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## Prevention in Inflammatory Bowel Disease: An Updated Review



Millie D. Long

**Patients with inflammatory bowel disease (IBD) are subject to complications from the disease itself and also from the immunosuppressive therapies used for treatment. To optimize the care of patients with IBD, providers need to consider primary, secondary and tertiary prevention. Primary prevention is employed to prevent a disease or complication from developing, such as immunizations. Secondary prevention detects a disease early to prevent disability, such as through screening programs. Tertiary prevention employs measures to reduce the impact of long-term disease and disability. This review highlights methods of prevention that can be utilized in patients with IBD via partnership between the primary care and gastroenterology provider.**

### INTRODUCTION

Inflammatory bowel disease (IBD), including both Crohn's disease (CD) and ulcerative colitis (UC), causes inflammation and ulceration in the gastrointestinal tract. This inflammation results in considerable morbidity for patients, including symptoms such as diarrhea, abdominal pain, rectal bleeding, and weight loss. The prevalence of IBD is increasing in the United States (US) and worldwide. It is estimated that 2.2 million Americans will be living with IBD by 2025.<sup>1,2</sup> With this growing population, there is an increasing need for effective and safe therapies for management of inflammation. Currently, there are a large number of classes

of agents available for treatment of IBD, with varying relationships between safety and efficacy. Immunosuppressive agents used in the treatment of IBD include corticosteroids, biologic agents [anti-tumor necrosis factor alpha (anti-TNF), anti-integrin therapies, anti IL-12/23 inhibitors, janus kinase (JAK) inhibitors, and immunomodulators such as thiopurines or methotrexate]. As we target goals of mucosal healing in our IBD population using immunosuppressive agents, we must also use a patient-centered approach to prevent downstream complications, either of IBD itself, or of the therapies used for treatment of IBD. To do so, a partnership must exist between gastroenterology and primary care providers to target primary, secondary and tertiary prevention for our patients. This article will discuss current guidelines and recommendations for prevention specific to patients with IBD.<sup>3,4</sup>

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### Primary Prevention

Primary prevention is defined as prevention of

**Table 1. Primary Prevention Recommendations in Inflammatory Bowel Disease\***

Intervention	Population	Frequency
<b>Vaccines (inactivated)</b>		
Influenza	All	Annual
Pneumococcal vaccination	Immunosuppressed	Pneumococcal 13 valent (PCV13) vaccine, then pneumococcal polysaccharide (PPSV-23) vaccine after 2-12 months
Shingles vaccination	≥ 50 years of age	Time 0 and then 2-6 months later
<b>Sunscreen use; sun-protective clothing</b>	All	Continuous
<b>Weight bearing exercise; calcium and vitamin D (if appropriate)</b>	All	Regularly

\*In addition to those highlighted, individuals with IBD should have all age-appropriate vaccinations with the exception of live vaccines which need to be avoided in patients on immunosuppression

\*\*Immunosuppression defined as use of ongoing corticosteroids, biologic agents (anti-tumor necrosis factor alpha, anti-integrin, anti-IL 12/23), immunomodulators (azathioprine or methotrexate) or small molecules (tofacitinib)

disease development. Examples of primary preventive efforts include immunizations against infectious diseases or educational interventions on regular exercise. Primary preventive efforts can occur at an individual level or at a population level. One example of a population level primary preventive effort is fluoridation of the water supply to prevent dental caries. As compared to the age-matched general population, patients with IBD are at increased risk for vaccine-preventable illnesses, such as influenza,<sup>5</sup> pneumococcal pneumonia,<sup>6</sup> and shingles.<sup>7</sup> Inactivated vaccines are safe to administer in patients with IBD, regardless of immunosuppression status. Therefore, adherence to vaccination guidelines of inactivated vaccines can reduce these infectious complications. Annual influenza vaccination is indicated in all patients with IBD, pneumococcal vaccination series is indicated in all immunosuppressed patients with IBD and herpes zoster vaccination is indicated in all patients with IBD ≥ 50 years of age. Due to increased risk of shingles in younger IBD populations,<sup>7</sup> consideration can be given for earlier vaccination while on certain high risk therapies. In particular, tofacitinib is associated with an increased risk of shingles, particularly at higher doses.<sup>8</sup> However, more data are needed on safety, efficacy and durability in younger populations

prior to a definitive recommendation. The human papillomavirus (HPV) vaccine has been shown to protect against specific serotypes of HPV linked to cervical dysplasia and genital warts. This vaccine has been studied specifically in IBD populations. The HPV vaccine has demonstrated both efficacy and safety.<sup>9</sup> Another method of primary prevention in IBD patients is sunscreen use to prevent skin cancer. Patients with IBD have increased risks of both non-melanoma (NMSC) and melanoma skin cancer.<sup>10, 11</sup> Evidence has demonstrated that thiopurines specifically increase the risk of NMSC and that the mechanism of action is associated with photosensitivity to ultraviolet-A light.<sup>12</sup> Therefore, this is a potentially preventable complication of therapy through broad-spectrum sunscreen use. Finally, weight bearing exercise and calcium/vitamin D supplementation, when appropriate, can prevent downstream osteoporotic fracture in these patients who may require recurrent courses of corticosteroids during their lifetimes with IBD. Table 1 shows a summary of primary preventive measures recommended in IBD patients.

