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HERE AND NOW: CLINICAL PRACTICE

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Preventive Medicine in Inflammatory Bowel Disease

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The prevalence of inflammatory bowel disease (IBD) is increasing worldwide. The therapeutic options available to our patients are also increasing. These therapies offer patients the prospect of clinical and endoscopic remission, as well as improved quality of life. However, the management of IBD has become complex, including identification of specific risks associated with IBD and its therapies. The provider needs to consider forms of primary, secondary and tertiary prevention in his or her management of patients with IBD in order to prevent complications. We review the role of preventive medicine in IBD and provide specific preventive considerations for the clinician.

The prevalence of inflammatory bowel disease (IBD) is rising within the United States and worldwide.[1] There are currently 1.2 million Americans living with IBD, and it is estimated that this number will increase to 2.2 million Americans by 2025.[1,2] We have seen a rapid increase in the use of novel therapeutic agents in the management of IBD. Goals of therapy have shifted to achieving both clinical remission and mucosal healing.[3] However, we must also be mindful of the potential infectious and malignant complications of various immunosuppressive drugs used in the management of IBD. Studies suggest that IBD patients, particularly those on immunosuppression, do not receive adequate preventive health services.[2] This article highlights the importance of 3 forms of prevention in IBD care: primary, secondary, and tertiary prevention.

Primary prevention is defined as prevention of disease development. Immunizations against infectious diseases and education about leading a healthy lifestyle including regular exercise and eating a well-balanced diet are all examples of primary preventive measures. Secondary prevention aims to detect and treat disease in its earliest stage before the onset of signs or symptoms. Examples of secondary prevention include screening programs such as screening for breast cancer or colon cancer, as is recommended in the general population at appropriate ages. The goal of a secondary prevention screening program is to decrease the impact of a disease that has already occurred. Finally, tertiary prevention refers to the management of disease after diagnosis in an effort to reduce the impact of long-term disease by preventing disability and complications. Therefore, using tertiary prevention can maximize quality of life and potential life years. This framework of primary, secondary, and tertiary prevention is applicable to the management of IBD and should be continuously applied (Figure 1).

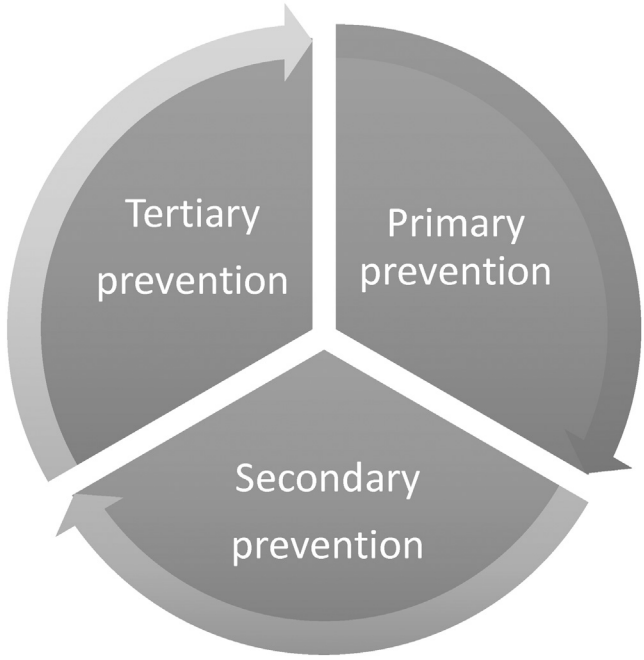

Figure 1. Forms of prevention applicable to the management of inflammatory bowel disease.

Preventive health recommendations for IBD patients are outlined in Table 1.[4] Patients with IBD are at increased risk of vaccine-preventable illnesses including influenza and pneumonia, as compared with age-matched patients without IBD.[4] Inactivated or killed vaccines do not increase the risk of infection and are safe to administer in all individuals with IBD,

Abbreviations used in this paper: **anti-TNF, anti–tumor necrosis factor alpha; IBD, inflammatory bowel disease.**

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Table 1. Primary, Secondary, and Tertiary Prevention Recommendations in Patients With Inflammatory Bowel Disease

