Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Viral screening before initiation of biologics in patients with inflammatory bowel disease during the COVID-19 outbreak

We read with interest the Comment by Ren Mao and colleagues on the implications of coronavirus disease 2019 (COVID-19) in patients with pre-existing digestive diseases, and the strategies implemented in China to restrict the risk of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in patients with inflammatory bowel disease.[1]

We agree with the current evidence that does not support drug suspension and also with the European Crohn's and Colitis Organisation COVID-19 Task Force's suggestion that, whenever possible during the COVID-19 pandemic, initiation of treatment with immunosuppressive drugs and biologics should be postponed based on an individual risk assessment.[2] However, for patients with substantial clinical activity, delaying the initiation of treatment might not always be possible.

A meta-analysis[3] of clinical trial data including 4135 patients given anti-tumor necrosis factor (TNF) therapy found that the relative risk of developing an opportunistic infection was 2·05 (95% CI 1·10–3·85) with anti-TNF therapy compared with placebo; opportunistic infections included tuberculosis, herpes simplex infection, oral or oesophageal candidiasis, herpes zoster virus, cytomegalovirus, and Epstein-Barr virus. A pooled analysis of 2266 patients given adalimumab found that higher disease activity was associated with significantly increased risks of both serious and opportunistic infections at 1 year.[4] Furthermore, vedolizumab, a humanised monoclonal antibody with gut selectivity, has been associated with airway and bowel infections, although to a lesser extent than with anti-TNF drugs.[5] The risk of opportunistic infection seems to be increased in patients with inflammatory bowel disease who are older than 50 years and receiving immunosuppression.[6,7]

As a result of this increased risk of opportunistic infections, inflammatory bowel disease guidelines suggest giving patients a viral screening before starting biologics.[8] In particular, the screening should include serology for hepatitis B virus, hepatitis C virus, HIV, and varicella zoster virus (in patients without a clear history of previous infection or vaccination), and tuberculosis screening through a combination of clinical risk stratification, chest x-ray, and IFN-γ release assays. Additionally, an assessment of history of specific infections is suggested, including herpes simplex virus, varicella zoster virus, and tuberculosis, and of immunisation status.[3]

Patients with inflammatory bowel disease might be at an increased risk of SARS-CoV-2 infection, and the risk of a severe clinical course of COVID-19 might be increased in individuals with chronic disease on immunomodulatory treatment. Furthermore, the risk of inducing clinical activation in individuals with asymptomatic SARS-CoV-2 infection cannot be excluded. As such, we believe that current recommendations for screening before initiation of biologics should be updated (at least temporarily) to include testing for SARS-CoV-2. In view of the rapid spread of the COVID-19 pandemic, we believe physicians should screen for COVID-19 even if patients are asymptomatic or do not have a history of high-risk travel or contact. However, importantly, the exact method of such screening should be decided on the basis of local policy and available health-care resources.

We declare no competing interests.

*Fabiana Zingone,
Edoardo Vincenzo Savarino
fabiana.zingone@unipd.it

Division of Gastroenterology, Department of Surgery, Oncology and Gastroenterology, University of Padua, 35121 Padua, Italy

1 Mao R, Liang J, Shen J, et al. Implications of COVID-19 for patients with pre-existing digestive diseases. *Lancet Gastroenterol Hepatol* 2020; published online March 11. https://doi.org/10.1016/S2468-1253(20)30076-5.
2 1st Interview COVID-19 ECCO Taskforce. ECCO Crisis Task Force, March 13, 2020. https://www.ecco-ibd.eu/images/6_Publication/6_8_Surveys/1st_interview_COVID-19%20ECCOTaskforce_published.pdf (accessed March 20, 2020).
3 Ford AC, Peyrin-Biroulet L. Opportunistic infections with anti-tumor necrosis factor-α therapy in inflammatory bowel disease: meta-analysis of randomized controlled trials. *Am J Gastroenterol* 2013; **108:** 1268–76.
4 Osterman MT, Sandborn WJ, Colombel JF, et al. Crohn's disease activity and concomitant immunosuppressants affect the risk of serious and opportunistic infections in patients treated with adalimumab. *Am J Gastroenterol* 2016; **111:** 1806–15.
5 Singh S, Murad MH, Fumery M, et al. First- and second-line pharmacotherapies for patients with moderate to severely active ulcerative colitis: an updated network meta-analysis. *Clin Gastroenterol Hepatol* 2020; published online Jan 13. DOI:10.1016/j.cgh.2020.01.008.
6 Naganuma M, Kunisaki R, Yoshimura N, Takeuchi Y, Watanabe M. A prospective analysis of the incidence of and risk factors for opportunistic infections in patients with inflammatory bowel disease. *J Gastroenterol* 2013; **48:** 595–600.
7 Toruner M, Loftus EV Jr, Harmsen WS, et al. Risk factors for opportunistic infections in patients with inflammatory bowel disease. *Gastroenterology* 2008; **134:** 929–36.
8 Lamb CA, Kennedy NA, Raine T, et al. British Society of Gastroenterology consensus guidelines on the management of inflammatory bowel disease in adults. *Gut* 2019; **68** (suppl 3)**:** s1–106.

