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- 3 Jordan RE, Adab P, Cheng KK. Covid-19: risk factors for severe disease and death. *BMJ* 2020; **368**: m1198.
- 4 Qin J, Li Y, Cai Z, et al. A metagenome-wide association study of gut microbiota in type 2 diabetes. *Nature* 2012; **490**: 55–60.
- 5 Ng SC, Hart AL, Kamm MA, Stagg AJ, Knight SC. Mechanisms of action of probiotics: recent advances. *Inflamm Bowel Dis* 2009; **15**: 300–10.

Emotional state should not be used to differentiate IBD from IBS

We congratulate Marietta Iacucci and colleagues on their recent Rapid Review¹ of recommendations to triage endoscopy during COVID-19. We would like to highlight several points with regard to their algorithm for a suspected new diagnosis of inflammatory bowel disease (IBD).

The authors state that “negative emotions...can cause symptoms that mimic IBD” and that emotional state must be assessed to help rule out irritable bowel syndrome (IBS). We argue that the inclusion of “negative emotions” in this context is potentially deleterious to patient care. To the public, IBS is already a highly stigmatised condition with the misconception that the illness might not be real.² Stigmatisation arises from medical providers, friends, and family members and can perpetuate feelings of shame and helplessness, leading to delayed management and its long-term consequences.³

In the authors’ diagnostic algorithm, an abnormal emotional state, along with normal blood tests and faecal calprotectin leads to “probably IBS”. Poor emotional health is common in IBS and IBD and does not serve to discriminate between the two conditions.⁴ Moreover, this might be exacerbated by the psychosocial shock precipitated by the COVID-19 pandemic. The dichotomised outcome of emotional state as normal versus abnormal is ambiguous and fails to capture the

complexities of psychological health; it is also pejorative and risks further stigmatisation of IBS.

Third, the step in the algorithm to “rule out IBS” after a negative stool test for infection does not follow the globally accepted diagnostic protocol for IBS. This fuels the commonly held misunderstanding among health-care professionals that IBS is a diagnosis of exclusion.⁴ Instead, this diagnosis can be made on clinical grounds using the Rome IV criteria, which has high specificity (97%) for IBS.⁵ Clinicians should not need to rule IBS out, but rather, should use clear evidence-based guidelines to make a diagnosis if patients meet criteria.⁶

We hope that the authors will consider a revision of their algorithm in figure 1 and the supporting text. We welcome a revision that eliminates the assessment of emotional state as part of the diagnostic algorithm or for differentiating IBS from IBD. We also recommend for the algorithm to be adapted to include the assessment of IBS using Rome IV criteria, which would lead to a positive diagnosis of IBS once criteria are met.

We declare no competing interests.

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- 1 Iacucci M, Cannatelli R, Labarile N, et al. Endoscopy in inflammatory bowel diseases during the COVID-19 pandemic and post-pandemic period. *Lancet Gastroenterol Hepatol* 2020; **5**: 598–606.
- 2 Taft TH, Bedell A, Naftaly J, Keefer L. Stigmatization toward irritable bowel syndrome and inflammatory bowel disease in an online cohort. *Neurogastroenterol Motil* 2017; **29**: 10.1111/nmo.12921.
- 3 Ruddy J. From pretending to truly being OK: a journey from illness to health with postinfection irritable bowel syndrome: the patient’s perspective. *Gastroenterology* 2018; **155**: 1666–69.

- 4 Spiegel BMR, Farid M, Esrailian E, Talley J, Chang L. Is irritable bowel syndrome a diagnosis of exclusion? A survey of primary care providers, gastroenterologists, and IBS experts. *Am J Gastroenterol* 2010; **105**: 848–58.
- 5 Palsson OS, Whitehead WE, van Tilburg MAL, et al. Rome IV diagnostic questionnaires and tables for investigators and clinicians. *Gastroenterology* 2016; published online Feb 13. DOI:10.1053/j.gastro.2016.02.014.
- 6 Talley NJ, Bollipo S. How can I diagnose IBS? In: Lacey B, ed. *Curbside consultation in IBS: 49 clinical questions*. Thorofare, NJ, USA: Slack, 2011.

Authors’ reply

We appreciate the comments made by Johannah Ruddy and colleagues in response to our Rapid Review,¹ the focus of which, in this unprecedented period, was on how to urgently adapt endoscopy in inflammatory bowel disease (IBD) during the COVID-19 pandemic and in the post-pandemic period. As endoscopy services in general have been severely disrupted, the article highlighted priority indications in IBD for endoscopy.

Our current practice has changed dramatically with the incorporation of telemedicine, recognition of risks to patients and staff from unnecessary visits to hospital and undergoing endoscopy, redeployment of staff, and severe curtailment of endoscopy capacity. We proposed practical triaging protocols that can be administered by a range of health-care providers for prioritisation.

The differential diagnosis between IBD and irritable bowel syndrome (IBS) was not the purpose of the algorithm that Ruddy and colleagues highlight. Selecting patients for urgent colonoscopy to investigate who might have a new diagnosis of moderate to severe IBD is one of the four essential indications in IBD for endoscopy during the pandemic.¹

Negative emotions such as anxiety and stress increase visceral sensitivity via the brain-gut axis, which is the crucial player in IBS symptoms.² Emotional state is an important component of triaging patients during the pandemic, with its serious effects on people’s emotional state, including stress, anxiety, and depression,^{3,4} which

might trigger IBS.⁵ Emotional state and stressful events might be related to health-care seeking behaviour in IBS.^{6,7}

While anxiety and depression are important in all chronic diseases, including IBS and IBD, this is not an immediate consideration in assessing a patient for a probable new diagnosis of IBD (unlike established IBD). Symptoms of IBS often begin during times of emotional stress.⁸ We did not propose to evaluate emotional state alone, but also faecal calprotectin, blood test, and clinical symptoms, to decide who should undergo colonoscopy.

