Optimal inflammatory bowel disease management during the global coronavirus disease 2019 pandemic

Sara El Ouali[a,b], *David T. Rubin*[c], *Benjamin L. Cohen*[b], *Miguel D. Regueiro*[b], *and Florian Rieder*[b,d]

Purpose of review
This review aims to summarize the current evidence regarding the risks and implications of coronavirus disease 2019 (COVID-19) in patients with inflammatory bowel disease (IBD) and discuss optimal management of IBD during this pandemic.

Recent findings
Patients with IBD are not at increased risk of COVID-19 but several risk factors for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2 infection) have been identified, such as active IBD, obesity, and corticosteroid use. COVID-19 outcomes are similar among patients with IBD and the overall population. Although biologics have not been shown to increase the risk of severe COVID-19 complications, several risk factors have been associated with negative COVID-19 outcomes in patients with IBD, including older age, obesity, the presence of comorbidities, active disease, and corticosteroid use. IBD therapy should, therefore, be continued with the aim of attaining or maintaining remission, except for corticosteroids, which should be held or reduced to the minimal effective dose. Although it has been recommended that immunosuppressive therapy be held during a case of COVID-19, the half-lives of these drugs and data on the timing of restarting therapy limit the strength of these recommendations. We recommend COVID-19 vaccination for IBD patients whenever available, as benefits to the individual and to society outweigh the risks.

Summary
As our understanding of SARS-CoV-2 and COVID-19 continues to evolve, we are learning more about its impact in patients with IBD and how to better manage patients in this setting. Managing IBD during this pandemic has also highlighted the importance of restructuring services in order to adapt to current and potential future outbreaks. The COVID-19 pandemic has transformed IBD care through the expansion of telemedicine and development of novel approaches to remote monitoring.

Keywords
coronavirus disease-2019, Crohn's disease, inflammatory bowel disease, severe acute respiratory syndrome coronavirus 2, ulcerative colitis

INTRODUCTION

As the world continues to grapple with the coronavirus disease 2019 (COVID-19) pandemic, our understanding of the disease and its impact on our patients with inflammatory bowel disease (IBD) is evolving. The pandemic has had a considerable impact on patients with IBD and their care [1]. Beyond the important influence on psychosocial aspects of patients [2], many other parts of their care have been affected [1]. In addition to a significantly reduced access to endoscopy, surgery, and laboratory testing [1,3], there have been extensive changes in the delivery of care in order to adapt to the pandemic through increased use of telemedicine and remote monitoring [4]. In this review, we provide an up-to-date summary of current evidence regarding the risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection in

[a]Digestive Diseases Institute, Cleveland Clinic Abu Dhabi, United Arab Emirates, [b]Department of Gastroenterology, Hepatology & Nutrition, Digestive Diseases and Surgery Institute, Cleveland Clinic Foundation, Cleveland, Ohio, [c]University of Chicago Medicine Inflammatory Bowel Disease Center, Chicago, Illinois and [d]Department of Inflammation and Immunity, Lerner Research Institute, Cleveland Clinic Foundation, Cleveland, Ohio, USA

Correspondence to Sara El Ouali, Digestive Disease Institute, Cleveland Clinic Abu Dhabi, PO Box 112412 – Abu Dhabi, UAE.
Tel: +971 25019000 x42659;
e-mail: elouals2@clevelandclinicabudhabi.ae

Curr Opin Gastroenterol 2021, 36:000–000
DOI:10.1097/MOG.0000000000000741

KEY POINTS

- Patients with IBD are not at increased risk of SARS-CoV-2 infection overall.
- Moderate-to-severe disease activity, obesity, and corticosteroids have been associated with an increased risk of COVID-19 infection.
- Although patients with IBD are not at increased risk of severe COVID-19, several factors, such as older age, comorbidities, active IBD, and corticosteroid use have been associated with worse COVID-19 outcomes.
- Nonlive COVID-19 vaccines should be offered to patients with IBD, regardless of immunosuppressant use.

patients with IBD and discuss optimal management of IBD during a pandemic.

RISK OF SEVERE ACUTE RESPIRATORY SYNDROME CORONAVIRUS 2 INFECTION IN INFLAMMATORY BOWEL DISEASE

On the basis of available evidence to date, patients with IBD are not at increased risk of SARS-CoV-2 infection. Several initial studies from North America, Asia, and Europe have found a similar incidence of COVID-19 among patients with IBD compared with the general population [5–9], and this remains the case in most recent literature [10]. In a large nationwide Dutch cohort study, the incidence of COVID-19 among patients with IBD and the general Dutch population were found to be similar [10]. In a Spanish cohort study, the rates of infection among patients with IBD were actually lower than in the general population [6].

