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May 31, 2020, compared with 155 in the same period in 2018 and 166 in the same period in 2019, representing a 26% decrease relative to the 2018–19 average. New referrals for colorectal cancer remained lower than that during previous years between June 1 and Oct 31, 2020, a decrease of 8% for colon cancers and 13% for rectal cancers, relative to the average in the same period of the previous 2 years (appendix).

The number of surgeries for colorectal cancer also fell between March 1 and May 31, 2020. 212 surgeries were done for newly referred colorectal cancers, compared with 323 in the same period of 2018 and 320 in the same period of 2019, representing a 34% decrease in 2020 relative to the 2018–19 average. Between June 1 and Oct 31, 2020, there were 439 surgeries for colorectal cancer, compared with 567 in the same period of 2018 and 494 in the same period of 2019, representing a 17% decrease relative to the 2018–19 average (appendix).

Other French studies complete the picture. A national-level study based on claims data also found a 17.7% decrease of colorectal resections in France between January to September, 2019, compared with January to September, 2020.² For radiotherapy, evidence of increased use of hypofractionation was reported in France, although not specifically for colorectal cancer.³ Indirect national-level information on screening has been published by the National Medication Safety Agency.⁴ During the spring lockdown of 2020, consumption of colonoscopy products decreased by 46.4% during March 16–29, by 85.6% between March 30 and April 12, by 77.4% during April 13–26, and by 66.1% between April 27 and May 10, compared with what was expected from data from the previous 2 years. A separate study concluded that, between Jan 1 and May 12, 2020, 152 114 fewer colonoscopies were

done in France compared with the same period in 2019, a 32% decrease.²

Because of delayed detection and inappropriate patient pathways, we join Morris and colleagues in their concerns about the probable mid-term impact of COVID-19's disruption on colorectal cancer prognosis.

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Sonia Priou, *Guillaume Lamé, Gilles Chatellier, Christophe Tournigand, Emmanuelle Kempf
guillaume.lame@centralesupelec.fr

Information Technology Department, Assistance Publique–Hôpitaux de Paris, Paris, France (SP, GC); Laboratoire Génie Industriel, CentraleSupélec, Université Paris-Saclay, Gif-sur-Yvette 91190, France (GL); Université de Paris, Paris, France (GC); IMRB, Université Paris-Est Créteil, INSERM, Créteil, France (CT); Assistance Publique–Hôpitaux de Paris, Department of Medical Oncology, Henri Mondor and Albert Chenevier Teaching Hospital, Créteil, France (CT, EK)

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The impact of SARS-CoV-2 variants on IBD management

The COVID-19 pandemic has revealed several challenges in inflammatory bowel disease (IBD) management. One of the initial key considerations

was the effect of immunosuppression on COVID-19 incidence and outcomes, as well as on immunity after infection or vaccination.^{1,2} With a rise in cases due to the emergence of SARS-CoV-2 variants, the question now is whether this information still applies.

A SARS-CoV-2 variant called B.1.1.7 was first identified in the UK, where it has now become the dominant strain; the variant has spread to more than 70 countries.² Another variant, B.1.351, emerged independently in South Africa, and the Brazil variant, P.1, was identified in January, 2021. The UK and South Africa variants have a mutation (N501Y) in the receptor-binding domain of the spike protein that is reported to be linked to a 40–70% higher transmission rate.³ Some early studies have suggested a higher incidence of death with B.1.1.7 than the original strain.^{2,4} Variable protection is provided by the current licensed SARS-CoV-2 vaccines against these emergent variants.^{3,5} Consequently, many countries have imposed further lockdowns, travel bans, and strict quarantine rules for those that have visited these areas where the variants are endemic.

The new variants share the same symptomatology with the initial strain; however, loss of taste or smell were observed slightly less often with B.1.1.7.⁶ Despite evidence of increased transmissibility, it is important to note that, as yet, there remains little evidence that this variant is associated with a more severe phenotype or an increase in mortality,⁴ although such observations might be confounded by advances in testing and therapeutic strategies against COVID-19 since SARS-CoV-2 first emerged.

