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Only with enhanced donor screening and validated stool tests for SARS-CoV-2 can we ensure safe and effective delivery of FMT to critically ill patients with recurrent and refractory *Clostridioides difficile* infection.

SCN reports grants from Ferring, personal fees from Takeda, AbbVie, Janssen, and Tillotts, outside the submitted work. SCN and FKLC have patents pending for faecal fungome and therapeutic efficacy of FMT, faecal virome and therapeutic efficacy of FMT, therapeutic and prophylactic use of microorganisms, and methods for treating bacterial infections. FKLC reports grants from Olympus Hong Kong and China, Pfizer, AstraZeneca, Takeda Pharmaceuticals, Takeda (China) Holdings, and Given Imaging; and personal fees from the American Gastroenterological Association, Medical Association of Guangdong Province, Olympus Hong Kong & China, Pfizer, AstraZeneca, Takeda Pharmaceuticals, EA Pharma, Takeda (China), Associacao Dos Medicos Hospitalares Da Funcao Publica De Macau, Pfizer Upjohn Korea, Fujifilm, Ministry of Health Singapore, and the Japanese Gastroenterological Endoscopy Society; and is also an advisor and commentator for evidence-based medicine for the Ministry of Health of the People's Republic of China, Pfizer, AstraZeneca, the Ministry of Health of Singapore, the American College of Physicians Journal Club, and *Nature Reviews Gastroenterology & Hepatology*. PKSC declares no competing interests.

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Determining risk factors for mortality in liver transplant patients with COVID-19

We read with great interest the Correspondence from Bhoori and colleagues¹ describing the effect of coronavirus disease 2019 (COVID-19) on their centre's adult liver transplant population.¹ Within their cohort of over 150 transplant recipients, the authors identified six patients with COVID-19, including three resulting deaths. Each of those who died was transplanted over 10 years previously and were older than 65 years, male, overweight, and had hypertension and diabetes. The authors speculated as to whether these characteristics might be major risk factors for mortality.

We operate two collaborating international registries (SECURE Cirrhosis covering the Americas, China,

Japan, and South Korea; and COVID-Hep covering the rest of the world) working to collate details of patients with chronic liver disease and post-liver transplantation who develop COVID-19. As of April 22, 2020, we have received submissions from 21 countries. Here, we summarise details of the 39 liver transplant recipients who developed COVID-19, including nine (23%) who died from respiratory failure (table).

By contrast with the experience of Bhoori and colleagues, the deaths in our cohort included four patients transplanted within the past 2 years, with a median age younger than 65 years, and 44% women. Among the patients who died, four (44%) had diabetes, four (44%) had hypertension, and three (33%) were obese. Although our numbers were small, the frequencies of these comorbidities were not significantly different between those of fatal and non-fatal cases of COVID-19 (table).



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For the COVID-Hep registry see

<http://www.COVID-Hep.net>

For the SECURE Cirrhosis registry see <https://covidcirrhosis.web.unc.edu>

	Survived (n=30)	Died (n=9)	p value
Age (years)	58 (50–64)	63 (61–67)	0.102
Sex	0.696
Male	20 (67%)	5 (56%)	..
Female	10 (33%)	4 (44%)	..
Overweight (BMI >25 kg/m ²)	19 (63%)	7 (78%)	0.695
Obese (BMI >30 kg/m ²)	7 (23%)	3 (33%)	0.679
Heart disease	4 (13%)	2 (22%)	0.607
Diabetes	11 (37%)	4 (44%)	0.711
Arterial hypertension	14 (47%)	4 (44%)	1.000
Time from transplant (years)	5 (2–11)	6 (1–8)	0.580
Baseline laboratory characteristics			
Serum sodium (mmol/L)	138 (137–141)	138 (136–139)	0.266
Serum total bilirubin (μmol/L)	10 (7–13)	10 (8–15)	0.570
Serum albumin (g/L)	40 (37–42)	37 (33–38)	0.025
Serum creatinine (μmol/L)	109 (80–133)	141 (111–186)	1.000
Prothrombin time (s)	12 (11–14)	12 (11–15)	0.930
Immunosuppressive drugs			
Prednisone or prednisolone	10 (33%)	6 (67%)	0.123
Tacrolimus	27 (90%)	8 (89%)	1.000
Sirolimus	2 (7%)	0 (0%)	1.000
Mycophenolate mofetil	16 (53%)	4 (44%)	0.716

Data are n (%) or median (IQR). BMI=body-mass index. p values were calculated using Wilcoxon rank-sum or Fisher's exact tests as appropriate.