Although SARS-CoV-2 infection rates are not increased in patients with IBD, several risk factors for infection and specifically development of COVID-19 have been identified in patients with IBD. Obesity, corticosteroids and moderate-to-severe disease activity were found to be associated with an increased risk of COVID-19 [8,11]. It is important to note that thiopurines and biologics have not been associated with an increased risk of SARS-CoV-2 infection [11,12].

CLINICAL MANIFESTATIONS OF CORONAVIRUS DISEASE 2019 IN INFLAMMATORY BOWEL DISEASE

In a systematic review of 23 studies assessing COVID-19 manifestations in 1028 patients with IBD, the most common symptoms were fever, cough, and diarrhea, which were present in 48.3, 46.5, and 20.5% of patients, respectively [13]. Although gastrointestinal symptoms have been commonly described in COVID-19 [14], patients with IBD appear to present with gastrointestinal symptoms more frequently than the general (non-IBD) population [13]. Compared with non-IBD-matched controls, not surprisingly, patients with IBD reported more frequent abdominal pain and diarrhea with COVID-19 [8]. In a Spanish case series, diarrhea was the predominant presenting symptom in 42% of patients with IBD who developed COVID-19 [6]. Importantly for clinical practice, SARS-CoV-2 infection may mimic relapses of IBD in these patients [15]. Patients with IBD who developed COVID-19 had an increased risk of abdominal pain, diarrhea, abnormal inflammatory markers (C-reactive protein and fecal calprotectin), as well as active disease on endoscopy as compared with noninfected IBD patients [8]. SARS-CoV-2 infection should, therefore, be considered in any patient presenting with gastrointestinal symptoms, especially if other typical manifestations of COVID-19 are also present, such as anosmia, dysgeusia, fever, or respiratory symptoms [15], and this is particularly true in patients with IBD.

Interestingly, de novo IBD has also been described in case reports in the setting of COVID-19. A young, otherwise healthy woman developed chronic bloody diarrhea after documented COVID-19 infection. A colonoscopy performed 5 months after COVID-19 showed left-sided ulcerative colitis and biopsies showed typical features of IBD [16]. Distinguishing between COVID-19 and new or relapsing IBD can, thus be challenging and requires a thorough clinical evaluation including a careful history, stool studies, endoscopic, and histopathologic assessment as well as SARS-CoV-2 testing [15]. Although fecal calprotectin can be used, it may not help differentiate between a relapse of IBD and COVID-19. COVID-19 patients presenting with diarrhea do have increased fecal calprotectin levels compared with COVID-19 patients without diarrhea [17] but this is usually in a range of 100–200 μg/g rather than the much higher levels that may be seen in actively inflamed IBD.

CORONAVIRUS DISEASE 2019 OUTCOMES IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

Multiple studies have evaluated the impact of COVID-19 and its complications in patients with IBD and have found similar outcomes compared with the general population [15]. Studies from the United States [7,8], Spain [6], France [9], and Italy [9]

have all shown comparable findings. In a large IBD cohort study of 34 763 patients, 20% of patients who developed COVID-19 had a severe course, as defined by the need for ICU admission, mechanical ventilation, or death [10]. However, rates of COVID-19 complications were found to be similar to a reference population. The presence of one or more comorbidities was found to be independently associated with hospitalization [10]. In a systematic review, 30.6% of patients with IBD and COVID-19 required hospitalization, 11.4% required admission to an ICU, and 3.8% died. These rates were again found to be similar to the general population [13]. The Surveillance Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease (SECURE-IBD) registry has greatly contributed to our current understanding of COVID-19 outcomes in IBD [18]. This ongoing global effort has helped collect data on patients with IBD and COVID-19 from 64 countries. As of 13 February 2021, out of 5081 included patients, hospitalization, ICU admission and mortality rates were 16, 3, and 2%, respectively [18]. We strongly encourage our colleagues to enter their patients into this registry in order to expand the understanding of COVID-19 and IBD [18].