### Secondary Prevention

Secondary prevention is defined as detecting a disease early to prevent disability; such as through screening programs. Therefore, there are

**Table 2. Secondary Prevention Recommendations in Inflammatory Bowel Disease**

Intervention	Population	Frequency
<b>Skin cancer screening</b>	All	Initial; subsequent interval by dermatology
<b>Cervical cancer screening</b>	Immunosuppressed* Others	Annual Per standard recommendations
<b>Colorectal cancer screening</b>	Colonic inflammation  Primary Sclerosing Cholangitis + colon inflammation	At 8-10 years of disease duration, with subsequent interval based on results Annual starting at diagnosis
<b>Osteoporosis/osteopenia screening</b>	Women $\geq$ 65 years All with $\geq$ 3 months steroid use	Once, with subsequent screening based on results
<b>Anxiety/depression screening</b>	All	Annual

\*Immunosuppression defined as use of ongoing corticosteroids, biologic agents (anti-tumor necrosis factor alpha, anti-integrin, anti-IL 12/23), immunomodulators (azathioprine or methotrexate) or small molecules (tofacitinib)

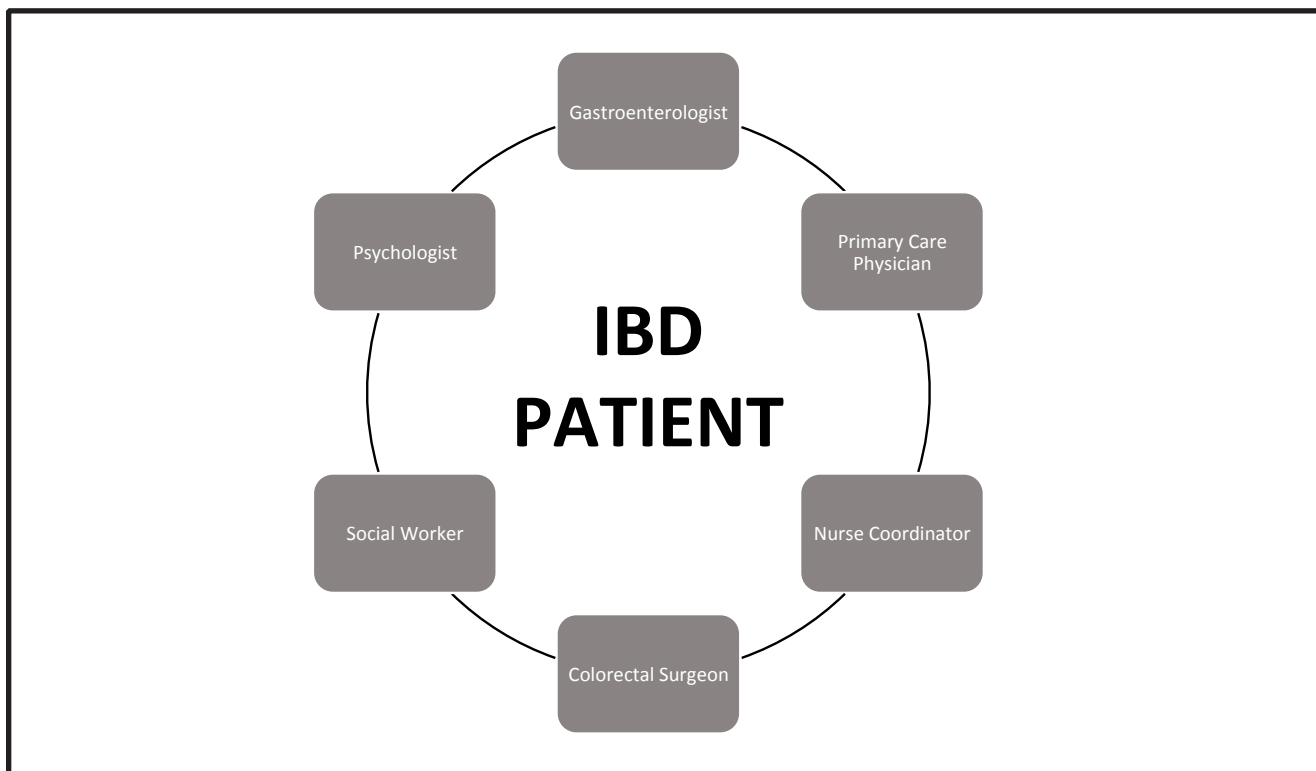
a number of important opportunities for secondary prevention in IBD patients. For example, patients with IBD are known to have an increased risk of melanoma, regardless of immunosuppressive therapy. Individuals on anti tumor necrosis factor alpha (anti-TNF) agents have nearly a two-fold further increased risk of developing melanoma.<sup>10</sup> Therefore, a dermatology skin screening program is recommended in all patients with IBD.<sup>3</sup> Prior studies have suggested an increased risk of abnormal Pap smear and/or cervical dysplasia in patients with IBD on immunosuppression.<sup>13</sup> Therefore, annual cervical cancer screening is recommended in patients with IBD on immunosuppression.<sup>3</sup> Patients with IBD who have longstanding colonic inflammation (> 10 years of duration) have an increased risk of developing colorectal dysplasia and cancer. Therefore, patients with longstanding colonic inflammation should undergo routine colonoscopy starting at 8-10 years of colonic disease duration, with subsequent colonoscopy intervals based on the results (often every 1-3 years). From a bone health perspective, all individuals (regardless of gender) with  $\geq$  3 months duration of corticosteroid use are at risk for osteopenia or osteoporosis. Therefore, screening with DEXA scan for these individuals and in women age  $\geq$  65 years is recommended. Subsequent DEXA screening can be determined based on the initial

