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.

6 Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; **395:** 507–13.

7 Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalised patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020; published online Feb 7. DOI:10.1001/jama.2020.1585.

8 Shi H, Han X, Jiang N, et al. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study. *Lancet Infect Dis* 2020; published online Feb 24. DOI:10.1016/S1473-3099(20)30086-4.

9 Xu X-W, Wu X-X, Jiang X-G, et al. Clinical findings in a group of patients infected with the 2019 novel coronavirus (SARS-Cov-2) outside of Wuhan, China: retrospective case series. *BMJ* 2020; published online Feb 19. DOI:10.1136/bmj.m606.

10 Yang X, Yu Y, Xu J, et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med* 2020; published online Feb 24. DOI:10.1016/S2213-2600(20)30079-5.

11 Yeo C, Kaushal S, Yeo D. Enteric involvement of coronaviruses: is faecal–oral transmission of SARS-CoV-2 possible? *Lancet Gastroenterol Hepatol* 2020; published online Feb 19. DOI:10.1016/S2468-1253(20)30048-0.

12 Chai X, Hu L, Zhang Y, et al. Specific ACE2 expression in cholangiocytes may cause liver damage after 2019-nCoV infection. *bioRxiv* 2020; published online Feb 4. https://doi.org/10.1101/2020.02.03.931766 (preprint).

13 Xu Z, Shi L, Wang Y, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med* 2020; published online Feb 18. DOI:10.1016/S2213-2600(20)30076-X.

Screening of faecal microbiota transplant donors during the COVID-19 outbreak: suggestions for urgent updates from an international expert panel

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As the outbreak of coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has rapidly spread from China to other countries, governments and the medical community are taking steps to prevent transmission, from common sense recommendations to radical quarantine measures.[1]

In that context, timely recommendations concerning the screening of donors of human cells, tissues, or cellular or tissue-based products have been released, as the potential for transmission of COVID-19 through transplant is not yet known. Several institutions have recommended interim precautions to screen new donors. The US Food and Drug Administration has suggested considering a donor's history of travel to areas of outbreak, cohabitation with infected individuals, or diagnosis or suspicion of COVID-19 within the 28 days before recovery of donor tissue.[2] Similar measures have been taken by the Global Alliance of Eye Bank Associations and by the Joint United Kingdom Blood Transfusion Services Professional Advisory Committee to rule out potential donors.[3,4] The European Society for Blood and Marrow Transplantation has recommended excluding potential donors who have been diagnosed with COVID-19, and waiting at least 21 days before donation in those with a history of high-risk travel or contact.[5] In Italy, where the COVID-19 outbreak is spreading rapidly, the national transplant centre has taken stronger measures and has recommended testing all potential tissue and stem-cell living donors, as well as dead donors, through real-time RT-PCR assays of nasopharyngeal swab samples (or bronchoalveolar lavage in deceased individuals).[6]

Faecal microbiota transplantation is a novel treatment that has rapidly earned a major role in the management of recurrent *Clostridioides difficile* infection because of its clear advantages over antibiotics.[7] It is becoming increasingly more widespread and standardised around the world. Last year, an international expert panel, including several authors of this Comment, released recommendations on how to screen faecal microbiota transplant donors, including a medical history and blood and stool examinations.[8]

Given the global COVID-19 outbreak, we, as an international group of experts in faecal microbiota transplantation and stool banking, believe that recommendations to update (at least temporarily) the screening of stool donors are urgently needed, as the risk of transmitting SARS-CoV-2 by faecal microbiota transplantation might be higher than that in other tissue transplants. Evidence has shown that the SARS-CoV-2 can be found in faeces, and that stool samples can remain positive for the virus even when it is no longer detectable in the respiratory tract, suggesting the possibility of a faecal–oral route of transmission.[9] This concept is supported by the presence of gastrointestinal symptoms in some patients affected by COVID-19.[10] Another relevant issue is that faecal microbiota transplantation is not classified in the same way worldwide, as some countries regulate these transplants as a drug (eg, the USA, the UK, and France), some as

a tissue (eg, Italy), and others do not provide specific regulation (eg, Australia).[8] This discrepancy results in a confusing scenario, in which some countries will apply rules for human cells, tissues, or cellular or tissue-based products, and others will not, potentially contributing to the spread of the infection. A more alarming issue is represented by the uncontrolled practice of homemade faecal microbiota transplantation, which is widespread among patients who want to try this treatment for indications outside of clinical guidelines or clinical trials.[11]