Table 1. Risk factors for severe coronavirus disease 2019 outcomes in patients with inflammatory bowel disease

Risk factor	References
Comorbidities[a]	Bezzio *et al.* [19] Brenner *et al.* [20▪▪] Derikx *et al.* [10] D'Amico *et al.* [21]
Active IBD	Bezzio *et al.* [19]
Older age	Bezzio *et al.* [19] Brenner *et al.* [20▪▪] Burke *et al.* [11]
Systemic corticosteroids	Brenner *et al.*[b] [20▪▪] Ungaro *et al.*[b] [22▪]
Obesity	Burke *et al.* [11]
5-Aminosalicylates	Brenner at al.[b] [20▪▪] Ungaro *et al.*[b] [22▪]
Thiopurines[c]	Ungaro *et al.* [22▪]
Combination therapy (thiopurine with anti-TNF)	Ungaro *et al.* [22▪]

IBD, inflammatory bowel disease.
[a]Definitions of comorbidities varied among studies but generally included hypertension, diabetes, cardiovascular disease, and lung, kidney, or liver disease.
[b]These studies partially included the same patient population as part of the SECURE-IBD registry.
[c]When compared with anti-TNF therapy.

RISK FACTORS FOR SEVERE CORONAVIRUS DISEASE 2019 IN INFLAMMATORY BOWEL DISEASE

Although COVID-19 outcomes are overall similar in patients with IBD and the overall population, several risk factors for severe COVID-19 among patients with IBD have been identified and are listed in Table 1.

Similar to the general population, the presence of comorbidities has been frequently associated with worse outcomes in patients with IBD [10,19,20▪▪,21]. Older age and obesity have also been linked with a more severe course of COVID-19 [11,19,20▪▪]. Furthermore, actively inflamed IBD was found to be associated with severe COVID-19 outcomes in a prospective cohort study, including a higher risk of COVID-19-related death [19]. Corticosteroid use has been identified as an important risk factor for negative outcomes in the SECURE-IBD registry [20▪▪,22▪]. Of note, short-term dexamethasone has been shown to improve mortality in patients with severe COVID-19 requiring respiratory support in the RECOVERY trial [23]. However, this may be related to the inhibition of the acute cytokine release storm in these patients, whereas baseline corticosteroid use among patients with IBD at the time of infection may potentially negatively impact the future course of COVID-19 [22▪]. The association with corticosteroid therapy and worse COVID-19 outcomes spans beyond just patients with IBD and has also been found in a cohort of patients with other immune-mediated diseases [7]. In addition, corticosteroids have been previously associated with worse outcomes in patients with other coronavirus outbreaks, the Middle East respiratory syndrome (MERS-CoV) and the first severe acute respiratory syndrome (SARS-CoV, now called SARS-CoV-1) [15].

Finally, an intriguing risk factor identified in the SECURE-IBD registry was 5-aminosalicylate (5-ASA) use, which was associated with an increased risk of severe COVID-19 compared with patients not using 5-ASAs [20▪▪,22▪]. However, patients receiving 5-ASAs were not at increased risk of negative outcomes compared with patients receiving no IBD medications. In addition, no dose relationship was found [22▪]. Further data are, therefore, needed in order to clarify whether this is related to unmeasured confounders, such as active IBD or use of 5-ASA for Crohn's disease, a protective effect of other therapies, or if this is because of a true biologic effect on the enzymes and mode of entry of the coronavirus [24].

INFLAMMATORY BOWEL DISEASE THERAPIES AND THEIR IMPACT ON CORONAVIRUS DISEASE 2019 OUTCOMES

Importantly, the available biologic therapies for IBD have not been associated with worse outcomes from

COVID-19 [7,19,20▪▪,25]. Several biologics are in fact being studied as potential COVID-19 treatment options in ongoing randomized controlled trials, including anti-TNFs (adalimumab, ChiCTR2000030089; infliximab, NCT#04425538) and several Janus kinase inhibitors including tofacitinib (NCT#04469114) [26]. Interestingly, infliximab has been successfully used to simultaneously treat COVID-19 and severe IBD in two case reports. The course of COVID-19 in both patients improved significantly after the administration of infliximab [27,28].

