Title: Regional variability in fecal microbiota transplantation practices: a descriptive study of the Southern Ontario Fecal microbiota Transplantation (SOFT) Movement

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Running Title: Fecal microbiota transplantation in Ontario, Canada

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Potential Competing Interests

S.S. Hota has received a grant and honoraria from serving as a consultant and on the advisory board of Cubist (Merck) pharmaceuticals. S. M. Poutanen has received honoraria related to advisory boards from Merck, Paladin Labs, and Accelerate Diagnostics and honoraria from Merck related to talks. C. Lee is a member of advisory board for Rebiotix and received grants from Merck, Actelion and Rebiotix for clinical research. E.O. Petrof is a co-founder and serves on the Scientific Advisory Board of Nubiyota

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Abstract

Background: There is growing evidence that fecal microbiota transplantation (FMT) is a cost-effective treatment for recurrent *Clostridium difficile* infection. However, little guidance exists for implementation of FMT programs. This study summarizes the program characteristics and protocols of 9 planned or operating FMT programs in Southern Ontario (Southern Ontario Fecal microbiota Transplantation – SOFT- Movement), in order to inform FMT policy in Canada.

Methods: A 59-item survey was administered electronically to clinical leads of the SOFT Movement on June 2, 2016. Six domains were evaluated: 1) FMT program characteristics; 2) FMT recipients; 3) donor screening and selection; 4) FMT manufacturing; 5) FMT administration; 6) good manufacturing procedures/biosafety procedures; and, 7) infection control procedures. Descriptive statistics were used to analyze quantitative data.

Results: All nine programs responded to the survey. Of nearly 1300 FMT performed between 2003 and 2016 within these programs, most (5/6 operating programs) utilized enema administration. Programs were primarily driven by physicians. All programs used universal FMT donors and followed Health Canada screening guidelines, with significant variability in screening frequency (every 3 – 6 months) and modality. Locations for FMT preparation and manufacturing protocols were heterogeneous. FMT stool masses ranged from 20g to 150g and FMT volume, from 25mL to 300mL.

Interpretation: The experience of this high-volume, Canadian, regional FMT network highlights current challenges in program development, including a high reliance upon physicians and the costly nature of donor screening. Standardization and optimization through development of regional centers of excellence for FMT donor recruitment and administration should be explored.

Introduction

Over the past decade, fecal microbiota transplantation (FMT) has emerged as a novel option for the treatment of recurrent *Clostridium difficile* infection (rCDI). To date, multiple randomized controlled trials have demonstrated that FMT using various methodologies is at least as effective if not superior to conventional antibiotic treatments for rCDI, and several cost-effectiveness analyses have demonstrated its value (1-10). However, for clinicians and centers considering offering FMT, little to no guidance exists on how to optimally approach program development. In part, this stems from a lack of accepted standards for FMT methodologies. Within FMT research, variables such as FMT patient selection, timing of FMT, FMT pre-treatment (with suppressive antibiotics and bowel lavage), donor selection, donor screening, FMT manufacturing and storage conditions, FMT route of administration, and number of FMT administrations have not been adequately standardized and validated (11, 12). The impact of heterogeneity in FMT methodologies on recipient outcome remains unclear.

In 2015, Health Canada issued brief, interim guidance regarding the use of FMT in patients with *C. difficile* infection (CDI) not responding to conventional treatment, focusing primarily on the safety aspects of donor selection and screening (13). While various expert bodies have produced guidelines for FMT that include further details on how to manufacture and perform FMT, these recommendations are predominantly based on expert opinion (14, 15). In the absence of evidence-informed guidance, individual centers in Canada offering the treatment have largely created their own protocols. The characteristics of Canadian FMT programs have not been summarized and widely shared.

In November 2015, the Southern Ontario Fecal microbiota Transplantation (SOFT) Movement was created with the dual purpose of sharing FMT experience between long-standing and new programs and removing barriers to FMT provision in Ontario, Canada. As an initial step, we performed an environmental scan of practices by surveying our members on FMT program characteristics and methodologies. Here, we describe the key features of FMT programs in Southern Ontario.

