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ECCO Guideline

ECCO Guidelines on the Prevention, Diagnosis, and Management of Infections in Inflammatory Bowel Disease

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1. Introduction

The therapeutic landscape of inflammatory bowel disease [IBD] has undergone a profound transformation with the advent of novel immunosuppressive and biologic agents. These advancements have revolutionized the management of Crohn's disease [CD] and ulcerative colitis [UC], enabling tighter control of inflammation and significantly improved patient outcomes. However, while older treatment strategies, including prolonged corticosteroids, purine analogs, and anti-tumor necrosis factor [TNF]/thiopurine combination therapy, carried a substantial immunosuppressive burden, the expanding therapeutic armamentarium introduces new agents with distinct infection risk profiles that require updated, evidence-based guidance. By definition, opportunistic infections are infections caused by organisms that infrequently induce disease in immunocompetent hosts but can result in significant morbidity or mortality in immunocompromised individuals. As treatment strategies increasingly rely on potent modulation of the immune system, ranging from traditional thiopurines to advanced small molecules, a structured, evidence-based approach to infection prevention, diagnosis, and management has become indispensable for the clinician. The European Crohn's and Colitis Organisation [ECCO] has long recognized this clinical imperative, previously publishing consensus statements in 2009 and 2014, followed by a comprehensive guideline in 2021. This 2026 update is warranted by the rapid expansion of the therapeutic armamentarium, specifically the introduction of newer small molecules, advanced biologics, and evolving vaccination strategies. This update integrates the most recent data on risk stratification, viral, bacterial, mycobacterial, and vaccine-preventable infections, emphasizing a preventative strategy tailored to the contemporary IBD treatment paradigm.

2. Methodology

This consensus guideline was developed in strict accordance with standard ECCO methodology for guideline production. The project was led by two coordinators from the ECCO Guidelines Committee [GuiCom]. In April 2024, a call for participation was extended to all ECCO members from a competitive pool of applicants. The Guidelines Committee selected a panel of expert gastroenterologists and three infectious disease specialists. Four multidisciplinary working groups [WGs] were established to address the following major domains of infection management as outlined here: WG1, Viral infections; WG2, *Mycobacterium tuberculosis*, Bacterial, Parasitic, and Fungal infections; WG3, Risk factors, Degree of immunosuppression, Screening, and Special situations; and WG4, Vaccination strategies.

For each domain, clinically relevant questions were formulated to define a Population, Intervention, and Comparator of interest. These questions informed a systematic literature search conducted by a professional librarian using PubMed/Medline, Embase, and the Cochrane Central databases. Abstracts were screened by two participants, and full texts of potentially relevant articles were retrieved and evaluated to inform the clinical questions [search strings provided in the Supplementary material]. A consensus statement and supporting text were drafted for each topic. The Evidence Level [EL] was graded according to the Oxford Centre for Evidence-Based Medicine [2011] criteria (https://www.cebm.ox.ac.uk/resources/levels-of-evidence/explanation-of-the-2011-ocebm-levels-of-evidence). Consensus was achieved through two rounds of online voting and a final web-based video conference in September 2025. Consensus was defined as agreement by 80% or more of participants. The final manuscript was critically reviewed by external experts.

3. Defining the immunocompromised patient in IBD

3.1. Degree of immunosuppression with IBD medications

Patients with IBD are at increased risk of serious and opportunistic infections, a risk driven by both disease-related immune dysregulation and, for certain agents, the iatrogenic effects of immunosuppressive therapy. This risk is not uniform; rather, it is shaped by the mechanism of action, dose, and duration of individual therapeutic agents, and is further amplified by the concomitant or sequential use of multiple immunosuppressants. Systemic corticosteroids, particularly at higher doses (≥20 mg/day prednisone equivalent for ≥2 weeks)[1] and when used in combination with thiopurines and anti-TNFs, are consistently associated with increased infection rates. Host factors play a critical role in this risk equation. Older age, comorbidities such as chronic pulmonary disease, and concomitant medications such as opioids further amplify risk.[2,3] In a 2025 Veterans Affairs cohort analysis, advanced age and systemic corticosteroid exposure were strongly associated with infection-related hospitalizations.[4] Conversely, in the same cohort, vedolizumab, ustekinumab, and tofacitinib were not associated with higher infection-related hospitalization rates compared with traditional regimens, suggesting no excess risk in that specific setting.[4] Nevertheless, vigilant monitoring remains warranted, especially in older patients and those with additional risk factors. The assessment of immunocompromise must therefore integrate both host-related characteristics and the cumulative immunosuppressive burden associated with current and recent therapies.

> ***Statement 1: Patients with IBD receiving immunosuppressive treatment do not have an increased risk of opportunistic infections per se. The incidence of these infections varies based on the specific immunosuppressive treatment employed [EL2]. To better assess risk, immunosuppressive agents and the degree of immunosuppression can be categorized according to their mechanism of action, dosage, duration, and route of administration [EL5] [Agreement 95%]***

Data on the effect of immunosuppressive drugs on development of opportunistic infections have historically been conflicting, due largely to heterogeneous definitions of "opportunistic infections" across studies. A systematic review and network analysis of 38 randomized controlled trials [RCTs] did not detect a significant increase in infections with different treatments compared with placebo.[5] However, a subsequent meta-analysis including 49 RCTs with 14590 patients revealed an increased rate for opportunistic infections with biologics (odds ratio [OR]: 1.9; 95% confidence interval [CI]: 1.2–3.0), although no increased risk for serious infections was noted.[6]

A recent meta-analysis of 90 RCTs found no overall increased risk of opportunistic infections, but noted that the lack of a universal definition for infection makes cross-trial comparison difficult.[7] Crucially, this analysis highlighted considerable differences between drug classes, as follows: anti-TNF agents, highest incidence (0.83/1000 patient-years [py]); Janus kinase [JAK] inhibitors, intermediate incidence (0.55/1000 py); anti-interleukin [IL] 12/23 [IL-12/23] agents (predominantly ustekinumab), lower incidence [0.27/1000 py]; anti-integrins, very low incidence [0.05/1000 py]; sphingosine-1-phosphate [S1P] receptor modulators, lowest incidence [0/1000 py].[7] Notably, the above IL-12/23 class data derive predominantly from ustekinumab trials, as the pivotal phase 3 programs for selective anti-IL-23p19 agents post-dated the meta-analysis search period. Subsequent phase 3 data for risankizumab, mirikizumab, and guselkumab in both CD and UC have demonstrated favorable safety profiles with low rates of serious and opportunistic infections suggesting that selective anti-IL-23p19 agents carry a comparable or potentially lower infection risk relative to other advanced therapies, though longer-term surveillance data are needed.[8–10]

This heterogeneity is mirrored in large observational cohorts. An analysis of more than 190000 patients with IBD in France revealed an increased risk for opportunistic infections, particularly with combination treatment, and an increased risk for mycobacterial and bacterial infection with anti-TNF agents compared with thiopurines, but not viral infections.[2] Similarly, a Swedish nationwide register study found that while vedolizumab was associated with a lower risk of serious infections compared with anti-TNF agents in UC, this difference was not observed in CD, challenging the assumption that anti-integrins carry substantially lower infection risk across all IBD subtypes.[11] Consistent with this, the formal post-authorization safety study [PASS] of vedolizumab, a prospective observational cohort of 5008 patients with a mean follow-up of 37 months, found no significant difference in serious infection rates between vedolizumab and other biologics in either UC (adjusted hazard ratio [aHR]: 0.89; 95% CI: 0.69–1.15) or CD (aHR: 1.15; 95% CI: 0.95–1.40).[12] It is important to interpret RCT meta-analyses with caution, as strict inclusion and exclusion criteria and limited follow-up may underestimate risks that manifest in real-world settings. Life-long frequency of relevant infections in patients with IBD under immunosuppression has been reported at up to 5%.[13] Retrospective case-control studies and prospective registries have consistently demonstrated increased infection risk for patients on infliximab, steroids, azathioprine, or mercaptopurine, as well as those on combination therapies.[14,15] Infliximab appears to carry a particularly high risk compared with other IBD drugs.[2,15,16] This finding should be interpreted with caution, as infliximab is more frequently used in combination with thiopurines than other biologics, which may partly explain the higher observed infection rates rather than an intrinsically higher risk of infliximab monotherapy per se. Furthermore, meta-analyses of observational studies confirm an increased risk of infections with combination therapy compared with anti-TNF agent monotherapy.[17]

Specific Drug-Class Risks:

Vedolizumab: no increases in opportunistic infections have been reported, probably due to its gut selectivity,[17,18] although enteric infections such as *Clostridioides difficile* may occur.[19] In RCT meta-analyses, vedolizumab has been associated with low rates of opportunistic infections compared with other drug classes.[7] However, the PASS found no significant difference in serious infection rates between vedolizumab and other biologics in either UC or CD.[12] **Ustekinumab:** data from rheumatologic and dermatologic trials suggest reduced rates of serious infections compared with anti-TNF agents.[20,21] Long-term analysis [5 years in CD, 4 years in UC] revealed no increased risk of opportunistic infections, including tuberculosis.[22] **Anti-IL-23 (p19) agents (risankizumab, mirikizumab, guselkumab):** long-term extension studies report low rates of opportunistic infections.[23,24] **JAK inhibitors:** generally associated with low rates of opportunistic infections, with herpes zoster [HZ] being the main notable exception. For upadacitinib, HZ occurs more frequently than with placebo or some active comparators, whereas overall opportunistic infection rates remain low.[25] A similar pattern has been observed with tofacitinib: opportunistic infections excluding HZ occur at rates of <1/100 py, while HZ remains the principal excess risk.[26] In contrast, a systematic review and network meta-analysis found no significant increase in HZ risk with filgotinib compared with placebo, whereas tofacitinib and higher-dose upadacitinib were associated with significantly higher HZ rates.[27] In comparative claims-based data, the overall risk of infections with tofacitinib was similar to that observed with anti-TNF agents rather than lower, with HZ again representing the main distinguishing safety signal.[28] **S1P receptor modulators:** data are limited, but recent analyses of etrasimod showed no increased risk of infections or HZ.[29]

Figure 1 categorizes IBD therapeutic agents into the following three degrees of immunosuppression: (1) no immunosuppression, (2) low immunosuppression, and (3) moderate–severe immunosuppression.

When interpreting these data, it is important to recognize that active, poorly controlled IBD is itself an independent risk factor for infection.[2,30] Consequently, higher infection rates observed with certain agents may partly reflect their preferential use in more severe or refractory disease and in combination regimens, rather than a direct drug effect alone.

4. Viral infections

4.1. Screening and management of ongoing viral infections

Prevention of viral reactivation and primary infection is a cornerstone of IBD management. A proactive screening strategy allows for vaccination or prophylactic management prior to induction of significant immunosuppression.

Statement 2: Serological screening for hepatitis B, hepatitis C, HIV, and Epstein-Barr virus is suggested for all patients with IBD, ideally at diagnosis [EL4]. These are recommended before immunosuppressive treatment [EL1]. In the absence of documented immunity [past infection or vaccination] for hepatitis A, varicella zoster virus, mumps, measles, and rubella virus, serological screening may be considered, ideally at diagnosis [EL4]. These are recommended before immunosuppressive treatment [EL1]. We suggest cervical screening for human papillomavirus in female patients with IBD [EL4] [Agreement 100%]

Therapy/class	Degree of immunosuppression	Clinical interpretation
5-ASA		No systemic effects.
Topically acting oral steroids		Limited systemic exposure: risk increases with dose and duration.
Systemic steroids		Strong infection risk signal related to dose and duration.
MTX		Dose-dependent immunosuppressive effect.
Thiopurines [AZA/MP]		Sustained systemic immunosuppression; higher risk in combination.
Ciclosporin		Potent T-cell suppression used in high-risk settings.
Tacrolimus		
Vedolizumab		Gut-selective mechanism with low systemic infection signal.
Anti-TNF agents		Highest observed infection incidence among biologics.
Combination therapy		Additive immune effects drive infection risk.
Ustekinumab		Lower observed serious infection rates vs anti-TNF agents.
Anti-IL23 agents		Emerging safety data suggest low infection incidence.
S1P receptor modulators		Long-term infection risk still evolving.
JAK inhibitors		Overall low infection risk, but increased HZ signal

Drugs are categorized by their general immunosuppressive potential and risk of infections. Note that dosage significantly impacts risk categorization for steroids and immunomodulators. Abbreviations: 5-ASA, 5-aminosalicylic acid; AZA, azathioprine; HZ, herpes zoster; IL, interleukin; JAK, Janus kinase; MP, mercaptopurine; MTX, methotrexate; S1P, sphingosine-1-phosphate; TNF, tumour necrosis factor.

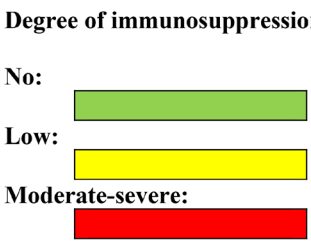

Figure 1. IBD therapies and degrees of immunosuppression.

