBD have an increased risk of infections, colorectal cancer, and skin cancer, especially those who are immunocompromised; however, preventive care utilization may not be adequate
- Health maintenance in patients with IBD includes vaccination; smoking cessation; and screening for malnutrition, colorectal, skin, and cervical cancer, and bone and mental health
- Health maintenance should be comanaged by the gastroenterologist and PCP, and gastroenterologists should proactively communicate with PCPs about the unique needs of patients with IBD

IBD=inflammatory bowel disease; PCP=primary care physician.

Available Resources

- American College of Gastroenterology
  - Clinical guidelines
- American Gastroenterological Association
  - Clinical guidelines
- American Society for Colposcopy and Cervical Pathology
  - Clinical guidelines
- Centers for Disease Control and Prevention
  - Health effects of cigarette smoking
  - Picture of America
- Cornerstone Health
  - Health maintenance checklist
- Crohn's & Colitis Foundation
  - Health maintenance checklists
  - Health maintenance technical guide for pediatric patients
- Crohn's & Colitis UK
  - Smoking and IBD
- International Organization for the Study of IBD
  - Expert opinion
- National Osteoporosis Foundation
  - Clinical guidelines
- United States Preventive Services Task Force
  - Clinical guidelines

References

- Abegunde AT, Muhammad BH, Ali T. Preventive health measures in inflammatory bowel disease. *World J Gastroenterol.* 2016;22(34):7625-7644.
- Ali T, Lam D, Bronze MS, Humphrey MB. Osteoporosis in inflammatory bowel disease. *Am J Med.* 2009;122(7):599-604.
- Allegretti JR, Barnes EL, Cameron A. Are patients with inflammatory bowel disease on chronic immunosuppressive therapy at increased risk of cervical high-grade dysplasia/cancer? a meta-analysis. *Inflamm Bowel Dis.* 2015;21(5):1089-1097.
- Andersen NN, Jess T. Has the risk of colorectal cancer in inflammatory bowel disease decreased? *World J Gastroenterol.* 2013;19(43):7561-7568.
- Anderson A, Ferris LK, Click B, et al. Low rates of dermatologic care and skin cancer screening among inflammatory bowel disease patients. *Dig Dis Sci.* 2018;63(10):2729-2739.
- Balestrieri P, Ribolsi M, Guarino MPL, Emerenziani S, Altomare A, Cicala M. Nutritional aspects in inflammatory bowel diseases. *Nutrients.* 2020;12(2):372.
- Bernstein CN, Leslie WD, Leboff MS. AGA technical review on osteoporosis in gastrointestinal diseases. *Gastroenterology.* 2003;124(3):795-841.
- Bischoff SC, Escher J, Hébuterne X, et al. ESPEN practical guideline: clinical nutrition in inflammatory bowel disease. *Clin Nutr*. 2020;39(3):632-653.
- Blackwell J, Saxena S, Alexakis C, et al. The impact of smoking and smoking cessation on disease outcomes in ulcerative colitis: a nationwide population-based study. *Aliment Pharmacol Ther.* 2019;50(5):556-567.
- Campbell-Sills L, Norman SB, Craske MG, et al. Validation of a brief measure of anxiety-related severity and impairment: the Overall Anxiety Severity and Impairment Scale (OASIS). *J Affect Disord*. 2009;112(1-3):92-101.
- Centers for Disease Control and Prevention. Health effects of cigarette smoking. https://www.cdc.gov/tobacco/data_statistics/fact_sheets/health_effects/effects_cig_smoking/index.htm. Accessed March 22, 2021.
- Centers for Disease Control and Prevention. Picture of America prevention. https://www.cdc.gov/pictureofamerica/pdfs/Picture_of_America_Prevention.pdf. Accessed March 20, 2021.
- Cornerstones Health. IBD checklist for monitoring & prevention. https://www.cornerstoneshealth.org/wp-content/uploads/2020/08/NEW-IBD-Checklist-for-Monitoring-Prevention-526a.pdf. Accessed March 22, 2021.
- Cosnes J, Beaugerie L, Carbonnel F, Gendre JP. Smoking cessation and the course of Crohn's disease: an intervention study. *Gastroenterology.* 2001;120(5):1093-1099.
- Crohn's & Colitis Foundation. Health maintenance checklist for pediatric IBD patients. https://www.crohnscolitisfoundation.org/sites/default/files/2019-07/Health%20Maintenance%20Checklist%20Pediatric%202019-ESA-P55-19.pdf. Accessed March 22,2021.
- Crohn's & Colitis Foundation. Health maintenance checklists. https://www.crohnscolitisfoundation.org/science-and-professionals/education-resources/health-maintenance-checklists. Accessed March 22, 2021.
- Crohn's & Colitis Foundation. Malnutrition and IBD. https://www.crohnscolitisfoundation.org/diet-and-nutrition/malnutrition-and-ibd. Accessed March 22, 2021.

