CADTH

ENVIRONMENTAL SCAN

Fecal Microbiota Therapy in Canada: An Environmental Scan

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Abbreviations

CDI	*Clostridioides difficile* infection
CAD	Canadian dollars
ECRI	Emergency Care Research Institute
FMT	fecal microbiota therapy
GI	gastrointestinal
HTA	health technology assessment
IBD	inflammatory bowel disease
IBS	irritable bowel syndrome
MDRO	multi-drug resistant organism
rCDI	recurrent *Clostridioides difficile* infection
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SOFT	Southern Ontario Fecal Microbiota Transplantation Movement

Summary

- The findings of this Environmental Scan are based on a literature review, 17 stakeholder survey responses, and email-based follow-up consultations with select stakeholders. Eight Canadian jurisdictions are represented by the survey respondents, who were primarily physicians involved in fecal microbiota therapy (FMT) research (i.e., clinical trials) and providing FMT from screening to follow-up.
- FMT is currently being offered at facilities in at least seven Canadian jurisdictions (with some having programs in development). More populated provinces, including Alberta, British Columbia, Quebec, and Ontario, have the highest number of facilities offering FMT, the most established programs, and the highest number of active clinical trials for non-recurrent *Clostridioides difficile* infection conditions. Respondents reported treatment capacity ranging from zero to 80 patients per year.
- FMT is approved in Canada for clinical use in patients with recurrent *C. difficile* infection; though, in general, patients must meet specific clinical criteria to receive treatment. FMT may not be a treatment option due to clinical contraindications, inability to identify a donor, or if they are unable to tolerate the administration method.
- Patients with conditions other than recurrent *C. difficile* infection may be able to access treatment through participation in clinical trials. In Canada, clinical trials are ongoing in seven Canadian jurisdictions for a range of gastrointestinal and other conditions.
- Various barriers and facilitators to FMT implementation and access were identified by survey respondents and from published literature. The majority pertained to evidence; public perception; and factors related to donors, screening, manufacturing practices, patients' health status and discomfort, finances, infrastructure, treatment, and ethical, legal or social issues.
- Strategies to address barriers include the adoption of universal stool banks; the amendment of regulations to enable broader access; implementing mechanisms to ensure funding and reimbursement; the provision of dedicated facilities and infrastructure for FMT; and broader education of donors, patients, and care providers.
- The COVID-19 pandemic has introduced new barriers and safety concerns regarding FMT access and procedures. Regulatory guidance now requires adequate screening and testing for severe acute respiratory syndrome coronavirus 2 (COVID-19) and FMT program operations may be impacted.

Context

Clostridioides difficile Infection

Gut dysbiosis, or imbalances in gut microbiota, occurs when the proportion of bacteria associated with a positive effect on human health is reduced, and the proportion of bacteria with a negative effect is increased.[1] *C. difficile* is a bacterial species that colonizes the gastrointestinal (GI) tract after disruption of normal gut microbiota.[1,2] It is the most common cause of health care–associated infections in Canada. In 2016, the pooled incidence of hospital-acquired *C. difficile* infection (CDI) ranged from 2.3 to 4.6 cases per 10,000 inpatient days.[3] While the rate of hospital-acquired CDI in Canada has decreased over time, the rate of community-acquired cases has increased.[3-5] Common factors associated with CDI include previous hospitalization, underlying disease, advanced age, and the use of antibiotics.[6]

Standard therapy for CDI is antibiotics, yet even with treatment, the rate of treatment failure and recurrence is high.[7] Recurrent CDI (rCDI) is common and can lead to increased health care visits, longer hospital stays, and persistent symptoms.[8,9] Health care costs attributed to CDI have been estimated at over CA$280 million annually.[10,11] Given the detrimental changes CDI imposes on the microbiome (e.g., overpopulation and toxin expression causing a range of mild-to-severe gastrointestinal symptoms),[12] strategies aimed at restoring normal gut flora have been explored as a method of avoiding recurrence.[5]

Fecal Microbiota Therapy

Fecal microbiota therapy (FMT) — also referred to as fecal microbiota transplant, fecal probiotic therapy, fecal bacteriotherapy, stool transplant, and microbial ecosystem therapeutics — involves the processing and transfer of microbiota in screened stool from a healthy donor to a patient with compromised gut microbiota due to CDI or other gastrointestinal conditions.[13] Donor stool samples are screened for both blood-borne and enteric pathogens, and donors undergo a clinical risk assessment and blood tests for other transmittable diseases. The transfer is made by administering fresh, frozen, or freeze-dried products via nasogastric tube, gastroscopy, colonoscopy, or retention enema, or providing oral capsules. Most FMT evidence and guidance is for individuals with rCDI, yet interest is growing in its use for other gastrointestinal conditions, such as inflammatory bowel disease (IBD; e.g., ulcerative colitis and Crohn disease) and irritable bowel syndrome (IBS). FMT studies are planned or ongoing for more than 30 conditions.[14]

FMT is purported to resolve CDI through the restoration of a healthy gut ecosystem that reduces pathogen advantage, as well as through modulation of the immune system.[14] Numerous evidence syntheses have reported that FMT is potentially more effective and cost-effective for treating rCDI than placebo or standard therapy.[15-25] The most common adverse effect associated with FMT is abdominal discomfort.[26] Serious adverse events are rare but include death, infection, and disease relapse.[26] There is also concern over the possible transmission of known and unknown pathogens.[26] Recently, alerts have been issued due to deaths in the US caused by donor stools containing organisms that caused invasive *Escherichia coli* infections.[27]

Clinical societies and guideline developers have issued recommendations about the use of FMT for rCDI.[28-31] Despite this, there is still uncertainty about the appropriate dose, frequency of administration, route of delivery (e.g., upper versus lower GI tract) and preparation (e.g., fresh versus frozen).[16] There is also uncertainty surrounding which conditions other than

rCDI are most likely to benefit,[32] and the durability of the effect.[14] Furthermore, substantial heterogeneity has been documented in the conduct and findings of studies investigating the effectiveness of FMT.[33]

Canadian Context

In Canada, there has been documented use of FMT as salvage therapy for CDI since 1996.[34] Historically, health care facilities were averse to onsite procedures, leading many specialists to resort to administering FMT in patients' homes.[34] This aversion was based mainly on the state of the evidence at the time — confined primarily to case studies — and uncertainty regarding safety and the risk of disease transmission.[34]

In 2011, Alberta's Institute of Health Economics evaluated the clinical evidence and cost-effectiveness of FMT, and reported that there was limited clinical evidence and a lack of guidelines on the use of FMT in Canada. The report concluded that the potential for FMT as an experimental or accepted procedure for patients with rCDI was yet to be determined.[35] In 2012, a two-day Canadian Institutes of Health Research–sponsored meeting was held to evaluate the available FMT evidence and experience among experts, and to explore factors influencing slow implementation.[36] At the time, questions were raised about whether there was sufficient evidence to support widespread adoption, and there was uncertainty about treatment composition, preparation and delivery, and how FMT should be regulated.[36] A 2014 Canadian Association of Gastroenterology position statement reflected these uncertainties.[37]

In 2015, following the emergence of new supportive evidence, Health Canada approved the use of FMT for patients with rCDI outside of the clinical trial setting using a directed donor model (i.e., the patient or physician must identify a stool donor).[38,39] The guidance did not address the manufacturing, preparation, and delivery of FMT, and stated that FMT would be regulated as a "new biologic drug," falling under the purview of the Biologic and Genetic Therapies Directorate.[39] Health Canada's guidance replicated the US FDA's 2013 enforcement policy, which stated that patients receiving FMT therapy must have first tried conventional treatment.[39]

In 2016, Health Quality Ontario conducted a health technology assessment (HTA) that led to an Ontario Health Technology Advisory Committee recommendation to fund FMT for patients with CDI based on its clinical benefit and value for money.[40] In 2018, it was reported that from 2013 onward, approximately 1,300 FMT procedures had been performed across six institutions in Southern Ontario.[41] Currently, research is active in Canada, with clinical trials of FMT ongoing in seven jurisdictions for a range of conditions,[42] and many individuals gaining access to care through participation in these trials.

