

# Preventive Care and Health Maintenance in Patients with Inflammatory Bowel Disease

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## ABSTRACT

Health maintenance in patients with inflammatory bowel disease (IBD) is essential. In order to achieve clinical and endoscopic remission, many patients will require treatment with steroids, immunomodulators, biologics or small molecules, which place them at a higher risk of serious infections as well as certain malignancies. Some of these adverse events are preventable through vaccination and adherence to cancer screening guidelines, making preventive care and health maintenance in this patient population crucial. Gastroenterologists should take a proactive role in health care maintenance and collaborate with the patient's primary care provider. The aim of this article is to review and provide guidance on preventive care and health maintenance in patients with IBD, including vaccinations, cancer screening, bone health, nutrition, and mental health assessment as well as smoking cessation.

**KEYWORDS:** health maintenance; inflammatory bowel disease (IBD); preventive medicine; screening

## INTRODUCTION

Inflammatory bowel disease (IBD) consists of a spectrum of diseases including ulcerative colitis (UC), Crohn's disease (CD) and indeterminate colitis. These are chronic inflammatory conditions of the bowel that may affect patients of any age range with a peak incidence during the second to fourth decade of life.<sup>1</sup> It has been estimated that the number of people worldwide living with IBD had increased from 3.7 million to more than 6.8 million between 1990 and 2017, with nearly a quarter of these patients living in the United States.<sup>1</sup> IBD is a complex condition and many patients with IBD will require immunosuppressing therapies with corticosteroids, immunomodulators, small molecules and/or biologic agents. For this reason, many patients with IBD are at an increased risk of infections, malignancy and other complications.<sup>2</sup> Up-to-date health maintenance is paramount in patients with IBD as a means of limiting morbidity from the disease itself and its treatment. Data suggests that patients with IBD do not receive adequate preventive care as compared to the general population,<sup>3</sup> and even though health

maintenance guidelines from different GI societies are available, adherence to preventive care recommendations, especially vaccination, remain low.<sup>4</sup> Moreover, many patients with IBD consider their gastroenterologist as their primary care provider (PCP).<sup>2</sup> For these reasons, it is imperative that gastroenterologists take a proactive role in health maintenance in these patients. It is of equal importance to partner with PCPs in optimizing health maintenance. The intent of this article is to review and provide guidance on preventive care and health maintenance in patients with IBD, including vaccinations, cancer screening, bone health, nutrition, and mental health assessment as well as smoking cessation.

## VACCINES

Patients with IBD are susceptible to acquiring infections for two reasons: immunological disorder caused by the disease itself, as well as treatment side effects.<sup>5</sup> Over the last two decades, the advent of new biologic agents and small molecules revolutionized the treatment of IBD. These medications are proven to be beneficial in controlling disease activity but may also place the patient at a higher risk for serious and/or opportunistic infections, a number of which are vaccine preventable.<sup>6</sup> In general, patients with IBD are recommended to follow standard, age-appropriate immunization schedules, with immunizations occurring ideally prior to initiation of immunosuppressive therapy, as some of these therapies may blunt vaccine response.<sup>3</sup> Special consideration must be kept for live-attenuated vaccines, which are contraindicated in immunosuppressed patients, particularly those who are moderately-severely immunosuppressed. Patients with IBD are considered to be moderately-severely immunosuppressed if taking any of the following medications: systemic steroids with doses of  $\geq 20$  mg for  $\geq 2$  weeks, methotrexate (MTX)  $> 20$  mg per week or  $> 0.4$  mg/kg/week, azathioprine (AZA)  $> 3$  mg/kg/day, 6-mercaptopurine (6-MP)  $> 1.5$  mg/kg/day, cyclosporine, biologic agents (except for vedolizumab) and small molecules.<sup>7</sup> Of note, significant protein calorie malnutrition is also linked with immunosuppression.<sup>8</sup> Low dose immunosuppression includes receiving treatment with topical steroids (oral budesonide  $> 6$  mg/day) and those on lower doses of systemic steroids, MTX, AZA and 6-MP.<sup>7</sup> In contrast to patients who are moderately-severely immunosuppressed, certain live vaccines may be safe