Table: Baseline characteristics of 39 patients with previous liver transplant and laboratory-confirmed COVID-19 submitted to the COVID-Hep and SECURE Cirrhosis registries



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These conflicting findings are further reinforcement that greater case numbers are urgently required to accurately inform our understanding of individual risk.

Collating and analysing rapidly emerging data will be vital for identifying modifiable risk factors for severe COVID-19 among liver transplant recipients. For example, different immunosuppression regimens might confer differential risk and changes to these medications might mitigate the risk of COVID-19 complications.

Although early data suggest that the effects of COVID-19 on the liver might be modest and reflect infection severity among patients without pre-existing liver disease, the effects of COVID-19 on those with liver transplants or established liver disease remain unclear.² We call on all those caring for patients with previous liver transplantation and other forms of chronic liver disease to use registries to pool details of COVID-19 cases and so permit the rapid large-scale collaborative analyses that are required to inform clinical care.

We declare no competing interests.

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- 2 Zhang C, Shi L, Wang F-S. Liver injury in COVID-19: management and challenges. *Lancet Gastroenterol Hepatol* 2020; 5: 428–30.

Probiotics and COVID-19: one size does not fit all

As of April 20, 2020, coronavirus disease 2019 (COVID-19) has affected more than 2 million people globally. In February, 2020, China's National Health Commission and National Administration of Traditional Chinese Medicine suggested the use of probiotics in patients with severe COVID-19.¹ We reviewed the evidence for the role of probiotics in COVID-19-related illnesses (appendix).

In China, 58–71% of patients with COVID-19 were given antibiotics, and diarrhoea occurred in 2–36% of patients.^{2–4} When antibiotics are used, reinforcement of colonic flora using probiotics has been proposed to reduce susceptibility to subsequent infections. Although a 2012 meta-analysis⁵ showed that probiotics have modest efficacy in reducing antibiotic-associated diarrhoea, the largest randomised, placebo-controlled trial (involving 2941 participants) showed that a 21-day treatment of combined *Lactobacilli* and *Bifidobacteria* did not reduce antibiotic-associated diarrhoea.⁶ Even if probiotics are useful, they are unlikely to have a direct effect on severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection; most patients with COVID-19 present with respiratory symptoms. However, gut-lung crosstalk has been proposed in the pathogenesis of certain respiratory conditions. Two meta-analyses reported modest efficacy of probiotics in reducing the incidence and duration of respiratory tract infections of viral origin.^{7,8} During the COVID-19 pandemic, 2–47% of infected patients required invasive mechanical ventilation.^{3,4} Two randomised controlled trials showed that critically ill patients on mechanical ventilation who were given probiotics (*Lactobacillus rhamnosus* GG, live *Bacillus subtilis*, and *Enterococcus faecalis*) developed substantially less ventilator-associated

pneumonia compared with placebo.^{9,10} However, the efficacy of probiotics in reduction of intensive care unit mortality and inpatient mortality is uncertain.

Scarce data are available on the effect of COVID-19 on intestinal microbiota. A small case series from China revealed that some patients with COVID-19 showed microbial dysbiosis with decreased *Lactobacillus* and *Bifidobacterium*.¹¹ However, animal studies (as yet, not peer-reviewed) showed that *Lactobacillus acidophilus* and *Bacillus clausii* did not reduce coronavirus receptor expression in the murine small intestine compared with control and post-*Salmonella* infection models.¹² Not all probiotics are likely to be the same. *Lactobacilli* and *Bifidobacteria* are only two types of non-pathogenic bacteria and we must consider whether they can really tip the balance of a diverse gut ecosystem in combating COVID-19. To date, the rationale for using probiotics in COVID-19 is derived from indirect evidence. Blind use of conventional probiotics for COVID-19 is not recommended until we have further understanding of the pathogenesis of SARS-CoV-2 and its effect on gut microbiota. It is likely that a novel and more targeted approach to modulation of gut microbiota as one of the therapeutic approaches of COVID-19 and its comorbidities will be necessary.

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