FMT has been covered extensively by Canadian media,[43] with headlines noting its growing popularity and suggesting a paradigm shift of the public perception of the treatment from novel to mainstream. Media reports of patients seeking and providers offering unregulated within or out-of-country FMT for non-approved conditions have raised concern about patient safety risks.[44-46] Debate persists over the classification of this therapy and where it best fits within Health Canada's regulatory framework.[36] The approval of FMT for new clinical indications and its associated demand may increase in the future. Nevertheless, the infrastructure and standardized processes needed are not in place. The 2016 Ontario Health Technology Advisory Committee report stated that an estimated 500 to 1,000 patients in the province would be eligible for FMT based on referral experience,[40] but given the evolving landscape, it is hard to quantify demand. Implementation of FMT programs and the rate of adoption may also depend on the ability to address current barriers.

Objectives

This Environmental Scan was initiated to provide information on the current context of FMT in Canada to inform future research and document barriers and strategies to improve access and ensure quality of care. The objectives of this Environmental Scan were to:

1. identify centres where FMT is available in Canada
2. identify the level of access to FMT across Canada
3. identify current barriers and facilitators to providing and accessing FMT therapy in Canada.

This Environmental Scan does not include an assessment of the clinical or cost-effectiveness of FMT. Thus, conclusions or recommendations about the value of FMT or its place in therapy are outside of the scope of this report.

Research Questions

The Environmental Scan aimed to address the following questions:

1. Where is FMT currently available in Canada (either through regular health care treatment, special access, or through clinical trials)?
2. What systems and services are in place in Canadian jurisdictions for the provision of FMT to patients with *C. difficile* infection or other conditions for which FMT may be effective?
3. What are the current barriers to Canadian patients accessing FMT?
4. What facilitators could improve access to FMT in Canada?

Methods

A limited literature search, responses to the CADTH survey titled *Access to and Availability of Fecal Microbiota Transplantation Therapy in Canada* (Appendix 1), and focused follow-up consultations with select stakeholders by email were used to inform the report.

Literature Search

A literature search was conducted to address specific research questions related to the objectives of the report. The search strategy is available upon request.

The limited literature search was conducted by an information specialist on key resources, including MEDLINE, the Cochrane Library, and the University of York Centre for Reviews and Dissemination databases. The grey literature search included the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords, and developed in consultation with the project team.

The database search was run in two parts: for the first part, the main search concepts were "Canada" and "fecal microbiota therapy"; for the second, the main search concepts were "barriers/implementation issues" and "fecal microbiota therapy." No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English-language documents published until November 21, 2019,

and the search for barriers was also limited to documents published after January 1, 2014. Search alerts were run on a monthly basis until the end of the stakeholder feedback period (August 2020).

Screening and Study Selection

One author assessed titles and abstracts of the database search for eligibility. Articles were selected for full-text review and inclusion using the components outlined in Table 1. Reference lists of selected articles were also scanned for potentially relevant records, and broad scoping searches were utilized selectively to pursue relevant themes. No restrictions were made regarding study design or type of publication. We included studies with both qualitative and quantitative data collection methods, as well as commentaries and editorials, when applicable. Search alerts were screened by two authors.

Table 1: Components for Literature Screening and Information Gathering

Population	Patients with *C. difficile* infection or other conditions that affect gut microbiota (e.g., inflammatory bowel disease, ulcerative colitis, Crohn disease), or other emerging indications for this treatment
Intervention	FMT
Settings	Any (such as hospitals, endoscopy clinics, primary care) in Canada
Types of information	Locations and types of facilities where FMT is available Level of access (i.e., capacity, patient eligibility, accessibility) Barriers to the provision of and access to FMT Facilitators of the provision of and access to FMT

FMT = fecal microbiota therapy.

Survey

A 19-item questionnaire was developed, reviewed for content validity by three CADTH staff, and tested for usability by two other staff. The questionnaire included a combination of demographic, dichotomous (yes or no), multiple-choice, and open-ended questions covering the topics addressed by the project objectives (Appendix 1). It was designed using Survey Monkey and launched electronically on February 12th, 2020. An email invitation containing the link to the online questionnaire was sent to a list of contacts identified by CADTH liaison officers and through the literature search. Participants were given 10 business days to complete the questionnaire. Two reminders were sent to nonresponders with two 10–business day extensions. Before starting the survey, participants provided written consent for their information to be used in this Environmental Scan report. The survey was closed on March 20, 2020.

Consultations

Initially, telephone and video consultations with key Canadian stakeholders (including some survey respondents) were planned. The purpose of these consultations was to fill knowledge gaps identified during synthesis of the literature and survey findings. Due to circumstances of the COVID-19 pandemic, and with minimal information gaps remaining after the synthesis of findings, brief email-based consultations with several of the survey respondents occurred instead (i.e., respondents were sent specific questions by email in June 2020 and responses were used to inform the report).

Synthesis Approach

Relevant findings from the literature search were grouped thematically according to the objectives of the report. Information was then integrated with the survey and consultation findings.

Feedback from respondents who gave consent to use their survey and consultation information was included in the report. Final survey results were downloaded from Survey Monkey to Microsoft Excel. Survey questionnaire feedback was excluded when the respondent's demographic and contact information were unavailable, and when more than than 75% of the survey was incomplete. Survey responses were abstracted by question, and were summarized by jurisdiction, when possible, or were pooled and presented from a pan-Canadian perspective. Quantitative responses were summarized using descriptive statistics. Qualitative (open-ended) responses were analyzed using basic thematic synthesis and summarized according to the objectives of the report.

Feedback was solicited on an earlier draft of the Environmental Scan report through an open call to the public, and targeted invitations were sent to survey participants (and their referrals) and key stakeholders. This stakeholder feedback opportunity included specific questions aimed at obtaining feedback on information gaps. Input received through this stakeholder feedback process, and through follow-up consultations with selected stakeholders over email (see Consultations), informed revisions made to the report.

Findings

The findings presented are based on the results of a literature search, a survey of Canadian stakeholders, and targeted email-based consultations with select stakeholders.

Summary of Information Sources

Literature Search Results

The literature search retrieved 393 potentially relevant references, with 92 full-text papers retrieved for further evaluation. In addition, 20 full-text papers were retrieved from the subsequent search alerts run between December 2019 and August 2020, and four papers were retrieved from the grey literature search.

Of the 116 full records screened, nine reports were included in the findings of this Environmental Scan.[36,40,41,47-52] Four additional records were included from other sources.[43,53-55] Ultimately, 13 sources were referenced in the findings of the review. In addition, 17 clinicaltrials.gov records for ongoing FMT trials in Canada are cited.