during low-dose immunosuppression or in patients on certain biologic agents; however, the decision to administer any live vaccine should be considered on a case-by-case basis.<sup>7,8</sup> Examples of commonly used live-attenuated vaccines include measles-mumps-rubella (MMR) vaccine, varicella (VAR) vaccine, nasal influenza and the live herpes zoster vaccine (no longer available in the United States). Other live vaccines include yellow fever, cholera and one of the existing typhoid vaccines which are usually administered for travel purposes.<sup>2</sup> Otherwise, all adult patients with IBD may receive non-live vaccines including inactivated influenza vaccine, pneumococcal vaccines, hepatitis A and B vaccine, tetanus-diphtheria and pertussis (Tdap), human papillomavirus (HPV) vaccine, meningococcal vaccine, inactivated recombinant herpes zoster vaccine and adenovirus, subunit or messenger RNA (mRNA) vaccines directed against coronavirus virus disease (COVID-19).<sup>2</sup> Current vaccination recommendations in adult patients with IBD are summarized in **Table 1**, see **Appendix**. Given COVID-19 vaccinations are dynamically changing as the pandemic evolves, would recommend visiting the Center for Disease Control and Prevention websites for updated information. Pediatric recommendations on regards to COVID-19 vaccination are also available in these websites: (<https://www.cdc.gov/coronavirus/2019-ncov/vaccines/stay-up-to-date.html> and <https://www.cdc.gov/coronavirus/2019-ncov/vaccines/recommendations/immuno.html>).

Regarding optimal timing for vaccination, the Infectious Diseases Society of America (IDSA) guidelines recommend that the administration of live vaccines should occur at least 4 weeks prior to initiating immunosuppression and should be avoided within 2 weeks of initiation of immunosuppression.<sup>9</sup> On the other hand, if a live vaccine is required and the patient has discontinued immunosuppressive therapy, it is recommended to at least wait for 1–6 months (five times the elimination half-life of a drug) prior to the live vaccine administration,<sup>7</sup> or if there is no detectable drug in the system for medications in which there are options to measure. For inactivated vaccines, the IDSA recommends administration at least 2 weeks prior to initiating immunosuppression.<sup>9</sup>

Employing a “cocoon strategy”, vaccinating household and close contacts is also an important approach. Healthy immunocompetent individuals who live in a household with immunocompromised patients should receive inactivated vaccines as per their age-appropriate schedules, and the following live vaccines based on the Centers for Disease Control and Prevention (CDC) annual schedule: MMR vaccine, rotavirus vaccine in infants 2–7 months (immunocompromised patients should avoid handling diapers of vaccinated infants for 4 weeks following vaccination), VAR vaccine, and in cases when the inactive zoster vaccine is not available, the live zoster vaccine is recommended. Immunocompromised patients should avoid individuals who develop skin lesions after receiving the VAR or the live zoster vaccines until the

lesion disappear.<sup>9</sup> Household and close contacts may also receive the following live vaccines for travel: yellow fever and oral typhoid vaccine, while the oral polio vaccine should not be administered under any circumstances.<sup>9</sup>

**CANCER SCREENING**

**Colon Cancer**

Colonoscopy remains the primary modality used for colorectal cancer and dysplasia surveillance in patients with IBD. Two-step modalities such as fecal immunochemical test (FIT) or multi-targeted stool DNA tests (like Cologard™) are not appropriate for CRC surveillance in the IBD population.<sup>10</sup> The interval of screening and/or surveillance differs based on the duration and extent of disease. Dysplasia surveillance using high-definition colonoscopy should begin 8 years after disease diagnosis in patients with UC with involvement extending proximal to the rectum, or in patients with CD who have more than 1/3 of the colon involved.<sup>11–13</sup> Subsequent surveillance colonoscopies should be completed every 1-5 years following a negative colonoscopy based on additional patient risk factors for developing dysplasia or clinical features that could potentially obscure the detection of dysplasia (**Table 2**).<sup>12</sup> A personal history of dysplasia, adenomatous polyps, primary sclerosing cholangitis, family history of CRC, degree and extent of colonic inflammation, extensive pseudopolyps all inform increased frequency of surveillance. Patients with primary sclerosing cholangitis (PSC) should undergo a colonoscopy at time of

