# CLINICAL PRACTICE UPDATES

## AGA Clinical Practice Update on Noncolorectal Cancer Screening and Vaccinations in Patients With Inflammatory Bowel Disease: Expert Review

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**DESCRIPTION:** **The aim of this American Gastroenterological Association (AGA) Clinical Practice Update (CPU) is to provide Best Practice Advice statements for gastroenterologists and other healthcare providers who provide care to patients with inflammatory bowel disease (IBD). The focus is on IBD-specific screenings (excluding colorectal cancer screening, which is discussed separately) and vaccinations. We provide guidance to ensure that patients are up to date with the disease-specific cancer screenings and vaccinations, as well as advice for mental health and general well-being.**

**METHODS:** **This expert review was commissioned and approved by the AGA CPU Committee and the AGA Governing Board to provide timely guidance on a topic of high clinical importance to the AGA membership and underwent internal peer review by the CPU Committee and external peer review through standard procedures of *Clinical Gastroenterology and Hepatology*. The Best Practice Advice statements were drawn from reviewing existing literature combined with expert opinion to provide practical advice on the screening for noncolorectal cancers and vaccinations in patients with IBD. Because this was not a systematic review, formal rating of the quality of evidence or strength of the presented considerations was not performed.**

**BEST PRACTICE ADVICE STATEMENTS**

**BEST PRACTICE ADVICE 1:** **All adult patients with IBD should receive age-appropriate cancer screening.**

**BEST PRACTICE ADVICE 2:** **Adult women with IBD should follow age-appropriate screening for cervical dysplasia. Data are insufficient to determine whether patients receiving combined immunosuppression or thiopurines require more frequent screening. Shared decision making and individual risk stratification are encouraged.**

**BEST PRACTICE ADVICE 3:** **All adult patients with IBD should follow skin cancer primary prevention practices by avoiding excessive exposure to the sun's ultraviolet radiation. Patients on immunomodulators, anti-tumor necrosis factor biologic agents, or small molecules should undergo yearly total body skin exam. Patients with any history of thiopurine use should continue with yearly total body skin exam even after thiopurine cessation.**

**BEST PRACTICE ADVICE 4:** **At every colonoscopy, a thorough perianal and anal examination should be performed. Special attention should be made to inspection of the anal canal of patients with perianal Crohn's disease, with anal stricture, with human papillomavirus, with human immunodeficiency virus, and who engage in anoreceptive intercourse.**

*Abbreviations used in this paper:* ACIP, Advisory Committee on Immunization Practices; AGA, American Gastroenterological Association; anti-HBs, hepatitis B surface antibody; anti-TNF, anti-tumor necrosis factor; BMD, bone mineral density; CDC, Centers for Disease Control and Prevention; CI, confidence interval; CIN, cervical intraepithelial neoplasia; CPU, Clinical Practice Update; HD, high dose; HIV, human immunodeficiency virus; HPV, human papillomavirus; HR, hazard ratio; HZ, herpes zoster; IBD, Inflammatory bowel disease; MMR, measles, mumps, and rubella; mRNA, messenger RNA; RSV, respiratory syncytial virus; RZV, recombinant herpes zoster vaccine; SD, standard dose; TBSE, total body skin exam; USPSTF, U.S. Preventive Services Task Force; VPD, vaccine-preventable disease.

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**BEST PRACTICE ADVICE 5:** **Gastroenterology clinicians should discuss age-appropriate vaccines with adult patients who have IBD and share responsibility with primary care providers for administering these vaccines. Patients with IBD should follow the adult immunization schedule advised by the Centers for Disease Control and Prevention (CDC) for all vaccines with the exception of live vaccines; Patients receiving immune-modifying agents should be counseled against receiving live vaccines; Immunization history to the 2 live pediatric vaccines, varicella and measles, mumps, and rubella vaccine series, is presumptive evidence of immunity. All adults 18 to 26 years of age should receive human papillomavirus vaccine series, and those between 27 and 45 of age years should be vaccinated if they are likely to have a new sexual partner.**

**BEST PRACTICE ADVICE 6:** **Inactivated vaccines are safe in patients with IBD, and their administration is not associated with exacerbation of IBD activity. We suggest that patients receive vaccines at the earliest opportunity and preferably be off corticosteroids or at the lowest tolerable corticosteroid dose.**

**BEST PRACTICE ADVICE 7:** **All adult patients with IBD should be evaluated for latent hepatitis B infection. Patients who have previously completed a full hepatitis B vaccine series but are not seroprotected (hepatitis B surface antibody [anti-HBs] <10 mIU/mL) should receive a single challenge dose of hepatitis B vaccine; Four to 8 weeks after this challenge dose, their anti-HBs levels should be measured to evaluate for an amnestic response. An amnestic response, indicated by an anti-HBs level ≥10 mIU/mL (seroprotection), suggests immunologic memory, and no further doses are needed. If no amnestic response is observed, the patient should complete a second full 2- or 3-dose series of hepatitis B vaccination.**

**BEST PRACTICE ADVICE 8:** **All adult patients with IBD should receive an annual inactivated influenza vaccine. Patients receiving anti-tumor necrosis factor monotherapy or who have undergone a solid organ transplant recipients can benefit from a high-dose influenza vaccine. Adults 65 years of age and older should receive a high-dose, recombinant, or adjuvanted influenza vaccine. Live attenuated intranasal vaccines should be avoided.**

**BEST PRACTICE ADVICE 9:** **All adult patients with IBD 19 to 64 years of age should receive an initial pneumococcal vaccine, with an subsequent second pneumococcal vaccine administered at 65 years of age and older.**