Published **Online**
March 25, 2020
https://doi.org/10.1016/S2468-1253(20)30085-6

Prevention of COVID-19 in patients with inflammatory bowel disease in Wuhan, China

As recently outlined by Ren Mao and colleagues[1] in *The Lancet Gastroenterology & Hepatology*, patients with inflammatory bowel disease (IBD) are at increased risk of opportunistic infections. Particular attention is therefore required for these patients during the ongoing

Published **Online**
April 17, 2020
https://doi.org/10.1016/S2468-1253(20)30121-7

coronavirus disease 2019 (COVID-19) pandemic.

318 patients with IBD (114 with Crohn's disease, 204 with ulcerative colitis) were registered in a prospective database at the Regional Medical IBD Center of China, Renmin Hospital of Wuhan University, Wuhan, China, between Jan 1, 2000, and Dec 8, 2019. Patients' clinical characteristics and their location relative to the COVID-19 outbreak are shown in the appendix (pp 2–4). Median age was 39·2 years (IQR 15–79); 33 (10%) were older than 60 years. 49 (15%) patients (22 [19%] of those patients with Crohn's disease, 27 [13%] of those with ulcerative colitis) had other chronic medical conditions (appendix p 2). 35 (31%) of the patients with Crohn's disease and 93 (46%) of those with ulcerative colitis had active IBD. More than two-thirds (246 [77%]) lived and worked near Huanan seafood supermarket (≤30 km), the suspected location from which SARS-CoV-2 emerged (appendix p 4). We recorded the times and frequency of received alerts and information from our team, self-prevention measures, and confirmed or suspected diagnosis of COVID-19 between Dec 8, 2019, and March 30, 2020.

See Online for appendix

Between Jan 3 and March 30, 2020, five (2%) patients had been hospitalised for severe active IBD during the COVID-19 outbreak, including one with Crohn's disease, who underwent emergency surgery for intestinal perforation, and one pregnant patient with Crohn's disease in whom preterm delivery was induced (appendix pp 2–3). Before the outbreak, 40 (13%) patients had been treated with corticosteroids, 35 (11%) with azathioprine, 37 (12%) with thalidomide, and 20 (6%) with infliximab; nine (3%) patients were enrolled in clinical trials (appendix pp 2–3). Between Jan 31 and March 30, 20 (6%) patients required medical management of disease flare, which was treated preferentially with exclusive enteral nutrition for Crohn's disease (n=15) and steroids (n=18), with a median time to review of 1·3 days (IQR 1·0-2·3).

On Jan 3, 2020, we temporarily ceased infliximab infusions and immunosuppressive treatment for all patients, in accordance with national Chinese Society of Gastroenterology guidelines,[2] altering treatment to 5-aminosalicylic acid (37 patients) or thalidomide (43 patients; with 25 patients receiving both medications) depending on the patients' condition. On Jan 3, we sent educational and instructional alerts and messages to the online IBD groups of our outpatients via WeChat, with all patients responding to our alerts (table). Within 3 days, most patients reported that they maintained good hand hygiene, sought medical assistance online rather than in person, and kept track of fever and respiratory symptoms; all confirmed notification of our information for self-prevention and all patients kept up to date on official news on COVID-19 (table). Most patients decreased the time they spent outside the home, wore masks when outside, and purchased masks for storage; most patients were very satisfied with our team's work (table).