In contrast, in a more recent expanded analysis of the SECURE-IBD registry on 1439 patients from 47 countries, thiopurines were associated with an increased risk of severe COVID-19 compared with anti-TNF monotherapy, whether alone (adjusted OR (aOR) 4.08, 95% CI 1.73 to 9.61) or in combination therapy with anti-TNFs (aOR 4.01, 95% CI 1.65 to 9.78) [22▪]. Mesalamine was also found to be associated with an increased risk of severe COVID-19 (aOR 1.70, 95% CI 1.26 to 2.29), with a further increased risk when compared to anti-TNF monotherapy (aOR 3.52, 95% CI 1.93 to 6.45). Although these findings suggest thiopurines or mesalamine may be associated with worse outcomes, they may also be due to a potential protective effect of anti-TNFs or unmeasured confounders [29]. Further data are therefore needed before changing clinical practice.

Finally, in an analysis of 37 patients on tofacitinib in the SECURE-IBD database, tofacitinib was not associated with an increased risk of severe COVID-19 [30], and there are multiple ongoing studies of tofacitinib as a treatment for COVID-19. Moreover, despite the increased risk of thrombosis associated with COVID-19, there were no reported thrombotic events among patients on tofacitinib [30].

OPTIMAL MANAGEMENT OF INFLAMMATORY BOWEL DISEASE DURING A PANDEMIC: GENERAL RECOMMENDATIONS

Many questions arose at the onset of the pandemic regarding the management of patients with IBD. However, several societies came together early on to provide expert opinion-based guidance, because of the initial lack of data on outcomes in IBD [31,32▪▪,33]. Although there are some practical issues regarding the half-lives of IBD therapies and recommendations to hold or discontinue them at the time of a SARS-CoV-2 infection or COVID-19, most recommendations are still valid and are in line with the accumulating evidence on IBD and COVID-19 outcomes. A summary of general recommendations can be found in Table 2.

Patients should remain on their maintenance regimen, if in remission, in order to avoid the risk of relapse. The exception is for oral systemic corticosteroids, which should be tapered, reduced to the minimal effective dose, or stopped [32▪▪,33]. Nonadherence to maintenance therapy may lead to disease relapse, which in turn may be associated with an increased risk of COVID-19 [8], increased corticosteroid use, and SARS-CoV-2 exposure through more frequent hospital visits [33]. Biologic infusions should be continued at centers with a COVID-19-screening protocol and adequate hygiene and safety standards, as recommended by the International Organization for the Study of Inflammatory Bowel Disease (IOIBD) taskforce [34]. De-escalation of therapy doses or discontinuation of therapies otherwise has not been recommended for risk of relapse. Similarly, elective transition from intravenous anti-tumor necrosis factor (anti-TNF) therapy to an injectable anti-TNF therapy should not be electively performed, as this can be associated with a loss of drug efficacy and tolerance [33,43].

Although endoscopy remains a crucial diagnostic and monitoring tool in IBD, elective endoscopic procedures have had to be canceled or postponed because of the pandemic, leading to a significant drop in endoscopic volume [1]. IOIBD experts have compiled a list of recommendations for IBD endoscopy during the pandemic [37]. Procedures should be performed according to adequate safety measures and prioritized according to the urgency of their indication. High priority procedures include acute severe ulcerative colitis, cholangitis in the case of concurrent primary sclerosing cholangitis, partial bowel obstruction, new diagnosis of IBD and acute gastrointestinal bleeding. If endoscopy is not readily available, fecal calprotectin and serum inflammatory markers should be used for disease monitoring, in addition to clinical evaluation [37].

MANAGEMENT OF THE PATIENT WITH INFLAMMATORY BOWEL DISEASE AND CORONAVIRUS DISEASE 2019

In the case of SARS-CoV-2 infection, it is generally recommended to hold immunosuppressive therapies [32▪▪]. However, current recommendations are mostly based on expert consensus and recent evidence does not demonstrate worse outcomes among patients with IBD on biologics, further supported by the fact that the half-lives of these therapies are such that the drugs are still present even with short-term discontinuation. IBD management should, therefore, be individualized and adapted to the severity of SARS-CoV-2 infection and disease activity [15].