**BEST PRACTICE ADVICE 10:** **All adult patients with IBD who are 60 years of age and older should receive a respiratory syncytial virus vaccine. There is no preference for any of the available respiratory syncytial virus vaccines.**

**BEST PRACTICE ADVICE 11:** **All adult patients 19 years of age and older receiving immune-modifying therapies, or with plans to initiate immune-modifying therapies, should receive a recombinant herpes zoster vaccine series, regardless of their prior varicella vaccination status.**

**BEST PRACTICE ADVICE 12:** **Bone densitometry should be considered in patients with IBD, regardless of age, when risk factors for osteopenia and osteoporosis are present. These risk factors include low body mass index (<20 kg/m$^2$), >3 months of cumulative corticosteroid exposure, current smoking, postmenopausal status, or hypogonadism. In the absence of other factors, bone densitometry should be considered for postmenopausal women and men 65 years or older.**

**BEST PRACTICE ADVICE 13:** **All adult patients with IBD should be screened for depression and anxiety annually. Patients who screen positive for depression or anxiety should be referred to the appropriate specialist, be it their primary care physician or a mental health specialist.**

## Introduction

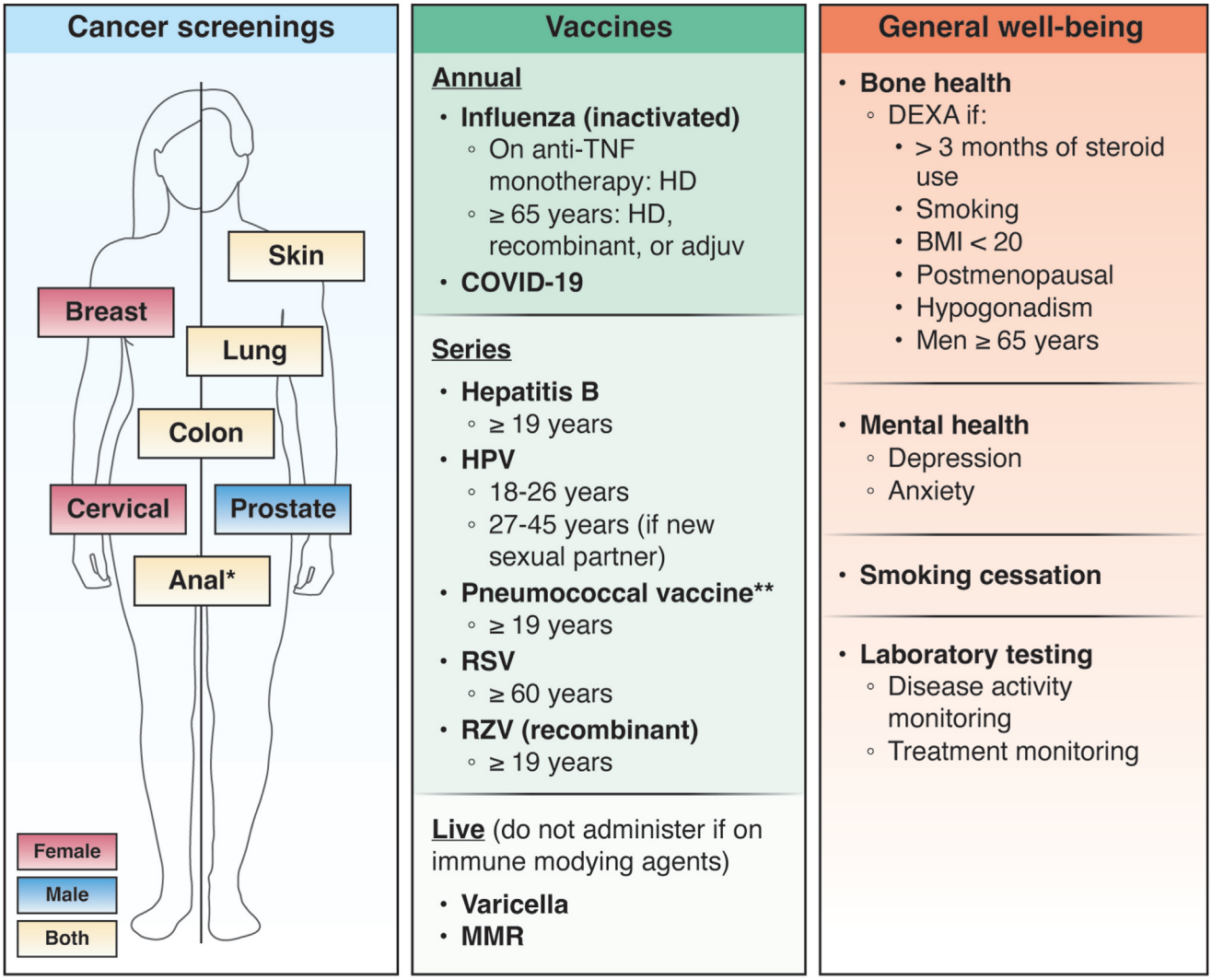
Advances in the treatment of inflammatory bowel disease (IBD) with the use of novel biologic agents and small molecules have enhanced treatment response and overall health-related quality of life. The use of these agents is associated with increased rates of clinical remission and mucosal healing; however, in some cases, they are also associated with an increased risk of serious and opportunistic infections.[1] Many of the serious infections, defined as those requiring hospitalization, may be preventable with routine vaccination.[2] Furthermore, patients with inflammatory bowel disease (IBD) are at increased risk for certain cancers due to their disease state or immune-modifying therapy. Therefore, health maintenance is a crucial aspect

in the treatment of patients with IBD. This review focuses on providing best practice advice on noncolorectal cancer screening and vaccination in patients with IBD (Figure 1). Also, general advice focusing on a patient's general well-being, including bone health and mental health, are included. All patients with IBD should be counseled to stop smoking and also be advised to remain up to date with their disease- and therapy-related monitoring labs.

