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.

promotes gut motility) an increase of metagenomic richness was detected.[8] Likewise, other life style factors, most prominently nutrition, affect intestinal motility and gut microbiota composition. Thus, although subclinical endotoxaemia can affect hepatic steatosis and inflammation, based on the observations of the lubiprostone trial and the available literature, it seems likely that additional microbiota-associated factors are contributing.

The effect size of the primary endpoint in this phase 2 trial, which enrolled patients with ALT above 40 U/L, was moderate, with a mean decrease of ALT by 15 U/L in the 24 µg group and 12 U/L in the 12 µg group. The on-treatment effect was reversible after cessation of lubiprostone, suggesting a transient change. Although this moderate decrease in ALT levels was sufficient to show superiority of lubiprostone versus placebo in this 12-week trial, larger and later stage clinical trials have observed a higher placebo response rate.[9] Indeed, the placebo response rate is considered a major weakness of ongoing clinical trials for NAFLD, even though it was favourable in the current study.

It is intriguing to speculate that intestinal motility (through its effect on the gut microbiome, short chain fatty acid production, and or the effect on the intestinal permeability) affects disease severity in NAFLD. The most important question will be how to most effectively transform these early data into benefit for patients with NAFLD. One aspect could be the standardised promotion of supportive measures including regular physical exercise or standardised lifestyle changes. An old question in the treatment of patients with NALFD still remains: which patients require specific pharmacotherapy versus lifestyle modification only? If pharmacotherapy is chosen, the choice of mechanism of drugs to be considered (traditionally antisteatotic, anti-inflammatory, or antifibrotic[10]) could be expanded to include modulators of intestinal permeability and motility in the future. Importantly, here the compounds with the highest synergism in specific patient subgroups need to be defined and the current study provides early evidence that a history of constipation could be a treatment-relevant subgroup. Increasing bowel motility is a therapeutic goal that hepatologists and gastroenterologists are well acquainted with. The added benefit in the subgroup of patients with a history of constipation will need to be established in larger trials.

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SARS-CoV-2 infection in liver transplant recipients: collaboration in the time of COVID-19

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See **Articles** page 1008

In *The Lancet Gastroenterology & Hepatology*, Gwilym Webb and colleagues present a multicentre analysis of outcomes for 151 liver transplant recipients with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, with data collected from March 25, 2020, to June 26, 2020.[1] The study, which included liver transplant recipients from 18 countries, represents the largest reported series of liver transplant recipients with confirmed SARS-CoV-2 infection to date. The study is also the first to include a comparison with patients

with COVID-19 who have not received a liver transplant (n=627), having collected data from the electronic patient records of group of four hospitals in Oxford, UK. Importantly, the report provides an estimation of the risks for liver transplant recipients—who must balance the need for ongoing medical care with the need to remain isolated to reduce exposure to SARS-CoV-2—and also demonstrates the power of international collaboration in solving critical health-care challenges.

The study found no difference in the proportion of patients hospitalised between the liver transplant (124 [82%] patients) and the non-liver transplant cohort (474 [76%] patients; p=0·106). Despite an increased need for invasive ventilation support among recipients of liver transplants (30 [20%] *vs* 32 [5%] in the comparison cohort, p<0·0001), mortality was significantly lower in liver transplant recipients (28 [19%]) than in patients who had not received a liver transplant (167 [27%]; p=0·046). In a propensity score-matched analysis (adjusting for age, sex, creatinine concentration, obesity, hypertension, diabetes, and ethnicity), liver transplantation did not significantly increase the risk of death in patients with SARS-CoV-2 infection (absolute risk difference 1·4% [95% CI –7·7 to 10·4]).

COVID-19 lung disease was the main cause of death in both groups and, importantly, there were no liver-related deaths among the transplant recipients. Multivariable analysis showed that factors associated with death among liver transplant recipients included age and creatinine concentration, as well as the presence of non-liver malignancy, whereas time from transplantation and type of immunosuppression were not related to risk of death. In the control population, multivariable analysis showed age, male sex, and diabetes to be the major risk factors for death. An additional notable finding was the higher rates of gastrointestinal symptoms in the liver transplant cohort, with 30% having abdominal pain, vomiting, or diarrhoea at diagnosis compared with just 12% of the control group having abdominal symptoms (p<0·0001).