Methods

A 59-item survey on FMT program characteristics and protocols (Appendix 1) was developed by two study investigators (SH and SMP) and reviewed for content validity by a third investigator (BC). Open-ended and multiple-choice questions were used to evaluate the following domains: 1) FMT program characteristics; 2) FMT recipients; 3) donor screening and selection; 4) FMT manufacturing; 5) FMT administration; 6) good manufacturing procedures/biosafety procedures; and, 7) infection control procedures.

The survey was built using SurveyGizmo© and administered electronically on June 2, 2016. Twelve SOFT Movement members representing 9 hospital corporations in Southern Ontario (Figure 1) received the survey by email, with instructions to complete one survey per institution. One reminder email was sent. The data were analyzed using standard descriptive statistics on Microsoft Excel©. Consent to participate in this study was implicit to completing the survey. Institutional research ethics board approval was not deemed necessary as participation was voluntary, the survey did not request patient information or elicit personal opinions, and results were to be presented in aggregate.

Results

All 9 institutions responded to the survey request, with 6 providing complete responses. One institution shared FMT standard operating procedures that were developed but did not have clinical experience to report. Two institutions were in the process of forming FMT programs and therefore provided incomplete or no survey responses.

FMT program characteristics

Since 2003, approximately 1300 FMT have been administered across 6 institutions in Southern Ontario (Figure 1). The earliest program began in 2003, with the remainder of programs starting after 2008. Two programs had not yet launched their programs. One program performed FMT for clinical care only while

the other respondents planned or performed FMT for both clinical care and research purposes. Programs were all staffed by physicians, with five programs having inter-professional clinical support (program co-ordinator, clinical nurses and infectious diseases physician assistant) and two employing research staff (research nurse and summer student).

FMT recipients

All active programs administered FMT for adult patients with CDI. One center additionally performed research into FMT for inflammatory bowel disease, another had planned or ongoing research on FMT for non-alcoholic fatty liver disease and multiple sclerosis and a third was planning research into FMT for obesity and bipolar depression. FMT indications used by the programs for CDI patients are summarized in Figure 2. Major exclusions for FMT recipients included: severe, uncontrollable diarrhea (n = 3); bloody diarrhea (n = 2); any immunocompromise (n = 1); neutropenia (n = 1), irreversible bleeding disorder (n = 1). No center had an upper limit of age for FMT recipients.

Donor screening and selection

All surveyed programs used or planned to use universal FMT donors. At all sites, universal donors underwent screening at baseline. Five of the 7 institutions (71%) screened universal donors every 6 months thereafter, while one institution screened every 3 months and another screened every 3 months and at the end of the donation cycle. Three programs performed microbiota analysis of the donor feces but none used these data as selection criteria for donors.

All programs applied the following suggested donor exclusions recommended by Health Canada: recent antibiotics; systemic immunosuppressive or biological agents; systemic antineoplastic agents; exogenous glucocorticoids; antidiarrheal drugs; mineral oil; bismuth; and kaolin. One program allowed magnesium consumption in donors. Additional exclusions used by all programs included a history of cancer, and by some programs, a history of chronic medical conditions, ongoing use of medications, and certain food consumptions depending on recipients' allergies.

Figure 3, which lists Health Canada-recommended donor exclusion criteria, summarizes the infectious diseases laboratory screening modalities used by programs to adhere to these guidelines. A significant proportion of infectious diseases screening occurred through reference laboratories. Gastroenteritis (diarrhea) due to agents not directly screened for in laboratory tests (e.g. *Listeria*), malaria, Chagas disease, babesiosis, Creutzfeld-Jacob disease and other prion disease exclusions were derived from medical assessment in all cases, with one center also performing laboratory testing for malaria. Although not specifically recommended by Health Canada, 71% and 57% of programs additionally screened for carbapemenase-producing *Enterobacteriaceae a*nd extended spectrum beta-lactamase-producing organisms.