Best Practice Advice 1: All adult patients with IBD should receive age-appropriate cancer screening.

Available evidence pertaining to when and how to screen for a specific cancer is constantly reviewed by the U.S. Preventive Services Task Force (USPSTF), which provides updated guidelines for implementation. It is important to ensure that patients with IBD follow age-appropriate cancer screenings, including breast cancer screening for females and prostate cancer screening for males. Based on the USPSTF recommendations, starting at 40 years of age, average-risk women should have breast cancer screening every other year, while other societies advise screening every 1 to 2 years.[3] As for males, screening for prostate cancer should be individualized between 55 and 69 years of age, per the USPSTF.[4] The USPSTF also recommends lung cancer screening for high-risk adults between 50 and 80 years of age who have a 20-pack-year smoking history, those with active smoking, or those who quit within the past 15 years. Cervical cancer, skin cancer, and anal cancer are discussed in more detail in separate best practice advice.

Best Practice Advice 2: Adult women with IBD should follow age-appropriate screening for cervical dysplasia. Data are insufficient to determine whether patients




HD, high dose influenza vaccine; adjuv, adjuvanted influenza vaccine; HPV, human papilloma virus; RSV, respiratory synctial virus; RZV, recombinant zoster vaccine; MMR, measels mumps rubella

*Special attention: perianal Crohn's disease, anal stricture, HPV, HIV, and ano-receptive intercourse
**Refer to Figure 2

**Figure 1.** Healthcare maintenance checklist for patients with IBD.

receiving combined immunosuppression or thiopurines require more frequent screening. Shared decision making and individual risk stratification are encouraged.

For cervical cancer screening, per the USPSTF, women between 21 and 29 years of age should be screened every 3 years with cervical cytology, while women between 30 and 65 years of age should be screened with cervical cytology every 3 years, high-risk human papillomavirus (HPV) testing every 5 years, or cotesting every 5 years.[5] Women under 21 years of age and those over 65 years of age who have had adequate prior screening and are at low risk for cervical cancer do not require screening.[5] Also, women who have had a hysterectomy with cervix removal and who have had no history of high-grade lesions or cervical cancer do not require continued cervical cancer screening.[5]

Cervical cancer is caused by persistent infection with oncogenic HPV. Known factors associated with an increased risk of cervical cancer include cigarette smoking. The data regarding an increased risk of cervical dysplasia and cancer from simply having a diagnosis of IBD are conflicting, but select studies suggest an increased risk associated with the use of immunosuppressants. In a Dutch study, investigators examined adult women with IBD and available cervical records in a nationwide cytopathology database for the incidence rates of cervical intraepithelial neoplasia (CIN) 2+ in patients exposed to immune modulators and biologics.[6] In 1981 women, 99 (5%) developed CIN 2+ lesions during a median follow-up of 17.2 years. CIN 2+ risk increased per year of exposure to immunomodulators (hazard ratio [HR], 1.16; 95% confidence interval [CI], 1.08–1.25). In multivariable analysis, smoking and 5-year screening frequency were also risk factors for CIN 2+ detection. The authors concluded that cumulative exposure to immunomodulators as well as prolonged screening periods increase the risk for cervical lesions and that intensified screening was warranted, thus concluding that more intensive screening was warranted for these adult patients. Actually, this literature indicated the need for annual cervical cancer screening in women who have a history of chronic immunosuppression; however, recent data do not support this increased risk.[7] In a comprehensive meta-analysis by Mann et al[8] that identified 5 population-based studies, including 74,310 patients with IBD and 2,029,087 reference patients across 5 different countries, there was no statistically significant increased risk for cervical cancer in IBD patients compared with the general population (HR, 1.24; 95% CI, 0.94–1.63). This held true regardless of disease subtype or by medication use (anti-tumor necrosis factor or thiopurine). Interestingly, they did note a slightly elevated risk for low-grade cervical lesions in adult women with IBD (HR, 1.15; 95% CI, 1.04–1.28).[8]

The discrepancy highlights the need for nuanced, individualized risk assessment and screening strategies for adult women with IBD. Despite the conflicting data on cancer risk, HPV vaccination remains recommended for adult women 18 to 45 years of age, underscoring the importance of preventive measures in this adult population.

Best Practice Advice 3: All adult patients with IBD should follow skin cancer primary prevention practices by avoiding excessive exposure to the sun's ultraviolet radiation. Patients on immunomodulators, anti-tumor necrosis factor (anti-TNF) biologic agents, or small molecules should undergo a yearly total body skin exam (TBSE). Patients with any history of thiopurine use should continue with a yearly TBSE even after thiopurine cessation.

Patients with IBD are at an increased risk for the development of nonmelanoma skin cancers. As such, all patients are encouraged to practice primary skin cancer prevention strategies.[9] IBD-related therapies including immunomodulators, anti-TNF biologics, and small molecules further increase the risk of skin cancers (either melanoma and/or nonmelanoma skin cancers) so TBSE on a yearly basis should be advised.

Best Practice Advice 4: At every colonoscopy, a thorough perianal and anal examination should be performed. Special attention should be made to inspection of the anal canal of patients with perianal Crohn's disease, with anal stricture, HPV, with human immunodeficiency virus (HIV), and who engage in anoreceptive intercourse.