Summary of Survey Responses

Surveys were distributed to 52 contacts in all provinces and territories, except for Nova Scotia and Saskatchewan, as no potential contacts were identified. A total of 19 survey responses were received; 17 responses were complete and included. Responses were received from Alberta (two), British Columbia (three), Manitoba (one), Newfoundland and Labrador (one), Nunavut (one), Ontario (six), Prince Edward Island (one), and Quebec (two). Responses were received from provincial health authorities, academic institutions, hospital networks, and individual hospitals. The organizations represented by respondents are reported in Appendix 2.

Respondents identified primarily as physicians (i.e., gastroenterologists [four], other physician specialists [eight], infectious disease specialists [one]) but also included academic researchers (two), government employees (two), and a physician's assistant (one). One of the respondents identified as both a physician specialist and government employee.

Respondents were involved in FMT provision in various capacities. Of the 17 respondents, 15 were directly involved in FMT provision at the patient level as directors or coordinators of provincial, regional, or hospital-based FMT programs or clinics (three); by providing FMT as part of regular clinical care (for rCDI) or clinical trials (eight); by conducting non-clinical trial research on FMT (three); and by assessing provincial or regional programs (one).

Those engaged in research noted that they were conducting studies on the use of FMT for indications other than rCDI (e.g., ulcerative colitis, Crohn disease, and IBD). Respondents involved in running FMT programs and providing clinical care noted that their responsibilities ranged from finding, screening, and testing universal donors, to preparing and administering FMT interventions, and providing follow-up patient care.

Four survey contacts were followed up with to engage in brief email consultations aimed at addressing knowledge gaps.

FMT Infrastructure in Canada

Location of Facilities

Based on responses from the Environmental Scan survey, sites in Alberta, British Columbia, Newfoundland and Labrador, Nova Scotia, Ontario, Prince Edward Island, and Quebec have operational FMT programs or patient access via clinical trials. A full list of the facilities identified is available in Appendix 3. Most facilities providing FMT are hospitals (teaching or community), specialty clinics (including dedicated FMT clinics), or regional health authorities (specific locations not specified). Some survey respondents identified sites providing FMT in jurisdictions other than their own.

Overall, based on the available information, Ontario currently has the largest number of sites providing FMT, followed by British Columbia, Alberta, and Quebec. A 2016 survey of the Southern Ontario Fecal Microbiota Transplantation Movement (SOFT) — a collective of physicians performing FMT in Ontario — practitioners determined that, since 2013, six institutions in Ontario have provided FMT, and two additional institutions were in the process of forming programs at that time.[41] CADTH's survey indicated that the number of operational programs has increased at least twofold. Some smaller provinces provide FMT at a single location, and others, like Manitoba, are in the process of establishing programs.[51]

Level of Access to FMT Across Canada

What systems and services are in place in Canadian jurisdictions for the provision of FMT?

Clinical Indications and Eligibility Criteria

A 2016 survey of Ontario programs noted that all active programs performed FMT for clinical purposes in patients with rCDI.[41] Some have FMT research programs for other indications, including IBD, non-alcoholic fatty liver disease, multiple sclerosis, obesity, and bipolar depression.[41]

Fourteen survey respondents provided information on the eligibility criteria for receiving FMT. Eight survey responses indicated that individuals seeking care must have rCDI. In some cases, respondents specified that they must have experienced at least two episodes of rCDI requiring hospital admission, or three episodes of mild-to-moderate rCDI. Some respondents further specified that the individual seeking treatment must have had a failed vancomycin taper, presented with symptomatic and toxin-positive disease, and irritable bowel post-CDI must be ruled out. Individuals must also have no predictable need for antibiotics in the future. Some respondents noted that the individual patient must be able to provide a donor who meets their program site's requirements. Individual patients may also be able to gain access by participating in clinical trials.

Clinical Exclusion Criteria

In Ontario, SOFT programs noted that they applied the following exclusion criteria for patients seeking FMT:[41]

- severe uncontrollable diarrhea
- bloody diarrhea
- immunocompromised
- neutropenia
- irreversible bleeding disorder.

Further exclusion criteria noted by survey respondents included individuals on antibiotic regimens, and those unable to receive treatment by oral routes or by retention enema without sedation. Survey responses also noted that severely immunocompromised patients, those with decompensated liver disease, and those with mucosal breakdown (e.g., due to colorectal cancer or IBD) might be considered ineligible.

Clinical Trial Criteria

Survey respondents indicated that clinical trials in Canada were recruiting patients with the following criteria for treatment with FMT:

- ulcerative colitis (British Columbia)
- kidney transplant recipients colonized with multi-drug resistant organisms (British Columbia)
- crohn disease (Ontario)
- pouchitis (Ontario)
- conditions other than rCDI (not specified) (British Columbia).

An informal search of clinicaltrials.gov for upcoming and active trials (i.e., not yet recruiting, recruiting, enrolling by invitation, active [not recruiting]) identified trials for the following conditions:

- rCDI (Alberta and British Columbia)[56,57]
- severe or fulminant CDI (Alberta)[58]
- dysbiosis due to IBD or IBS (British Columbia)[59]
- asymptomatic carbapenemase-producing Enterobacteriaceae–colonized patients (Ontario)[60]
- primary *C. difficile*-associated diarrhea (Newfoundland)[61]
- pouchitis (Ontario) [62]

- crohn disease (Ontario; pediatric) [63] (Ontario, Alberta, and British Columbia; adult)[64,65]
- ulcerative colitis (Ontario)[66]
- hepatic encephalopathy (Alberta)[67]
- organ transplant (to prevent post-transplant infection) (British Columbia)[68]
- renal carcinoma patients preparing for cancer immunotherapy (Ontario)[69]
- melanoma patients preparing for cancer immunotherapy (Ontario)[70]
- bipolar disorder (Ontario)[71]
- obesity (Ontario).[72]

Trials may require that patients meet additional inclusion criteria beyond the disease phenotype for enrollment.

Volume of Care

Several survey respondents (12) disclosed the approximate number of patients treated with FMT at their site within the last year (leading up to the survey); these numbers ranged from zero to 80 per site.

The COVID-19 pandemic has presented operational challenges for some programs. Notably, some may have suspended operations, or may be evaluating the feasibility of continuing with current program models in the context of organizational changes and pressures resulting from the pandemic (Dr. Susy Hota, Infection Prevention and Control, University Health Network, Toronto, Ont: personal communication, Jun 25, 2020).

Barriers and Facilitators to Provision of and Access to FMT in Canada

In addition to the survey and consultation responses, 11 literature sources informed this section of the report. This includes a 2011 survey of physician perspectives conducted at three academic hospitals in Ontario;[48] a 2012 Canadian working group report on FMT, including an overview of FMT practices and challenges;[36] a 2016 HTA by Health Quality Ontario on FMT for CDI;[40] a 2017 pilot study on the implementation of a stool banking program (including self stool donation) in Ontario;[47] a 2017 study of the costs associated with selecting donors for FMT in Ontario;[50] a 2018 survey of regional variability in FMT practices in Ontario;[41] a 2019 analysis of press coverage of FMT in Canada;[43] a 2019 overview of the challenges of establishing an FMT program in Toronto;[53] a 2020 survey of potential stool donors' perceptions in Canada, the UK, and the US;[52] and two recent study abstracts (2019 and 2020) discussing patient perceptions based on a pediatric clinical trial in patients with ulcerative colitis and IBD unclassified in Ontario.[49,55]

The following barriers and facilitators to implementation of or access to FMT were identified via the survey or literature search.