The emergence of SARS-CoV-2 variants poses several questions for the IBD community. Our initial experience of COVID-19 has suggested that the medications used for patients with IBD do not seem to confer an increased risk of infection, severity, or poorer outcomes.⁷ It might not be possible to

currently confirm that the same is true for the new variants. Moreover, further mutations of SARS-CoV-2 are likely to develop in the future, which might lead to altered infectivity, virulence, and severity. What effect this will have on patients with IBD remains to be seen.

A notable additional consideration is whether immunosuppression affects antiviral⁸ and immune responses⁹ for patients with IBD. The combination of viral mutation plus immunosuppression might be enough to weaken anti-vaccine responses to the point that available vaccines no longer confer meaningful anti-SARS-CoV-2 immunity, at least with respect to the mutant viral forms.

Therefore, we suggest that patients with IBD should still proceed with caution in the current pandemic. Furthermore, we suggest that vaccine efficacy in the general population should be extrapolated to the immunosuppressed population very cautiously. Considering there is already evidence for a lower immunogenic response to the new variants with the currently licensed vaccines,⁴ the fact that immunosuppression can further reduce immunogenicity is cause for concern for patients with IBD.

Despite a plethora of research into the effects of the primary sequenced SARS-CoV-2, there is now a need to develop observational prospective studies to evaluate the effect of new variants on patients with IBD. It is essential that the health-care community promotes ongoing research into the efficacy of available and new vaccines as they become available. An exemplar model has been the UK CLARITY IBD initiative to assess seroconversion after SARS-CoV-2 infection in patients with IBD receiving systemic anti-tumour necrosis factor therapy (infliximab) or gut-selective anti- $\alpha 4\beta 7$ integrin therapy (vedolizumab). Promoting such research will ensure adaptable and resilient future strategies

to enable rapid evidence-based adaptations to vaccination strategies, which might include vaccine selection, combination vaccines, or use of boosters to confer optimal immunity to patients with IBD.

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*Jonathan P Segal, Aditi Kumar, Timothy Raine, Christopher A Lamb, Matthew J Brookes
jonathansegal1@nhs.net

Department of Gastroenterology and Hepatology, Hillingdon Hospital, Uxbridge UB8 3NN, UK (JPS); Royal Wolverhampton Trust New Cross Hospital, Wolverhampton, UK (AK); Department of Gastroenterology, Cambridge University Hospitals, Cambridge, UK (TR); Translational & Clinical Research Institute, Faculty of Medical Sciences, Newcastle University, Newcastle upon Tyne, UK (CAL); Department of Gastroenterology, Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle upon Tyne, UK (CAL); Faculty of Science and Engineering, University of Wolverhampton, Wolverhampton, UK (MJB); Department of Gastroenterology, Royal Wolverhampton NHS Trust, Wolverhampton, UK (MJB)

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Gastrointestinal sequelae 90 days after discharge for COVID-19

Huang and colleagues recently reported that as many as 76% of patients discharged after hospitalisation for COVID-19 had at least one symptom persisting 6 months after disease onset,¹ including fatigue or muscle weakness (63%), sleep difficulties (26%), and anxiety or depression (23%). Additionally, more than 50% of the patients had abnormal chest CT images indicating impaired pulmonary function.

Although SARS-CoV-2 mainly affects the lungs, many other organs are also affected. Enteric symptoms are common in COVID-19, and gastrointestinal symptoms can be the only symptom, or can be present before respiratory symptoms.² The cellular receptor for SARS-CoV-2, ACE2, is highly expressed in the gut, and SARS-CoV-2 has been observed in the colonic tissue³ and faeces⁴ of patients with COVID-19. Therefore, we examined the long-term gastrointestinal sequelae of SARS-CoV-2 infection in patients who were admitted for



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For more on the UK CLARITY IBD initiative see <https://www.clarityibd.org/>