The majority of anal cancers are due to squamous cell carcinomas, and a recent meta-analysis showed that patients with IBD are at an increased risk for anal cancer, with an incidence rate of 10.2 per 100,000 person-years in ulcerative colitis and 7.7 per 100,000 person-years in Crohn's disease.[10] Incidence is further increased in patients with anal/perianal Crohn's disease (19.6 per 100,000 person-years).[10] Other risk factors include smoking and a persistent HPV infection, as seen in patients on chronic immunosuppression. Additional risk factors include having HIV, men who have sex with men, women with HPV-associated genital cancers, and solid organ recipients.[11] HPV infection is necessary but insufficient for the development of squamous intraepithelial neoplasia. For at-risk populations, screening constitutes discussion of the risks and assessment of symptoms such as anorectal bleeding, pain, or growths. There are a few screening tests available for anal cancer and anal high-grade squamous intraepithelial lesions, including the digital anal rectal exam, cytology, high-risk HPV testing with or without genotyping, or a combination of these, depending on a patient's risk factors.[11] If there are concerns for anal cancer, a digital anorectal examination is performed. Performance data for anal cytology in the non-HIV population are scarce and anal cytology is not yet utilized for routine screening.

Best Practice Advice 5: Gastroenterology clinicians should discuss age-appropriate vaccines with adult patients who have IBD and share responsibility with primary care providers for administering these vaccines. Patients with IBD should follow the adult immunization schedule recommended by the Centers for Disease

Control and Prevention (CDC) for all vaccines with the exception of live vaccines. Patients receiving immune-modifying agents should be counseled against receiving live vaccines. Immunization history to the 2 live pediatric vaccines, varicella and measles, mumps, and rubella (MMR) vaccine series, is presumptive evidence of immunity. All adults 18 to 26 years of age should receive the HPV vaccine series and those between 27 and 45 years of age should be vaccinated if they are likely to have a new sexual partner.

Patients with IBD are at an increased risk for infections as a consequence of their disease, and this risk may be amplified by certain immune-modifying therapies.[12,13] Many of these infections are vaccine-preventable diseases (VPDs). Previous studies have shown that patients with IBD have lower vaccine uptake than the general population; however, these rates have improved, but remain suboptimal.[14,15] Several factors contribute to the lower vaccine uptake among patients with IBD, including primary care providers' insufficient awareness of the necessity of these vaccines, patients' apprehensions regarding vaccine safety, and ambiguity regarding which healthcare provider, whether primary care provider or gastroenterologist, is responsible for advising and administering age-appropriate vaccines.[16] To mitigate the morbidity and mortality associated with VPDs, it is imperative for gastroenterologists to encourage age-appropriate vaccines and share the responsibility of administering these vaccines with primary care providers. Implementing vaccination programs in outpatient gastroenterology practices is crucial.[17] The first step in this process is identifying a vaccine champion (physician, advanced practice provider, or pharmacist) who will stay up to date with patient vaccinations and disseminate information and optimal workflows throughout the practice.[18] While patients with IBD typically follow the adult immunization schedule, optimal immunization tailored to their heightened risk for certain VPDs is essential.[19] Patients receiving immune-modifying agents should avoid live vaccines, as outlined in Table 1.

The varicella and MMR vaccine series are 2 live vaccines typically given to children.[19] Recent measles outbreaks have prompted concerns among healthcare providers and patients regarding the immune status of immunosuppressed patients with IBD.[20] Live pediatric vaccines elicit immune responses similar to those of natural infections, providing immunity to nearly all recipients.[21] Although vaccine-induced antibody concentrations are typically lower than those of primary infections, they still offer sustained protection.[22,23] However, commercially available serologic tests may inadequately measure vaccine-induced antibody concentrations, with a reported 34% false negative rate when evaluating varicella vaccine-induced antibody concentrations compared with more sensitive assays by researchers from the CDC.[24] Additionally, systemic immunosuppression appeared to have no significant impact on sustained antibody concentrations against MMR in adults with IBD who completed the vaccine series approximately 17 years earlier compared with healthy control subjects.[25] Consequently, it is advised to follow the Advisory Committee on Immunization Practices (ACIP) guidance, considering appropriate immunization history as acceptable evidence for immunity against MMR and varicella. Serologic screening for presumed immunity to MMR or varicella is discouraged because of the potential for false negative results per the ACIP.

Patients with IBD should not be discouraged from traveling but should be referred for a pretravel consultation to address potential risks. During these consultations, preventive measures against vector-borne diseases such as yellow fever, dengue, and malaria can be discussed, including vaccination when appropriate, the use of proper insect repellents, protective clothing, and bed nets. While yellow fever vaccine can be safely given to patients with IBD not on immunosuppression, those on immune-modifying therapy should consider modifying travel plans to avoid yellow fever endemic areas. Other inactivated vaccines, such as injectable typhoid, are safe for all patients with IBD. The consultation should also include education about managing IBD during travel and strategies to minimize travel-associated health risks.[26]

Best Practice Advice 6: Inactivated vaccines are safe in patients with IBD, and their administration is not associated with exacerbation of IBD activity. We suggest that patients receive vaccines at the earliest opportunity and preferably be off corticosteroids or at the lowest tolerable corticosteroid dose.