References

- Crohn's & Colitis Foundation. Pediatric health maintenance technical guide. https://www.crohnscolitisfoundation.org/sites/default/files/2021-01/Health%20Maintenance%20Technical%20Guide%20for%20Pediatric%20Patients.pdf. Accessed March 22, 2021.
- Crohn's & Colitis UK. Smoking and IBD. https://www.crohnsandcolitis.org.uk/about-crohns-and-colitis/publications/smoking-and-ibd. Accessed April 26, 2021.
- Farraye FA. Vaccination of patients with inflammatory bowel disease. *Gastroenterol Hepatol (N Y).* 2017;13(7):431-434.
- Farraye FA, Melmed GY, Lichtenstein GR, Kane SV. ACG clinical guideline: preventive care in inflammatory bowel disease. *Am J Gastroenterol.* 2017;112(2):241-258.
- Franch AM, Soriano YJ, Perez MGS. Dental management of patients with inflammatory bowel disease. *J Clin Exp Dent*. 2010;2(4):e191-e195.
- Gasparetto M, Guariso G. Crohn's disease and growth deficiency in children and adolescents. *World J Gastroenterol.* 2014;20(37):13219-13233.
- Gisbert JP, Chaparro M. Systematic review with meta-analysis: inflammatory bowel disease in the elderly. *Aliment Pharmacol Ther.* 2014;39(5):459-477.
- Hagen JW, Pugliano-Mauro MA. Nonmelanoma skin cancer risk in patients with inflammatory bowel disease undergoing thiopurine therapy: a systematic review of the literature. *Dermatol Surg.* 2018;44(4):469-480.
- Halmos EP, Gibson PR. Dietary management of IBD—insights and advice. *Nat Rev Gastroenterol Hepatol*. 2015;12(3):133-146.
- Harbord M, Annese V, Vavricka SR, et al. The first European evidence-based consensus on extra-intestinal manifestations in inflammatory bowel disease. *J Crohns Colitis.* 2016;10(3):239-254.
- Jansen FM, Vavricka SR, den Broeder AA, de Jong EM, Hoentjen F, van Dop WA. Clinical management of the most common extra-intestinal manifestations in patients with inflammatory bowel disease focused on the joints, skin and eyes. *United European Gastroenterol J.* 2020;8(9):1031-1044.
- Johnson SU, Ulvenes PG, Oktedalen T, Hoffart A. Psychometric properties of the General Anxiety Disorder 7-Item (GAD-7) Scale in a heterogeneous psychiatric sample. *Front Psychol.* 2019;10:1713.
- Karr JR, Lu JJ, Smith RB, Thomas AC. Using computerized physician order entry to ensure appropriate vaccination of patients with inflammatory bowel disease. *Ochsner J.* 2016;16(1):90-95.
- Katsanos KH, Torres J, Roda G, Brygo A, Delaporte E, Colombel JF. Review article: non-malignant oral manifestations in inflammatory bowel diseases. *Aliment Pharmacol Ther.* 2015;42(1):40-60.
- Keller DS, Windsor A, Cohen R, Chand M. Colorectal cancer in inflammatory bowel disease: review of the evidence. *Tech Coloproctol.* 2019;23(1):3-13.
- Kim ER, Chang DK. Colorectal cancer in inflammatory bowel disease: the risk, pathogenesis, prevention and diagnosis. *World J Gastroenterol.* 2014;20(29):9872-9881.
- Krasteva A, Panov V, Krasteva A, Kisselova A. Oral cavity and systemic diseases—inflammatory bowel diseases. *Biotechnol Biotechnol Equip*. 2011;25(2):2305-2309.