Hepatitis B virus [HBV]: universal screening with HBsAg, anti-HBs, and anti-HBc is recommended before immunosuppressive therapy to identify active, resolved, or occult infection and guide antiviral prophylaxis (see Section 4.2.2). Seronegative patients should be vaccinated before immunosuppressive therapy (see Section 7.2). **Hepatitis C virus [HCV]:** screening with anti-HCV antibodies allows identification of patients who may benefit from direct-acting antiviral therapy (see Section 4.2.3). **Human immunodeficienct virus [HIV]:** screening with a combination HIV-1/2 antigen/antibody test is recommended to guide safe use of immunosuppressants (see Section 4.3). **Hepatitis A virus [HAV]:** patients without documented vaccination may be considered for screening. Fulminant HAV infection rates and severity are higher in immunosuppressed patients[31–33] (see Section 4.2.1). HAV vaccination is suggested for all patients with IBD without evidence of prior infection or vaccination, regardless of serological screening (see Section 7.2). **Epstein-Barr virus [EBV]:** screening is critical, especially in young males prior to starting thiopurines, due to the increased risk of lymphoproliferative disorders.[34–36] (see Section 4.5). **Varicella zoster virus:** determining serological status in patients without documented history identifies candidates for vaccination.[37] Seronegative immunosuppressed individuals are at risk of severe varicella and may require post-exposure prophylaxis. In patients with IBD, HZ is increased compared with the general population, with pooled estimates of relative risk [RR] of 1.74 [95% CI: 1.57–1.92] for CD and RR 1.40 [95% CI: 1.31–1.50] for UC.[38] This risk may be further increased in patients treated with JAK inhibitors[39] (see Section 7.2). **Measles and mumps:** serological testing for IgG is recommended in the absence of vaccination history due to poorer outcomes in the immunosuppressed[40–43] (see Section 7.2). **Severe acute respiratory syndrome coronavirus 2:** screening asymptomatic patients before biologic initiation remains controversial.[44] Data from the SECURE-IBD registry indicate that while systemic corticosteroids increase the risk of severe COVID-19, anti-TNF agents do not and may even be protective.[45] **Human papillomavirus [HPV]:** cervical screening is advised in female patients with IBD receiving immunosuppressive therapy, as some studies have reported an increased risk of cervical high-grade dysplasia or cancer [OR: 1.34; 95% CI: 1.23–1.46],[46] although this association may be attenuated after adjustment for confounders such as oral contraceptive use and number of sexual partners [aHR: 1.07; 95% CI: 0.79–1.45],[47] and the overall risk has been described as equivocal.[48] HPV vaccination is recommended as the primary preventive measure, and cervical screening in accordance with national guidelines is additionally advised (see Sections 4.6 and 7.2). **Influenza:** testing is indicated only in symptomatic patients.[49]

Statement 3: Temporary discontinuation of immunosuppressive therapy may be considered in patients with IBD with acute severe or disseminated viral infections [EL4] [Agreement 100%]

The decision to interrupt therapy balances the risk of infection progression against the risk of IBD flare.

Varicella/herpes simplex virus: severity supports withdrawing immunosuppressants during active infection. **HZ:** is frequent in immunosuppressed patients with IBD. In severe cases [multi-dermatomal, disseminated, ophthalmic], biologics and small molecules should be discontinued.[50] Continuing JAK inhibitors after an HZ episode does not significantly increase recurrence risk.[51] For recurrent HZ reactivation, temporary or definitive discontinuation of immunosuppressants, or switching to a lower-risk agent, should be individually evaluated.[13] Vaccination with the recombinant zoster vaccine [RZV] is recommended for prevention, particularly in patients initiating JAK inhibitors (see Section 7.2 for detailed vaccination guidance). **Influenza:** generally mild and self-limited;[52] however, in cases complicated by pneumonia or multiorgan failure, temporary withdrawal is advised.[53] **Measles:** discontinuation is reasonable due to the risk of life-threatening complications, such as giant-cell pneumonitis[42,43] and prolonged immunosuppression with lymphopenia, which increases the risk of opportunistic infections and higher mortality.[54] **COVID-19:** treatment with biologics [anti-TNF, anti-IL-12/-23, anti-integrin] should generally be continued. However, systemic corticosteroids should be tapered and thiopurines discontinued in severe cases.[55–58] Temporary discontinuation of small molecules is reasonable in severe infection.[45,59,60] Treatment with thiopurine monotherapy or in combination with anti-TNF agents is linked to an increased risk of severe adverse outcomes.[61]

Statement 4: Immunosuppressed patients with IBD with an acute viral infection may benefit from appropriate antiviral therapy [EL4] [Agreement 100%]

The decision to start antiviral therapy should be evaluated on a case-by-case basis and consultation with an infectious disease expert is advised, if possible.

Influenza: all immunosuppressed IBD patients with suspected or confirmed influenza should receive antiviral therapy [oseltamivir, zanamivir] promptly, regardless of disease severity. Extended treatment duration may be considered.[49,53,62] **Herpes simplex virus [HSV]:** evidence on managing HSV in IBD is limited; however, data from HIV and transplant patients suggest that immunocompromised patients with a primary HSV infection should be treated with acyclovir, valacyclovir, or famciclovir. Intravenous [IV] therapy should be considered for encephalitis, herpes dermatitis complicating atopic dermatitis, ocular herpes, and genital disease. Suppressive or episodic treatment is advised for recurrent herpes.[63–67] **HZ:** antiviral therapy is recommended for all immunocompromised patients. Uncomplicated HZ is treated with oral valacyclovir or famciclovir. Complicated cases [multi-dermatomal, ophthalmic, visceral, or disseminated HZ] require IV acyclovir. Treatment should start within 72 h of rash onset and continue for 7–10 days. If temporarily withheld, it may be reasonable to resume immunosuppressive therapy once anti-varicella zoster virus [VZV] therapy has been started and skin lesions have resolved.[68–71] **COVID-19:** in patients with IBD and severe COVID-19, treatment with antivirals [nirmatrelvir/ritonavir] or monoclonal antibodies is associated with reduced disease severity.[59] Initiation of these treatments in accordance with national guidelines seems reasonable in patients with IBD receiving immunosuppressive therapy who develop severe COVID-19.

4.2. Hepatitis A, B, C, D, and E

In patients with IBD who are diagnosed with viral hepatitis, specialist hepatology consultation should be sought, and management should follow contemporary international hepatology society guidelines and relevant national recommendations.

4.2.1. Hepatitis A

Statement 5: There is no specific treatment for hepatitis A other than supportive care and avoidance of hepatotoxic substances in patients with IBD [EL5] [Agreement 100%]

HAV is a common cause of acute hepatitis and is transmitted via the fecal–oral route. There is no specific antiviral therapy for hepatitis A; management is supportive, with attention to hydration, monitoring for complications, and strict avoidance of hepatotoxic substances [including alcohol and potentially hepatotoxic medications], which is particularly important in patients with IBD who may be receiving such drugs. Vaccination is the primary method of preventing hepatitis A infection and is also recommended for post-exposure prophylaxis. The recommendations for hepatitis A vaccination differ by region. In many places, vaccination is advised only before traveling to areas where the disease is prevalent.[72,73]

4.2.2. Hepatitis B and hepatitis D

Statement 6: We suggest initiating antiviral treatment with a high-barrier nucleos(t)ide analog in all HBsAg-positive patients with or without hepatitis D virus co-infection with IBD before starting immunosuppressive therapy, including corticosteroids [EL4] [Agreement 100%]

Statement 7: We suggest either the use of antiviral prophylaxis or close monitoring for risk of hepatitis B virus reactivation in immunosuppressed patients with IBD with previous hepatitis B virus infection. We suggest antiviral prophylaxis should be considered if patients are HBs-Ag negative but anti-HBc positive, with detectable hepatitis B virus DNA levels [EL4] [Agreement 100%]

HBV reactivation can occur in patients with chronic or occult infection and has been reported in patients with IBD treated with corticosteroids, anti-TNF agents, and other immunosuppressants.[74–76] Reactivation is largely preventable with prophylactic high-barrier nucleos(t)ide analogs such as entecavir or tenofovir, which are standard of care in HBsAg-positive patients, irrespective of HBV disease phase.[77,78] Active hepatitis D virus co-infection further increases the risk of cirrhosis and hepatocellular carcinoma, although data on its epidemiology, host–viral

interactions, and specific treatments remain limited; eradication with pegylated interferon-α or bulevirtide alongside HBV therapy is generally advised.[79,80] Even in regions with variable rates of prior HBV exposure, previous infection is an important consideration in immunosuppressed patients with IBD.[79,81] In patients with previous or resolved HBV infection, the absolute risk of reactivation is lower than in HBsAg-positive patients but remains clinically relevant after starting immunosuppressive therapy. Two retrospective studies [64 and 90 patients] support both close monitoring and antiviral prophylaxis, provided that antivirals are promptly initiated if reactivation occurs.[82,83] The risk is lower in HBsAg-negative than HBsAg-positive patients.[78,84] In practice, for HBsAg-negative/anti-HBc-positive patients, monitoring should be performed primarily via HBV DNA testing, as HBsAg seroreversion and ALT/AST [alanine aminotransferase/aspartate aminotransferase] elevation are late markers that may detection of reactivation.[85] The following stepwise approach is recommended: (1) test HBV DNA; (2) if detectable, initiate antiviral prophylaxis as for HBsAg-positive patients;[78] (3) if undetectable, monitor HBV DNA every 3–6 months during immunosuppressive therapy; and (4) initiate antivirals promptly if HBV DNA becomes detectable.

Hepatitis B vaccination is recommended for all seronegative patients with IBD, ideally before initiation of immunosuppressive therapy (see Section 7.2).

4.2.3. Hepatitis C

Statement 8: It is suggested to treat patients with IBD and hepatitis C virus in accordance with national and international guidelines [EL5]. Direct-acting antiviral agents are effective and safe in patients with IBD on immunosuppressive treatment [EL3] [Agreement 100%]

Direct-acting antivirals have revolutionized the treatment of hepatitis C virus [HCV] treatment. Recent cohort studies confirm their efficacy [sustained virologic response 96%] and safety in patients with IBD on immunosuppressants.[86] Immunosuppressive therapy for IBD does not need to be delayed for HCV treatment. Patients who achieved sustained virological response should be aware that successful eradication does not confer immunity to reinfection. Retesting for HCV RNA may be considered in patients with ongoing risk behaviors or those belonging to high-risk groups.[87,88]

4.2.4. Hepatitis E

Statement 9: It is suggested to screen for hepatitis E virus in patients with IBD presenting with abnormal liver enzymes similarly as for any hepatitis [EL4]. Immunosuppressive treatment de-escalation, antiviral treatment, or both may be considered in patients with no spontaneous clearance of hepatitis E virus [EL4] [Agreement 100%]

Hepatitis E virus can progress to chronic hepatitis in immunosuppressed individuals. Systematic screening is not recommended, but testing is indicated in the presence of abnormal liver enzymes.[89] Treatment may involve reducing immunosuppression or using ribavirin.[90]

4.3. HIV

Statement 10: Patients with IBD with HIV infection may be treated with immunosuppressive therapy when on antiretroviral therapy with stable CD4 counts and undetectable viral load. CD4 count should be closely monitored [EL4] [Agreement 100%]

Patients infected with HIV on antiretroviral therapy with stable CD4 counts do not appear to have an increased risk of opportunistic infections when treated with immunosuppressants for IBD. Anti-TNF agents can be used regardless of HIV status.[91] Vedolizumab appears safe and does not impair HIV control, although its theoretical benefit for HIV remission remains unproven.[91,92] Ustekinumab and anti-IL-23p19 agents have limited specific data in HIV-positive IBD patients but are not expected to exacerbate HIV based on their mechanism of action.[91] S1P receptor modulators lack data in this setting. Thiopurines should be used with particular caution given the additive immunosuppression and risk of lymphoproliferative disease in the context of chronic viral infection.[91] Caution is advised with JAK inhibitors due to reports of iatrogenic Kaposi sarcoma.[93]

4.4. Cytomegalovirus

Statement 11: Immunosuppressed patients with IBD with acute severe UC or refractory disease could benefit from testing to exclude cytomegalovirus colitis [EL3] [Agreement 100%]

Statement 12: Immunosuppressive therapy can be continued in patients with IBD with intestinal cytomegalovirus reactivation [EL3]. Patients with symptomatic disseminated cytomegalovirus infection may benefit from discontinuation of immunosuppressive therapy [EL4]. Antiviral therapy should be considered in steroid-refractory patients with IBD with cytomegalovirus colitis [EL3] [Agreement 100%]

Cytomegalovirus [CMV] colitis is relatively common in immunosuppressed patients with IBD with severe flares, and may act more as a marker of disease severity than as the primary cause of symptoms. The strongest evidence supports routine CMV testing in patients with steroid-refractory acute severe UC, where prevalence is approximately 10%–30%; across broader IBD flare cohorts, reported prevalence ranges from 1% to 33%, varying with IBD subtype, flare severity, immunosuppression, CMV definition, and diagnostic method.[94,95] As blood-based tests for CMV viremia (polymerase chain reaction [PCR] or pp65 antigenemia) have limited sensitivity for CMV colitis [pooled sensitivity approximately 50%], tissue immunohistochemistry [IHC], tissue PCR, or both are preferred. Compared with tissue PCR, IHC has lower sensitivity but high specificity, and a tissue viral load cut-off >250 viral copies/mg has been proposed to define clinically relevant infection.[96–98] Severe UC, pancolitis, older age at UC onset, and use of glucocorticoids, immunosuppressants, and azathioprine increase the risk of