Multiple studies have evaluated the safety of inactivated vaccines (eg, influenza, pneumococcal, hepatitis B) and have found that even vaccines with adjuvants (eg, recombinant herpes zoster [HZ]) are safe and not associated with exacerbation of IBD activity.[27,28] A meta-analysis found that postvaccination adverse events are mainly local or mildly systemic and do not significantly differ from those seen in the general population.[27] Furthermore, inactivated messenger RNA (mRNA) COVID-19 primary vaccine series or boosters have not been associated with disease flares or increased adverse events compared with the general population.[29,30]

We suggest that patients receive appropriate boosters or catch-up vaccines during any in-person clinic visit. The most opportune times to provide these vaccines are during the transition of care to a new gastroenterology provider or during periods of remission at routine visits. Whenever feasible, vaccines should be administered before the commencement of immune-modifying therapy, as certain agents may diminish the immune response to vaccines; however, vaccination should not delay the initiation of appropriate immune-modifying therapy. Vaccines should preferably be administered when not on corticosteroids or at the lowest dose, as concomitant corticosteroids have been associated with lower vaccine-induced humoral immune responses for

**Table 1.** Adult Immunization Schedule for Patients with Inflammatory Bowel Disease

| Vaccine | Patient Group | Schedule |
|---|---|---|
| COVID-19 (Moderna, Novavax, Pfizer) | All adults. | Follow current ACIP recommendations for the general population. |
| SD quadrivalent influenza vaccine, inactivated | All adult 18–64 y of age. | Annually |
| HD quadrivalent influenza vaccine, inactivated: Flublok (recombinant), Fluad (adjuvanted) | All adults ≥65 y of age.<br>All adults on anti-TNF monotherapy or with a concomitant solid organ transplant. | Annually |
| Pneumococcal vaccine (PCV15, PCV20, PCV21, or PPSV23) | All adults ≥19 y of age. | See Figure 2. |
| Recombinant herpes zoster vaccine, adjuvanted nonlive: Shingrix (GlaxoSmithKline) | All adults ≥19 y of age. | 2-dose series.<br>For patients not on immune-modifying therapy: 2-dose series 8–12 wk apart.<br>For patients on immune-modifying therapy: 2-dose series 4–8 wk apart. |
| Human papillomavirus: Gardasil 9 (Merck) | All adults ages 18–26 y of age.<br>Adults 27–45 y of age who are likely to have a new sexual partner. | 3-dose series: at 0, 1–2, and 6 mo. |
| RSV<br>Recombinant vaccine: Abrysvo (Pfizer)<br>Adjuvanted recombinant vaccine: Arexvy (GlaxoSmithKline)<br>Messenger RNA vaccine: mRESVIA (Moderna) | Adults with IBD ≥75 y of age.<br>Adults with IBD 60–74 y of age with certain medical conditions or risk factors for severe RSV disease.<br>Pregnant persons during 32–36 weeks' gestation (September 1 to January 31) only Abrysvo. | Single dose. |
| HepB | Universal vaccination is recommended for all adults 19–59 y of age.<br>All adults starting immune-modifying therapy. | HEPLISAV-B: Two-dose series (HepB-CpG) at 0 and 1 mo.<br>ENGERIX-B or Recombivax HB: 3-dose series at 0, 1, and 6 mo.<br>Twinrix (HepA-HepB): 3-dose series at 0, 1, and 6 mo.<br>PreHevbrio: 3 dose series at 0, 1, and 6 mo. |
| TD<br>Tdap<br>HepA<br>Meningococcal ACWY; meningococcal B | All adults | Follow recommendations from the ACIP for the general population. |
| MMR (live vaccine) | Patients not immune to MMR.<br>If immune status is uncertain, obtain immunization history.<br>Serology to determine seroprotection status is not recommended with appropriate immunization history. | 2-dose series, at least 4 wk apart. |
| Varicella 2-dose series (live vaccine) | Documentation of 2 doses or varicella vaccine.[2]<br>If immune status is uncertain, obtain immunization history. Serology to determine seroprotection status is not recommended with appropriate immunization history. | All patients who are not immune should receive a 2-dose series (Figure 1). |

ACIP, Advisory Committee on Immunization Practices; HD, high dose; HepA, hepatitis A; HepB, hepatitis B; MMR, measles, mumps, and rubella; RSV, respiratory syncytial virus; SD, standard dose; TD, tetanus and diphtheria; Tdap, tetanus, diphtheria, and pertussis; TNF, tumor necrosis factor.

certain vaccines. Nevertheless, annual seasonal vaccinations such as influenza or COVID-19 boosters should be offered to patients regardless of their treatment regimen, even if they are receiving high doses (HDs) of corticosteroids. Moreover, as previous studies have shown that immune responses to influenza and COVID-19 vaccines are not influenced by the timing of biologic therapy administration, vaccines should be provided irrespective of the biologic dosing schedule.[31,32]

Best Practice Advice 7: All adult patients with IBD should be evaluated for latent hepatitis B infection. Patients who have previously completed a full hepatitis B vaccine series but are not seroprotected (hepatitis B surface antibody [anti-HBs] $<$ 10 mIU/mL) should receive a single challenge dose of hepatitis B vaccine. Four to 8 weeks after this challenge dose, their anti-HBs levels should be measured to evaluate for an amnestic response; An amnestic response, indicated by an anti-HBs level $\geq$10 mIU/mL (seroprotection), suggests immunologic memory, and no further doses are needed. If no amnestic response is observed, the patient should complete a second full 2- or 3-dose series of hepatitis B vaccination.

Patients with IBD are at an increased risk of hepatitis B virus (HBV) reactivation, particularly when receiving immunosuppressive therapy. This reactivation can lead to several complications including death in approximately 5% of patients.[33,34] Given this risk, patients with IBD should be screened for HBV infection, and those not previously vaccinated should receive a HBV vaccination series. Seroprotection against hepatitis B can be determined by measuring serum hepatitis B surface antibody (anti-HBs) levels. Vaccinated patients achieving an anti-HBs level $\geq$10 mIU/mL are considered seroprotected and clinically protected against hepatitis B infections.[35] For previously immunized vaccinated individuals with anti-HBs $<$10 mIU/mL, a challenge dose should be given to determine their seroprotection status. Given the higher seroconversion rates from HEPLISAV-B, it should be considered a preferred option rather, than the aluminum 3-dose series ENGERIX-B. Patients who are not seroprotected after the challenge dose should receive a new hepatitis B vaccination series, preferably with HEPLISAV-B, and be evaluated if they achieved seroprotection 4 weeks after finishing the series.