References

- Lankarani KB, Sivandzadeh GR, Hassanpour S. Oral manifestation in inflammatory bowel disease: a review. *World J Gastroenterol.* 2013;19(46):8571-8579.
- Levine A, Rhodes JM, Lindsay JO, et al. Dietary guidance from the International Organization for the Study of Inflammatory Bowel Diseases. *Clin Gastroenterol Hepatol.* 2020;18(6):1381-1392.
- Lewis K, Marrie RA, Bernstein CN, et al. The prevalence and risk factors of undiagnosed depression and anxiety disorders among patients with inflammatory bowel disease. *Inflamm Bowel Dis.* 2019;25(10):1674-1680.
- Lichtenstein GR, Loftus EV, Isaacs KL, Regueiro MD, Gerson LB, Sands BE. ACG clinical guideline: management of Crohn's disease in adults. *Am J Gastroenterol.* 2018;113(4):481-517.
- Lochs H, Basics in clinical nutrition: nutritional support in inflammatory bowel disease. *E Spen Eur E J Clin Nutr Metab*. 2010;5(2):e100-e103.
- Long MD. Prevention in inflammatory bowel disease: an updated review. *Pract Gastroenterol*. 2020;44(2):32-37.
- Long MD, Martin C, Sandler RS, Kappelman MD. Increased risk of herpes zoster among 108 604 patients with inflammatory bowel disease. *Aliment Pharmacol Ther.* 2013;37(4):420-429.
- Long MD, Martin C, Sandler RS, Kappelman MD. Increased risk of pneumonia among patients with inflammatory bowel disease. *Am J Gastroenterol.* 2013;108(2):240-248.
- Long MD, Martin CF, Pipkin CA, Herfarth HH, Sandler RS, Kappelman MD. Risk of melanoma and nonmelanoma skin cancer among patients with inflammatory bowel disease. *Gastroenterology.* 2012;143(2):390-399.
- Long MD, Porter CQ, Sandler RS, Kappelman MD. Suboptimal rates of cervical testing among women with inflammatory bowel disease. *Clin Gastroenterol Hepatol.* 2009;7(5):549-553.
- Mady R, Grover W, Butrus S. Ocular complications of inflammatory bowel disease. *ScientificWorldJournal.* 2015;2015:438402.
- Mahid SS, Minor KS, Soto RE, Hornung CA, Galandiuk S. Smoking and inflammatory bowel disease: a meta-analysis. *Mayo Clin Proc.* 2006;81(11):1462-1471.
- Marrie RA, Walld R, Bolton JM, et al. Rising incidence of psychiatric disorders before diagnosis of immune-mediated inflammatory disease. *Epidemiol Psychiatr Sci.* 2019;28(3):333-342.
- Mikocka-Walus A, Knowles SR, Keefer L, Graff L. Controversies revisited: a systematic review of the comorbidity of depression and anxiety with inflammatory bowel diseases. *Inflamm Bowel Dis.* 2016;22(3):752-762.
- Mir FA, Kane SV. Health maintenance in inflammatory bowel disease. *Curr Gastroenterol Rep.* 2018;20(5):23.
- National Institutes of Health. PROMIS: clinical outcomes assessment. https://commonfund.nih.gov/promis/index. Accessed April 15, 2021.

References

- National Osteoporosis Foundation. Bone density exam/testing. https://www.nof.org/patients/diagnosis-information/bone-density-examtesting/. Accessed March 22, 2021.
- Nazarenkov N, Seeger K, Beeken L, et al. Implementing dietary modifications and assessing nutritional adequacy of diets for inflammatory bowel disease. *Gastroenterol Hepatol*. 2019;15(3):133-144.
- Neuendorf R, Harding A, Stello N, Hanes D, Wahbeh H. Depression and anxiety in patients with inflammatory bowel disease: a systematic review. *J Psychosom Res.* 2016;87:70-80.
- Nguyen GC, Munsell M, Harris ML. Nationwide prevalence and prognostic significance of clinically diagnosable protein-calorie malnutrition in hospitalized inflammatory bowel disease patients. *Inflamm Bowel Dis.* 2008;14(8):1105-1111.
- Nimmons D, Limdi JK. Elderly patients and inflammatory bowel disease. *World J Gastrointest Pharmacol Ther.* 2016;7(1):51-65.
- Nunes T, Etchevers MJ, Merino O, et al. Does smoking influence Crohn's disease in the biologic era? the TABACROHN study. *Inflamm Bowel Dis.* 2013;19(1):23-29.
- Papageorgiou SN, Hagner M, Nogueira AV, Franke A, Jäger A, Deschner J. Inflammatory bowel disease and oral health: systematic review and a meta-analysis *J Clin Periodontol.* 2017;44(4):382-393.
- Parkes GC, Whelan K, Lindsay JO. Smoking in inflammatory bowel disease: impact on disease course and insights into the aetiology of its effect. *J Crohns Colitis.* 2014;8(8):717-725.
- Pereira MS, Munerato MC. Oral manifestations of inflammatory bowel diseases: two case reports. *Clin Med Res.* 2016;14(1):46-52.
- Perkins RB, Guido RS, Castle PE, et al. 2019 ASCCP risk-based management consensus guidelines for abnormal cervical cancer screening tests and cancer precursors. *J Low Genit Tract Dis.* 2020;24(2):102-131.
- Reich JS, Farraye FA, Wasan SK. Preventative care in the patient with inflammatory bowel disease: what is new? *Dig Dis Sci.* 2016;61(8):2205-2216.
- Reich JS, Miller HL, Wasan SK, et al. Influenza and pneumococcal vaccination rates in patients with inflammatory bowel disease. *Gastroenterol Hepatol (N Y).* 2015;11(6):396-401.
- Rex DK, Boland CR, Dominitz JA, et al. Colorectal cancer screening: recommendations for physicians and patients from the U.S. Multi-Society Task Force on Colorectal Cancer. *Gastroenterology.* 2017;153(1):307-323.
- Ribaldone DG, Brigo S, Mangia M, Saracco GM, Astegiano M, Pellicano R. Oral manifestations of inflammatory bowel disease and the role of non-invasive surrogate markers of disease activity. *Medicines (Basel).* 2020;7(6).
- Rosen MJ, Dhawan A, Saeed SA. Inflammatory bowel disease in children and adolescents. *JAMA Pediatr.* 2015;169(11):1053-1060.
- Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol.* 2019;114(3):384-413.