CMV colitis. CMV colitis is associated with poorer outcomes, including higher colectomy risk in acute severe colitis, especially when tissue CMV burden is high.[99–101] CMV is frequently detected in colonic tissue of patients with IBD refractory to immunosuppressants, and corticosteroids and azathioprine are independent predictors of CMV reactivation in the colon.[102–104] Therapeutic strategies include rapid steroid tapering and use of infliximab, which may carry a lower risk of CMV reactivation than corticosteroids, methotrexate, or thiopurines.[105–108] Despite concerns about exacerbating CMV colitis, case series and retrospective cohorts indicate that immunosuppressive therapy is usually maintained to control IBD activity, and CMV clearance often parallels remission induced by immunosuppressants, even without antivirals. In a prospective cohort of biologic-naive moderate-to-severe UC with biopsy-proven CMV colitis, infliximab [with or without thiopurines], but not antivirals, achieved CMV clearance in most patients.[109–111] Meta-analyses and small retrospective studies provide conflicting evidence on the effect of antiviral therapy [eg, ganciclovir or valganciclovir] on colectomy risk and complications in UC or acute severe colitis with CMV, suggesting that benefit may depend on CMV burden. Therefore, antivirals are generally reserved for steroid-refractory disease or high-burden CMV.[100,104,112–114] In contrast, disseminated CMV infection, usually primary infection, presents with a mononucleosis-like "CMV syndrome" with viremia and systemic features in immunosuppressed patients with IBD; in these cases, discontinuation of immunosuppressive therapy is recommended, with IV ganciclovir followed by oral valganciclovir and, when there is inadequate response, genotypic resistance testing and use of alternative antivirals such as maribavir, foscarnet, or cidofovir.[111,115–117]

4.5. Epstein-Barr virus

Statement 13: Epstein-Barr virus infection is associated with an increased risk of lymphoma in Epstein-Barr virus-negative patients on immunosuppressive therapy, primarily thiopurines. Thus, the use of thiopurines in Epstein-Barr virus-IgG negative patients should be carefully considered [EL3] [Agreement 100%]

Statement 14: We suggest stopping immunosuppressive treatment in Epstein-Barr virus-related lymphoproliferative disease in patients with IBD [EL3] [Agreement 100%]

EBV infection in pediatric and adult IBD cohorts is usually self-limiting or asymptomatic, even under immunosuppression, but impairment of T-cell function may lead to loss of control over B-cell proliferation and EBV-driven lymphoproliferative disease, particularly in EBV-IgG-negative patients exposed to thiopurines.[34,118,119] Up to 95% of adults are EBV-seropositive from childhood or adolescence. However, as EBV seropositivity in pediatric and young adult IBD cohorts ranges from 48% to 76%, a sizeable subgroup is EBV-IgG-negative at treatment start.[120–123] In EBV-IgG-negative transplant patients on immunosuppressants, primary EBV infection markedly increases the risk of post-transplant lymphoproliferative disease, and several case reports and small series describe lymphoma occurring after primary EBV infection in thiopurine-treated patients with IBD.[124–129] Thiopurines, alone or combined with anti-TNFs, are associated with an increased, although still very small, absolute risk of mainly non-Hodgkin lymphoma; some series also suggest excess risk with anti-TNF agent monotherapy. In large IBD lymphoma cohorts, diffuse large B-cell and follicular lymphoma predominate and a high proportion of tumors are EBV-positive.[130–134] These data support considering baseline EBV serology in candidates for thiopurines and avoiding or using thiopurines with particular caution in EBV-IgG-negative patients, although there are no comparative or prospective data proving benefit of routine screening. Although the increased risk of EBV-positive lymphoma with thiopurine monotherapy and combined thiopurine–anti-TNF therapy is well established, current evidence does not suggest an increased risk of lymphoproliferative disease with JAK inhibitors, ustekinumab, or vedolizumab. Current practice is to stop thiopurines and anti-TNF agents when EBV-related lymphoma or other lymphoproliferative disease is diagnosed.[135] In the ENEIDA and ECCO series, most patients with IBD with lymphoma had thiopurines or biologics withdrawn at diagnosis; many remained in IBD remission off treatment and some later restarted biologic therapy. Relapse or mortality did not clearly correlate with prior immunosuppressive exposure, consistent with a meta-analysis showing similar cancer recurrence rates in patients with immune-mediated diseases and prior malignancy irrespective of immunosuppressive treatment.[136–138] Similar principles apply to EBV-triggered hemophagocytic lymphohistiocytosis or EBV-positive mucocutaneous ulceration, in which withdrawal of immunosuppression is standard and usually leads to remission, often alongside targeted therapies such as rituximab.[139–141]

4.6. Human papillomavirus

Statement 15: Immunosuppressed female patients with IBD should undergo age-appropriate screening for cervical dysplasia, in line with general population guidelines [EL3]. Routine anal cancer screening is not currently supported by evidence in immunosuppressed patients with IBD; however, targeted screening might be considered in individuals with additional high-risk factors [EL4] [Agreement 100%]

Statement 16: Screening with cervical cytology and high-risk human papillomavirus testing should be considered in patients initiating or on immunosuppressive therapy, particularly in women with additional risk factors [EL3]. Patients with IBD who are positive for high-risk human papillomavirus should not delay initiating immunosuppressive therapy when clinically indicated [EL3]. Anal human papillomavirus screening may be considered on a case-by-case basis depending on individual risk factors [EL4] [Agreement 100%]

Current evidence indicates that HPV 16/18 infections contribute to approximately 70% of cervical cancers, 78% of HPV-related vulvar cancers, 65% of vaginal cancers, and

90% of anal cancers globally. A nationwide study reported that patients with IBD exhibit a significantly higher incidence of cervical [5.2 vs 4.6 per 100000; $P = .042$] and anal cancers [5.5 vs 1.8 per 100000; $P = .001$] compared with the general population.[142] HPV 16/18 is recognized as the primary risk factor for cervical dysplasia,[143] and immunosuppressive therapy in patients with IBD is associated with an increased risk of persistent HPV infection and subsequent cervical neoplasia.[144] An umbrella review showed that immunosuppressants increase the risk of persistent HPV infection, cervical dysplasia, and cervical cancer in IBD [RR: 1.33; 95% CI: 1.23–1.46], and a meta-analysis reported a similar increase compared with the general population [OR: 1.34; 95% CI: 1.23–1.46].[46,144] Observational studies have corroborated these findings. A cross-sectional study including 124 women with IBD and 372 controls showed that HPV 16/18 infection [7.3% vs 0.3%; $P < .001$] and cervical dysplasia [3.2% vs 0%; $P = .004$] were more prevalent in women with IBD, and additional series have reported similar associations between immunosuppressant exposure and cervical dysplasia.[143,145–149] However, a large meta-analysis including 74000 patients with IBD and more than 2 million controls from five countries found no statistically significant increase in cervical cancer incidence among women with IBD [HR: 1.24; 95% CI: 0.94–1.63], irrespective of disease subtype or exposure to thiopurines or anti-TNF agents. Nonetheless, methotrexate and use of two or more immunosuppressants increased the risk of high-risk HPV infection and combination therapy was associated with higher cervical dysplasia risk.[145,146,150] Data on progression risk with vedolizumab, ustekinumab, and JAK inhibitors are limited. Anal cancer risk is elevated in specific high-risk groups, including HIV-positive individuals, those with prior cervical, vulvar, or vaginal cancer, solid organ transplant recipients, and patients with autoimmune diseases.[151] Some studies reported increased anal cancer and dysplasia in IBD compared with the general population, whereas others showed no clear increase or no consistent association with immunosuppressant use.[142,152–157] Anal HPV-related disease and anal cancer may be more common in patients with IBD, particularly in those with perianal CD.[142,158,159] However, data on anal high-risk HPV infection and squamous intraepithelial lesions remain limited and heterogeneous, and current evidence does not support routine anal HPV screening for all patients with IBD.[160,161] Overall, the available data support age-appropriate cervical dysplasia screening for immunosuppressed female patients with IBD consistent with general population guidelines and consideration of cervical cytology with high-risk HPV testing before or during immunosuppressive therapy in women with additional risk factors.[144] The presence of high-risk HPV infection should not delay the initiation of clinically indicated immunosuppressive therapy, as most HPV infections are transient; however, enhanced cervical surveillance and HPV vaccination according to national guidelines are recommended in this setting (see Section 7.2).[144] Anal cytology and high-risk HPV testing may be considered on an individual basis, particularly in patients with additional risk factors, such as HIV infection, prior high-grade cervical dysplasia, or cervical, vaginal, or vulvar cancer, solid organ transplantation, or CD with chronic perianal fistulae, where individual risk assessment should guide screening decisions.

5. Non-viral infections

5.1. *Mycobacterium tuberculosis*

Statement 17: Latent tuberculosis infection screening is recommended before starting anti-TNF agents or JAK inhibitors, ideally off immunosuppressive medication [EL1]. For lower-risk agents (vedolizumab, ustekinumab, anti-IL-23p19 agents, S1P receptor modulators), screening is recommended if additional risk factors are present [EL3] Latent tuberculosis infection treatment lowers, but does not eliminate, the risk of reactivation [EL2] [Agreement 100%]

Statement 18: Mycobacterium tuberculosis infection screening should be performed before immunosuppressive therapy [EL3]. Prior to immunosuppression, a single test, either tuberculin skin test or interferon gamma release assay, is suggested [EL4]. Following the initiation of immunosuppression, both tuberculin skin test and interferon gamma release assay should be combined to improve diagnostic sensitivity [EL5] [Agreement 95%]

Screening for latent tuberculosis infection [LTBI] is advised before initiating corticosteroids or advanced therapy, ideally before the commencement of immunosuppressive therapy, as this improves diagnostic yield and can reduce reactivation of *Mycobacterium tuberculosis* [TB].[162–174] TB screening is particularly crucial in patients receiving anti-TNF agents, in whom the incidence of active TB is 2- to 4.5-fold higher than in the general population, and 1%–3% of patients with IBD develop TB depending on local burden. Severe presentations, including miliary and pleural TB, are more frequent, and combination of anti-TNF agents with methotrexate or azathioprine confers a 13-fold increased risk of reactivation compared with monotherapy.[164,175–185] In contrast, non-anti-TNF biologics present a much lower TB risk. In population-based analyses, the RR of TB for vedolizumab or ustekinumab compared with anti-TNF agents was 0.31 [95% CI: 0.07–1.26]. Large cohorts report no or only single TB cases with vedolizumab or ustekinumab, suggesting that reactivation risk appears to be extremely low, particularly in low-endemic areas. Screening can therefore be guided by individual risk factors [history of TB exposure, previous untreated or partially treated LTBI, concomitant immunosuppression or immunosuppression due to other causes, and living or working in high-risk settings] and local TB prevalence. Evidence for newer agents, such as anti-IL-23 agents, remains sparse.[22,177,179,182,186–189]

Among small molecules, tofacitinib is probably associated with an increased TB risk [200–210/100000 py], with rare but potentially severe TB cases reported. Data for upadacitinib are limited and warrant caution. Data for filgotinib are limited but reassuring; TB cases have not been prominently reported in the IBD filgotinib program, although vigilance is warranted given the potential JAK1-inhibitor class effect.[190] Current data on S1P receptor modulators do not suggest increased TB risk. As methotrexate, azathioprine, short corticosteroid courses [<15 mg/day, <1 month], or ciclosporin are not associated with excess TB risk compared with placebo, systematic LTBI

screening is not recommended when these agents are used alone.[29,182,187,191–194]

The diagnosis of LTBI requires exclusion of active TB and is based primarily on a positive tuberculin skin test [TST] or interferon-gamma release assay [IGRA]; in patients with negative tests, LTBI may still be diagnosed if there is epidemiological evidence of inadequately treated previous TB or recent exposure to a smear-positive case. In high-risk individuals, a positive result on either test is sufficient to confirm infection.[195] The TST, which uses purified protein derivative tuberculin to detect cell-mediated immunity to TB, is inexpensive but requires a return visit for reading, may yield false-positive results in Bacillus Calmette-Guérin [BCG]-vaccinated individuals or those exposed to nontuberculous mycobacteria, and can be falsely negative in young children, recent infection, severe illness, extensive TB, or immunosuppression.[196] IGRA offers a more specific alternative by measuring T-cell responses to TB antigens and is not affected by BCG vaccination or most nontuberculous mycobacteria, although its reproducibility can be inconsistent. There is no universal preference between TST and IGRA, but IGRA may be favored in BCG-vaccinated patients and in accordance with local TB prevalence and national recommendations.[196,197]

In low-burden TB settings, initial screening before immunosuppression may be performed with a single IGRA or TST in adults, while in young children both tests [IGRA and TST] prior to anti-TNF treatment are suggested.[198] If pre-treatment screening is not feasible, using both TST and IGRA should be considered to maximize diagnostic yield.[162,163,165,167,171,196,199–201] If both tests are required, they should be performed simultaneously or ensure the IGRA is drawn within 3 days of the TST. A longer delay may allow the TST to "boost" interferon-γ response levels, leading to a false IGRA result. Conversely, performing the IGRA first does not affect subsequent TST results.[202] Adding chest radiography to IGRA screening in low-endemic populations offers limited additional clinical benefit and is unlikely to justify the added costs, patient burden, radiation exposure, and resource use.[203]