Primary hepatitis B vaccine responders remained protected, even if the anti-HBs wanes to $<$10 mIU/mL over time, as immunological memory persists in memory B and T cells that can still mount a humoral and cell-mediated immune response upon encountering HBV.[36,37] This phenomenon is known as an anamnestic response and is considered to be a reliable measure of preserved immunological memory. Studies in immunocompetent individuals have shown that the majority of responders to hepatitis B vaccination who are found to have anti-HBs $<$10 mIU/mL remain seroprotected when given a challenge dose.[38,39] Providing a challenge dose is different from a booster dose because its goal is to elicit an anamnestic response and not to boost the immune response to maintain seroprotection, as is needed with other inactivated vaccines. A hepatitis B challenge dose to elicit an anamnestic response is recommended by numerous public health agencies such as CDC and by the World Health Organization to determine true seroprotection status.[35,40–43] Previous studies in previously vaccinated patients with IBD have shown low rates of sustained seroprotection (anti-HBs $<$10 mIU/mL), but these studies failed to provide a hepatitis B challenge dose. A recent study in which a challenge dose was provided to previously vaccinated patients with an anti-HBs $<$10 mIU/mL found sustained seroproteciton rates $>$90%.[44]

Patients with IBD have been found to have lower seroconversion rates to the 3-dose recombinant series of aluminum hydroxide, especially those on anti-TNF therapy or those older than 40 years of age. HEPLISAV-B (HepB-CpG) is a 2-dose adjuvanted recombinant hepatitis B vaccine series approved by the U.S. Food and Drug Administration in 2017, with a new cytosine phosphoguanine adjuvant that is more immunogenic in the general adult population and in those with chronic kidney disease or diabetes mellitus.[17,18] Studies evaluating the immunogenicity of HepB-CpG have shown higher rates of seroconversion compared with historical rates, and that primary nonresponders to the 2 dose series may benefit from a third dose of the vaccine.[45,46]

While hepatitis B is a significant concern, other viral infections also pose substantial risks to patients with IBD. Hepatitis C infection may result in chronic liver disease and is a major source of morbidity and mortality.[47] Similarly, untreated HIV infection can lead to significant health complications. The estimated prevalence of HIV infection among persons 13 years of age and older in the United States is 0.4%.[48] Timely treatment of both hepatitis C and HIV can significantly reduce their associated morbidity. Recognizing the importance of early detection and treatment, the CDC recommends universal screening for HIV in all adults 18 to 64 years of age and in all pregnant women with unknown HIV status.[48] Likewise, they recommend universal screening for hepatitis C in all adults 18 years of age and older at least once in a lifetime, and in all pregnant women during each pregnancy.[47]

Best Practice Advice 8: All adult patients with IBD should receive an annual inactivated influenza vaccine. Patients receiving anti-TNF monotherapy or who have undergone a solid organ transplant recipients can benefit from an HD influenza vaccine. Adults 65 years of age and older should receive an HD, recombinant, or adjuvanted influenza vaccine. Live attenuated intranasal vaccines should be avoided.

Influenza virus infection results in respiratory illnesses, and most people recover without serious complications. The risk is further increased in older adults $\geq$65 years of age, those with certain chronic medical conditions, pregnant women, and immunosuppressed patients. All of those patients also have a risk of severe

illness and complications from influenza infections.[49,50] Influenza vaccination provides protection against influenza and its potential complications.[51] The ACIP recommends annual influenza vaccination for all persons >6 months of age who do not have contraindications.[51] Older adults are more likely to have a lower humoral immune response to standard-dose (SD) influenza vaccines.[51] Three different types of influenza vaccine are approved for older adults: HD influenza vaccine, recombinant influenza, and adjuvanted influenza vaccine.[51] These vaccines are associated with higher effectiveness against influenza and are more likely to induce higher antibody concentrations than SD vaccines. In solid organ transplant recipients, the HD influenza vaccine is also associated with higher antibody concentrations compared with the SD vaccine.[52]

Patients with IBD are at an increased risk of influenza compared with non-IBD control subjects and are more likely to have complications from influenza, resulting in hospitalization or pneumonia, and as such, influenza has been identified as one of the most common VPDs leading to serious infections among patients with IBD.[53] Patients on systemic corticosteroids are at a further increased risk of influenza.[49] The vaccine-induced humoral immune response triggered by the influenza vaccine may be influenced by a patient's treatment regimen, similar to other inactivated vaccines. Patients receiving anti-TNF monotherapy or combination therapy (anti-TNF and immunomodulator) might exhibit a diminished immune response compared with those solely on immunomodulators.[54–56] Various strategies have been explored to enhance influenza vaccine responses in patients receiving anti-TNF therapy and whether providing a booster dose or administering the vaccine concurrently with anti-TNF agent or midway through the dosing interval have not improved vaccine response.[31,56,57] In a randomized controlled trial comparing HD vs SD influenza vaccine in patients with IBD on anti-TNF monotherapy, those who received the HD influenza vaccine exhibited higher postimmunization antibody levels.[58] Live attenuated intranasal vaccines should be avoided in patients receiving immune-modifying therapy.

Best Practice Advice 9: All adult patients with IBD 19 to 64 years of age should receive an initial pneumococcal vaccine, with a subsequent vaccine administered at 65 years of age and older.