Evidence and Public Perception

Several reports noted that the perceived lack of evidence for the effectiveness and safety of the procedure and the need for further research might impact the use of FMT.[36,48,55] The need for more evidence on safety was echoed by a survey respondent from Alberta. A lack of consensus on the appropriate method of administration was also noted.[36] Feelings of "disgust" surrounding the procedure might also impact public perception,[43] along with a lack

of understanding about what FMT entails.[55] FMT may also be perceived as a last-resort treatment option.[55]

One source suggested that efforts to educate the public about FMT, including about stool donations and the clinical potential of FMT, may improve perception.[52]

Donor Recruitment and Engagement

Insufficient availability of stool donors and biological material, as well as challenges with recruitment and retention, were reported.[53] Likewise, survey respondents from multiple jurisdictions reported challenges with the identification of eligible donors. Once identified, potential donors may be unable or unwilling to comply with rigorous and repetitive screening or donation protocols, particularly without compensation.[52,53] Survey respondents noted challenges in organizing regular donor recruitment. Focusing on donors who are willing to donate without financial compensation or who are driven by the desire to help others (altruism) could help to address the inconvenience of donating.

Economic compensation or the prospect of obtaining health information (e.g., about gut microbiome health) for donations, and efforts to inform donors about the potential benefit of stool donations, may improve donor participation.[52] The perception that out-of-pocket costs of donor participation (e.g., transportation costs, lost wages) would be covered could also improve participation.[52] Efforts to improve the convenience and ease of donation may also increase donors. One survey respondent advocated for the standardization of donor screening. Another suggested that there may be benefits in providing an option for anonymous donation, which is not possible with a directed-donor model.

Donors may find the process of collecting their own stool unpleasant or awkward (the "ick factor"), and may perceive the physical examination to be invasive.[52] Fear of societal stigma or embarrassment was also reported.[52] Some donors may fear potential harmful effects to themselves or the recipient (e.g., risk of infection transmission).[52] Demographic factors might also influence a potential donor's likelihood to participate in an FMT program. For instance, females may be less likely to donate than males, though the reasons for this are unclear.[52]

To address issues of donor reluctance, one survey respondent suggested the need for improved awareness about FMT. Funding for donor-targeted advertising and communication strategies was suggested in one report.[53] To address likely variation in willingness to be a donor in the general population, targeted recruitment among populations more likely to agree to donation requirements (e.g., by pursuing donors based on proximity to the donation centre, targeting existing blood donors or allogenic living tissue donors, or pursuing donors with positive attitudes toward FMT or those interested in contributing to scientific research) has been suggested.[52,53] Donors may be more willing to donate to friends or family members.[52]

Donor and Sample Screening

Survey responses suggested that the extensiveness of screening and regulatory requirements (i.e., number of criteria or procedures) may also present challenges for donor and sample eligibility. Also, survey respondents commented that serological testing and re-testing protocols and long turnaround times might impact the viability of donor stool.

Some survey respondents proposed the need for standard screening guidelines, including specific criteria for selecting donors and recipients. One report suggested that less extensive donor screening based on selective recruitment of donors could be an option.[53] This report

further suggested initial self-screening before in-person assessments and not requiring physical examinations as measures that could help ease the screening process.[53]

Programs also struggle with a low return on investment for donor screening efforts. For instance, one program reported that only 1.6% of 322 prospective donors met the screening criteria over two years, with only two (0.6%) becoming active donors.[53] One survey respondent recalled low and evolving donor eligibility. Some donors who initially qualify may subsequently be disqualified due to changes in health status or other factors.

Once donors are secured, the donor screening process can also present challenges. First, the sequence of donor and sample screening may be an issue. There may be contamination risks if the timing of donor screening cannot or does not adequately account for the sample donation period (i.e., if there is a considerable lapse of time from initial donor screening to sample donation).[36] One survey respondent also observed that with the absence of stool banks, live donors must be screened for each treatment, which contributes to time requirements and treatment delays. The lack of standardization of the screening process is also a noted barrier.[41] The cost of laboratory tests and procedures required for screening and rescreening donors can also be substantial.[36,40,41,53] Costs may be higher if there is a need to screen for conditions requiring stringent exclusion criteria.[50] Depending on lab access, reference laboratories may be required for specialized testing.[41] The results of screening tests may take days to weeks to process, which may also delay treatment.[36] Furthermore, there is still uncertainty over the necessary screening standards, such as whether or not measures are required to assess the unknown long-term risks of commensal gut bacteria or bacterial profiles associated with chronic diseases,[36] and lack of consensus on standards for donor exclusions and frequency of rescreening.[53] One survey respondent commented that donor screening requirements are extensive and evolving.

Several strategies have been suggested to address screening challenges. Calls have been made for standardization,[53] both in the literature and by survey respondents. Still, there was a lack of suggestions from survey respondents on specific measures to achieve standardization.

Stool Banking

Donor-centered programs, such as stool banks or biobanks, or archives were noted by survey respondents to be lacking. The inability to develop local libraries and reliance on outside sources of FMT material (e.g., from other Canadian centres) was also an issue raised by survey respondents. The use of a directed donor model in Canada (where the provider or recipient must know the donor) places the burden on physicians to find and screen donors.[38] The use of universal stool donors, who, if approved, could provide stool on an ongoing basis for multiple patients[53] may address issues with the number of eligible donors, and with the directed donor model. The challenges of the directed donor model could theoretically be addressed if users of an FMT stool bank were to sign an agreement delegating donor assessment (e.g., medical, microbiologic screening tasks, donor ongoing health monitoring) to stool bank medical directors, and ensuring manufactured products sent outside of the stool bank have proper certification that screening and manufacturing requirements from Health Canada are met and have proper labelling (including expiry dates) (Dr. Susy Hota: personal communication, Jun 25, 2020).

Survey respondents expressed support for stool banks with screened donors and suggested that providers could work with health authorities to provide funding for stool bank infrastructure and FMT programs. Survey respondents provided the example of OpenBiome (Cambridge, Massachusetts, US), a non-profit stool bank based in the US that currently provides FMT products for some clinical trials based in Canada.[73] One suggestion was a national library of stool samples that could distribute FMT products to Canadian sites, and multiple suggestions for centralized donation and screening were made. In addition, one survey respondent suggested that research aimed at identifying the ideal components of FMT to enable individualized or lab-derived treatment may circumvent the need for stool donors and reduce risk and cost.

The current Health Canada regulations requiring a directed-donor model are not compatible with a national stool bank program; however, some programs have operations that function like a small stool bank. One respondent noted that University Health Network and Sinai Health System in Toronto operate this type of model to support clinical and research programs, but they do not provide services outside of their own systems (Dr. Susy Hota: personal communication, Jun 25, 2020).

Preparation and Manufacturing

Two literature sources report a lack of equipment and support from hospitals and clinical laboratories for sample preparation.[36,41] Survey respondents also commented on the lack of services for sample preparation, as well as on the time and biosafety provisions required for sample preparation. Similar to earlier steps in the FMT process, a lack of standardization for sample processing or manufacturing and storage conditions was noted.[41] One survey respondent commented that preparation techniques are laborious and lack automation. Survey respondents observed a lack of preprepared, screened products for treatment.