On Jan 8, 2020, the first confirmed case of COVID-19 was diagnosed at our hospital, in the pulmonology department. On Jan 12, a second patient was diagnosed, in our gastroenterology department (appendix p 5). On Jan 13, we updated our alerts (table) and actions and implemented an updated model of care. All inpatients with IBD were placed in single-occupancy rooms. We sent daily alerts to outpatients with IBD with recommendations to stay at home if possible, encourage use of N95 masks for those with recent treatment with biologics and immunosuppressants, and to keep in daily contact with our IBD team. For patients with low health literacy and education, we remained in contact via phone calls. We mailed trial

	Alerts on Jan 3, 2020 (n=318)	Upgraded alerts on Jan 13, 2020 (n=318)
Time from alert to patient response (days; median [IQR])	1·8 (1·0–3·4)	1·2 (1·0–2·3)
Responded to our alert	318 (100%)	318 (100%)
Overall service satisfaction		
Very satisfied	300 (94%)	318 (100%)
Satisfied	18 (6%)	0
Not satisfied	0	0
Reduced time spent outside*	291 (92%)	318 (100%)
Attended any social gathering	0	0
Wore masks when outside	284 (89%)	318 (100%)
Purchased masks for storage	246 (77%)	318 (100%)
Maintained hand hygiene†	296 (93%)	318 (100%)
Route of care		
Sought medical care or contacted doctors and pharmacies online	289 (91%)	318 (100%)
Sought medical care in person	27 (8%)	0
Did not seek care	2 (1%)	0
Noted educational and instructional information sent by mobile messages and WeChat	318 (100%)	318 (100%)
Maintained awareness of COVID-19 symptoms‡	318 (100%)	318 (100%)
Monitored social news on COVID-19	318 (100%)	318 (100%)

COVID-19=coronavirus disease 2019. *Patients who had to leave their homes were outside for the shortest time necessary. †Cleaning hands with soap and using an alcohol-based sanitiser, especially before meals, after toilet use, and immediately after returning home. ‡Fever and respiratory symptoms.

Table: **Responses to WeChat alerts**

drugs to those in clinical trials who lived further from our hospital (>1 h driving distance), to reduce exposure to hospital facilities. By Jan 13, most patients with IBD in our hospital were discharged, IBD clinics were closed, and routine, non-urgent medical care was moved online. We published online recommended guidelines and precautions for prevention of COVID-19 in the IBD population.[2]

On Jan 22, we sent alerts to outpatients to be aware of atypical COVID-19 (ie, confirmed COVID-19 with only gastrointestinal symptoms and no fever) and to maintain self-isolation, and sent alerts via public news media (major newspapers and periodicals) on Jan 24, when the shutdown of Wuhan was announced and domestic social lockdown and quarantine controls were instituted.

With the escalation of our alerts, all of our patients reported within 2 days that they wore masks when outside, purchased masks for storage, decreased time spent outside, and were very satisfied with our information and service (table). Throughout this period (Jan 3 to March 30), a weekly multidisciplinary meeting with surgical, medical, and radiological teams was maintained to discuss hospitalised patients in critical or severe condition and formulate management plans.

We sent a questionnaire to our patients on Feb 10, regarding their exposure history (ie, contact with confirmed or suspected cases of COVID-19), potential risk factors for exposure (eg, populated places and contact with health-care workers), telehealth outpatient visits, and recent symptoms (including fever and respiratory and gastrointestinal symptoms). In response, 24 (8%) patients reported risk factors for exposure to SARS-CoV-2, including one patient who reported contact with an individual with confirmed COVID-19 (appendix p 2).

As of March 30, none of our registered patients with IBD had reported concern over respiratory symptoms and none had confirmed or suspected COVID-19. COVID-19 was excluded in 29 patients, including 20 patients with disease flare and six active cases, by diagnostic chest CT scans and virological testing.