*Streptococcous pneumonia* is a common cause of otitis media, sinusitis, and community-acquired pneumonia in addition to causing more severe infections that require hospitalization such as sepsis and meningitis. Pneumococcal pneumonia is the most common cause of community-acquired pneumonia. Patients with IBD are at increased risk for pneumoccal pneumonia compared with age-matched control subjects.[59] Additionally, the risk for invasive pneumoccal disease starts years prior to their diagnosis of IBD.[60] The risk is increased in patients treated with thiopurines, anti-TNF therapy, and/or corticosteroids. A study from the U.S. Department of Veterans Affairs showed that patients on immune-modifying therapies are also at increased risk for hospitalization.[61] Moreover, pneumococcal pneumonia has been identified as the third most common VPD leading to serious infections among patients with IBD.[53]

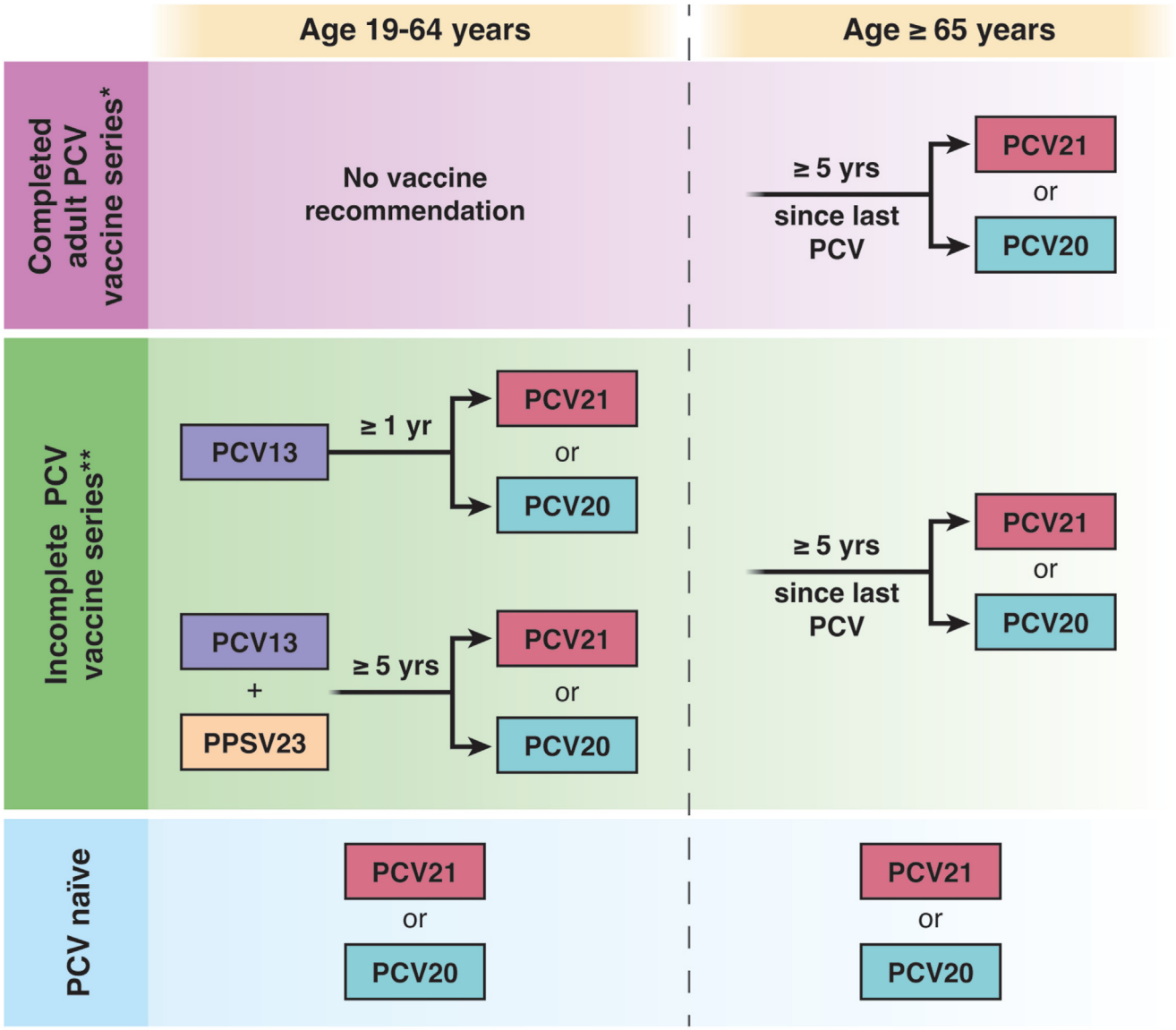
Previous studies have evaluated the immunogenicity of PCV13 and/or PPSV23 and have shown that, similar to the response to influenza vaccine, patients on anti-TNF monotherapy or combination therapy may have a blunted vaccine response to pneumococcal vaccines.[62] Vaccination with a pneumococcal vaccine (PCV13 or/PPSV23) is associated with decreased risk of severe pneumococcal disease.[63] Since 2021, 3 new pneumococcal vaccines (PCV15, PCV20, and PCV21) with broader serotype spectrum are currently recommended by the ACIP (Figure 2). Providing the single-dose PCV20 or PCV21 is preferred to the 2-dose PCV15 followed by PPSV23.

Best Practice Advice 10: All adult patients with IBD who are 60 years of age and older should receive an respiratory syncytial virus (RSV) vaccine. There is no preference for any of the available RSV vaccines.