FMT manufacturing

Three (3/6) active programs manufactured FMT within a clinical microbiology laboratory, 2 performed these steps in a research laboratory and one used a shared clinical/research space. In 3 programs, a physician manufactured the FMT all or some of the time; in other programs, FMT manufacturing involved a: nurse (n=1); laboratory technologists (n=1); research technologist (n=1), PhD microbiologist (n=1) or physician assistant (n=1).

Four (4/7) respondents undertook manufacturing validation studies prior to finalizing protocols. The majority (4/7) recommended that donor feces be stored in household refrigerators prior to transporting to the FMT program. Most strived to manufacture FMT within 24 hours of donation, although 2 centers accepted samples up to 48 and 72 hours after donation.

There was a wide range of donor stool mass and diluent volume used in manufacturing FMT (Table 1). Diluents varied with 50% of programs using saline, 17% using water, and 33% using saline for FMT administered by enema and water for FMT administered by nasoduodenal/nasojejunal (ND/NJ). Six programs manufactured frozen FMT, with one institution additionally offering lyophilized FMT. Only

one program used a cryoprotectant (glycerol) in the frozen FMT product. When frozen, FMT was maintained at both -20°C and -80°C.

FMT administration

The most common route of FMT administration was enema, with 3 programs offering FMT by enema alone, 1 providing enema and colonoscopy administration and 1 providing enema and ND/NJ administration. One institution performed FMT by ND/NJ route only.

FMT was performed in either a clinic setting, inpatient room or day unit. FMT was most commonly administered by a physician (n = 5 programs), sometimes with assistance from a physician trainee, physician assistant, or nurse. In the majority of cases when FMT was being administered to patients with CDI, oral vancomycin therapy was stopped 24-48 hours before FMT, although one site stopped it 48-96 hours prior and another, <24 hours before FMT. Only one program used a bowel preparation after stopping vancomycin before FMT administration. In those performing FMT by enema, 2 programs administered FMT once, 3 provided it up to 3 times and 1 provided more than 5 FMT if necessary. In the 2 programs providing FMT by colonoscopy, a single administration was given. One program provided a single FMT by ND/NJ route-time while another provided up to 3 ND/NJ administrations. When multiple FMT administrations were given, they were most frequently given 2-4 days apart.

At 3 sites, patients were not routinely followed post-FMT, whereas 4 sites reported variable follow-up durations ranging from 1-36 months. For CDI, failure of FMT was based on return of CDI symptoms alone at 2 programs while 5 programs additionally required laboratory confirmation.

Good manufacturing procedures/biosafety procedures

All programs manufactured FMT in a biosafety cabinet. Two programs used disposable equipment for manufacturing and the remainder disinfected the manufacturing equipment and space using a sporicidal agent.

Infection control procedures

Fluid-resistant gowns and gloves were used by all programs during FMT manufacturing and administration, while procedure masks and face shields were used variably. Shoe covers were only used during FMT administration at one institution. Four programs performed more than one FMT per day. Between cases, two of these programs requested environmental services to disinfect rooms with a sporicidal agent; one relied on FMT program staff do this; and one only changed linens between cases. All programs requested environmental services to disinfect rooms used for FMT with a sporicidal agent after the last or only procedure of the day was completed.

Interpretation

We provide a comprehensive description of a high volume network of FMT programs in Canada. National surveys of FMT practices in the UK and Ireland have focused primarily on identifying hospitals where FMT is offered, and analysing barriers to FMT uptake without detailing protocols for manufacturing and administration (16-18). Others have reported on the development of single-site FMT programs (19, 20) but to our knowledge, a larger scale comparison of protocols and practices between FMT programs has not been performed. Collectively, our programs have performed about 1300 FMT primarily on patients with rCDI, but programs are expanding to include other indications in the context of research. FMT is most commonly administered by enema, although colonoscopic and NJ administrations are also available. To date, no definite data supports one route of administration over another in terms of FMT efficacy for rCDI (3, 21-25).