Table 2. Inflammmatory bowel disease management during the coronavirus disease 2019 pandemic: general recommendations

Aspects of IBD care	Recommendations	Guidance
Medication management	Infusions should be continued at a center with a COVID-19-screening protocol and appropriate safety measures Intravenous medications should not be switched to a different subcutaneous medication IBD therapy should not be held except for corticosteroids, which should be tapered or stopped In case of SARS-CoV-2 infection, immunosuppressive therapy should generally be held for at least 10 days from symptom onset	IOIBD [33] AGA [34] AGA [33] IOIBD [34] IOIBD [32▪▪] AGA [33] IOIBD [35]
Disease monitoring	Telemedicine is encouraged Endoscopy: procedures should be performed according to adequate safety measures and prioritized according to the urgency of their indication Laboratory tests: clinical evaluation combined with fecal calprotectin and serum inflammatory markers can be used as alternative monitoring tools if endoscopy is not readily available The implementation of point-of-care biomarkers and home fecal calprotectin tests is encouraged	IOIBD [36,37] ECCO [38]
Hospitalization	Hospitalization should only be pursued if absolutely necessary Endoscopic or radiologic procedures should only be performed if urgently required or if susceptible to change management Length of stay should be minimized	IOIBD [39]
Surgery	Preoperative SARS-CoV-2 testing is required prior to surgery Surgery should be postponed in uncomplicated IBD	IOIBD [40] ECCO [38]
Preventive care	Inactivated influenza vaccine and pneumococcal vaccine are strongly encouraged	ECCO [38]
COVID-19 prevention	Usual preventive measures should be encouraged: social distancing, hand hygiene, using a mask, avoidance of travel and crowds Nonlive COVID-19 vaccine should be recommended to all patients with IBD, regardless of immunosuppressive therapy	AGA [33] ECCO [38] CDC [41] IOIBD [42▪]

AGA, American Gastroenterological Association; CDC, Centers for Disease Control and Prevention; COVID-19, coronavirus disease 2019; ECCO, European Crohn's and Colitis Organisation; IBD, inflammatory bowel disease; IOIBD, International Organization for the study of Inflammatory Bowel Disease; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

If immunosuppressives are held, IOIBD generally advises to resume therapy at least 10 days after the onset of symptoms and at least 3 days after resolution of fever, once there is 'clinically meaningful improvement in respiratory symptoms' [35]. However, it is important to note that there are limited data regarding the safety and timing of restarting immunosuppressives after SARS-CoV-2 infection and that other approaches might also be considered, such as a test-based strategy [35]. There are case reports suggesting that active therapy for IBD may also address the inflammatory activity of COVID-19, including the rare multisystem inflammatory syndrome in children, and the co-existing active IBD [27,28,44].

CORONAVIRUS DISEASE 2019 VACCINE AND INFLAMMATORY BOWEL DISEASE

Several vaccines have been approved for COVID-19 prevention in a number of countries, including mRNA, inactivated, and viral vector-based vaccines [42▪,45,46]. Several other vaccines are being investigated in randomized controlled trials and are at different stages of development [47].

Although these nonlive vaccines have not been specifically studied in patients with IBD, their safety profile and underlying mechanism suggest they can safely be used in patients with IBD, including immunosuppressed patients [42▪,48]. Recent IOIBD consensus guidance, therefore, recommends nonlive COVID-19 vaccine administration to all our patients with IBD [42▪]. There are, however, no data thus far regarding the efficacy of these vaccines in the context of immunosuppression. This should be discussed with patients, especially if they are receiving systemic corticosteroids [42▪].

CONCLUSION

The COVID-19 pandemic has had a considerable impact on our patients. As our understanding of

COVID-19 and its implications in patients with IBD is evolving, several questions remain regarding the safety of certain therapies, such as thiopurines or mesalamine, the timing of restarting therapy after COVID-19 convalescence, as well as regarding the safety and efficacy of COVID-19 vaccines in the patients with IBD. Managing IBD in this context has also led us to appreciate the importance of quickly adjusting to changing norms and restructuring care in order to adapt to future waves or outbreaks. COVID-19 will undoubtedly transform IBD care through the expansion of telemedicine and the development of point-of-care testing and novel approaches for remote monitoring, which may in fact benefit our patients in the long-term through access to convenient and well tolerated IBD care well beyond the expected control of the COVID-19 global burden.

Acknowledgements

None.

Specific author contributions: S.E. and F.R. planned and conducted the study. All authors have contributed to drafting and approving the final version of the manuscript.

Financial support and sponsorship

This work was supported by the Helmsley Charitable Trust through the Stenosis Therapy and Anti-Fibrotic Research (STAR) Consortium and National Institutes of Health [K08DK110415 and R01DK123233] to F.R.