LTBI treatment is indicated for patients with a positive TST or IGRA or for those with negative tests but epidemiological evidence of improperly treated previous TB or recent contact with a smear-positive patient. LTBI treatment reduces but does not entirely eliminate the risk of active TB.[167,182,183,204] A positive LTBI test should not contraindicate any specific biologic or small molecule class but should prompt LTBI treatment initiation. For anti-TNF agents and JAK inhibitors, LTBI treatment should ideally be started at least 3–4 weeks before immunosuppressive therapy. For lower-risk agents (vedolizumab, ustekinumab, anti-IL-23p19 or S1P receptor modulators), concurrent initiation may be acceptable when treatment delay is clinically undesirable.[205,206]

Statement 19: Patients on anti-TNF therapy should be rescreened for TB following substantial exposure to respiratory TB. Rescreening is suggested annually for those from high-prevalence areas or with other TB risk factors [EL4] and may be considered if baseline testing was performed under immunosuppression [EL5]. Evidence is insufficient to recommend rescreening in patients receiving advanced therapies other than anti-TNF agents [EL5] [Agreement 100%]

Patients treated with anti-TNF agents who live in high TB prevalence areas, have TB risk factors [persons from or born in high-prevalence areas, healthcare workers, close contacts of persons with known or suspected active TB, injectable drug users, and residents or employees of high-risk settings, such as correctional facilities, long-term care facilities, and homeless shelters], or both should undergo annual TB screening.[207,208] Serial universal rescreening in low-prevalence populations is not recommended due to high false-positive rates, unnecessary diagnostic work-up and treatment, and increased risk of adverse effects.[207,209,210] In most studies, rescreening with TST or IGRA is performed 1 year after anti-TNF agent initiation, when TB reactivation risk is highest.[167,211–215] However, TST and IGRA have limited diagnostic accuracy in immunocompromised patients and in low-prevalence regions and do not reliably predict TB reactivation; annual IGRA-based screening shows frequent false-positive conversions and reversions.[165,187,216,217] When rescreening is positive and active TB is excluded, LTBI treatment is recommended without suspending ongoing IBD-related therapy.[167]

Statement 20: We suggest that patients diagnosed with LTBI complete a full therapeutic regimen for LTBI [EL1]. Therapy with anti-TNF agents or JAK inhibitors should be delayed for at least 3–4 weeks after starting LTBI treatment [EL5] In cases of clinical urgency, simultaneous initiation of LTBI and biological therapy may be considered [EL4]. Therapy with α4β7 integrin inhibitors, anti-IL-12/-23p40 or IL-23p19 agents, or S1P receptor modulators may be started concomitantly with treatment for LTBI [EL5] [Agreement 100%]

Patients diagnosed with LTBI while on high-dose steroids [prednisolone ≥15 mg daily for >1 month] and those starting anti-TNF agents or JAK inhibitors should complete a full LTBI treatment regimen.[187,205,214,218–220] LTBI therapy should ideally start at least 3–4 weeks before these drugs, based on studies mainly in rheumatoid arthritis that show that initiating anti-TNF agents 3–4 weeks after LTBI prophylaxis significantly reduces TB reactivation.[77,167,205,221–223] In urgent IBD situations, simultaneous initiation of LTBI treatment and biologic therapy may be considered with specialist consultation and close monitoring.[205,224] For JAK inhibitors, LTBI treatment should be initiated at least 3–4 weeks before starting therapy, consistent with the approach recommended for anti-TNF agents. Concurrent use of JAK inhibitors and LTBI treatment is acceptable thereafter, and completion of the full LTBI treatment course while on therapy is the standard approach. Evidence specific to individual JAK inhibitors [upadacitinib, filgotinib] remains limited, but the same principles are applied across the class.[205]

In patients with LTBI requiring urgent IBD therapy, gut-selective agents such as vedolizumab may be preferred due to their lower systemic immunosuppression and minimal TB reactivation risk, allowing concurrent LTBI treatment without significant delay. LTBI treatment likewise does not need to delay methotrexate or azathioprine.[205,206] Concomitant therapies do not change the recommended LTBI duration.[187,205,218–220] Patients who convert from negative to positive LTBI tests while already on advanced therapy should receive LTBI treatment without interrupting IBD therapy.[167,225]

The most commonly used LTBI regimen is isoniazid [INH] for 6–9 months; randomized studies show >75% efficacy when

completed for 9–12 months [up to 90% with high adherence], decreasing to approximately 60% with 6 months of therapy.[226] This regimen is recommended by the World Health Organization for low-prevalence countries and widely endorsed by guidelines. Alternatively, shorter regimens include 3 months of once-weekly rifapentine plus INH or 4 months of daily rifampicin; both have better adherence than the standard INH regimen.[227,228] Monitoring for toxicity, particularly hepatotoxicity and neurotoxicity, is essential. High-risk patients [eg, with liver injury risk factors, such as excessive alcohol use, age >65 years, malnutrition, or concurrent hepatotoxic drugs] should have monthly liver function tests.[205] INH-related hepatotoxicity occurs in approximately 0.15% of patients and may be severe.[229] Treatment should be discontinued immediately if jaundice develops. Otherwise, treatment should be adjusted or discontinued if transaminases increase to >3× the upper limit of normal with symptoms of hepatitis, or to >5× the upper limit of normal without symptoms.[222,228]

See Table 1 for recommended TB chemoprophylaxis regimens.

5.2 *Clostridioides difficile*

Statement 21: Screening for Clostridioides difficile infection in patients with IBD under immunosuppression [steroids, immunomodulators, biologicals, small molecules] with a disease flare should be based on a two-step algorithm with a highly sensitive test, such as glutamate dehydrogenase antigen enzyme immunoassay or nucleic acid amplification tests initially, followed by a second test with high specificity, such as toxin A/B enzyme immunoassays [EL3] [Agreement 100%]

Clostridioides difficile infection [CDI] diagnosis requires compatible symptoms [diarrhea] plus evidence of toxigenic *C. difficile* or toxin in stool. Only liquid or unformed stools should be tested to minimize detection of asymptomatic carriers, and samples should be processed promptly, ideally within 2 A rectal swab is an acceptable alternative in ileus with reasonable sensitivity and specificity. Endoscopy is not recommended for CDI diagnosis, as pseudomembranes are uncommon and absence does not exclude CDI; histology also rarely distinguishes CDI from an IBD flare.[230–234] No single laboratory assay performs well as a stand-alone test in low-prevalence settings [limited positive predictive value], and reference methods [stool cytotoxicity assay and toxigenic culture] are impractical for routine care.[230–233] A two-step approach is therefore preferred. An initial high-sensitivity test with high negative predictive value, such as glutamate dehydrogenase [GDH] enzyme immunoassays [EIAs] or nucleic acid amplification technology [NAAT] should be performed. If positive, this should be followed by a high-specificity toxin A/B EIA to confirm CDI. If results are GDH-positive and toxin-negative, NAAT can be used as the confirmatory test.[230–233,235] Some multiplex NAAT platforms increase overall pathogen detection and may reduce IBD treatment modification during flares when an alternative cause is identified.[236,237]

Statement 22: For mild-to-moderate CDI in IBD, we recommend oral vancomycin or fidaxomicin as first-line treatment. Both are equally effective, although fidaxomicin is associated with a lower rate of recurrence [EL2]. We do not recommend oral metronidazole as first-line therapy in CDI related to IBD [EL2]. Severe cases require IV metronidazole in addition to oral vancomycin [EL3]. We suggest pulse-tapered schemes with oral vancomycin, fidaxomicin, or fecal microbiota transplantation for recurrent CDI [EL3]. Fecal microbiota transplantation is suggested for the prevention of CDI recurrence in IBD [EL4] [Agreement 90%]

Table 1. Tuberculosis chemoprophylaxis regimens.

Regimen	Dose	Duration [months]	Estimated protection	Notes
Isoniazid [daily]	Adults: 5 mg/kg/day [maximum 300 mg/day] Children: 10 mg/kg/day [maximum 300 mg/day]	6–9	9 months: ~90%6 months: ~60–80%	Pyridoxine supplementation recommended to reduce neurotoxicity. Longer regimen—lower completion.
Rifapentine plus isoniazid [once weekly, 12 doses]	Isoniazid: ≥12 years 15 mg/kg [maximum 900 mg per dose]; 2–11 years 25 mg/kg [maximum 900 mg per dose]Rifapentine: 10.0–14.0 kg 300 mg; 14.1–25.0 kg 450 mg; 25.1–32.0 kg 600 mg; 32.1–50.0 kg 750 mg; >50 kg 900 mg	3	Non-inferior to 9 months of isoniazid	Higher completion than isoniazid monotherapy. Check drug–drug interactions [rifamycins].
Rifapentine plus isoniazid [daily, 28 doses]	Age ≥13 years: isoniazid 300 mg/day plus rifapentine 600 mg/day	1	Non-inferior to 9 months isoniazid [randomized trial data]	Very short regimen—high completion. Check drug–drug interactions [rifamycins].
Rifampicin (daily)	Adults: 10 mg/kg/day [maximum 600 mg/day]Children: 15 mg/kg/day [range 10–20 mg/kg/day; maximum 600 mg/day]	4	Non-inferior to 9 months isoniazid	Better safety and completion than longer isoniazid regimens. Check drug–drug interactions.
Isoniazid plus rifampicin [daily]	Isoniazid: adults 5 mg/kg/day [maximum 300 mg/day]; children 10 mg/kg/day [range 7–15 mg/kg/day; maximum 300 mg/day] Rifampicin: adults 10 mg/kg/day [maximum 600 mg/day]; children 15 mg/kg/day [range 10–20 mg/kg/day; maximum 600 mg/day]	3–4	Comparable efficacy to longer isoniazid regimens	Shorter regimen with good completion. Monitor liver tests and drug–drug interactions.

Table 2. Treatment options for *Clostridioides difficile* infection in patients with IBD.

	Treatment options	Observations
Mild-to-moderate [10 days of therapy]	VAN 125 mg orally QIDORFDX 200 mg orally BID	FDX associated with lower recurrence than VANMetronidazole: not recommended as first-line (inferior efficacy); limited exception in low-risk mild disease when other agents unavailable
Severe [leucocytosis >15000 or creatinine >1.5 mg/dL]	VAN 125–500 mg PO QID for 10–14 daysADD IV metronidazole [500 mg Q8H] when systemic toxicity is present	Higher VAN dosing may be used based on clinical severityIV metronidazole added for systemic toxicity
Fulminant [hypotension, toxic megacolon, or ileus]	VAN 500 mg QID [PO, NG, or rectal]Rectal VAN when ileus limits oral delivery and/or IV metronidazole [500 mg TID]	Rectal VAN and IV metronidazole may be used alone or in combination with oral VANEarly surgical consultation for severe sepsis, perforation, or toxic megacolon
First recurrence	VAN 125 mg orally QID for 10–14 daysIf VAN was used for the initial episode: prolonged tapered and pulsed VAN regimen [125 mg QID for 10–14 days, then BID for 7 days, once daily for 7 days, then every 2–3 days for 2–8 weeks]ORFDX 200 mg BID for 10 days	Recurrence rate up to 33% in IBDExtended regimens allow microbiome recovery
Second and subsequent recurrence	Extended-pulsed FDX regimen [200 mg BID for days 1–5, then once every other day from days 7 to 25]ORVAN in a tapered and pulsed regimenORFecal microbiota transplantation	Extended-pulsed FDX: superior sustained cure vs standard VAN (EXTEND trial)FMT effective in recurrent CDI including IBD with high reported cure rates
IBD therapy management during CDI	Discontinuation of IBD therapy not routinely requiredIndividualize based on CDI severity, IBD activity, and overall risk	Avoid corticosteroid escalation during CDI (associated with higher colectomy risk)CDI treatment type did not drive IBD outcomes

Treatment should be guided by CDI severity and recurrence risk. Dosing regimens are for adult patients. See Statements 21–23 for full recommendations and supporting evidence.
Abbreviations: VAN, vancomycin; FDX, fidaxomicin; PO, by mouth; NG, nasogastric; IV, intravenous; QID, four times daily; BID, twice daily; Q8H, every 8 h; TID, three times daily; FMT, fecal microbiota transplantation; CDI, *Clostridioides difficile* infection.