Ruling out a diagnosis for the purpose of prioritising colonoscopy is not the same as establishing a diagnosis.⁹ The term "probable IBS" was included as a triaging decision during this period and eventually the patient will be reviewed in clinic to establish a positive diagnosis and recommend a management plan upon resumption of near-normal service. At this stage we are in full agreement with the comments made by Ruddy and colleagues. Our algorithm does not attribute any pathogenetic interpretation of the emotional state.

We declare no competing interests.

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- Iacucci M, Cannatelli R, Labarile N, et al. Endoscopy in inflammatory bowel diseases during the COVID-19 pandemic and post-pandemic period. *Lancet Gastroenterol Hepatol* 2020; 5: 598–606.
- Tanaka Y, Kanazawa M, Fukudo S, Drossman D. Biopsychosocial model of irritable bowel syndrome. *J Neurogastroenterol Motil* 2011; 17: 131–39.
- McKay D, Yang H, Elhaj J, Asmundson G. Anxiety relating to contracting COVID-19 related to interoceptive anxiety sensations: the moderating role of disgust propensity and sensitivity. *J Anxiety Disorders* 2020; 73: 102233.
- Park CL, Russell BS, Fendrich M et al. Americans' COVID-19 stress, coping, and adherence to CDC guidelines. *J Gen Intern Med* 2020; published online May 29. DOI:10.1007/s11606-020-05898-9.

- Pellissier S, Bonaz B. The place of stress and emotions in the irritable bowel syndrome. *Vitam Horm* 2017; 103: 327–54.
- Choung R, Locke G. Epidemiology of IBS. 3rd Ed. *Gastroenterol Clin North Am* 2011; 40: 1–10.
- Muscatello MRA, Bruno A, Mento C, et al. Personality traits and emotional patterns in irritable bowel syndrome. *World J Gastroenterol* 2016; 22: 6402–15.
- Crohn's and Colitis Foundation. IBD vs IBS. <https://www.crohnscolitisfoundation.org/what-is-ibd/ibs-vs-ibd> (accessed June 4, 2020).
- Spiegel BM, Farid M, Esrailian E, Talley J, Chang L. Is irritable bowel syndrome a diagnosis of exclusion? A survey of primary care providers, gastroenterologists, and IBS experts. *Am J Gastroenterol* 2010; 105: 848–58.

COVID-19 in liver transplant recipients: preliminary data from the ELITA/ELTR registry

Whether liver transplant recipients are at a particularly high risk for critical COVID-19 needs clarification. To date, data are scarce^{1–4} and results conflicting.

On March 30, 2020, the European Liver and Intestine Transplantation Association (ELITA) sent out a call to establish a COVID-19 registry for liver transplant recipients to 149 liver transplant centres affiliated to the European Liver Transplant Registry (ELTR) located in 30 European countries. 114 (77%) centres responded to the call, with 56 (49%) of these having observed cases of COVID-19 in their liver transplant recipients. We report data from the first 103 COVID-19 cases observed between March 1, and April 24, 2020, mainly from centres located in specific areas of Italy, Spain, and France. The cutoff for follow-up for this analysis was April 24, 2020. Eight patients have also been included in the COVID-Hep registry but were not among the cases reported by Webb and colleagues.³

76 (74%) recipients were male and 27 (26%) were female. The median age was age 65 years (range 11–82). Around half of patients had hypertension and two-fifths had diabetes (appendix).

13 (13%) patients had a history of tobacco smoking. 86 (85%) of 101 patients with available data were receiving tacrolimus as their primary immunosuppressant. Severe acute respiratory syndrome coronavirus 2 infection was confirmed by RT-PCR of respiratory swabs in 100 (97%) of 103 cases. The most common presenting symptoms were fever, cough, and shortness of breath (appendix). 20 (19%) patients without clinically significant respiratory symptoms were monitored at home, 68 (66%) were admitted to a general ward, and 15 (15%) were admitted to intensive care units. 64 (62%) hospitalised patients had radiological findings that were consistent with viral pneumonia. 68 (66%) patients required respiratory support, including oxygen supplementation (40 [59%] patients), non-invasive ventilation (15 [22%] patients), and mechanical ventilation (ten [15%] patients). The most frequent treatments for COVID-19 are reported in the appendix.

At a median follow-up of 18 days (range 1–121), 16 (16%) liver transplant recipients, including four (44%) of the nine patients on mechanical ventilation, had died. Mortality was observed only in patients aged 60 years or older (16 [22%, 95% CI 13–33] of 73 patients vs none [0%, 0–13] of 27 patients younger than 60 years), and was more common in male recipients than in female recipients (appendix). Although not statistically significant, more patients who were transplanted at least 2 years previously died than did those who received their transplant within the past 2 years (15 [18%, 95% CI 11–28] of 82 patients vs one [5%, 0–24] of 21 patients; appendix).

The results from the ELITA/ELTR COVID-19 registry suggest that mortality in liver transplant recipients might be higher in older recipients than in younger patients and could be worse in patients with longer



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See Online for appendix