Conflicts of interest

F.R. is on the advisory board or consultant for Agomab, Allergan, AbbVie, Boehringer-Ingelheim, Celgene, CDISC, Cowen, Genentech, Gilead, Gossamer, Guidepoint, Helmsley, Index Pharma, Janssen, Koutif, Metacrine, Morphic, Pfizer, Pliant, Prometheus Biosciences, Receptos, RedX, Roche, Samsung, Takeda, Techlab, Theravance, Thetis, UCB. S.E. has no conflict of interest. D.T.R. has received grant support from Takeda; and has served as a consultant for Abbvie, Abgenomics, Allergan Inc., Arena Pharmaceuticals, Bellatrix Pharmaceuticals, Boehringer Ingelheim Ltd., Bristol-Myers Squibb, Celgene Corp/Syneos, Check-cap, Dizal Pharmaceuticals, GalenPharma/Atlantica, Genentech/Roche, Gilead Sciences, Ichnos Sciences S.A., InDex Pharmaceuticals, Iterative Scopes, Janssen Pharmaceuticals, Lilly, Materia Prima, Narrow River Mgmt, Pfizer, Prometheus Laboratories, Reistone, Takeda, and Techlab Inc. B.L.C. receives the following financial support: Advisory Boards and Consultant for Abbvie, Celgene-Bristol Myers Squibb, Pfizer, Sublimity Therapeutics, TARGET RWE; CME Companies: Cornerstones, Vindico; Speaking: Abbvie. M.D.R. is on the advisory board or consultant for Abbvie, Janssen, UCB, Takeda, Pfizer, Miraca Labs, Amgen, Celgene, Seres, Allergan, Genentech, Gilead, Salix, Prometheus, Lilly, TARGET Pharma Solutions, ALFA-SIGMA, S.p.A., Bristol Meyer Squibb (B.M.S.).

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

- ■ of special interest
- ■■ of outstanding interest

1. Kennedy NA, Hansen R, Younge L, *et al.* Organisational changes and challenges for inflammatory bowel disease services in the UK during the COVID-19 pandemic. Frontline Gastroenterol 2020; 11:343–350.
2. Grunert PC, Reuken PA, Stallhofer J, *et al.* Inflammatory bowel disease in the COVID-19 pandemic - the patients' perspective. J Crohns Colitis 2020; jjaa126. [Epub ahead of print]
3. Shields S, Dunlop A, Seenan JP, Macdonald J. Disease monitoring of biologic treatment in IBD: early impact and future implications of COVID-19 pandemic. 2020.
4. Lees CW, Regueiro M, Mahadevan U; International Organization for the Study of Inflammatory Bowel Disease. Innovation in inflammatory bowel disease care during the COVID-19 pandemic: results of a Global Telemedicine Survey by the International Organization for the Study of Inflammatory Bowel Disease. Gastroenterology 2020; 159:805.e1–808.e1.
5. Mak JWY, Weng M-T, Wei SC, Ng SC. Zero COVID-19 infection in inflammatory bowel disease patients: findings from population-based inflammatory bowel disease registries in Hong Kong and Taiwan. J Gastroenterol Hepatol 2021; 36:171–173.
6. Taxonera C, Sagastagoitia I, Alba C, *et al.* 2019 novel coronavirus disease (COVID-19) in patients with inflammatory bowel diseases. Aliment Pharmacol Ther 2020; 52:276–283.
7. Haberman R, Axelrad J, Chen A, *et al.* Covid-19 in immune-mediated inflammatory diseases — case series from New York. New Engl J Med 2020; 383:85–88.
8. Lukin DJ, Kumar A, Hajifathalian K, *et al.,* Jill Roberts Center Study Group Study Group, Weill Cornell Medicine-Gastrointestinal Study Group. Baseline disease activity and steroid therapy stratify risk of COVID-19 in patients with inflammatory bowel disease. Gastroenterology 2020; 159:1541.e2–1544.e2.
9. Allocca M, Fiorino G, Zallot C, *et al.* Incidence and patterns of COVID-19 among inflammatory bowel disease patients from the Nancy and Milan Cohorts. Clin Gastroenterol Hepatol 2021; 18:2134–2135.
10. Derikx LAAP, Lantinga MA, de Jong DJ, *et al.* Clinical outcomes of covid-19 in patients with inflammatory bowel disease: a nationwide cohort study. J Crohn Colitis 2020. [Epub ahead of print]
11. Burke KE, Kochar B, Allegretti JR, *et al.* Immunosuppressive therapy and risk of COVID-19 infection in patients with inflammatory bowel diseases. Inflammatory Bowel Dis 2020; 27:155–161.
12. Khan N, Patel D, Xie D, *et al.* Impact of anti-TNF and thiopurines medications on the development of COVID-19 in patients with inflammatory bowel disease: a nationwide VA cohort study. Gastroenterology 2020; 159:1545.e1–1546.e1.
13. D'Amico F, Danese S, Peyrin-Biroulet L. Systematic review on IBD patients with COVID-19: it is time to take stock. Clin Gastroenterol Hepatol 2020; 18:2689–2700.
14. Ouali SE, Achkar J-P, Lashner B, Regueiro M. Gastrointestinal manifestations of COVID-19. Cleveland Clin J Med 2021. [Epub ahead of print]
15. El Ouali S, Philpott J, Vargo J, Regueiro M. COVID-19 in patients with IBD and pancreaticobiliary disorders. Cleveland Clin J Med 2020. [Epub ahead of print]
16. Taxonera C, Fisac J, Alba C. Can COVID-19 trigger de novo inflammatory bowel disease? Gastroenterology 2020; 160:1029–1030.
17. Effenberger M, Grabherr F, Mayr L, *et al.* Faecal calprotectin indicates intestinal inflammation in COVID-19. Gut 2020; 69:1543–1544.
18. Brenner EJ, Ungaro RC, Colombel JF, Kappelman MD. SECURE-IBD Database Public Data Update. covidibd.org. (Accessed 13 February 2021)
19. Bezzio C, Saibeni S, Variola A, *et al.,* Italian Group for the Study of Inflammatory Bowel Disease (IG-IBD). Outcomes of COVID-19 in 79 patients with IBD in Italy: an IG-IBD study. Gut 2020; 69:1213–1217.
20. ■■ Brenner EJ, Ungaro RC, Gearry RB, *et al.* Corticosteroids, but not TNF antagonists, are associated with adverse COVID-19 outcomes in patients with inflammatory bowel diseases: results from an international registry. Gastroenterology 2020; 159:481.e3–491.e3.