**Table 2.** Interval of time to next colonoscopy following a colonoscopy negative for dysplasia

1 year	2–3 years	5 years
Ongoing moderate or severe inflammation	Mild inflammation	Continuous disease remission with mucosal healing on colonoscopy and one of the following: No dysplasia on ≥2 consecutive colonoscopy Minimal historic colonic involvement i.e. <1/3 of the total colon
PSC	Family history of CRC but no first degree relative <50 years	
Family history of CRC in first degree relative diagnosed age <50 years	Endoscopic evidence of prior severe colitis such as scarring or moderate polyposis	
Extensive pseudopolyps	History of invisible dysplasia or high-risk visible dysplasia* diagnosed > 5 years prior	
History of invisible dysplasia or high-risk visible dysplasia* in last 5 years	History of lower risk visible dysplasia diagnosed in the last 5 years	

\*High risk visible dysplasia: >2cm, lateral spreading, irregular boarder, local recurrence, incomplete prior resection.

Table published in the 2021 AGA Clinical Practice Update on Endoscopic Surveillance of Colonic Dysplasia (12).

diagnosis and then annually. Chromoendoscopy during surveillance can be used at the discretion and expertise of the endoscopist with the potential of increasing detection of subtle lesions.

**Cervical Cancer**

Women with IBD on immunosuppressants are at an increased risk of developing cervical cancer or high-grade dysplasia.<sup>14</sup> For this reason, the American College of Obstetrics and Gynecology and American College of Gastroenterology (ACG) recommend an increased frequency of cervical cancer screening with annual cytology.<sup>8,15</sup> Furthermore, the increased risk of cervical dysplasia and malignancy emphasizes the importance of vaccination for HPV when indicated.

**Skin Cancer**

Both melanoma, and non-melanoma skin cancers (NMSC) are observed more frequently in patients with IBD. Immunosuppression with either immunomodulators or biologics confer additional risk. For patients taking chronic thiopurines for longer than 1 year, the risk of developing NMSC was at least four times that of matched healthy controls.<sup>16</sup> This association applies to both current and prior exposure to thiopurines.<sup>17</sup> Similarly, there is a higher risk of being diagnosed with melanoma (OR 1.88, 95% CI 1.08-3.29) in patients with a history of IBD, and particularly in patients treated with biologic therapy.<sup>18,19</sup> Primary prevention through behavioral modification such as sun avoidance and sunscreen use should be discussed with all patients with IBD. Furthermore, all patients with IBD should be referred for skin exam with a dermatologist.<sup>8</sup> Given the durability of risk despite cessation of immunomodulators, annual skin exams should be continued lifelong in select patients as directed by dermatology.

**BONE HEALTH/OSTEOPENIA-OSTEOPOROSIS**

Patients with IBD are at increased risk of osteopenia, osteoporosis, and bone fractures due to multiple factors, including type of IBD, history of corticosteroid use, low body mass index, malnutrition, vitamin D deficiency, calcium malabsorption, underlying chronic inflammatory state, and immobilization.<sup>4,20</sup> Published literature indicates that the risk of osteoporosis is estimated to be 15–40%.<sup>4</sup> Recommendations on screening of osteopenia/osteoporosis and prevention in patients with IBD are detailed in **Table 3**.<sup>21</sup>

**NUTRITIONAL ASSESSMENT**

Iron deficiency anemia is observed in approximately 45% of patient with IBD and occurs through multiple mechanisms, including luminal blood loss and decreased iron absorption.<sup>22</sup>