There are some important caveats to the current analysis, such as the significant differences between the two cohorts. Although age, a key risk factor, was higher in the comparison cohort (median 73 years [IQR 55–84]) than the liver transplant cohort (median 60 years [47–66]), the liver transplant group had significantly greater proportions of men (68% *vs* 52% in the comparison cohort) and patients with diabetes (43% *vs* 23% in the comparison cohort). In addition, testing rates and thresholds for hospitalisation and admission to an intensive care unit might have differed across different centres and between the cohorts. Furthermore, the liver transplant cohort might have been subject to reporting bias because the data were collected from two registries of clinician-submitted cases; those clinicians might have been more likely to be aware of, and thus submit data on, hospitalised liver transplant recipients with more severe infections (as compared with the comparison cohort, which was drawn from consecutive cases of patients testing positive for SARS-CoV-2). However, this bias would only serve to strengthen the main conclusion that liver transplant recipients are not at a higher risk of death than patients who have not undergone transplantation.

It is essential to note that the median time from transplantation in this liver transplant cohort was 5 years (IQR 2–11), and thus the current experience cannot be extrapolated to patients who might acquire SARS-CoV-2 infection in the perioperative period.

Despite these limitations, Webb and colleagues' study[1] represents the largest experience of SARS-CoV-2 infection in liver transplant recipients to date, and found no adverse effect of liver transplantation on survival following COVID-19 compared with a UK population cohort of patients without liver transplant.

A recently published single-centre study of 36 kidney transplant recipients in the USA showed a similar rate of hospitalisation (78%), with a potentially higher rate of death (28%), although, unlike the present series of liver transplant recipients, at least some kidney transplant recipients were within weeks of transplantation.[2] A larger multicentre series of 144 kidney transplant recipients, which included only hospitalised patients, found a mortality rate of 32% in a cohort with a median time from transplantation of 5 years, although that study also included some patients with less than 1 year since transplantation.[3]

Whether there are actually differences in outcome between patients undergoing liver or kidney transplantation, or transplantation of other organs, remains to be determined, although the question is likely to be answered best by large collaborative efforts, as reflected in Webb and colleagues' study.[1] Despite the

unprecedented challenges imposed by the current pandemic on all aspects of our lives, centres across the globe were able to work together to collect and analyse detailed outcome data for more than 700 patients with SARS-CoV-2 infection, thus providing crucial information on a potentially at-risk population, with an efficiency and scale only possible through international collaboration.

We declare no competing interests.

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COVID-19 as a barrier to attending for gastrointestinal endoscopy: weighing up the risks

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See **Online** for appendix

Gastrointestinal endoscopy is the cornerstone of gastrointestinal cancer diagnostics. Services were largely suspended during the peak of the COVID-19 pandemic (appendix p 1),[1] with procedures done during April and May, 2020, representing only 12% of pre-COVID-19 activity.[2] Following British Society of Gastroenterology[3] guidance on recommencing gastrointestinal endoscopy at the end of April, 2020, UK services have increased; however, levels vary by procedure type and unit. According to the National Endoscopy Database, by July 5, 2020, activity had only reached 42% of pre-COVID levels.

For more on the **National Endoscopy Database** see https://nedpilot.thejag.org.uk

After recommencement of endoscopy procedures in April, 2020, delivery issues, including reduced staff and room capacity, need for enhanced personal protective equipment, creation of COVID-minimised pathways, including room downtime, enhanced cleaning, and need for linear flow of patients through units, have resulted in substantially reduced services (appendix p 1). Reluctance of patients to attend for investigations is also a major factor contributing to the reduction in services, and despite the implementation of measures to protect patients and staff,[4] many services have reported a substantial number of patients are not attending appointments.

During the peak of the COVID-19 epidemic, people were strongly encouraged to avoid attending hospital. Many patients remain concerned about this: a UK YouGov survey done in June, 2020,[5] indicated that 42% of respondents felt uncomfortable about attending a routine hospital appointment. Research done before the COVID-19 epidemic identified anxiety as a major factor for patients attending endoscopy, affecting experience; patients feel anxious about why they have been referred, what the test involves, whether it will be painful or embarrassing, and what results might show. COVID-19 adds further complexity and UK endoscopy units have reported many patients citing anxiety about contracting COVID-19 as an important factor in deciding whether to attend.

Decision making about attendance, what factors influence this, and how patients assess competing risks that cancer (and other conditions detected by endoscopy) and COVID-19 pose, are poorly understood. Anxiety about COVID-19, family pressures, logistical considerations, such as carer responsibilities, and travel to and from the hospital while adhering to social distancing, might also be barriers. The cultural attitude of sparing health services is important and varies between countries but is likely to have been reinforced during COVID-19, when for example the message from the UK Government was to protect health services. The scarcity of evidence on what influences behaviour hinders our ability to take action to reassure patients and increase uptake.

To minimise the potential impact of COVID-19 associated diagnostic and treatment delays on patients with cancer, it is vital that endoscopic procedures are safely and effectively reinstated and that patients feel reassured that it is safe to attend. In June, 2020, an