This important study is the first analysis of the SECURE-IBD registry. It greatly contributed to our knowledge about the impact of IBD therapies in the setting of COVID-19.

21. D'Amico F, Danese S, Peyrin-Biroulet L. Systematic review on inflammatory bowel disease patients with coronavirus disease 2019: it is time to take stock. Clin Gastroenterol Hepatol 2020; 18:2689–2700.

22. ■ Ungaro RC, Brenner EJ, Gearry RB, *et al.* Effect of IBD medications on COVID-19 outcomes: results from an international registry. Gut 2020; 70:725–732.

This study is an expanded analysis of the SECURE-IBD registry and provides further insights on the impact of IBD therapies in the context of SARS-CoV-2 infection.

23. Dexamethasone in hospitalized patients with Covid-19 — preliminary report. New England Journal of Medicine 2020.

24. Magro F, Dias CC, Morato M. Aminosalicylates and COVID-19: facts or coincidences? Gastroenterology 2021; 384:693–704.

25. Papa A, Gasbarrini A, Tursi A. Epidemiology and the impact of therapies on the outcome of COVID-19 in patients with inflammatory bowel disease. Am J Gastroenterol 2020; 115:1722–1724.

26. Rizk JG, Kalantar-Zadeh K, Mehra MR, *et al.* Pharmaco-immunomodulatory therapy in COVID-19. Drugs 2020; 80:1267–1292.

27. Dolinger MT, Person H, Smith R, *et al.* Pediatric Crohn's Disease and Multisystem Inflammatory Syndrome in Children (MIS-C) and COVID-19 treated with infliximab. J Pediatr Gastroenterol Nutr 2020; 71:153–155.

28. Bezzio C, Manes G, Bini F, *et al.* Infliximab for severe ulcerative colitis and subsequent SARS-CoV-2 pneumonia: a stone for two birds. Gut 2020; 70:623–624.

29. Lees CW, Irving PM, Beaugerie L. COVID-19 and IBD drugs: should we change anything at the moment? Gut 2020; 70:632–634.

30. Agrawal M, Brenner EJ, Zhang X, *et al.* Characteristics and outcomes of IBD patients with COVID-19 on tofacitinib therapy in the SECURE-IBD Registry. Inflamm Bowel Dis 2020; 27:585–589.

31. Kennedy NA, Jones G-R, Lamb CA, *et al.* British Society of Gastroenterology guidance for management of inflammatory bowel disease during the COVID-19 pandemic. Gut 2020; 69:984–990.