References

- Ryan WR, Allan RN, Yamamoto T, Keighley MR. Crohn's disease patients who quit smoking have a reduced risk of reoperation for recurrence. *Am J Surg.* 2004;187(2):219-225.
- Sapir T, Moreo K, Carter JD, Greene L, Patel B, Higgins PD. Continuing medical education improves gastroenterologists' compliance with inflammatory bowel disease quality measures. *Dig Dis Sci.* 2016;61(7):1862-1869.
- Selby L, Hoellein A, Wilson JF. Are primary care providers uncomfortable providing routine preventive care for inflammatory bowel disease patients? *Dig Dis Sci.* 2011;56(3):819-824.
- Shaukat A, Kahi CJ, Burke CA, Rabeneck L, Sauer BG, Rex DK. ACG clinical guidelines: colorectal cancer screening 2021. *Am J Gastroenterol.* 2021;116(3):458-479.
- Shrestha MP, Ruel J, Taleban S. Healthcare maintenance in elderly patients with inflammatory bowel disease. *Ann Gastroenterol.* 2017;30(3):273-286.
- Singh S, Nagpal SJ, Murad MH, et al. Inflammatory bowel disease is associated with an increased risk of melanoma: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol.* 2014;12(2):210-218.
- Troncoso LL, Biancardi AL, de Moraes HV, Jr., Zaltman C. Ophthalmic manifestations in patients with inflammatory bowel disease: a review. *World J Gastroenterol.* 2017;23(32):5836-5848.
- US Preventive Services Task Force. Behavioral counseling to prevent skin cancer: US Preventive Services Task Force recommendation statement. *JAMA.* 2018;319(11):1134-1142.
- US Preventive Services Task Force. Interventions for tobacco smoking cessation in adults, including pregnant persons: US Preventive Services Task Force recommendation statement. *JAMA.* 2021;325(3):265-279.
- US Preventive Services Task Force. Primary care interventions for prevention and cessation of tobacco use in children and adolescents: US Preventive Services Task Force recommendation statement. *JAMA.* 2020;323(16):1590-1598.
- US Preventive Services Task Force. Screening for colorectal cancer: US Preventive Services Task Force recommendation statement. *JAMA.* 2016;315(23):2564-2575.
- US Preventive Services Task Force. Screening for osteoporosis to prevent fractures: US Preventive Services Task Force recommendation statement. *JAMA.* 2018;319(24):2521-2531.
- Vavricka SR, Schoepfer A, Scharl M, Lakatos PL, Navarini A, Rogler G. Extraintestinal manifestations of inflammatory bowel disease. *Inflamm Bowel Dis.* 2015;21(8):1982-1992.
- Wasan SK, Coukos JA, Farraye FA. Vaccinating the inflammatory bowel disease patient: deficiencies in gastroenterologists knowledge. *Inflamm Bowel Dis*. 2011;17(12):2536-2540.