In patients with IBD with confirmed CDI, treatment should be guided by CDI severity and recurrence risk (Table 2), recognizing the association of CDI with poorer outcomes [eg, higher hospitalization and colectomy rates], which supports early diagnosis and prompt therapy. For mild-to-moderate CDI, oral vancomycin [125 mg QID for 10 days] or fidaxomicin [200 mg BID for 10 days] are first-line options. Although initial efficacy is broadly similar, fidaxomicin is associated with lower recurrence, albeit at higher cost; recent IBD-specific retrospective cohort data also support its safety and effectiveness.[238–240] Metronidazole is no longer recommended as first-line therapy due to inferior efficacy,[241] with limited exceptions when other agents are unavailable in low-risk mild disease.[242] For severe CDI [eg, leucocytosis >15000 cells/μL or creatinine >1.5 mg/dL], vancomycin [125–500 mg PO QID for 10–14 days] is recommended, with IV metronidazole [500 mg Q8H] added when systemic toxicity is present.[243] Fulminant CDI [hypotension, toxic megacolon, or ileus] requires high-dose vancomycin [500 mg PO/NG QID], rectal vancomycin when ileus limits delivery or IV metronidazole [500 mg TID] or both; early surgical consultation is needed for severe sepsis, perforation, or toxic megacolon.[244–246] Recurrence is more frequent in IBD [up to 33%].[243] Options for recurrence include specific extended-dosing regimens to allow for microbiome recovery. Vancomycin pulse-taper regimens are frequently used to suppress *C. difficile* spores while allowing gut flora to recover. A typical 6–12-week regimen includes 125 mg QID for 10–14 days, followed by 125 mg BID for 7 days, then 125 mg once daily for 7 days, and finally 125 mg every 2 or 3 days [pulsed] for 2–8 weeks.[247] Based on the EXTEND trial, an extended-pulsed fidaxomicin regimen [200 mg BID for days 1–5, then 200 mg once every other day from days 7 to 25] has shown superior sustained clinical cure compared with standard vancomycin.[248] This approach may be particularly beneficial in IBD to minimize further microbiome disruption. Fecal microbiota transplantation is also effective in recurrent CDI, including in IBD, with high reported cure rates.[249,250]

Statement 23: Discontinuation of IBD therapy is not routinely required in the case of CDI and should be considered on an individual basis [EL5] [Agreement 95%]

CDI superimposed on IBD is associated with adverse outcomes, including treatment failure, higher hospitalization and surgery rates, and increased mortality. Enteric infection at flare, particularly CDI, is also associated with poorer longer-term IBD outcomes.[251,252] In broader real-world datasets, patient factors [eg, comorbidity burden and prior healthcare utilization] are linked to higher complication risk after CDI.[253] Because symptoms overlap with IBD activity and molecular tests may detect colonization, CDI diagnosis and subsequent IBD management require careful clinical correlation. In hospitalized UC, CDI is associated with higher early mortality, increased subsequent treatment intensification, and readmission.[254] Decisions on continuing, withholding, or escalating immunosuppression should therefore be individualized after considering CDI severity, IBD activity, and overall risk.[255] Notably, corticosteroid escalation during CDI is associated with a higher risk of colon surgery, whereas CDI treatment type did not appear to drive IBD outcomes in that analysis.[256] Further studies are needed to better define optimal integrated management strategies in this setting.

5.3. Other bacterial pathogens

Statement 24: In patients with severe systemic infection caused by Salmonella enteritidis, Salmonella typhimurium, or Listeria monocytogenes, immunosuppressive therapy should be temporarily withheld until resolution [EL5] [Agreement 100%]

Evaluation for enteric or systemic infection in immunosuppressed patients with IBD may prevent unnecessary escalation of immunosuppressants, particularly during acute flares and combination therapy. Preventive measures against *Salmonella* spp. and *Listeria monocytogenes* should be emphasized for patients treated with steroids, immunomodulators, biologics, or small molecules, focusing on food hygiene and avoidance of high-risk foods [eg, raw eggs, unpasteurized milk or raw-milk cheeses, and undercooked or raw meat]. Immunosuppression confers a high risk for intestinal or systemic *Salmonella* infection,[257] and anti-TNF agents may carry a particular risk for serious infection. *Listeria* infections reported after infliximab initiation often occur early [after three or fewer infusions], suggesting possible reactivation in some cases.[258,259] When severe systemic infection is confirmed, immunosuppressive therapy should be temporarily withheld until clinical resolution. Evidence is insufficient to define the optimal duration of withholding; however, case reports describe reinstitution of immunosuppression after successful treatment of active infection.[258] Salmonellosis is typically treated with antibiotics [eg, fluoroquinolones or third-generation cephalosporins], although fluoroquinolone resistance is increasing. Complicated infections, such as osteomyelitis, aortitis, or septic arthritis, may require both medical and surgical management.[260–263] *Listeria monocytogenes* is treated with ampicillin or amoxicillin or trimethoprim–sulfamethoxazole [TMP-SMX] in patients with allergy to penicillin. A high index of suspicion is warranted in immunosuppressed patients presenting with meningitis or neurological symptoms.[264,265] Prompt recognition and appropriate management are important to optimize outcomes when infection is suspected or confirmed.[266–268] In addition to *Salmonella* and *Listeria*, other enteric pathogens such as *Shigella*, *Escherichia coli*, and *Campylobacter* are of special interest as they can mimic or precipitate IBD flares.[269,270] Routine testing for these organisms via stool culture or multiplex PCR is recommended in symptomatic patients.[237,271] When confirmed, targeted antimicrobial therapy should be initiated, with careful consideration given to temporarily withholding immunosuppressive therapy in severe or refractory presentations.

Statement 25: In patients with IBD under immunosuppressive therapy presenting with severe pneumonia, we recommend empirical antibiotic coverage for Legionella pneumophila [EL3]. If Legionella pneumophila infection is confirmed, immunosuppressive therapy may be paused [EL5] [Agreement 95%]

Legionella pneumophila pneumonia occurs more frequently in patients receiving anti-TNF agents [notably infliximab and adalimumab] than in the general population. In the French RATIO registry, the standardized incidence ratio for *Legionella* infection in patients treated with anti-TNF agents was 13.1, with the highest risk reported for adalimumab and infliximab.[272] Severe presentations, including intensive care unit [ICU] admission and fatalities, have been reported in patients with IBD on infliximab.[273,274] In biologic-treated populations, *Legionella* has been identified among common opportunistic pathogens, with mortality up to 19% in some series.[275] Accordingly, *Legionella* testing should be considered in immunosuppressed patients with IBD with pneumonia, particularly if hospitalized, severe, or requiring ICU care, as delayed diagnosis may worsen outcomes.[273,276,277] Urinary antigen testing provides rapid detection [mainly for *L. pneumophila* serogroup 1], while PCR, culture, or both from respiratory specimens can support diagnosis in higher-risk cases. Paired serology [4-fold increase] may be used when required for confirmation.[278–280] Given the potential morbidity in immunocompromised hosts, empirical *Legionella*-active therapy is appropriate while awaiting results in severe pneumonia.[279] Recommended first-line options include fluoroquinolones or macrolides, with fluoroquinolones often preferred in severe disease due to intracellular activity; combination regimens may be considered in critically ill patients.[273,275,281] Treatment duration should be individualized based on severity, with longer courses sometimes needed in ongoing immunosuppression.[278] If *L. pneumophila* is confirmed, biologic or advanced therapy [anti-TNF agents, ustekinumab, vedolizumab, tofacitinib] may be temporarily withheld until pneumonia resolves.[273,282] Corticosteroid tapering should be considered where feasible, and re-initiation of therapy should be individualized, particularly in patients with recurrent infections or additional risk factors.[279,283] Preventive advice includes avoiding high-risk water exposures [eg, poorly maintained water systems, hot tubs, cooling towers] and educating patients, especially those on anti-TNF therapy, to seek early assessment for pneumonia symptoms.[277,284]

Statement 26: In patients with Nocardia spp. infection, immunosuppressive therapy should be withheld. Resumption of immunosuppressive therapy can be considered after multidisciplinary discussion [EL5] [Agreement 100%]

Nocardia spp. infections are rare but can cause invasive disease in immunosuppressed patients with IBD, including those treated with anti-TNF agents, vedolizumab, and tofacitinib.[206,285–290] Management should include early infectious disease consultation and targeted antimicrobial therapy with TMP-SMX, ceftriaxone, or carbapenems, used alone or in combination depending on severity. Antibiotics should be continued until complete resolution of all lesions. In immunocompromised patients and those with neurological involvement, prolonged therapy [≥1 year] is recommended, and longer or indefinite courses may be required when immunosuppression cannot be fully stopped.[291] As relapse risk increases with ongoing immunosuppression, indefinite discontinuation of anti-TNF therapy has been proposed,[292,293] and similar caution may be considered for other biologics and small-molecule therapies.

5.4. Parasitic and fungal infections

Statement 27: We suggest that screening for parasitic or fungal infections should be considered in residents of endemic areas or with relevant travel history [EL5]. Chemoprophylaxis following systemic fungal infection should be discussed with an infectious disease specialist [EL5] [Agreement 100%]

Parasites causing human disease are broadly classified as protozoa, helminths, and ectoparasites.[294] Because most patients with IBD do not develop these infections and no validated tool reliably predicts individual risk, a targeted approach is appropriate. Screening for parasitic or fungal infections should be focused on those with epidemiologic exposure [residence in endemic areas or relevant travel history]. General preventive measures [eg, food and hand hygiene, patient education, and pharmacovigilance through registries] remain important during immunosuppressive therapy.[295] Fungal infections reported in IBD include candidiasis, cryptococcosis, aspergillosis, coccidioidomycosis, histoplasmosis, blastomycosis, and *Pneumocystis* pneumonia.[296–298] The most common systemic fungal infection is histoplasmosis, a disease of nearly worldwide distribution due to its tendency to be endemic near large cities. Histoplasmosis should be considered in patients with IBD from endemic areas who present with fever, pulmonary infiltrates, hepatosplenomegaly, or pancytopenia during immunosuppressive therapy, particularly anti-TNF agents.[299] Diagnosis relies on urine and serum *Histoplasma* antigen testing, fungal cultures, and tissue histopathology. Treatment follows Infectious Diseases Society of America [IDSA] guidelines: liposomal amphotericin B for severe disease, followed by itraconazole for mild-to-moderate cases or as step-down maintenance therapy.[300] Following a systemic fungal infection, the need for secondary chemoprophylaxis should be individualized and discussed with an infectious disease specialist.

Statement 28: Patients with IBD living in endemic regions or with known travel history to such countries may benefit from screening for Trypanosoma cruzi [EL5]. Prophylaxis for trypanosomiasis is not recommended in patients with IBD [EL5] [Agreement 100%]

Trypanosomiasis (Chagas disease) is caused by *Trypanosoma cruzi*.[301,302] *T. cruzi* is endemic in South America and can be transmitted via insect vectors, blood transfusion, vertical transmission, or oral exposure.[301] Acute infection may present with non-specific symptoms [eg, fatigue, headache, fever], while chronic disease can emerge years to decades later with cardiac, digestive, and neurological manifestations. After acute infection, some patients enter a chronic latent phase. Reactivation has been reported in immunocompromised hosts, including people with HIV and those receiving immunosuppressive therapy. Although data in IBD are limited, reactivation has been described in other immune-mediated diseases treated with steroids, anti-TNF agents, azathioprine, and ustekinumab.[303–305] Reactivation is typically assessed using qPCR positivity.[305]

Statement 29: In visceral leishmaniasis, we recommend temporarily discontinuing immunosuppressive therapy [EL5], particularly anti-TNF agents [EL4] [Agreement 100%]

Immunosuppression, particularly anti-TNF therapy, increases the risk of leishmaniasis in endemic regions [Mediterranean basin, South America, and Asia].[306–308] In a Spanish multicenter study, nearly all patients with IBD with leishmaniasis were receiving biologics [94.5%], while a minority were treated with immunosuppressants [5.5%]; reactivation of latent infection was reported in 8.8% of asymptomatic patients treated with anti-TNF agents. Visceral disease accounted for 32.65% of cases, cutaneous for 57.14%, and mucocutaneous for 10.2%.[309] Clinical manifestations vary by species and geography; visceral leishmaniasis is typically caused by *L. donovani*/*L. infantum*, cutaneous forms by *L. major*/*L. tropica*, and mucocutaneous disease is most commonly linked to *L. braziliensis*. In endemic settings, screening should be considered before initiating biologics and in patients with suggestive features, such as unexplained fever, hepatosplenomegaly, or pancytopenia.[310] Diagnosis relies on serology [eg, ELISA], PCR, and, when needed, parasitological confirmation [eg, bone marrow aspiration].[309–311] Prevention is based on reducing sandfly exposure, such as via protective measures and insect-proof housing.[312] In active infection, biologic therapy should be temporarily withheld,[312] particularly anti-TNF agents, with careful reassessment in patients with a history of prior infection.[310] Although IBD-specific treatment studies are lacking, IV liposomal amphotericin B is first-line for visceral disease; pentavalent antimonials or miltefosine are used for cutaneous or mucocutaneous disease.[309,312,313] Given increasing reports in IBD, clinicians should maintain a high index of suspicion, particularly with unexplained fever, weight loss, hepatosplenomegaly, or chronic skin lesions.