To prevent SARS-CoV-2 transmission, we propose additions to the current donor screening measures. In all countries, before each donation, physicians should screen for two main items: the presence of typical COVID-19 symptoms (including fever, fatigue, dry cough, myalgia, dyspnoea, and headache) within the previous 30 days; and the donor's history of travel to regions known to be affected by COVID-19 or close contact with individuals with proven or suspected infection, within the previous 30 days. If either of these items is positive, the potential donor should either be rejected or tested with RT-PCR assay for SARS-CoV-2. In endemic countries, the RT-PCR assay should be considered in all donors, even if they are asymptomatic or do not have a history of high-risk travel or contact. Alternatively, donor stools should be stored and quarantined for 30 days before use, and released only if the donor has not developed symptoms. Finally, stool banks should retrospectively check the health status of the donor before using frozen faeces, according to local epidemiology, to avoid further potential spreading of SARS-CoV-2. These suggestions should be tailored to local health-care organisations, and should be updated accordingly as further insight into COVID-19 and SARS-CoV-2 is gained.

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1 Xiao Y, Torok ME. Taking the right measures to control COVID-19. *Lancet Infect Dis* 2020; published online March 5. https://doi.org/10.1016/S1473-3099(20)30152-3.

2 US Food and Drug Administration. Important Information for human cell, tissue, or cellular or tissue-based product (HCT/P) establishments regarding the 2019 novel coronavirus outbreak. 14 Feb, 2020. https://www.fda.gov/vaccines-blood-biologics/safety-availability-biologics/important-information-human-cell-tissue-or-cellular-or-tissue-based-product-hctp-establishments (accessed March 6, 2020).

3 Global Alliance of Eye Bank Associations. ALERT: Coronavirus (COVID-2019) and ocular tissue donation. Feb 3, 2020. https://www.gaeba.org/2020/alert-coronavirus-2019-ncov-and-ocular-tissue-donation/ (accessed March 6, 2020).

4 Joint United Kingdom (UK) Blood Transfusion and Tissue Transplantation Services Professional Advisory Committee. Coronavirus infection. 2020. https://www.transfusionguidelines.org/dsg/wb/guidelines/coronavirus-infection (accessed March 6, 2020).

5 European Society for Blood and Marrow Transplantation. Coronavirus disease COVID-19: updated EBMT recommendations. 2020. https://www.ebmt.org/ebmt/news/ebmt-recommendation-coronavirus-disease-covid-19 (accessed March 6, 2020).

6 Ministero Della Salute. Oggetto: aggiornamento delle misure di prevenzione della trasmissione dell'infezione da nuovo coronavirus (SARS-CoV-2) in Italia attraverso il trapianto di organi, tessuti e cellule. March 3, 2020. http://www.trapianti.salute.gov.it/imgs/C_17_cntAvvisi_231_0_file.pdf (accessed March 6, 2020).

7 Ianiro G, Murri R, Sciumè GD, et al. Incidence of bloodstream infections, length of hospital stay, and survival in patients with recurrent *Clostridioides difficile* infection treated with fecal microbiota transplantation or antibiotics a prospective cohort study. *Ann Intern Med* 2019; **171:** 695–702.

8 Cammarota G, Ianiro G, Kelly CR, et al. International consensus conference on stool banking for faecal microbiota transplantation in clinical practice. *Gut* 2019; **68:** 2111–2121.