In terms of possible solutions, survey respondents suggested the automation of FMT material preparation. Suggestions were made for industry-supplied FMT products and against local sample preparation using underequipped facilities or personnel, as this could be a recipe for poor practice, inadequate screening, and increased risks. Automation and centralization of preparation and manufacturing may address the limited infrastructure and resources currently available to conduct these aspects of the intervention at the clinical site.

Infrastructure

Insufficient infrastructure is also a challenge for providing FMT, and lack of support for the procedure by health care institutions has been observed.[48] Survey respondents noted that some hospitals do not provide dedicated facilities for FMT outside of clinical trial purposes. To address physical infrastructure challenges, one survey respondent thought that it should be possible to administer FMT in patient homes or outpatient settings, and that this may help address logistical barriers for frail patients or those otherwise unable to attend the hospital or clinic.

One report suggested that separate FMT centres could be established,[41] while one survey respondent suggested that financial assistance from jurisdictional governments to operationalize centres of excellence for FMT would be beneficial.

Patient-Related

Lack of patient education[49] and patient discomfort were raised as barriers to a patient receiving FMT.[47] Two studies (one reported as a conference abstract) identified fear of negative external opinions about receiving FMT, and aversion to the use of stool (e.g., due to smell) among the participants.[47,55] In the context of prospective self-banking, patient health status may prevent donation.[47] Several studies noted that some patients may also be uncomfortable receiving donor stool rather than their own manipulated stool due to fear of communicable risks.[47,49,55] Some delivery methods (e.g., enema) may also be a deterrent for some patients who may prefer oral medications.[47,49]

Few patient-related facilitators were noted; though one such example would be prioritizing treatment for patients whose current treatments are not working as they may be more open to FMT.[49] One survey respondent suggested moving to capsule-only delivery, which may address administration issues. The concept of prospective self-stool banking reported in one study could address some of the issues raised with donor screening, infection transmission, and discomfort with receiving donor stool.[47]

Treatment and Access

One report commented that physicians might assume a lack of patient acceptance for treatment.[48] Furthermore, some physicians may lack general knowledge about the treatment, as well as awareness of where to refer patients for treatment (e.g., to which providers or programs).[48] One survey respondent commented that the service was simply unavailable in their province, and another noted limited patient access despite demand, observing that eligibility criteria had to be tightened as a result.

General uncertainty about the appropriate method and route of administration, and the optimal number of treatments may also discourage practitioners from providing FMT.[36,41] Similar to donor and patient perceptions, the general "ick factor" is also a deterrent for those providing care.[48]

On the practical side, depending on the route and method of administration, the need for substantial facility and personnel resources is a barrier;[36,41] for example, the use of the endoscopy suite for colonoscopy and the need for the presence of a physician with expertise in gastroenterology, infectious disease, microbiology, or other specialty practice areas.[36,41] One survey respondent suggested that limited availability of infectious disease specialists to see patients referred from outside of the hospital could limit patient access. Another observed that without support staff to coordinate donors, donations, sample preparation, and administration, it is not possible to provide FMT. This lack of resources may contribute to long patient wait times.

One survey respondent suggested that certain care providers, such as physician's assistants and nurse practitioners, should be allowed to deliver FMT to take the pressure off specialists, and one physician consulted further added that these practitioners can be valuable assets that are also cost saving (Dr. Susy Hota: personal communication, Jun 25, 2020). Furthermore, physician's assistants and nurse practitioners could potentially be involved in assessing patient eligibility, administering FMT, and evaluating clinical response to treatment, allowing physicians to focus on research instead of routine FMT treatment (Dr. Peter Daley, Medicine and Laboratory Medicine, Memorial University and Eastern Health, St. John's, NFLD: personal communication, Jun 18, 2020).

A suggestion was made to develop standard FMT infusion protocols, with a call for regulators to coordinate this.

One respondent suggested that care could be improved by ensuring supervision of care teams, measures to reinforce the quality of care, and mechanisms for follow-up with patients. Follow-up post-FMT is an important, yet underemphasized, aspect of FMT programs. Having formal, dedicated employees responsible for evaluating and managing recipients of FMT, as well as program evaluation and donor procurement, could help to address this (Dr. Susy Hota: personal communication, Jun 25, 2020).

Financial

Given that FMT is an emerging therapy, perceived high cost may deter patients and providers, and[55] survey respondents noted many financial challenges to providing FMT. Some examples include a lack of formal funding mechanisms for FMT programs (including salaries for support staff), absence of practitioner reimbursement and formal billing codes, the need to pay donors out of research funds, and the general costs of developing a donor library. This was reflected in the literature, with some reports commenting on the lack of established mechanisms for clinician reimbursement, and the reliance on existing limited hospital budgets, in-kind contributions, and research funding to support patient care.[41,53] Logistical expenses such as the cost of patient travel may also impact the feasibility of treatment. Survey respondents also noted a lack of funds to conduct the necessary research for new indications.

Survey respondents suggested that financial challenges could be improved by providing reimbursement to practitioners, including both physicians and other clinicians and practitioners involved in FMT provision. Formalizing the payment structure for donor screening was also suggested, as this would help transition away from grant funding models. Overall, respondents felt that increased financial support through ministry or hospital funding or dedicated funds for FMT programs would be beneficial.

Regulatory

Survey respondents commented that there were regulatory challenges, though no specific issues were identified.

Several areas for improvement were noted. General comments that regulation and guidelines could be improved were made without specific direction. One respondent suggested that regulation amendments that allow for the import of FMT products from outside of Canada (e.g., from international stool banks) could help address supply issues. Another called for an amendment to the requirement for the physician to have a relationship with the stool donor (directed donor model) as this prevents wider sharing of FMT materials with other practitioners and increases the requirement for patient travel.

Ethical, Legal, or Social

Several barriers related to ethical, legal, or social considerations relevant to FMT were noted in one of the included studies.[36] One of these is the perceived risk to the patient from potential unknown pathogens. Another is the lack of standardization and knowledge of true risk-benefit considerations in the context of informed consent procedures. The ownership of donor stool and whether it should be subject to legislation for human tissue or other laws has been discussed. Another issue is the potential for inappropriate financial gain by manufacturers

or programs standing to profit from the use of human tissue (stool), and whether payment is used or perceived to coerce donors to supply stool for FMT. Practically, consideration of potential aversion and discomfort of patients, hospital staff, or others asked to administer FMT or to be involved in treatment, and associated sensitivities (e.g., aversion to handling feces) were raised. Finally, general ethical arguments against FMT versus the risk of not allowing such procedures (e.g., for patients who have exhausted other treatment options) were noted.

Limitations

The findings of this Environmental Scan are based on the perspective of a limited number of Canadian stakeholders and a targeted literature review of Canadian studies and reports. While attempts were made to identify and contact stakeholders from all Canadian jurisdictions, CADTH did not obtain responses from all jurisdictions. Furthermore, with the exception of Ontario, three or fewer responses were received from each jurisdiction. Similarly, most of the literature identified was from studies conducted in Ontario, or commentary presented from the Ontario or pan-Canadian perspective. As a result, the views represented in this report may not be applicable in jurisdictions without representation or in broader contexts such as rural, remote, and Northern settings. Most respondents were intimately involved in FMT as clinicians or researchers running clinical or research programs; thus, the views expressed may not directly represent those in the broader clinical or policy community.

Other than an earlier list prepared by the Association of Medical Microbiology and Infectious Disease Canada, CADTH did not identify any formal inventories of Canadian FMT centres; as such, survey responses and documented programs informed the summary of locations providing FMT across Canada. Consequently, some centres may have been missed.