Statement 30: Every patient with IBD originating from an endemic region might benefit from serological testing for Strongyloides stercoralis [EL4]. Empiric treatment for Strongyloides stercoralis is recommended if serology is not available [EL5] [Agreement 100%]

Strongyloidiasis is a helminth infection caused by *Strongyloides stercoralis*, which is common in tropical regions and uncommon in many Western settings.[314] Infection may remain asymptomatic for prolonged periods, but can progress to severe or disseminated disease that is potentially fatal, particularly under immunosuppression. Seroprevalence data suggest clinically relevant background exposure, including in individuals about to start biologics.[315] Infections are frequently reported in older patients and in those with additional risk factors, such as corticosteroid exposure and comorbidities.[316] Patients with IBD receiving steroids, immunomodulators, or anti-TNF agents are at increased risk of life-threatening hyperinfection syndrome or disseminated strongyloidiasis.[294,317–319] In endemic or tropical settings, *Strongyloides* has been detected among patients with IBD presenting with diarrhea.[320] Clinicians should suspect infection in immunosuppressed patients with relevant epidemiologic exposure [origin from, or travel to, endemic areas].[314,315,317] Although peripheral eosinophilia and stool

testing may support diagnosis, neither is sufficiently sensitive nor specific, which reinforces the role of serology when available. When serology is positive, treatment with ivermectin (200 µg/kg/day for 2 days) is recommended before initiating immunosuppressive therapy to prevent hyperinfection syndrome. When serology is unavailable or results are delayed, empiric treatment with ivermectin should be considered in patients from endemic areas, given the potentially fatal consequences of untreated infection under immunosuppression.[321]

Statement 31: Pneumocystis jirovecii pneumonia prophylaxis in IBD should be individualized according to the degree of immunosuppression and patient comorbidities. In patients receiving triple immunosuppressive therapy, standard prophylaxis with TMP-SMX should be strongly considered [EL4]. In those receiving double immunosuppressive therapy, TMP-SMX prophylaxis may be considered, particularly when a calcineurin inhibitor is included [EL4]. Prophylaxis should also be considered in patients with additional high-risk features, including high-dose corticosteroids, lymphopenia, JAK inhibitor therapy, or combinations thereof, especially when these factors occur in combination [EL5] [Agreement 95%]

Although the absolute risk is very low [<0.2%], IBD is associated with an increased risk of *Pneumocystis jirovecii* pneumonia [PJP].[298,322–326] Nonetheless, incidence may be increasing and *P. jirovecii* pneumonia can be fatal, particularly in patients receiving calcineurin inhibitors.[327–329] No vaccine is available. Given the low population-level incidence, routine prophylaxis for all patients with IBD is not recommended.[297] Indeed, population-based data from Olmsted County identified only three PJP cases despite infrequent prophylaxis use,[330] and cost-effectiveness modeling relies on assumptions that may not reflect real-world incidence.[297] A risk-based approach is therefore preferred, as prophylaxis may be cost-effective in patients with additional risk factors, such as prolonged high-dose corticosteroids [≥15 mg/day prednisone for >4 weeks], lymphopenia [<200 cells/mm^3], older age [particularly with steroids], and chronic lung disease.[297,331] Prophylaxis may also be reasonable in triple immunosuppression, although population-based cohorts have not consistently confirmed multiple-agent exposure as an independent risk factor.[297,323,330,332] Cases have been reported with anti-TNF agents and JAK inhibitors;[327,329,333] reports are uncommon with other approved biologics.[18,325,329,334] Consistent with this, ESCMID [European Society of Clinical Microbiology and Infectious Diseases] guidance recommends considering prophylaxis in patients treated with JAK inhibitors who have additional risk factors, including high-dose steroids;[335] current evidence does not support routine prophylaxis for JAK inhibitor monotherapy. The most common first-line prophylaxis is a single- or double-strength dose of TMP-SMX, depending on local practices. Second-line options should be chosen based on local availability and recommendations from infectious disease experts. If a patient cannot tolerate or has a contraindication to the primary treatment, alternative options include aerosolized pentamidine, dapsone, or atovaquone. Caution is advised when co-administering these with methotrexate, although low-dose methotrexate may be acceptable in certain situations.[336] See Table 3 for PJP prophylaxis regimens.

6. Scenario-based management

6.1. Patients with IBD and a disease flare

Statement 32: Screening for C. difficile infection [EL3] and bacterial enteritis [EL4] is recommended in all patients with IBD and a disease flare [Agreement 100%]

Statement 33: Stool cultures for common enteropathogens are suggested in patients with IBD under immunosuppression who experience a disease flare [EL5]. A multiplex PCR panel might be used in place of general stool cultures if locally available [EL4]. Screening for parasites and fungal infections should also be considered in patients with relevant travel history or long-term residency in endemic areas [EL5] [Agreement 87%]

As outlined in Section 5.2, superimposed CDI significantly worsens short- and long-term IBD outcomes, making routine screening imperative during any disease flare. Given that biologic exposure is an independent risk factor for CDI, clinicians should maintain a high index of suspicion.[337] Prompt stool testing for *C. difficile* should be prioritized upon presentation of a flare, particularly in hospitalized patients where prevalence and complication rates are highest.[255] Beyond CDI, bacterial enteric infections may mimic or trigger IBD flares and should be considered in the differential diagnosis of suspected IBD and in established IBD, particularly before initiating or escalating immunosuppressive or advanced therapies.[270,338–341] Excluding

Table 3. *Pneumocystis jirovecii* pneumonia prophylaxis regimens.

Line of therapy	Medication	Dose and schedule	Observations/clinical notes
First-line	Trimethoprim-sulfamethoxazole	80/400 mg daily	Single-strength tablet daily [or half a double-strength tablet daily]
		160/800 mg 3 times per week	Alternatively, one double-strength tablet 3 times per week
Alternatives [may be less effective than trimethoprim-sulfamethoxazole]	Aerosolized pentamidine	300 mg once every 4 weeks	Risk of extrapulmonary pneumocystosis.
	Dapsone	100 mg daily	Contraindicated in patients with G6PD deficiency or severe allergy to sulfonamides
	Atovaquone	1500 mg daily	

bacterial enteropathogens during a flare under immunosuppression is also important to limit ongoing transmission and to avoid misclassifying infectious symptoms as refractory IBD activity.[342] Conventional stool cultures remain a reliable first-line approach for common bacterial enteropathogens. Where available, multiplex gastrointestinal PCR panels may be used as an alternative, as they identify pathogens more frequently than conventional testing and are associated with lower rates of IBD treatment escalation or modification compared with standard cultures.[237,271] Consistent with the targeted approach outlined in Section 5.4, routine screening for parasitic and fungal gastrointestinal infections during a flare is unnecessary in the absence of relevant epidemiological exposure [eg, specific travel history or residence in endemic areas] or strong clinical suspicion. When suspected based on these risk factors, an infectious disease consultation can help guide the diagnostic work-up.[343] Although parasitic and fungal gastroenteritis can occur in immunocompromised hosts, testing in patients with IBD receiving immunosuppressive therapies should remain exposure-driven, and infectious disease consultation may be helpful to guide diagnostic work-up when suspected.[344–349]

6.2. Traveling

Statement 34: Pre-travel counseling regarding safety measures [including vaccinations and malaria chemoprophylaxis] is recommended for all patients with IBD under immunosuppression [EL4]. Traveling to endemic regions with potentially increased infection rates should be discussed on a case-by-case basis. Currently, no recommendation against traveling can be made [EL4] [Agreement 100%]

Travel is an important component of quality of life for many patients with IBD, and blanket restrictions are not justified. Pre-travel counseling, preferably in a specialized travel clinic, is recommended to review infection-prevention measures, vaccination planning [including contraindications to live vaccines under immunosuppression and potentially reduced responses to prior inactivated vaccines], and potential drug–drug interactions between IBD therapies and antimalarial or antidiarrheal agents.[350] In a retrospective case-control study [222 IBD vs 224 controls], patients with IBD reported more travel-related illness compared with controls during travel to industrialized countries but not during travel to developing or tropical regions. Reported events appeared more consistent with sporadic IBD relapse than increased susceptibility to enteric infection. Prior IBD hospitalizations and frequent flares predicted travel-associated illness, whereas immunosuppressive therapy did not.[351] For travel to TB-endemic areas, clinicians should be more cautious with combination immunosuppression [eg, anti-TNF plus azathioprine] than with vedolizumab or azathioprine monotherapy; repeat TB screening after return may be considered, although supporting data are limited.[352]

Statement 35: There is insufficient evidence to suggest that patients with IBD under immunosuppression are at an increased risk of disease flare after travel-related enteric infections [EL4] [Agreement 100%]

Enteric pathogens are linked to IBD onset and relapse.[353–355] In symptomatic patients with IBD, non-*C. difficile* enteric infections occur in a relevant minority [18.1% in CD and 16.1% in UC], although endoscopic and histologic features often do not clearly distinguish infection from an IBD flare.[269] Despite this, available data do not show an increased rate of IBD flares after travel.[356] Traveler's diarrhea, including prolonged symptoms, can occur in IBD and should not automatically be interpreted as a flare. Patients with prior IBD-related hospitalizations and frequent flares appear more prone to travel-associated illness episodes. In one study, 32% of patients with IBD reported new-onset diarrhea after travelling; patients variably attributed this to flare [58%] or infection [28%].[356] Other travel-related exposures [eg, high-altitude travel or long-haul flights] have been associated with higher flare rates in retrospective analyses, possibly related to mucosal hypoxia, but evidence remains limited.[357,358]

Statement 36: Patients with IBD, including those on immunosuppressive therapy, do not appear to be at increased risk for acquiring malaria or other tropical diseases or for having a more severe disease course and should follow standard guidelines for prevention [EL5] [Agreement 91%]

Available data suggest that immunosuppression does not increase overall travel-related illness rates in IBD,[351,359] and case-control studies do not show a higher risk of traveler's diarrhea. Clinicians may still discourage travel to TB-endemic regions in some patients receiving anti-TNF agents plus azathioprine, and practice varies regarding continuation of therapy during such travel.[360] Notably, many immunocompromised travelers undertake high-risk itineraries, including malaria-endemic destinations.[350] Traveler's diarrhea is the most frequent travel-associated illness and can be prolonged and should not be automatically interpreted as an IBD flare.[361,362] Consistent with this, increased post-travel flare rates have not been demonstrated.[356] Patients with IBD, including those under immunosuppression, should follow standard prevention advice [eg, safe food and water practices] and may be provided with standby antibiotics for self-treatment. Where fluoroquinolones are unsuitable [prior fluoroquinolone exposure, resistance, lack of response within 36–48 h, or contraindications], azithromycin is an alternative.[363] Increasing fluoroquinolone resistance, particularly in parts of Southeast Asia, limits empiric use in some settings.[364] Rifaximin is not recommended as it is only effective for non-invasive *E. coli*. Immunocompromised travelers should have a lower threshold to start self-therapy and, if symptoms persist, stool testing [including ova or parasites and *C. difficile*] should be performed. Evidence guiding continuation of immunosuppression during acute diarrhea is limited; given that an IBD flare remains an important differential, therapy is generally continued unless severe systemic infection occurs. Severe malaria has rarely been described under anti-TNF therapy.[365] Experimental data suggest TNF blockade could theoretically modulate malaria pathogenesis.[366] Standard malaria prevention measures [avoidance of mosquito bites and chemoprophylaxis when indicated] should be followed; pregnant women, asplenic individuals, and those with HIV are at higher risk. Drug–drug interaction checks are advised, including the reduced atovaquone absorption with metoclopramide.[367]

6.3. Special risk factors

6.3.1. Healthcare workers

Statement 37: Healthcare workers with IBD do not appear to have an increased risk of severe opportunistic infections compared with other patients with IBD, except for TB [EL4]. Repeating TB screening might be considered in patients with IBD exposed to occupational risk, particularly those under anti-TNF treatment [EL4] [Agreement 100%]

In a retrospective cohort of 44 patients with IBD with initially negative TB screening who later developed TB, the median time from starting anti-TNF therapy to TB diagnosis was 14.5 months; TB exposure was suspected in one-third, and half of those had occupational exposure.[276] In contrast, a case-control study found no increased risk of COVID-19 among healthcare workers with IBD compared with other patients with IBD.[368] A large multicenter case-control study evaluating severe infections reported similar overall incidence and severity of infections between healthcare workers and non-healthcare worker controls with IBD. However, healthcare workers face a recognized, increased occupational risk of TB. Therefore, as recommended in Section 5.1, routine annual TB rescreening should be provided for healthcare workers with IBD, particularly those receiving anti-TNF agents.[369] This is consistent with the recognized higher occupational risk of TB among healthcare workers in general.[370]

6.3.2. Elderly patients

Statement 38: There is insufficient evidence to recommend against immunosuppression in elderly patients with IBD based solely on an increased risk of opportunistic infections [EL5] [Agreement 100%]

Elderly patients with IBD are under-represented in clinical trials as many studies have excluded individuals aged >65 years; consequently, treatment targets often follow algorithms developed in younger populations.[371] Older patients are nonetheless a distinct group due to higher comorbidity burden, polypharmacy [with drug–drug interaction risks], and age-related changes in renal and hepatic function.[372–374] Advanced age is associated with increased risk of opportunistic infections, including CMV, CDI, and HZ,[14,294,375–380] partly due to immunosenescence and impaired barrier function.[372,381] Immunosuppression, particularly anti-TNF therapy, may further increase serious infection risk in older patients, especially with underlying comorbidities, and infections may follow a more severe course.[14,16,381] An increased risk of severe infections has been reported in patients aged >65 years treated with adalimumab or infliximab [11% vs 0.5% in younger patients].[382] Older age and comorbidities are also associated with higher mortality under anti-TNF treatment.[383] However, treatment decisions should be individualized, balancing risks against the harms of undertreatment; many elderly patients receive prolonged systemic steroids, which have substantial adverse effects.[384–387] Real-world data suggest elderly-onset IBD is often managed with less immunosuppression and more surgery in UC.[388] Where immunosuppression is indicated, agents with more favorable safety profiles may be preferred. In clinical trials, vedolizumab and anti-IL-12/-23 or anti-IL-23 agents did not have increased infection risk versus placebo. A retrospective cohort found lower infection-related hospitalizations with vedolizumab compared with anti-TNF agents in older patients with IBD.[389] Registry data suggest ustekinumab is effective in elderly patients with CD without increased severe infection risk versus younger patients.[390] Overall, strategy should be individualized[391] and favor lower-risk options [eg, vedolizumab or anti-IL-23 agents], with JAK inhibitors reserved for selected elderly patients after failure of alternatives.