9 Xiao F, Tang M, Zheng X, Liu Y, Li X, Shan H. Evidence for gastrointestinal infection of SARS-CoV-2. *Gastroenterology* 2020; published online March 3. DOI:10.1053/j.gastro.2020.02.055.

10 Wang D, Hu B, Hu C, et al. Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020; published online Feb 7. DOI:10.1001/jama.2020.1585.

11 Ekekezie C, Perler BK, Wexler A, Duff C, Lillis CJ, Kelly CR. Understanding the scope of do-it-yourself fecal microbiota transplant. *Am J Gastroenterol* 2020; published online Jan 10. DOI:10.14309/ajg.0000000000000499.

Is it unethical to conduct placebo-controlled trials of faecal microbiota transplantation for recurrent *Clostridioides difficile* infection?

Patients encountered early in our experience of using faecal bacteriotherapy to treat recurrent *Clostridioides difficile* infection included a woman admitted to hospital six times with severe complicated infections and a toddler who had been on antibiotics for more than half of his life, who had relentless severe diarrhoea and weight loss due to recurrent *C difficile* infection. Both were cured with a single dose of stool donated by a family member, a procedure now known as faecal microbiota transplantation (FMT). Previously considered to be a last resort, the practice of FMT has greatly increased since the first randomised controlled trial (RCT) was published in 2013,[1] with strong consensus among doctors doing the procedure that FMT is the most effective option for recurrent *C difficile* infection. Nevertheless, placebo-controlled FMT trials designed to show efficacy and safety in recurrent *C difficile* infection are ongoing, placing enrolled patients at risk of further recurrence.

Vast clinical experience and existing data confirm the superiority of FMT over antibiotics for prevention of recurrent *C difficile* infection in adults.[1,2] As such, placebo-controlled trials of FMT do not meet the requirement for clinical equipoise—ie, the genuine uncertainty that one treatment is superior to another. Given this lack of equipoise, the high efficacy of FMT and the substantial morbidity and mortality associated with recurrent *C difficile* infection, should placebo arms still be used in trials of FMT for this indication? Although considered to be the most rigorous means by which to analyse the effect of an intervention, placebo-controlled trials must balance the value of adherence to scientific methods with also protecting research participants. Because of potential ethical concerns, internationally accepted guidelines support the use of a placebo only in specific circumstances: when there is no proven effective treatment for the condition under study, when withholding treatment poses negligible risk to patients, when there are compelling methodological reasons to use a placebo, or when the trial does not require participants to forgo treatment they would otherwise receive.[3] None of these criteria applies to the treatment of recurrent *C difficile* infection with FMT.

Meta-analyses of RCTs investigating FMT for prevention of recurrence of *C difficile* infection after standard antibiotic treatment show high efficacy, with a number needed to treat of three.[2] In fact, the thousands of patients treated essentially served as their own controls: failing multiple antibiotic courses, including tapering regimens drawn out over months, and only achieving long-term cure after FMT from any healthy donor. Furthermore, microbiome analyses have shown dramatic resolution of dysbiosis in recipients and suggested mechanisms of therapeutic effect.[4] FMT is now strongly recommended by expert treatment guidelines[5] and is rapidly becoming standard of care.

Patients come to us hopeless and debilitated, having received endless cycles of antibiotic courses for recurrent *C difficile* infection. Some describe their lives as being on hold, as they miss school or work, become socially isolated, spend thousands of dollars on treatments, and are consumed with anxiety over the possibility of further episodes. More than merely causing diarrhoea, *C difficile* infection can be fatal: mortality in hospitalised patients is high, with nearly 29 000 Americans per year dying within 30 days of a diagnosis of *C difficile* infection.[6] Withholding FMT from these patients can result in serious harm or death, therefore a placebo has no role. As such, the first RCT of FMT was stopped early because of high recurrence rates in the control groups.[1] A search