The publication date of some of the literature cited may present certain limitations. For instance, some references were published before the 2015 Health Canada approval of FMT for patients with rCDI, and prior to the publication of much of the new evidence informing current guidance and practice around FMT. It is not clear whether the observations in these earlier reports are still relevant.

The potential for using FMT for expanded indications is evolving. However, in Canada, outside of clinical trials, FMT is only approved for rCDI. It is unclear whether different barriers and facilitators may apply for other patient populations; however, factors related to standard procedures that do not vary by patient population could apply. The findings of this report may not be generalizable to all non-rCDI conditions.

There are some limitations to CADTH's Environmental Scanning methods. No critical appraisal of the literature cited is conducted for this type of report; therefore, this Environmental Scan does not comment on the validity of the observations and interpretations presented within these studies and reports.

Conclusions and Implications for Decision- or Policy-Making

This Environmental Scan was conducted to identify the locations of and level of access to FMT services and programs in Canada, and to identify the barriers and facilitators to providing and accessing FMT within the country. The report was informed by a literature review, a stakeholder survey, and targeted email-based consultations. FMT is an emerging therapy, and the findings of this report reinforce the inconsistent experiences and stages of implementation across and within Canadian jurisdictions, and the common challenges and potential solutions discussed by FMT providers, patients, and decision-makers.

Availability and Access in Canada

The clinical use and availability of FMT have grown over time. According to the survey respondents and the literature, FMT is currently offered in at least seven Canadian jurisdictions. Some jurisdictions had programs in development at the time of the survey, and their operational status may have changed, particularly in light of the challenges presented by the COVID-19 pandemic. Many of these programs are in larger, more populated provinces. They are often championed by clinicians and researchers heavily involved in FMT research and care, so their availability outside of specialty academic research and clinical practice is uncertain. Treatment capacity ranges (from zero to 80 patients per year) but capacity is low relative to demand. A survey of lived experiences of Canadians with CDI by the Gastrointestinal Society published in 2020 reported that of the 167 respondents, one had received FMT for initial CDI, and of the 67 with rCDI, five had received treatment.[74] Some respondents commented that they would have liked to receive FMT but did not have access. A formal assessment of patient access statistics was not identified.

Currently, regulatory approval has only been issued for rCDI in Canada; though, due to demand, patients must often meet criteria beyond their clinical diagnosis of rCDI to receive care. Patients with rCDI may also suffer from concurrent GI conditions,[75] which could potentially impact their eligibility for FMT. In addition, patient access to care is often contingent on donor availability, and acceptability of the administration method. Patients who do not meet these criteria may gain access through participation in clinical trials. Canada has numerous ongoing trials in seven jurisdictions that are investigating the use of FMT for treating many conditions other than rCDI.

Availability and access also vary outside of Canada. For example, in the US, the Washington State Health Care Authority Health Technology Clinical Committee decided in 2017 that FMT would be a covered benefit with conditions — coverage limitations were that patients with CDI must have failed an appropriate course of antibiotic therapy and that FMT was not covered for treatment of IBD.[76] ECRI published a 2016 report that included a search of third-party payers, which found that of 11 US payors, six had conditional coverage policies, and two were denied coverage.[77] At the time, one clinical expert commented that FMT was offered by about half of US hospital-based and academic practices and 15% to 25% of private and group practices.[77]

Addressing Barriers and Facilitators

Survey respondents and literature sources (from the Canadian perspective) presented a range of barriers and facilitators that potentially influence FMT implementation. These factors apply to various stages in the FMT process, from donor identification through to treatment and follow-up; and related to patient factors; and practical aspects like finances, infrastructure,

public perception, and ethical, legal, and social considerations. Similar barriers to those identified in this report have been identified in the international literature.[78-80]

Optimizing Donation With Stool Banks

One of the areas of FMT that has the most challenges is that of stool donors. The need for a new donor model in Canada was highlighted as a barrier by many survey respondents and in the literature.[38] Compared to the universal donor model utilized by stool banks, the 2015 Health Canada guidance decision to use a directed donor model puts a large amount of responsibility on the provider for elements such as donor screening, intervention preparation, and administration and monitoring.[38] The Canadian Association of Gastroenterology has voiced support for standardized rigorous screening protocols, stringent monitoring, and oversight, which is a challenge with the decentralized directed donor model.[38] Some have suggested that stool banks could reduce costs; centralize regulatory oversight, adverse event reporting, and patient access; and increase the efficiency of the FMT process for providers.[38,81] One survey respondent commented that, based on experience, a small number of viable donors might be able to support a large program with the right infrastructure. Individual facilities, such as North York General Hospital, have piloted local stool processing and banking services,[47] though no centralized stool banks were identified at the national or provincial level.

The importance of developing a frozen stool bank to prevent treatment delays, optimize donor recruitment and screening, and enable standardization and sample centralization has been discussed.[82,83] Stool banks (both public and private) have been established in multiple countries, including the US,[84] the Netherlands,[85] New Zealand,[86] Australia,[87] the UK,[88] Italy,[87] Hong Kong,[87] and Israel.[87] The example of OpenBiome (Cambridge, Massachusetts, US) is often highlighted as a model for an operational international public stool bank as it supplyies both the US and other countries.[89] Survey respondents noted the desire to have access to stool bank samples from outside of Canada. The benefits of stool banks have been reported, including the ability to scale FMT, as well as to centralize donor selection, material processing, and safety monitoring.[78] Geospatial analysis of FMT access in the US suggests that universal stool banks have positively impacted access.[90,91] There are also arguments that the universal stool bank model addresses multiple barriers to FMT, including reducing the burden on donor selection, material processing, and distribution.[78] This could reduce costs and allow the provider to focus on clinical care.[78] International consensus statements on stool banking for FMT have been issued, providing guidance on organizing and developing an FMT stool bank.[83]

Guidance, Policy, and Standardization

Calls for standardization at various stages of the FMT process have been made, including by respondents to the CADTH survey. Some level of standardization of clinical care may be possible through the adoption of evidence-based guidelines. Numerous Canadian and international guideline recommendations have been issued, and the strength of the recommendations and certainty in the evidence have increased. In 2016, ECRI's Emerging Technology Evidence Report summarized the available guidance and consensus statements, which varied at the time, but generally acknowledged the lack of evidence on efficacy and safety, and of an appropriate regulatory framework. This report only supported the use of the procedure for patients with rCDI resistant to standard treatment.[77]

The latest guideline from the Association of Medical Microbiology and Infectious Disease Canada (2018) on the treatment of *C. difficile*[92] recommends the use of FMT for recurrence

following a vancomycin taper in the case of second or subsequent recurrences in adults, but does not provide specific recommendations about the procedure's standardization. Some individual centres in Canada have created institutional protocols,[41] and networks such as SOFT have been created in Canada to share experiences and address barriers to implementation.[41]

Various organizations, including a range of clinical societies; public health bodies; and HTA agencies from the US, Europe, and Australia, also recommend FMT for adult patients with rCDI who have failed antibiotic treatment.[29-31,93-97]

In 2018, ECRI published a hotline response (rapid review), citing nine guidelines and consensus publications addressing FMT for adults, or adults and children, with seven recommending FMT for patients who are unresponsive to antibiotic treatment and have experienced more than one recurrence of CDI, four recommending FMT for refractory CDI, two recommending FMT not be used as first-line therapy, one suggesting that FMT could be used for individuals with IBD with rCDI, and one stating that FMT is not appropriate for use in complicated CDI.[98]