6.3.3. Frailty

Statement 39: There are insufficient data to recommend against treating frail patients with immunosuppressive therapies. Immunosuppression should be discussed on a case-by-case basis in these patients, with the aim of balancing risk versus benefits [EL5] [Agreement 100%]

Frailty is a clinically recognizable state of increased vulnerability due to reduced physiological reserve across organ systems, leading to impaired ability to cope with stressors. Frailty is increasingly prevalent in IBD and increases with age. In a large cohort study, 6% of patients with IBD had a frailty-related diagnosis and frailty was associated with nearly 3-fold higher mortality.[392] Importantly, frailty was also associated with immunosuppression-related infections after adjustment for age and comorbidities.[392] Additional predictors of significant infection include number of immunosuppressants, body mass index [BMI], inflammatory burden, and comorbidity load.[30] Data are not fully consistent across drug classes; one study reported an association between frailty and adverse outcomes in vedolizumab-treated patients but not with anti-TNF agents.[393] Comorbidities materially influence infection risk and treatment decisions. Diabetes increased infection risk in patients with IBD treated with immunomodulators,[394] and a Charlson comorbidity index ≥1 is strongly associated with infections; comorbidity also predicted infection-related hospitalizations.[394,395] Elderly-onset IBD is frequently accompanied by comorbidities,[374] and older age is linked to a higher risk of opportunistic infections, including CMV, *C. difficile*, and HZ.[379,380] In registry data, frailty was associated with less initiation of biologics or immunomodulators and greater prednisolone use.[396] Comorbidity [and older age] is associated with greater vedolizumab use and higher likelihood of colectomy; elderly-onset UC is often managed with less immunosuppression and more surgery.[388,397] Given the rising incidence of elderly-onset IBD,[398] these considerations are increasingly relevant. Frailty [and age] is also associated with higher postoperative morbidity and mortality in IBD, with low muscle mass emerging as an additional risk factor; however, results are mixed after multivariable adjustment in some cohorts.[399–403] Comorbidity rather than age at diagnosis may drive delayed immunomodulator initiation,[404] and some comorbid conditions (eg, chronic obstructive pulmonary disease [COPD] and hepato-pancreato-biliary disease) are linked to poorer anti-TNF outcomes.[405] Reassuringly, life expectancy in older patients with IBD appeared similar with immunomodulator versus biologic monotherapy in one population-based analysis.[406] Overall, frailty should prompt structured risk assessment and shared decision-making, including careful selection and intensity of immunosuppression and minimization of avoidable risk factors.

7. Vaccination

Although this guideline focuses on patients receiving or planning to receive immunosuppressive therapy, general infection prevention measures, including vaccination according to national schedules, food safety counseling, and hand hygiene, apply to all patients with IBD, as disease-related immune dysregulation may independently contribute to infection susceptibility.

7.1. Pre-treatment assessment

Statement 40: Before initiation of treatment, preferably at the time of IBD diagnosis, a standardized screening checklist regarding infection risk and immunization status should be completed to minimize the risk of infections [EL4] [Agreement 100%]

As mentioned, opportunistic infections are recognized complications of IBD therapy. While risk of opportunistic infections is not uniformly increased across all agents, this risk is particularly relevant with anti-TNF agents.[2,15,16] Safety concerns also include rare fatal outcomes after live vaccination during anti-TNF therapy[407] and an increased risk of virus-associated malignancies with thiopurines.[36] A standardized pre-treatment checklist is therefore recommended to support timely risk assessment, vaccination planning, and implementation of preventive measures, which appear effective when recommendations are followed.[408] While Statement 2 stratifies screening by strength of recommendation, in practice a standardized checklist approach at diagnosis ensures no actionable infection is missed before immunosuppressive therapy is initiated. This is particularly important given the suboptimal vaccination coverage in both pediatric and adult IBD populations,[409–411] frequent gaps in vaccine counseling in primary care,[412] and persistent adherence issues before biologic initiation.[413] Structured protocols can improve vaccination uptake,[414] and checklist implementation increases clinician vaccine recommendations.[415] Nevertheless, opportunistic infections may still occur despite appropriate preventive measures.[408]

Ideally, the checklist should be completed at IBD diagnosis and updated before treatment escalation, including the following: **Medical history**, prior bacterial, viral, or fungal infections [especially TB and EBV, HSV, VZV, HIV, HAV, HBV, HCV]; **Exposure risk**, travel or residence in endemic areas [eg, TB, malaria, yellow fever, Chagas disease, strongyloidiasis] and future travel plans; **Immunization status**, routine vaccines (diphtheria, tetanus, polio, pertussis, measles, mumps, and rubella [MMR], HPV, hepatitis A and B) and vaccines recommended for chronic disease or IBD (annual influenza, pneumococcal, severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]); **Physical examination**, focused assessment including chest, skin, oral cavity, and HPV screening [women]; **Laboratory screening**, full blood count [neutrophils and lymphocytes], C-reactive protein, urinalysis if symptomatic, hepatitis B and C serologies, EBV serologies, HIV testing after counseling, and TB screening [TST, IGRA, chest X-ray, or combinations thereof]; **Serology for uncertain immunity**, MMR and VZV serology if history is unclear, with vaccination where appropriate and no contraindication to live vaccines; **Returning travelers or immigrants from endemic areas**, eosinophil count, stool examination [ova and parasites], *S. stercoralis* and *T. cruzi* serology.

Appendix 1 provides a schematic checklist that summarizes key considerations across all infections discussed in this guideline

Statement 41: It is suggested to wait for at least 1 month after discontinuation of immunosuppressive therapy before the administration of a live attenuated vaccine [EL4]. However, live attenuated vaccines could be offered to selected immunosuppressed patients after carefully weighing the risks and benefits [EL4] [Agreement: 100%]

Clinical evidence supporting live attenuated vaccination in patients receiving immunosuppressive therapy is limited; most guidance is therefore based on uncontrolled data, small cohorts, and case series. Multiple professional societies and expert groups (IDSA/Centers for Disease Control and Prevention [CDC], American College of Gastroenterology [ACG], Canadian Association of Gastroenterology, European Alliance of Associations for Rheumatology [EULAR], American College of Rheumatology [ACR], National Psoriasis Foundation, and Japanese expert consensus) suggest that selected live vaccines may be administered during low-dose immunosuppression, following individual risk assessment.[416–422] Where possible, live vaccines should be given before starting immunosuppression. If immunosuppression is paused to allow vaccination, treatment should not be restarted until an adequate interval has elapsed. A minimum interval of 3–4 weeks is commonly used to allow vaccine virus clearance and to cover incubation periods. A systematic review of 64 studies in immunosuppressed populations found that adverse events after live vaccination were uncommon,[423] but evidence remains insufficient to support routine live vaccination in immunosuppressed patients with IBD. Decisions should therefore be individualized, balancing infection risk, vaccine urgency, degree of immunosuppression, and patient preferences; multidisciplinary discussion may be appropriate in selected cases. Vaccinating close contacts ["cocoon strategy"] is an additional protective measure.[423,424] MMR, live varicella, live smallpox, and rotavirus vaccines can be administered to household contacts of immunosuppressed individuals, as transmission is not expected or can be minimized with simple precautions. Transmission of live influenza vaccine virus is mainly a concern only for very severely immunocompromised patients requiring isolation. In contrast, oral polio vaccine in close contacts, although rarely used, can pose a significant risk for immunosuppressed patients.[425] Recommended washout intervals before live vaccination vary by agent and guideline. UK guidance suggests 3 months after high-dose steroids, thiopurines, or methotrexate, and 6 months after certain other immunosuppressants.[425] An alternative approach is to guide timing according to pharmacokinetics, pharmacodynamics, and immune reconstitution, commonly using approximately five drug half-lives as a pragmatic threshold to achieve negligible circulating drug levels.[426]

7.2. Specific vaccinations

Table 4 summarizes recommended vaccination schedules for patients with IBD.

Table 4. Recommended vaccination schedules for patients with inflammatory bowel disease.

Vaccine (Statement)	Vaccine type	Schedule and dose	IBD-specific considerations	Monitoring/booster	Key references
Hepatitis A (St. 42)	Inactivated	Two doses: 0, 6–12 monthsStandard adult dose	Administer before IS when possibleCan be given during IS (inactivated)Pre-vaccination serology not routinely required	Check anti-HAV IgG 1–2 months after seriesNo routine boosters if seroconverted	429–433
Hepatitis B (St. 43)	Inactivated (recombinant)	Standard: 3 doses at 0, 1, 6 months (20 μg)Alternative formulations (eg, high-dose, Heplisav-B®, accelerated schedule) proposed but insufficient data to recommend	Vaccinate as early as possible, ideally before ISResponse rates reduced (~60%) during ISAnti-HBs ≥10 IU/L=adequate; ≥100 IU/L=effectiveEnhanced vaccination strategies under investigation	Check anti-HBs ≥4 weeks after last doseIf anti-HBs <10 IU/L: revaccinate (optimal approach unclear; full series may be considered)Check anti-HBs in previously vaccinated newly diagnosed patients	434–452
Herpes zoster (RZV)(St. 44)	Recombinant Adjuvanted (non-live)	Standard: 2 doses at 0, 2–6 monthsAccelerated (IS patients): 0, 1–2 months	Preferred over ZVL in all IBD patientsCan be given during IS (non-live)Recommended for all adult IBD patients on IS	No routine serological monitoringNo booster currently recommended	453–465
Influenza (St. 45)	Inactivated (IIV or RIV)	One dose annuallyStandard or high-dose formulation	Administer annually regardless of IS statusAvoid LAIV (live attenuated) in IS patientsHigh-dose/adjuvanted may improve response in IS	No serological monitoring requiredAnnual revaccination	466–471
HPV (St. 46)	Inactivated (recombinant)	9-valent: 2 or 3 dosesBefore age 13: 2 doses at 0, 6–12 monthsAge ≥15: 3 doses at 0, 1–2, 6 months	Recommended up to age 26; catch-up not usually recommended for adults >26 yearsNot recommended for adults >45 yearsVaccinate before IS when possible	No routine serological monitoringNo boosters currently recommended	472–474
Pneumococcal (St. 47)	Conjugate (PCV) and polysaccharide (PPSV23)	IS patients: PCV20 or PCV21 (single dose)OR PCV15 → PPSV23 (≥8 weeks later)Previously unvaccinated: PCV first	Administer before IS when possibleAll IBD patients on IS should receive pneumococcal vaccinationPCV preferred as initial vaccine	Revaccination with PPSV23 after 5 years (if used)No routine serological monitoring	475–484
COVID-19 (St. 48)	mRNA or protein-based (non-live)	Primary series per local guidelinesAdditional (3rd) primary dose for IS patientsBoosters as recommended	IS patients may have attenuated responseNo delay necessary for non-live vaccinesAdditional doses recommended for IS patients	Boosters per local/national guidelinesSerological monitoring not routinely recommended	45,485–523
MMR (St. 49)	Live attenuated	Two doses: 0, ≥4 weeksStandard adult dose	Contraindicated during ISAdminister ≥4 weeks before starting ISCheck VZV and measles serology before IS	Check measles IgG if on borderline ISNo routine boosters if 2 doses completed	524–528
RSV (St. 50)	Recombinant (non-live)	Single doseAdults ≥60 years	Consider for IBD patients ≥60 yearsCan be given during IS (non-live)	No booster currently recommendedAnnual revaccination under evaluation	526–528

Schedules reflect recommendations for adult IBD patients. Live vaccines (MMR, LAIV, ZVL) are contraindicated during significant immunosuppressive therapy. Non-live vaccines can be administered during immunosuppressive therapy, although responses may be attenuated. Vaccination should ideally be initiated before starting immunosuppressive therapy when clinically feasible. Reference numbers correspond to the guideline bibliography.
Abbreviations: HAV, hepatitis A virus; HBV, hepatitis B virus; RZV, recombinant zoster vaccine; ZVL, zoster vaccine live; HPV, human papillomavirus; PCV, pneumococcal conjugate vaccine; PPSV23, pneumococcal polysaccharide vaccine 23-valent; MMR, measles, mumps, rubella; RSV, respiratory syncytial virus; IS, immunosuppression/immunosuppressive therapy; IIV, inactivated influenza vaccine; RIV, recombinant influenza vaccine; LAIV, live attenuated influenza vaccine; St., Statement.

Statement 42: HAV vaccination is suggested for all patients with IBD with no evidence of past infection or vaccination [EL4] [Agreement 96%]

HAV infection can be severe in immunosuppressed individuals; therefore, vaccination is suggested for patients with IBD without evidence of prior infection or vaccination. [79,427,428] Pre-vaccination serology [anti-HAV IgG] is not routinely required, as vaccination is safe even in those with pre-existing antibodies.[79,429] For this reason, universal HAV vaccination does not require prior serological screening; the lower screening tier assigned in Statement 2 reflects the limited clinical impact of HAV serostatus on immunosuppressive treatment decisions, not a lower priority for vaccination itself. After completion of the HAV vaccine series, seroconversion rates in patients with IBD are generally high; pediatric data suggest rates comparable with healthy controls, although responses may be lower in those receiving anti-TNF therapy or combination immunosuppression.[73,428,430] The standard schedule is two doses. Seroconversion after the first dose may be lower in IBD, but increases to near-normal levels after the second dose,[73,430] supporting timely booster administration [usually 6 months after dose 1].