	Intervention	Target population	Frequency	Specific considerations
Primary prevention				
Prevention of infectious complications	Influenza vaccination	All	Annual	Avoid live intranasal influenza vaccine in immunosuppressed
	Pneumococcal vaccination	Immunosuppressed	PCV13 ×1, then PPSV23 after 2–12 months	PPSV23 booster required 5 y after initial vaccination in those <age 65
	Shingles vaccination	≥50 years old, including those with prior shingles	2 doses administered at 0 and 2–6 months	Zoster vaccine recombinant adjuvanted (Shingrix) preferred, specific consideration with tofacitinib
Prevention of cervical dysplasia or genital warts	Human papilloma virus vaccination	All female and male patients between the ages of 11 and 45 years	3 doses administered at 0, 2, and 6 months	Studied in IBD populations with efficacy and no risk of flare
Prevention of skin cancer	Sunscreen use; sun protective clothing	All	Continuous	Anti-TNFs associated with increased risk of melanoma; thiopurines, tofacitinib with increased risk of NMSC
Prevention of osteoporotic fracture	Weight-bearing and muscle-strengthening exercises	All	Regularly	Improves strength and balance, maintains bone strength, decreases risk of falls and fractures
	Calcium and vitamin D measurement and supplementation as appropriate	All	Daily or weekly on the basis of dosing	Recommended calcium intake 1000–1200 mg/day Recommended vitamin D intake 800–1000 IU/day Supplement if not meeting dietary recommendations or deficient on the basis of laboratory studies
Secondary prevention				
Prevention of skin cancer	Skin screening examination	All patients on azathioprine to screen for NMSC, all patients with IBD to screen for melanoma	At diagnosis or initiation of therapy, with subsequent interval determined by dermatology	Anti-TNFs associated with increased risk of melanoma; thiopurines, tofacitinib with increased risk of NMSC
Prevention of colorectal cancer and dysplasia	Colonoscopy	Colonic inflammation	Surveillance colonoscopy recommended in those with disease duration ≥8 y and ≥30% colonic involvement, with subsequent intervals determined on the basis of results[3]	Proctitis and isolated ileal disease are not considered to be at increased risk for dysplasia; surveillance protocols not required Individuals with primary sclerosing cholangitis and IBD should initiate surveillance colonoscopy at time of diagnosis regardless of disease location or extent
Prevention of cervical dysplasia	Pap smear	All female patients	Annual if on immunosuppression; otherwise per national guidelines	
Prevention of osteoporotic fracture	DEXA scan	Women ≥65 y All with ≥3 months of corticosteroid use regardless of age or gender	Osteopenia or osteoporosis: repeat DEXA in 2 years; otherwise repeat in 5–10 years if no change in risk factors	Consider maximizing calcium and vitamin D, bisphosphonates if osteopenia/osteoporosis
Prevention of anxiety, depression	Clinic-based screening	All	Annual	Consider Patient Health Questionnaire-2 and Generalized Anxiety Disorder-7 as options
Tertiary prevention				
Treatment of IBD	Medical management of IBD to achieve mucosal healing	All		To prevent disability and complications including surgery, colorectal cancer

NOTE. These recommendations do not include the standard age-appropriate vaccination schedules that should also be followed PPSV23.
anti-TNF, anti–tumor necrosis factor-alpha; DEXA, dual-energy x-ray absorptiometry; IBD, inflammatory bowel disease; NMSC, non-melanoma skin cancer; PCV13, pneumococcal conjugate vaccine-13; PPSV23, pneumococcal polysaccharide vaccine-23.

Table 2. Routine Laboratory Monitoring Recommendations for Patients With Inflammatory Bowel Disease on Medical Therapy

Medication	Laboratory monitoring	Frequency	Special considerations
Mesalamine/sulfasalazine[5]	CBC Creatinine	Before initiation and then every 3–6 months	Folic acid supplementation with sulfasalazine
Thiopurines[6]	Thiopurine methyltransferase CBC with differential Liver enzymes	Once before initiation of therapy Every 2 weeks × 4 after initiation and with dose adjustment, then every 3 months thereafter	Avoid use of thiopurines in those with low enzyme activity and reduce dose in those with intermediate enzyme activity because of risk of myelosuppression
Methotrexate[7]	CBC Creatinine Liver enzymes Albumin	Induction weeks 2, 4, 8 and then every 4–12 weeks thereafter	All patients should receive folic acid supplementation Contraindicated in pregnancy because of potential teratogenicity; women should be off methotrexate for 3 months before trying to conceive Contraindicated among those with preexisting liver disease or alcoholism Consider CXR within 1 year of initiation to rule out interstitial lung disease
Tofacitinib[8]	HBsAg, HBcAb total, HBsAb to determine hepatitis B status QuantiFERON gold or PPD Lipid panel CBC with differential Liver enzymes	Before initiation Before initiation At initiation and then 4–8 weeks after starting drug At initiation, then 4–8 weeks after starting drug, and then every 3 months thereafter	Not recommended during pregnancy because of insufficient data Zoster vaccine recombinant adjuvanted (Shingrix) vaccine series recommended
Biologics[3]	HBsAg, HBcAb total, HBsAb to determine hepatitis B status QuantiFERON gold PPD CBC Creatinine Liver enzymes Albumin	Before initiation Before initiation At initiation and then with subsequent infusions or at least twice yearly for those receiving subcutaneous injections	Tuberculosis clinical risk factors assessed annually; but annual PPD or QuantiFERON gold not required in low-risk populations; anti-TNF biologics associated with specific increased risks of tuberculosis and hepatitis B reactivation; risks less clear with other biologics