**Table 3.** Bone Health – Screening and prevention of osteopenia and osteoporosis\*

	Recommendation
Screening Dual energy X-ray absorptiometry (DEXA)	All IBD patients should be screened for osteoporosis if any of the following risk factors is present: <ul style="list-style-type: none"> <li>• Low BMI</li> <li>• &gt;3 months of cumulative steroid use</li> <li>• Postmenopausal</li> <li>• Hypogonadism</li> <li>• Tobacco use</li> </ul> If osteoporosis is noted the patient should be referred to endocrinology for evaluation of bisphosphonate therapy. Repeat in 5 years if initial screen is negative.
Prevention Vitamin D 25-OH level assessment	Serial monitoring of vitamin D levels, supplement if deficient (levels <20 consider vitamin D3 50,000 units weekly for 8 weeks followed by vitamin D3 2,000 units daily)
Calcium and Vitamin D supplementation	Co-prescription of calcium and vitamin D for all patient receiving a course of oral corticosteroids

\*Adapted from Health Maintenance Checklist for adults from the Crohn’s & Colitis Foundation (21) and Cornerstones Health IBD Checklist for monitoring and prevention (23).

The presence of inflammation may confound the interpretation of iron studies, and a ferritin cut-off of 100 ng/mL should be considered as the lower limit of normal in patients with active IBD. A consequence of impaired absorption, oral iron repletion may be ineffective and parenteral infusions are often necessary. Similarly, vitamin B12 deficiency is well described in patients with ileal CD or those with a history of prior ileal resection. Cornerstones Health recommends screening for iron deficiency in all patients with IBD and vitamin B12 deficiency in patients with ileal CD or history of ileal resection.<sup>23</sup> In patients at risk of B12 deficiency, methylmalonic acid (MMA) levels should be checked simultaneously and B12 replacement therapy considered in all patients with elevated MMA level for a goal B12 level of greater than 400 pg/mL and normalization of MMA. Parenteral replacement should be considered in patients with greater than 20 cm of terminal ileal resection.

**MENTAL HEALTH – DEPRESSION AND ANXIETY SCREENING**

Depression and anxiety are common disorders in patients with IBD with pooled mean rates almost twice as high when compared to healthy controls.<sup>24</sup> While anxiety has been associated with decreased compliance to medications, increased risk of surgery and lower quality of life, depression has been linked with pain, IBD flare and lesser response to IBD treatment in some studies.<sup>25</sup> Furthermore, depression severity has been associated with suicidal ideation in this patient population.<sup>26</sup> Therefore, screening of these conditions is critical as they may cause significant morbidity. The Crohn’s & Colitis Foundation health maintenance checklist

recommends all patients with IBD should be screened at baseline and on a yearly basis for depression and anxiety.<sup>21</sup> Patients who are found to have anxiety or depression should be referred to their primary care physician or mental health for further evaluation and management.

In addition, fatigue has also been related to psychosocial factors, including depression and sleep disturbances.<sup>27</sup> Therefore, evaluation of fatigue, sleep quality and management of sleep disorders are equally important.

### TOBACCO USE/SMOKING CESSATION

Smoking and tobacco use remain a significant health risk for any patient with IBD. Multiple studies suggest that active tobacco use is associated with an increased risk for the development of CD and for disease specific complications such as progression, need for surgery, and surgical complications.<sup>28,29</sup> Although there are data demonstrating decreased disease activity in patients with UC, tobacco should not be recommended because the overwhelming detriments of smoking on extra-intestinal health outweigh any benefits.

Despite clear evidence for the negative effects of smoking, up to 20% of patients with CD and 60% of patients with UC reported believing that smoking was either neutral or beneficial for their disease activity.<sup>30</sup> Furthermore, 21% of patients with CD and 44% of patients with UC within the same cohort were never asked about their smoking status.<sup>30</sup> Society guidelines emphasize the need to screen for tobacco use at every encounter.<sup>8,23</sup> For those patients who engage in cessation planning, the alliance between the gastroenterologist and PCP is critical to coordinate adjunctive therapies and optimize success.

### CONCLUSION

Healthcare maintenance remains a crucial issue in the care of patients with IBD. Despite their importance, many physicians do not address these factors due to lack of knowledge, time constraints, or because they do not feel that this is their responsibility. Checklists are now available to help gastroenterologists and PCPs ensure that their patients with IBD are receiving appropriate vaccinations and other screenings.

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