Statement 43: HBV vaccination is recommended for all non-immune patients with IBD, preferably at diagnosis [EL2] [Agreement: 100%]

Patients with IBD are at risk of HBV infection; therefore, all non-immune patients should be vaccinated, ideally at diagnosis.[81,431] Vaccine responses are reduced compared with healthy controls, with pooled adequate immune response [approximately 60%, anti-HBs > 10 IU/L] and effective immune response [40%, anti-HBs > 100 IU/L] rates significantly lower in patients with IBD.[432–434] Timing is important, as immunosuppressive therapies, especially corticosteroids, thiopurines, and anti-TNF agents, are consistently associated with reduced likelihood of seroprotection, supporting vaccination as early as possible after IBD diagnosis.[435–443] Therefore, all non-immune patients should receive HBV vaccination immediately after an IBD diagnosis. We suggest measuring anti-HB levels at least 4 weeks after the final dose of the HBV vaccine, as well as in newly diagnosed patients with IBD who previously completed HBV vaccination. However, the optimal approach remains unclear if seroprotection is not achieved, including whether a single booster dose or a complete revaccination series is required.[436,441,442,444] Periodic monitoring of anti-HB levels may be advisable in patients on immunosuppressive therapy, with revaccination considered if titers decline below the protective threshold [<10 IU/L].[85,441] In adult patients who received the full vaccination series during childhood, full revaccination may be considered.[445] Several strategies have been proposed to enhance the immune response to HBV vaccination in patients with IBD, particularly those already receiving immunosuppressive or anti-TNF therapy. However, current data are insufficient to recommend for or against strategies such as double dosing, accelerated schedules with shorter intervals between doses, additional doses, use of specific vaccine formulations, or alternative routes of administration.[446–449]

Statement 44: Recombinant HZ vaccine is recommended for all adult patients with IBD receiving or planning to receive immunosuppressive therapy [EL2] [Agreement: 95%]

Patients with IBD have a higher risk of HZ, often at a younger age than the general population, and risk increases further with immunosuppression. Higher incidence has been reported with thiopurines, methotrexate, TNF agents, and corticosteroids.[38,450–453] JAK inhibitors, particularly at higher doses, confer an especially increased risk.[27,454,455] RZV is an adjuvanted recombinant vaccine [Shingrix® GSK] that was approved in 2017 for adults aged ≥50 years and subsequently extended to adults aged ≥18 years at increased risk of HZ. The standard regimen is two doses 2–6 months apart; in patients who are or will be immunosuppressed, the second dose may be given earlier [1–2 months after dose 1]. RZV is recommended even after prior HZ and can be used as a booster after live zoster vaccine.[456] Efficacy and safety in immunocompromised populations are supported by randomized trials, and meta-analytic data suggest higher efficacy than live zoster vaccine.[457] Data concerning safety and effectiveness of RZV specifically in patients with IBD have been evaluated in large retrospective cohort studies.[458–460] Risk of IBD flare post vaccination was low [1.5% in a prospective cohort of 67 patients].[461] Moreover, one cost-effectiveness model suggested that RZV vaccination for all adults with IBD is cost-effective.[462]

Statement 45: We suggest that patients with IBD receive annual influenza vaccination in accordance with national guidelines [EL3] [Agreement: 90%]

Annual influenza vaccination is an important preventive measure in IBD, given increased susceptibility to infections related to immune dysregulation, barrier dysfunction, nutritional factors, post-surgical status, and immunosuppressive therapies.[439,463] Observational data suggest that patients with IBD have a higher risk of influenza and related complications, independent of medication exposure.[53] In one study, IBD was associated with increased influenza risk [aHR: 1.28; 95% CI: 1.19–1.37] and higher hospitalization rates compared with non-IBD controls [5.4% vs 1.85%].[431] Vaccination is therefore expected to reduce complications, hospitalizations, and influenza-related mortality.[431,464]

Immune responses may be attenuated in patients receiving immunosuppression, particularly anti-TNF agents [with or without azathioprine] and corticosteroids.[463,465] In contrast, vaccination appears safe and immunogenic in vedolizumab-treated patients, with responses comparable with non-immunosuppressed individuals; repeated annual vaccination helps maintain seroprotection.[439] Data for anti-IL therapies and small molecules remain limited. Strategies, such as timing of vaccination around infliximab infusions or adding booster doses, have not consistently improved responses.[466] Higher-dose formulations may increase immunogenicity, although benefits may not persist beyond 6 months.[467]

Uptake remains suboptimal [reported 48%], often due to concerns about side effects or triggering flares; however, post-vaccination flares are uncommon [2%; 95% CI: 1%–4%] and typically mild.[468] Overall, cohort data support good

tolerability in IBD with adverse event rates similar to the general population.[466] Despite limitations, current evidence supports vaccination in patients with IBD to mitigate influenza risks. There are no specific data on influenza vaccination outcomes in patients with IBD stratified by age around the 60–65-year threshold.

Statement 46: Routine HPV vaccination is recommended for female and male patients with IBD in accordance with national guidelines [EL4] [Agreement: 100%]

HPV is a recognized cause of cancer. Although most HPV infections are asymptomatic and clear spontaneously, persistent infections can progress to precancerous lesions or cancer. HPV causes most cervical cancers and some cancers of the vagina, vulva, penis, anus, and oropharynx. It is estimated that only about 10% of cervical and anal cancers are HPV-negative. There are three available prophylactic vaccines for HPV. Gardasil 9 [9vHPV] is the main type of HPV vaccine in most countries where bivalent Cervarix [2vHPV] and quadrivalent Gardasil [4vHPV] are no longer available. Gardasil 9 contains seven oncogenic HPV types [16, 18, 31, 33, 45, 52, and 58] and two HPV types that cause most genital warts [6 and 11]. HPV vaccination can be initiated for all children at the age of 11 or 12 years. The Advisory Committee on Immunization Practices [ACIP] notes that vaccination may be started at age 9 years. Two doses are recommended if vaccination is completed before age 13 years; three doses are recommended if vaccination starts after age 15 years. Catch-up HPV vaccination is not usually recommended for adults aged >26 years. HPV vaccine should ideally be administered before potential exposure to HPV through sexual contact, as HPV acquisition generally occurs soon after first sexual activity. There are no data to support vaccination of all adults aged ≥27 years. Nonetheless, some adults who are not adequately vaccinated and might be at risk for new HPV infection [ie, new sexual partner] might benefit from vaccination in this age range.[469] HPV vaccines are not recommended for adults aged >45 years. Although anal cancer is rare, patients with IBD may have a higher rate of anal cancer than the general population, particularly those with CD and perianal fistulae. Thus, prophylactic HPV vaccination could be considered for such patients with additional high-risk features for anal cancer.[470] Only one small study has been conducted in young females with IBD on immunosuppression, which showed good immunogenic response of the HPV vaccine without significant vaccine-associated side effects.[471]

Statement 47: Pneumococcal vaccination is recommended for patients with IBD on immunosuppressive therapy [EL2] or with risk factors for pneumococcal disease [EL4] [Agreement: 100%]

Streptococcus pneumoniae can cause pneumonia, bacteremia, and meningitis with substantial morbidity and mortality. Observational studies suggest that IBD is associated with an approximately 1.5- to 2-fold higher risk of invasive pneumococcal disease compared with non-IBD controls.[472–474] Risk is further increased in patients receiving immunosuppressive therapy, including corticosteroids, and is associated with poorer outcomes.[475–478] However, available data cannot fully disentangle the contribution of IBD-related immune dysfunction, immunosuppressive exposure, and confounding by disease severity. Pneumococcal vaccination has evolved beyond 23-valent pneumococcal polysaccharide vaccine [PPSV23] and 13-valent pneumococcal conjugate vaccine [PCV13], with newer conjugate vaccines [PCV15, PCV20, PCV21] licensed since 2021 in the USA and Europe. Pneumococcal vaccines are generally safe and effective in adults with IBD and are associated with reduced infection-related hospitalizations, ICU admissions, and mortality.[477,479,480] Immunosuppression, particularly with anti-TNF agent monotherapy or combination therapy, may blunt serologic responses; a systematic review and meta-analysis reported lower seroconversion rates with anti-TNF exposure.[468] In contrast, a small study reported comparable seroconversion in vedolizumab-treated patients.[439] Vaccination schedules depend on age and prior vaccine history. Recent ACIP guidance recommends a single dose of PCV20 or PCV21 for adults aged ≥50 years with no prior or unknown vaccination. A similar recommendation is made for adults aged 19–49 years receiving immunosuppression who are unvaccinated or received PCV13 >1 year earlier; additional schedules and intervals are based on prior vaccination status.[481] Whether to vaccinate patients with IBD without immunosuppression and without other pneumococcal risk factors remains less clear, although vaccination may still be considered given the potential for future immunosuppressive therapy.

Statement 48: Additional booster doses of COVID-19 vaccines should be recommended to patients with IBD in accordance with national guidelines[EL2]. High-risk patients [older age, with comorbidities, or with active disease or highly immunosuppressed] should be prioritized [EL2] [Agreement 84%]

An increased risk of SARS-CoV-2 infection is not consistently demonstrated in IBD, but more severe COVID-19 outcomes have been reported, driven mainly by older age and comorbidities and also by IBD-related factors, such as active disease and corticosteroid exposure. Data for other therapies (eg, anti-TNF agents, 5-aminosalicylic acid [5-ASA], JAK inhibitors) are conflicting.[45,57,482–487] Vaccination against SARS-CoV-2 [including booster doses], particularly with mRNA platforms that are updated for emerging variants, has shown a favorable safety profile in IBD similar to the general population.[488–495] National recommendations commonly advise an interval of approximately 3–6 months after infection or after the last vaccine dose before an updated booster. In IBD, vaccine immunogenicity may be lower and wane faster than in healthy controls but improves with boosters; prior SARS-CoV-2 infection further augments responses.[496–504] Anti-TNF agents most consistently reduce antibody responses, and corticosteroids or combination immunosuppression may also blunt responses.[505–511] Despite this, real-world cohorts and meta-analyses support vaccine effectiveness in IBD, reinforcing booster recommendations and prioritization of higher-risk patients.[512–520]

Statement 49: MMR vaccination should be recommended in patients with IBD without documented MMR vaccination history prior to initiation of immunosuppressive therapy; serological screening is recommended when vaccination records are unavailable [EL4] [Agreement: 100%]

Documentation of vaccination with two doses of the live attenuated measles vaccine is recommended as an adequate measure to verify immunity.[521] Vaccinated immunocompromised patients with IBD have similar antibody titers as the general population.[522,523] Documented immunization supersedes serologic screening, as false negative results are common. Measles vaccination elicits a humoral and cell-mediated immune response, which leads to lower antibody titers compared with natural infection.[521] Serologic screening is recommended if documentation of vaccination is not feasible. Immunosuppressed individuals who are susceptible require post-exposure prophylaxis in the event of measles exposure. MMR vaccination for patients treated with immunosuppressive agents is generally contraindicated, although data are extremely limited. Recently, safety of MMR vaccination in 37 patients treated with vedolizumab was documented.[524] An additional study described inadvertent live vaccination of 35 patients with IBD on immunosuppressive agents [22 received MMR]; most patients were treated with anti-TNF agents or azathioprine and no breakthrough infections were recorded.[525]

Statement 50: Respiratory syncytial virus vaccination is suggested for patients with IBD on immunosuppressive therapy aged 60 years and above [EL4] [Agreement: 100%]

Respiratory syncytial virus [RSV] infection is an increasing medical concern regardless of patient age. Symptoms range from mild to severe, with hospitalization associated with an in-hospital mortality rate of up to 8%.[526] Currently, two non-live RSV vaccines are approved for use in adults aged ≥60 years.[527] A recent large retrospective multi-institutional study demonstrated that adult patients with IBD infected with RSV have a higher risk of hospitalization due to RSV compared with non-IBD cohorts. This risk is particularly elevated in those with concomitant cardiovascular disease, including ischemic heart disease, heart failure, cerebrovascular accident, or peripheral artery disease and in those who received steroid therapy within 3 months before infection onset. The study also showed that treatment with anti-TNF antibodies and immunomodulators did not influence hospitalization risk compared with 5-ASA therapy.[528] Despite the paucity of high-quality data, given the potential for significant mortality among hospitalized patients infected with RSV, we advocate for RSV vaccination for all patients with IBD aged ≥60 years. However, further studies are needed to assess the immunogenicity of both vaccines in immunocompromised individuals, especially those receiving immunosuppressive drugs, biologics, or both, as this may impact future dosing regimens.

8. Summary and conclusion

These updated ECCO guidelines provide a comprehensive, evidence-based framework for the prevention, screening, diagnosis, and management of infections in patients with IBD across contemporary therapeutic settings. By integrating evolving data on immunosuppressive and biologic therapies, patient-related risk factors, and vaccination strategies, the guidelines aim to support individualized, risk-adapted clinical decision-making. Emphasis is placed on prevention, early recognition, and multidisciplinary management to minimize infection-related morbidity and mortality while maintaining optimal control of IBD. As the therapeutic landscape continues to evolve, these recommendations should be applied alongside clinical judgement and updated as new evidence emerges.

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Supplementary material

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Conflicts of interest

ECCO has diligently maintained a disclosure policy of potential conflicts of interests [CoI]. The conflict-of-interest declaration is based on a form used by the International Committee of Medical Journal Editors [ICMJE]. The CoI disclosures are not only stored at the ECCO Office and the editorial office of JCC but are also open to public scrutiny on the ECCO website [https://www.ecco-ibd.eu/about-ecco/ecco-disclosures.html], providing a comprehensive overview of potential conflicts of interest of authors.

Data availability

Search strategy materials are provided in the Supplementary Material available online at *ECCO-JCC*.

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