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.

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Screening FMT donors during the COVID-19 pandemic: a protocol for stool SARS-CoV-2 viral quantification

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We read with interest the Correspondence by Christopher Green and colleagues[1] suggesting the need for a molecular test to screen faecal microbiota transplant (FMT) donors for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to prevent the potential risk of transmission. On March 12, 2020, the US Food and Drug Administration (FDA) issued safety alerts because of a death caused by transmission of drug-resistant *Escherichia coli* bacteraemia via FMT.[2] With more than 1 million people infected by SARS-CoV-2, screening policies for FMT donors should be stringent and scientifically validated. The presence of SARS-CoV-2 (including live virus) in stool of asymptomatic individuals implies that coronavirus disease 2019 (COVID-19) might be transmitted via the faecal route.[3,4] Development of stool tests has been slow, since real-time RT-PCR of respiratory samples is typically used to confirm the diagnosis of COVID-19.

At the time of writing, the FDA recommends that only FMT products generated from stool donated before Dec 1, 2019, should be used until proper testing and screening protocols are available.[5] As described by Green and colleagues,[1] the University of Birmingham Microbiota Treatment Centre (Birmingham, UK) is not actively processing new donors until a validated SARS-CoV-2 stool test is available. The FMT centre at the Chinese University of Hong Kong (Hong Kong) is one of the largest providers of FMT in Asia and is the sole provider of FMT to the Health Authority of Hong Kong. Although the first case of COVID-19 was reported in Hong Kong on Jan 22, 2020, we quarantined all donor material donated since Nov 1, 2019, from use. We developed a screening protocol that combines a questionnaire to identify donors who might be at risk of SARS-CoV-2 infection with an RT-PCR assay for detecting SARS-CoV-2 in donor stool. The assay (panel) allows SARS-CoV-2 viral quantification with a 3 h turnaround. We validated the assay in 81 stool samples from 21 confirmed SARS-CoV-2 cases and 114 stool samples from 114 asymptomatic non-infected individuals who had returned from high-risk areas. As per the diagnostic protocol of our local health authority, all COVID-19 cases had been confirmed by two RT-PCR tests targeting different regions of the *RdRp* gene in respiratory specimens. All 21 confirmed cases had positive stool tests (median two stool samples positive for SARS-CoV-2 per patient; viral load 2·9–7·1 $\log_{10}$ copies per mL). No stool samples from the 114 asymptomatic individuals tested positive for SARS-CoV-2.

We found that a single negative test, as in the current practice for screening other pathogens, is insufficient to exclude the presence of SARS-CoV-2 in stool. We recommend testing donors at multiple timepoints during the donation period, since the level of viral RNA present in stool can fluctuate around the margin of laboratory detection. Testing stool for SARS-CoV-2 should be done in appropriately equipped laboratories by trained staff; specimen handling would require biosafety level 2 laboratories or equivalent facilities.

***Panel*: Protocol for SARS-CoV-2 viral quantification in stool samples**

Stool collection and viral DNA extraction
- Collect stool in sterile plain bottles
- Suspend 0·1 g stool in 1 mL viral transport medium (in 1:10 dilution)
  - Centrifuge at 4000 g for 20 min
  - 140 µL aliquot of filtrate for following work
- Extract viral RNA using spin column-based extraction method
  - Kit example: QIAamp Viral RNA Mini Kit (Qiagen, Hilden, Germany), PureLink Viral RNA/DNA Mini Kit (ThermoFisher Scientific, Waltham, MA, USA)

SARS-CoV-2 viral load quantification
- SARS-CoV-2 RNA quantified using RT-quantitative PCR with following settings:
  - Primer-probe set N1
    - 2019-nCoV_N1-F: 5′-GAC CCC AAA ATC AGC GAA AT-3′
    - 2019-nCoV_N1-R: 5′-TCT GGT TAC TGC CAG TTG AAT CTG-3′
    - 2019-nCoV_N1-P: 5′-FAM-ACC CCG CAT TAC GTT TGG TGGACC-BHQ1-3′
  - Cycling conditions
    - One cycle: 25°C for 2 min, 50°C for 15 min, 95°C for 2 min
    - 45 cycles: 95°C for 15 s and 55°C for 30 s

SARS-CoV-2 RT quantitative PCR data analysis
- Samples are considered negative if cycle threshold values exceeded 39·9 cycles
- Detection limit of real-time RT-PCR is 347 copies per mL

SARS-CoV-2= severe acute respiratory syndrome coronavirus 2.

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.

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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 colleagues[1] 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).

	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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For the **COVID-Hep registry** see http://www.COVID-Hep.net

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