The recommendations specifically from guidelines for pediatric patients are less confident and acknowledge very low-quality evidence.[31] A recent 2019 joint position paper from the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology and Nutrition recommends the use of FMT in children with rCDI under conditions similar to those for adult populations.[99] The Pediatric Oncology Group of Ontario notably recommends that FMT not be routinely used in the treatment of CDI for pediatric patients with cancer and those undergoing hematopoietic stem cell transplantation.[100]

Several CADTH Rapid Responses, including searches for evidence-based guidelines, did not find any guidance on the use of FMT for those with autism,[101] overweight individuals,[102] and the use of lyophilized versus frozen FMT in rCDI, IBD, and IBS[103] — suggesting that the clinical consensus for new and emerging indications is not yet established. Recommendations for conditions other than CDI are not widely available. Of the available guidelines, many, particularly those published more recently, outline specific considerations to guide the donor, screening, and treatment delivery process, and provide implementation guidance, which may help in areas where knowledge deficits and lack of experience are hindering implementation. Consensus statements on best practice also exist,[104] which could inform care if they are adapted or created for the Canadian context.

Perception and Awareness

There was a paucity of patient-oriented facilitators or strategies to improve FMT implementation presented in the literature and by survey respondents. This suggests that further consultation with the individuals eligible for FMT on their perceived challenges and solutions that would optimize their care is warranted.

CADTH's survey, along with surveys conducted among practitioners in Canada[48] and the US,[105] highlight a lack of knowledge and experience with the procedure, and the need for better education. Potential frameworks for physician education have been published that may improve awareness for those less familiar with the procedure, who might feasibly provide care.[106] In the same vein, education for other practitioners who may be well-positioned to support the care of individuals receiving FMT (e.g., physician's assistants, nurse practitioners,

and other support staff) may help support operational requirements. Evidence-based guidance may be a valuable resource for facilities and individuals struggling with a lack of knowledge and experience.

One ongoing challenge is public perception, and the oft mentioned "ick factor" associated with the use of stool as a medical intervention. Analysis of the evolving media landscape has documented a positive shift in media representation of the intervention;[43] however, other developments suggest an industry and research shift towards products that distill the essence of traditional FMT into a more palatable format. In addition, a range of alternative treatments for CDI is emerging, including new oral antibiotics,[77] monoclonal antibiodies,[107] competitive inhibition with non-toxigenic strains of *C. difficile*,[107] and vaccines.[107]

In the context of FMT, manipulated stool products are generating interest, with some clinicians believing that wider FMT adoption is contingent on the availability of a "ready-to-use" product. Likewise, some survey respondents felt that oral or industry manufactured products might address some of the bottlenecks in the FMT process. In 2016, ECRI provided a list of groups developing fecal microbiota products, including the University of Guelph's Microbial Ecosystem Therapeutic and RePOOPulate synthetic fecal mixture.[77] More recently, clinical trials and feasibility testing of various manufactured stool-derived products are underway in Canada. Some examples of products under study include Microbial Ecosystem Therapeutics (MET), a defined mixture of pure live cultures of intestinal bacterial isolated from a healthy donor's stool sample,[108 109] Oral Full-Spectrum Microbiota (CP101), a drug product derived from the stools of normal healthy donors,[110,111] and RBX2660 (Rebiotix Inc.), a microbiota suspension of intestinal microbes prepared from human stool.[112-114] Many manufactured stool products are in early feasibility testing or being investigated in phase I to III clinical trials. The benefits and safety of these products are outside of the scope of this report, and timelines for their availability in the Canadian context are currently unclear.

Regulation and Adoption

There is still debate over the appropriate approach to regulating FMT, and what existing framework (i.e., regulating FMT as a drug versus a biologic) is the best fit when it comes to balancing safety, innovation, and access for patients with unmet needs.[87] FMT regulation varies across jurisdictions, with some similarities and notable differences;[87] however, most regulators in countries in North America (including Canada) and elsewhere currently regulate FMT as a biologic drug (or equivalent). Some jurisdictions, such as Australia[115] and the US,[87,116] have proposed provisions to allow for different levels of regulatory oversight depending on the level of processing and donor source of samples. In these models, the regulations would be moderate in cases where the donor is known (by the patient or physician), and the treatment is for an approved condition (i.e., rCDI), and stricter in cases of manipulated stool products and where the donor sample comes from a stool bank.

Cost (including capital costs and program operational costs) was identified as a common barrier to providing care by literature sources and survey respondents. There is evidence that FMT (administered by colonoscopy) may be a cost-effective strategy for recurrent (but not initial) CDI compared to other drug treatment options (based on systematic reviews of economic evaluations from high-income countries), though there are few studies from the Canadian perspective.[23,117]

Lack of access to well-regulated public FMT services may also put patients at risk. Some patients unable to access care in the current climate have sought out-of-country care or

unregulated care and paid out of pocket for services. In some cases, these FMT services are being targeted for populations for which the therapy is not approved for use in Canada, which introduces safety concerns, as well as ethical concerns about charging patients for experimental treatment.[44]

Evolving Safety Concerns

As with many procedures involving human tissue, the threat of transmitting harmful pathogens is continuously evolving and must be monitored with vigilance. The screening challenges noted in this report outline some of these issues.

Due to reports of multi-drug resistant organism (MDRO)–derived bacterial infections causing severe adverse reactions and deaths, donor screening must specifically address the risk of colonization with MDROs, include testing for them.[39,118] Existing samples not subject to these protocols must not be used until the safety of the sample is confirmed. According to the FDA, informed consent in the US must now also discuss the risk of MDRO transmission and subsequent infection.[118]

The recent emergence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and the associated COVID-19 pandemic has led to calls for increasingly rigorous screening protocols and has also impacted the viability of existing donor samples. In early 2020, new FDA communications were issued that outline potential risks of SARS-CoV-2 transmission via FMT due to documentation of the presence of the virus in the stool of infected individuals. In response, stool for FMT must have been donated before December 2019, and all stool donated after this date require donor screening to identify those possibly infected with SARS-CoV-2. The FDA also outlined testing for SARS-CoV-2, criteria for exclusion of donors and donor stool, and informed consent for these new risks.[119] Health Canada guidance was updated in March 2020 to reflect SARS-CoV-2 safety considerations.[39] An international position paper on adapting FMT procedures in light of circumstances of the pandemic also calls for SARS-CoV-2 testing of donors and samples, as well as adapted donor and patient screening and follow-up.[120] Protocols have been developed to facilitate SARS-CoV-2 screening,[121] though it is unclear whether FMT programs in Canada have ready access to screening. Donor screening for FMT may face future hurdles and require responsiveness to emerging safety considerations.[39] This suggests that programs need to be flexible and responsive to evolving screening and safety requirements to ensure patient safety and quality of care.

Final Remarks

Overall, the findings of this Environmental Scan indicate that FMT is still an emerging treatment across Canada, despite its availability in at least seven jurisdictions. The findings highlight the need for FMT infrastructure and policy, and point to opportunities for standardization across the country to address challenges limiting implementation and access.

Complementing this Environmental Scan, CADTH has prepared several recent Rapid Responses[101-103,122] and a Horizon Scanning *(Issues in Emerging Health Technologies)* bulletin about FMT[123] — all of which are freely available on the CADTH website.