results. Finally, depression and anxiety are common in IBD patients.<sup>14</sup> Earlier recognition and treatment of depression and anxiety can improve quality of life in patients with IBD. Screening for depression and anxiety is recommended in all patients with IBD.<sup>3</sup> Table 2 describes currently recommended secondary preventive efforts in IBD patients.

### Tertiary Prevention

Tertiary prevention refers to utilization of measures to reduce the impact of long-term disease and disability. In CD, ongoing inflammation can lead to development of strictures, which may cause obstruction and require bowel resection surgery. Additionally, inflammation can progress to fistulizing disease, including abnormal connections between the bowel and other organs. These fistulas can result in abscesses and other complications ultimately often requiring surgery. In UC, ongoing inflammation can increase the risk of colon cancer and dysplasia. Additionally, disease can extend from only left-sided involvement to pan-colonic involvement over time. Therefore, by intervening early and treating inflammation, with a goal of mucosal healing, we can potentially prevent these morbid and potentially life-threatening, complications of IBD. The paradigm in IBD management has shifted to one of a “treat to

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**Figure 1. A Patient-Centered Approach to Collaborative Care of the Inflammatory Bowel Disease Patient**

target” approach<sup>15</sup>. After initiation of medical therapy for the treatment of IBD, guidelines recommend subsequent reassessment to ensure that both symptoms and mucosal inflammation are improved.<sup>16,17</sup> This dual method of reassessment is important, as symptoms do not always correlate with ongoing inflammation. This standard of reassessing a current therapy is also important in post-operative CD, where early evaluation with colonoscopy in the first 6-12 months after a resection, with alteration of medical therapies based on this, has been shown to improve long-term endoscopic outcomes.<sup>18</sup> Therefore, by optimizing therapies to improve mucosal healing, we may be able to impact the long-term disability associated with irreversible bowel damage in IBD.

## CONCLUSION

Management of patients with IBD can be difficult. IBD itself can be associated with a number of complications for patients, including ongoing chronic bowel symptoms and structural bowel damage, as well as extra-intestinal manifestations of IBD. These extra-intestinal manifestations

can include significant joint symptoms, skin manifestations, anemia, and kidney stones. While there are a number of effective therapeutic agents for the treatment of IBD and these extra-intestinal complications, many of these therapies are themselves immunosuppressive. Therefore, the drugs themselves can result in therapy-related complications. These may include infectious, malignant, or idiopathic complications. As the patient may present to the primary care provider or the gastroenterologist for evaluation of symptoms or complications, it becomes very important for the entire care team to collaborate on diagnostic and management plans for individual patients with IBD. Importantly, prior studies have demonstrated that primary care physicians may not be comfortable addressing preventive care in IBD patients on immunosuppression.<sup>3</sup> However, the gastroenterologist may assume that all preventive activities are occurring in primary care. The gastroenterologist may also not be comfortable addressing all of an IBD patient’s preventive health needs. In fact, many patients with IBD consider their gastroenterologist to be their primary care

provider. Therefore, a collaboration between primary care and gastroenterology is needed to ensure appropriate adherence to preventive health recommendations in patients with IBD. Each IBD patient should have regular evaluation with both a primary care and gastroenterology provider. Through this partnership, an individualized plan for preventive medicine can be developed for each patient with IBD. This proactive approach of addressing primary, secondary and tertiary prevention in IBD patients can ultimately help to reduce infectious, malignant and long-term disease-related complications.

There is an old African proverb stating, “It takes a village to raise a child.” This reflects the emphasis that African cultures place on family and community. In fact, this community of support is also needed for each patient with IBD. By sharing the burden of the complete care of the IBD patient, a care team can deliver evidence-based, patient-centered care. Figure 1 shows the integral components of a care team for a patient with IBD. Through collaboration, a care plan can be implemented for each IBD patient addressing his or her individual needs and goals. By focusing on implementing the three forms of prevention: primary, secondary, and tertiary, we can improve the lives of our patients with IBD. ■

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Answers to this month’s crossword puzzle:

1	P	A	P	I	L	L	A	R	Y	5	S	A	C	S				
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