32. ■■ Rubin DT, Abreu MT, Rai V, Siegel CA; International Organization for the Study of Inflammatory Bowel Disease. Management of patients with Crohn's disease and ulcerative colitis during the coronavirus disease-2019 pandemic: results of an international meeting. Gastroenterology 2020; 159:6.e6–13.e6.

Important consensus guidance for the management of IBD during the COVID-19 pandemic.

33. Rubin DT, Feuerstein JD, Wang AY, Cohen RD. AGA clinical practice update on management of inflammatory bowel disease during the COVID-19 pandemic: expert commentary. Gastroenterology 2020; 159:350–357.

34. Dotan I, Panaccione R, Kaplan GG, *et al.* Best practice guidance for adult infusion centres during the COVID-19 pandemic: report from the COVID-19 International Organization for the Study of IBD [IOIBD] Task Force. J Crohns Colitis 2020; 14(Suppl 3):S785–S790.

35. Siegel CA, Christensen B, Kornbluth A, *et al.* Guidance for restarting inflammatory bowel disease therapy in patients who withheld immunosuppressant medications during COVID-19. J Crohns Colitis 2020; 14(Suppl 3):S769–S773.

36. Lewin S, Lees C, Regueiro M, *et al.,* Diseases ftIOftSoIB. International Organization for the Study of Inflammatory Bowel Disease: global strategies for telemedicine and inflammatory bowel diseases. J Crohns Colitis 2020; 14(Suppl 3):S780–S784.

37. Ng SC, Mak JWY, Hitz L, *et al.* COVID-19 pandemic: which IBD patients need to be scoped-who gets scoped now, who can wait, and how to resume to normal. J Crohns Colitis 2020; 14(Suppl 3):S791–S797.

38. Magro F, Rahier J-F, Abreu C, *et al.* Inflammatory bowel disease management during the COVID-19 outbreak: the ten do's and don'ts from the ECCO-COVID Taskforce. J Crohn Colitis 2020; 14(Suppl 3):S798–S806.

39. Allez M, Fleshner P, Gearry R, *et al.* Care of the patient with IBD requiring hospitalisation during the COVID-19 pandemic. J Crohn Colitis 2020; 14(Suppl 3):S774–S779.

40. Remzi FH, Panis Y, Spinelli A, *et al.* International organization for the study of ibd recommendations for surgery in patients with ibd during the coronavirus disease 2019 pandemic. Dis Colon Rectum 2020; 63:870–873.

41. CDC. Available at: https://www.cdc.gov/coronavirus/2019-ncov/prevent-getting-sick/prevention.html. [Accessed 13 February 2021]

42. ■ Siegel CA, Melmed GY, McGovern DP, *et al.,* International Organization for the Study of Inflammatory Bowel Disease (IOIBD), International Organization for the Study of Inflammatory Bowel Diseases (IOIBD). SARS-CoV-2 vaccination for patients with inflammatory bowel diseases: recommendations from an international consensus meeting. Gut 2021; 70:635–640.

Consensus recommendations regarding COVID-19 vaccinations in patients with IBD.

43. Van Assche G, Vermeire S, Ballet V, *et al.* Switch to adalimumab in patients with Crohn's disease controlled by maintenance infliximab: prospective randomised SWITCH trial. Gut 2012; 61:229–234.

44. Rosen MH, Axelrad J, Hudesman D, *et al.* Management of acute severe ulcerative colitis in a pregnant woman with COVID-19 infection: a case report and review of the literature. Inflamm Bowel Dis 2020; 26:971–973.

45. Baden LR, El Sahly HM, Essink B, *et al.* Efficacy and safety of the mRNA-1273 SARS-CoV-2 vaccine. New Engl J Med 2020; 384:403–416.

46. Polack FP, Thomas SJ, Kitchin N, *et al.,* C4591001 Clinical Trial Group. Safety and efficacy of the BNT162b2 mRNA covid-19 vaccine. New Engl J Med 2020; 383:2603–2615.

47. Knoll MD, Wonodi C. Oxford–AstraZeneca COVID-19 vaccine efficacy. The Lancet 2021; 397:72–74.

48. Melmed GY, Rubin DT, McGovern DPB. Winter is coming! Clinical, immunological, and practical considerations for vaccinating patients with IBD during the COVID pandemic. Gastroenterology 2020; 160:639–644.