RSV infection can often lead to significant health risks, especially among vulnerable populations such as young infants, older adults, and immunosuppressed individuals. Older adults (≥60 years of age) are at increased risk for serious complications of RSV such as respiratory failure and pneumonia, with mortality rates ranging between 2% and 5%.[64] A recent study found that adult patients with IBD have 30% higher risk of hospitalization due to RSV compared with non-IBD control subjects (adjusted odds ratio, 1.30; 95% CI, 1.06–1.59), with those on systemic corticosteroids being at the highest risk.[65] Currently, there are 3 RSV vaccines approved for adults 60 years and older. RSVPreF3 OA (Arexvy) from GlaxoSmithKline, RSVpreF (Abrysvo) from Pfizer, and mRESVIA (mRNA-1345) have been found to be safe and efficacious at preventing RSV in older adults in the general population.[66–68] The ACIP recommends that adults 60 years of age and older who are at increased risk of severe RSV infection and all adults 75 years of age and older receive a single dose of RSV vaccine. The ACIP also recommends RSV vaccination (Abrysvo) for pregnant individuals at 32 to 36 weeks' gestation, using seasonal administration (typically September to January in most of the United States) to protect infants under 6 months from RSV-associated lower respiratory tract infections.

Best Practice Advice 11: All adult patients 19 years of age and older receiving immune-modifying therapies, or with plans to initiate immune-modifying therapies, should receive a recombinant herpes zoster vaccine (RZV) vaccine series, regardless of their prior varicella vaccination status.

Patients with IBD are known to be at increased risk of HZ, irrespective of their immune-modifying therapy compared with the general population.[69] Certain immune-modifying therapies such as thiopurines, anti-




*Patient has completed one of the following vaccine regimens: PCV13 and two doses of PPSV23, PCV15 and PPSV23, PCV 20, or PCV 21

**Unknown vaccine history, PCV7 at any age, PPSV23 only, PCV 13 only, PCV 13 and one dose of PPSV23

**Figure 2.** Proposed pneumococcal vaccine (PCV) regimen for patients with IBD.

TNF agents, Janus kinase inhibitors, or corticosteroids amplify the risk of HZ in patients with IBD.[69,70] The RZV 2-dose series is recommended by the ACIP for all immunocompetent adults 50 years of age and older and adults 19 years of age and older who are immunosuppressed or at increased risk for HZ because of disease or therapy.[71] The RZV vaccine series has been found to be safe and not associated with disease flares.[28] Furthermore, an economic analysis showed that providing the RZV series is cost-effective for all patients with IBD 18 years of age and older.[72]

Best Practice Advice 12: Bone densitometry should be considered in patients with IBD, regardless of age, when risk factors for osteopenia and osteoporosis are present. These risk factors include low body mass index (<20 kg/m$^2$), >3 months of cumulative corticosteroid exposure, current smoking, postmenopausal status, or hypogonadism. In the absence of other factors, bone densitometry should be considered for postmenopausal women and men 65 years of age or older.

Bone densitometry should be considered in patients with IBD regardless of age depending on their risk factors for osteopenia and osteoporosis. Common risk factors include prolonged corticosteroid use, hypovitaminosis D, chronic inflammation, poor calcium intake, and cigarette smoking. It has been estimated that 14% to 42% of persons with IBD have osteoporosis, though the precise prevalence is unknown. Focused bone mineral density (BMD) screening is advocated for persons who have conventional risk factors for low BMD, specifically those individuals who

have identifiable medical conditions or use of medications (corticosteroids, parenteral nutrition) that are known to influence BMD. Screening is important because treatments can reverse bone loss and help prevent fracture.[73] If patients are found to have osteopenia and osteoporosis, further management with the primary care team or endocrinology should be encouraged. If the BMD is normal, timing of repeat evaluation will depend on the results of the initial BMD as well as patient risk factors such as the need for steroids, smoking status, weight loss, and low body mass index, but no more frequently than annually.

Best Practice Advice 13: All adult patients with IBD should be screened for depression and anxiety annually. Patients who screen positive for depression or anxiety should be referred to the appropriate specialist, be it their primary care physician or a mental health specialist.

Patients with IBD should be screened for depression and anxiety given its prevalence among this patient population.[74] The prevalence of depression in adults with IBD over 65 years of age has been found to be 22.6%. Those who were depressed had higher disease activity scores, lower quality-of-life scores, and reduced medication adherence (odds ratio, 2.18; 95% CI, 1.04–4.57). A systematic review found that anxiety is present in 19% of patients with IBD vs 9.6% of the background population and depression was found in 21.2% with IBD vs 13.4% in non-IBD control subjects. Both anxiety and depression were present in patients with inactive and active disease.[75] Screening is important because treatments are well tolerated and can change disease outcomes. Appropriate referral to crisis mental health is crucial if patients are suspected to have concerns for suicidality.[76] Several questionnaires exist for screening anxiety and depression. The 7-item Generalized Anxiety and Disorder Scale-7, the Beck Depression Inventory, and the Patient Health Questionnaire are of the most commonly used instruments. If the Patient Health Questionnaire-9 is used, this will also screen for suicide. Centers who do not have access to crisis mental health resources use the Patient Health Questionnaire-8 instead of the Patient Health Questionnaire-9.

## Conclusion

Comprehensive care for patients with IBD extends beyond managing intestinal symptoms. It is crucial to address overall healthcare maintenance, ensuring that patients are current with vaccines, cancer screenings, and other wellness measures. Gastroenterologists should stay well informed about VPDs and take responsibility for advising and administering appropriate vaccines to their patients. Additionally, they should encourage age-appropriate cancer screenings, particularly for those on immunosuppressive medications, as these measures can significantly contribute to associated comorbidities. To facilitate this holistic approach, the use of clinic-ready checklists (Figure 1) is highly encouraged. These tools can markedly improve adherence to best practice advice and should be widely implemented in clinical settings.

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