CBC, complete blood count; CXR, chest x-ray; HBcAb, hepatitis B core antibody; HBsAg, hepatitis B surface antigen; PPD, purified protein derivative; TNF, tumor necrosis factor.

including those on immunosuppression. It is therefore recommended that all IBD patients receive annual inactivated influenza vaccination. The pneumococcal vaccination series should be administered to all patients on immunosuppression. Further immunization recommendations are outlined in Table 1. Of note, live vaccines should generally be avoided in immunosuppressed patients. The Infectious Disease Society of America considers patients on anti–tumor necrosis factor alpha (anti-TNF) agents to have high-level immunosuppression; thus all live vaccines should be avoided. The package insert for vedolizumab states that patients on this biologic may receive live vaccines if the benefits outweigh the risks, whereas patients on ustekinumab or tofacitinib should not receive live vaccines.[4] Patients on low levels of immunosuppression (prednisone 20 mg/day $\leq$2 weeks, methotrexate $\leq$0.4 mg/kg/week, or azathioprine $\leq$3.0 mg/kg/day) can receive lower potency live attenuated vaccines (such as live attenuated zoster) but not other higher potency live vaccines.

In addition to the primary prevention of infectious complications, screening for colorectal cancer/dysplasia, bone density, and mental health screening are essential components of secondary prevention in IBD patients. All IBD patients should wear broad-spectrum sunscreen when outdoors, as well as sun-protective clothing. Because of the increased risk of melanoma among IBD patients and specifically those treated with anti-TNF agents, as well as the increased risk of non-melanoma skin cancer with the use of thiopurines and tofacitinib, all patients initiating therapy with an immunosuppressant should have a baseline skin check, with follow-up interval determined by the examining dermatologist.[2,4] Prior studies have suggested an increased risk of abnormal Pap smear and/or cervical dysplasia among women with IBD on immunosuppression. Therefore, it is recommended that women on immunosuppression undergo annual cervical cancer screening with Pap smear.[4] In addition, long-standing colonic inflammation among IBD patients is a risk factor for the development of colorectal cancer. Surveillance colonoscopy is recommended in specific populations (Table 1).[3] Osteopenia and osteoporosis as well as bone fracture are seen at increased rates in IBD patients compared with the general population.[2] All IBD patients should be counseled on the importance of regular exercise as well as adequate daily intake of calcium and vitamin D. In particular, individuals with IBD who have been exposed to more than 3 months of corticosteroids and all women $\geq$65 years old should have baseline dual-energy x-ray absorptiometry, with follow-up interval determined on the basis of the results of initial study. Screening for anxiety and depression is also essential in all patients with IBD because of associations with decreased quality of life and poor adherence.[3,4]

The ultimate goal in the treatment of patients with IBD is maintenance of corticosteroid-free clinical remission. By also achieving mucosal healing, we may prevent the need for surgery and/or the development of colorectal cancer. As the therapeutic armamentarium in IBD expands, specific laboratory monitoring of individual therapies is required to prevent therapy-specific adverse events. Recommendations for monitoring by specific type of medical therapy are outlined in Table 2.

Prevention is a central component in the care of IBD patients. Complications of IBD and its therapies can dramatically impact patients. Some patients remain fearful of medication-related complications and are therefore hesitant to initiate therapies, even when their IBD is quite severe. However, emphasizing the prevention of downstream consequences of inadequately treated disease and providing data on specific interventions that can prevent therapy-associated complications can better inform patients. A discussion of prevention is important initially at the time of therapy initiation and then subsequently in discussions of maintenance of therapy. Prior studies have shown that primary care providers often do not feel comfortable providing routine preventive care to IBD patients, particularly those on immunosuppression.[4] In addition, many patients with IBD consider their gastroenterologist to be their primary provider. As a result, it is important for gastroenterologists to share in the responsibility of health maintenance for IBD patients. Gastroenterologists may choose to manage preventive health measures themselves or communicate specific recommendations to the patient's primary care provider. By following preventive recommendations, we can improve disease-specific outcomes and quality of life and reduce complications in our patients with IBD.

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Conflicts of interest
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