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INVITED EDITORIAL

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Editorial: COVID-19 vaccines are safe and effective in patients with inflammatory bowel disease—but many unanswered questions remain

The rapid development, testing and regulatory approval of vaccines against SARS-CoV-2 were unprecedented, saving countless lives. However, people who are immunocompromised were excluded from the initial randomised trials despite concerns that they were at increased risk of severe COVID-19. This paradox and consequent lack of evidence resulted in recommendations for COVID-19 vaccines for inflammatory bowel disease (IBD) patients that were extrapolated from other populations.[1,3] The scientific community moved quickly to address vaccine safety and effectiveness with prospective observational research and routinely collected health data.

In a recent issue of AP&T, Bhurwal et al.[4] reported the effectiveness and safety of COVID-19 vaccines in IBD patients based on the systematic review of the literature to December 25, 2021. They included 21 non-interventional studies. Two doses of a COVID-19 vaccine (mRNA or adenovirus-vector) resulted in >90% seroconversion, irrespective of IBD therapy. However, antibody seroconversion may not reflect symptomatic or severe COVID-19 and therefore they assessed the risk of breakthrough infections. Three studies reported a similar risk of breakthrough infections after two doses in vaccinated individuals with and without IBD, and one study reported a lower risk of breakthrough infection in vaccinated compared to unvaccinated IBD patients. There was a high degree of statistical heterogeneity with meta-analysis, likely due to differences in study design and composition of control groups. The risk of severe adverse events in vaccinated IBD patients was reported to be 2.2%, however, this is likely an overestimate. Studies reporting adverse events did not assess risk compared to a control population or natural SARS-CoV-2 infection and included adverse events since proven to be unrelated to COVID-19 vaccines.

One source of between-study heterogeneity included the time at which seroconversion was assessed. We have since learned from seminal studies such as CLARITY-IBD[5,6] that patients with IBD on immunosuppressive medications (especially steroids, anti-TNF biologics and immunomodulators) are less likely to seroconvert and have a more rapid decay of antibody titres. Newer prospective serological studies have demonstrated a significant rise in antibody titres after a third vaccine dose,[7] and most vaccinologists now consider a two-dose regimen to be inadequate in the vaccine-evasive Omicron (B.1.1.529) era. Bhurwal et al.[4] did not assess vaccine effectiveness against Omicron. The need for additional doses remains an open question, although at the time of this writing, the CDC has recommended a fourth vaccine dose in people who were immunocompromised or over 50 years old.[8]

There is now little doubt that vaccines are safe and effective against severe COVID-19 in patients with IBD, and vaccine uptake has been high.[9,10] The systematic review from Bhurwal et al.[4] effectively synthesises knowledge accumulated to the end of 2021. However, many unanswered questions remain, including the durability of immunity, the association between dose and type of immunosuppression and the risk of breakthrough infection, and the effectiveness and frequency of additional doses to maintain immunity in IBD patients. New questions will undoubtedly arise as the pandemic continues. We are hopeful that many of these questions can be answered by well-designed prospective observational studies or research using routinely collected health data.

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AUTHOR CONTRIBUTIONS

Eric Ian Benchimol: Conceptualization (lead); project administration (lead); writing – original draft (lead); writing – review and editing (lead). **M Ellen Kuenzig:** Conceptualization (supporting); writing – review and editing (supporting).

LINKED CONTENT

This article is linked to Bhurwal et al papers. To view these articles, visit https://doi.org/10.1111/apt.16913 and https://doi.org/10.1111/apt.16935

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