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Appendix 1: Survey Questionnaire

Access to and Availability of Fecal Microbiota Transplantation Therapy in Canada (ES0341)

CONSENT FORM

Thank you for your interest in contributing to a CADTH report. Your input is both needed and highly valuable, as it will inform decision-making on the management of health technologies in Canada. The purpose of this survey is to gather information that will be used to prepare a CADTH Environmental Scan report, which will be published on the CADTH website.

Your participation in this survey is voluntary. You may choose not to participate, or you may exit the survey at any time without penalty. It should take approximately 15 minutes to complete.

Your identifiable private information will be kept confidential. This consent form does not give CADTH permission to disclose your name. If any direct quotes from the survey results are required, respondents will be contacted separately to sign a personal communication form before publishing.

CADTH will summarize your responses in the published report and your organization may be identified as a source. However, you and the organization you represent (if applicable) are not responsible for the analyses, conclusions, opinions, and statements expressed by CADTH in the report. For detailed information on the purpose of this Environmental Scan entitled Access to and Availability of Fecal Microbiota Transplantation Therapy in Canada: An Environmental Scan, please see the invitation email from Leigh-Ann Topfer (leigh-annt@cadth.ca).

1. ELECTRONIC CONSENT: Please select your choice from the following.

Clicking on the "Agree" button indicates that:

- ☐ you have read the aforementioned information
- ☐ you voluntarily agree to participate
- ☐ you authorize CADTH to use the information provided by you for the purpose as stated in this form.

If you do not wish to participate in the survey, please decline participation by clicking on the "Disagree" button.

☐ Agree ☐ Disagree

2. Name:
3. Title:
4. Organization:
5. Province:
6. Email:
7. Phone:
8. Date:

Demographics and Clinical Setting

9. Which province, territory, or federal government department do you work in?

- ☐ Alberta
- ☐ British Columbia
- ☐ Manitoba
- ☐ New Brunswick
- ☐ Newfoundland and Labrador
- ☐ Nova Scotia
- ☐ Nunavut
- ☐ Ontario
- ☐ Prince Edward Island
- ☐ Quebec
- ☐ Saskatchewan
- ☐ Yukon
- ☐ Federal Government Department

10. What is your profession? (Choose all that apply.)

- ☐ Registered Nurse
- ☐ Nurse Practitioner
- ☐ Physician – General Practitioner or Family Medicine
- ☐ Physician – Gastroenterologist
- ☐ Physician – Specialist
- ☐ Pharmacist
- ☐ Allied Health Professional
- ☐ Academic Researcher
- ☐ Government Employee
- ☐ Other (please specify)

11. Does your work involve the provision or management of fecal microbiota transplantation therapy (FMT)?

☐ Yes ☐ No

If yes, please describe:

12. If you work at a centre that provides FMT to patients, please state its name, and describe the type of facility (e.g., teaching hospital, hospital, primary care, clinic) and its location:

Name:

Type of facility (e.g., teaching hospital, hospital, primary care, clinic):

Location (city, province or territory):

13. What year did your centre irst provide FMT to patients?

14. At your centre, what eligibility criteria must be met for patients to receive FMT?

15. Approximately how many patients did your centre treat with FMT last year?

16. If you are aware of other centres that provide FMT to patients in Canada, please state their names and locations:

17. What are the barriers to the optimal provision of FMT at your centre, or in the broader Canadian context? Please describe:

18. Do you have any suggestions for changes or strategies that could improve access to FMT at your centre, or in the broader Canadian context? Please describe:

19. Following this survey, CADTH will be conducting short consultations to further understand challenges and opportunities as they relate to the provision of FMT in Canada. Would you be willing to participate in these consultations?

☐ Yes ☐ No

If yes, please provide the email and phone number we can reach you at:

Appendix 2: Information on Survey Respondents

Table 2: Information on Survey Respondents

Jurisdiction	Number of respondents (% total respondents)	Organization(s) represented by survey respondents
Alberta	2 (11.7%)	Alberta Health Services; University of Alberta
British Columbia	3 (17.6%)	University of British Columbia; Island Health
Manitoba	1 (5.9%)	University of Manitoba
Newfoundland and Labrador	1 (5.9%)	Memorial University
Nunavut	1 (5.9%)	Government of Nunavut, Department of Health
Ontario	6 (35.2%)	St. Joseph's Health Care (London); Hamilton Health Sciences; McMaster Children's Hospital (Hamilton); University Health Network (Toronto); Michael Garron Hospital (Toronto); McMaster University (Hamilton)
Prince Edward Island	1 (5.9%)	Health PEI
Quebec	2 (11.7%)	CHU de Québec; Jewish General Hospital

CHU = Centre hospitalier universitaire: PEI = Prince Edward Island.

Appendix 3: Location of FMT Programs in Canada

Table 3: Location of FMT Programs in Canada

Jurisdiction	Location[a]	Information source		
		Literature review	Survey (direct)	Survey (indirect)[b]
Alberta	University of Alberta Hospital (2012)		X	X
	University of Calgary			X
	Stollery Children's Hospital (Edmonton)	X[54]		X
British Columbia	Vancouver General Hospital (2015)		X	X
	Victoria General Hospital (inpatient only)			X
	Royal Jubilee Hospital, Victoria (both inpatient and outpatient) (2016)		X	
Manitoba	University of Manitoba (program under development)	X[51]	X	
New Brunswick	–			
Newfoundland and Labrador	Health Sciences Centre, Memorial University of Newfoundland (St. John's) (2019)		X	
Northwest Territories	–			
Nova Scotia	Queen Elizabeth II Health Sciences Centre (Halifax)			X
Nunavut	No locations		X	
Ontario[d,41]	St. Joseph's Hospital (London)[e]	X[41]	X	X
	St. Joseph's Healthcare (Hamilton)	X[c,41]		X
	McMaster University Medical Centre (2014) (Hamilton)		X	X
	McMaster Children's Hospital (2015) (Hamilton)		X	
	Trillium Health Partners (Mississauga)	X[41]		
	University Health Network (2011) (Toronto)	X[41]	X	X
	Sinai Health System (2011) (Toronto)	X[41]	X	X
	Michael Garron Hospital (2010) (Toronto)	X[41]	X	X
	Sunnybrook Health Sciences Centre (Toronto)	X[c,41]		
	Lakeridge Health (Oshawa)	X[c,41]		
	Kingston General Hospital (Kingston)	X[41]		
	Sudbury Health Sciences North			X[c]
Prince Edward Island	Queen Elizabeth Hospital (2016) (Charlottetown)		X	
Quebec	Centre hospitalier universitaire de Quebec (1998) (Quebec City)		X	X
	Centre hospitalier universitaire de Sherbrooke (Sherbrooke)			X
	McGill University Health Centre (Montreal)			X
	Jewish General Hospital (2011) (Montreal)		X	
Saskatchewan	–			
Yukon	–			

FMT = fecal microbiota therapy.

[a] Year of inception in parentheses, if specified.

[b] Reported by survey respondents, not their home site.

[c] Not fully operational at the time of the survey or report publishing.

[d] Some Ontario programs may have suspended FMT-related activities due to the COVID-19 pandemic (Dr. Susy Hota, Infection Prevention and Control, University Health Network, Toronto, Ont: personal communication, Jun 25, 2020).

[e] Specialty clinic.