Patients with IBD are susceptible to frequent and severe infections. IBD treatment teams need to put emphasis on risk assessment, prevention strategies, patient education, and effective therapies.[2] Mass awareness of important prevention and protection strategies is paramount and might go beyond what is currently recommended in some guidelines.[3] Despite such guidelines, cases of COVID-19 have been reported in patients with IBD in many countries, including France, Italy, Spain, and the USA.[4,5] Our recommendations extend beyond the so-called shielding procedures described in other guidelines and resulted in no cases of COVID-19 being reported among our patients. At the height of a pandemic, assuming mass community spread is vital and implementation of strict criteria for patients on immunosuppression is crucial.

We believe that our long-term relationships with our patients and understanding of their individual risk factors, along with routine emphasis on patient education, contributed to their adherence to our recommendations. Another crucial component is having a method of communication between patients and their IBD teams that allows concerns to be addressed in a timely fashion; our median times to response were within 1 day. We further discuss and evaluate our approach in the appendix (pp 6–9).

Of note, given high rates of community transmission and the large number of confirmed COVID-19 cases in China, the Chinese Society of Gastroenterology recommended withholding immunosuppressive therapies, on the basis of potential increased risk of infection and worsening of COVID-19 disease course, especially in high-risk areas such as Wuhan.[2] However, local guidelines and isolation measures should be dictated by the background rate of COVID-19 in the community. Nonetheless, we believe our experiences could provide a model of care to prevent COVID-19 in patients with IBD.

NSD reports personal fees from AbbVie and Janssen, outside of the submitted work. All other authors declare no competing interests. This work was partly supported by grants from the National Natural Science Foundation of China (81870392 to WD, 81302131 to PA, and 81901817 to MJ). PA, MJ, HR, JS, and NSD contributed equally.

*Ping An, Mengyao Ji, Haixia Ren, Juan Su, Nik Sheng Ding, Jian Kang, Anning Yin, Qian Zhou, Linyong Shen, Liang Zhao, Xiaoda Jiang, Yong Xiao, Wei Tan, Xiaoguang Lv, Jiao Li, Shuzhong Liu, Jing Zhou, Hongbin Chen, Yaqing Xu, Jun Liu, Mingkai Chen, Jiwang Cao, Zhongyin Zhou, Lei Shen, Shiyun Tan, Honggang Yu, Weiguo Dong, *Yijuan Ding*

dingyijuan88@163.com

Department of Gastroenterology, Key Laboratory of Hubei Province for Digestive System Disease, and Hubei Provincial Clinical Research Center for Digestive Disease Minimally Invasive Incision (PA, MJ, HR, JS, JK, AY, QZ, LiS, LZ, XJ, YX, WT, XL, JiL, SL, JZ, JuL, MC, JC, ZZ, LeS, ST, HY, WD, YD), Department of Respiratory Medicine (HC), and Infection Control Department (YX), Renmin Hospital of Wuhan University, Wuhan, China; and Department of Gastroenterology, St Vincent's Hospital Melbourne, University of Melbourne, Australia (NSD)

1 Mao R, Liang J, Shen J, et al. Implications of COVID-19 for patients with pre-existing digestive diseases. *Lancet Gastroenterol Hepatol* 2020; **5:** 426–28.

2 Wu KC, Qian JM. Management of patients with inflammatory bowel disease during epidemic of 2019 novel coronavirus pneumonia. *Chin J Dig* 2020; **40:** E001.

3 British Society of Gastroenterology. BSG expanded consensus advice for the management of IBD during the COVID-19 pandemic. April 6, 2020. https://www.bsg.org.uk/covid-19-advice/bsg-advice-for-management-of-inflammatory-bowel-diseases-during-the-covid-19-pandemic/ (accessed April 6, 2020).

4 Surveillance Epidemiology of Coronavirus Under Research Exclusion-Inflammatory Bowel Disease Database. Current data. April 6, 2020. https://covidibd.org/current-data/ (accessed April 6, 2020).

5 International Organization for the study of Inflammatory Bowel Disease. IOIBD update on COVID19 for patients with Crohn's disease and ulcerative colitis. April 7, 2020. https://www.ioibd.org/ioibd-update-on-covid19-for-patients-with-crohns-disease-and-ulcerative-colitis/ (accessed April 7, 2020).