With growing evidence to support the cost-effectiveness of FMT for rCDI, deregulation by Health Canada for this indication and increasing research applications of FMT for other health conditions, there has been renewed interest in FMT programs across Canada. In July 2016, Health Quality Ontario, an arms-length organization that advises the Ontario Ministry of Health and Long Term Care on quality in healthcare, made a recommendation for public funding of FMT for rCDI based on an independent review

of the cost-effectiveness of FMT and patient experience with rCDI (26). As individual centers and the provincial healthcare systems determine how to best structure and fund FMT programs, providing a view into current FMT programs can highlight successes and points of vulnerability.

In Southern Ontario, FMT programs are heavily driven by physicians. While FMT by enema or NJ tube may be administered by other health practitioners such as nurses and physician assistants, a physician with expertise in gastroenterology, infectious diseases and/or microbiology is required to oversee the procedure, the donor screening steps and recipient follow-up. As there is currently no mechanism for compensating physicians for this service in Ontario, physicians are donating time and expertise to provide this needed service. Likewise, hospitals are absorbing costs associated with building and supporting FMT programs. A fair, transparent and cost-effective means for providing seamless service should be developed in order to facilitate access to FMT.

Universal FMT donors are widely employed in these programs, primarily to provide stool samples that are processed then frozen and banked for later use. This approach is cost-effective, validated (4, 27-29) and favorable in terms of logistics for providing FMT on demand. The optimal frequency for screening universal donors is not clear and variability exists among the surveyed programs. Comprehensive donor screening, as recommended by Health Canada, is expensive, and not all tests are readily available to all institutions. There remains a heavy reliance upon reference laboratories for specialized testing (eg. stool for ova and parasites, enteric viruses). In some cases, validated or reliable tests do not exist (eg. testing of stool for *Listeria*) yet medical assessment alone may not necessarily exclude the possibility of infection or carriage.

FMT manufacturing is highly variable across sites. The total weight of stool used, the volume of diluent, and the method of preparation differed between programs. Locating a space for this task is a frequent barrier for FMT programs, and this has resulted in physicians using research laboratory space to manufacture a clinical therapeutic. The use of commercial systems that contain the FMT product and that

can be carefully disinfected between uses is highly desirable for infection control but these approaches are associated with significant costs and therefore are inconsistently used. Disposable equipment may be one alternative to decrease manufacturing costs (4, 30) but further research into validating FMT manufacturing is needed. While some sites in our survey did undertake validation studies to support their manufacturing processes and storage conditions, no industry standard exists regarding metrics for validation studies.

Our study has limitations. The study sites may not represent all sites where FMT has been performed within our region. Two of the surveyed sites were in the process of developing FMT programs and survey response may not represent their final approaches. Finally, we aimed to simply describe the FMT programs and did not collect data on clinical outcome of FMT recipients, which would be important for guiding future recommendations for FMT programs.

In summary, our study has identified a significant diversity in practices for FMT within a circumscribed region of Ontario, Canada servicing 12 million people. Site-based FMT protocols are driven by multiple factors including costs, local administrative pressures and availability of screening tests and these barriers have limited FMT uptake (16-18). The two largest costs of FMT in the region are physician time for coordinating, manufacturing and administering FMT and FMT donor screening. While public funding for FMT is being explored, FMT costs in Ontario are currently absorbed by individual hospital budgets and research funding. In planning future FMT programs in Canada, opportunities for systems-wide efficiencies should be explored – such as creating regional centers of excellence for FMT donor recruitment and administration. A recently released European guidance document on FMT echoes these concepts, recommending implementation of a clinical governance that would oversee the administrative aspects of FMT programs and deal with any organizational barriers that may hinder their efficiency to deliver FMT to rCDI patients in need (15). Such an approach would concentrate expertise in FMT, ensure consistency in procedures and practices, enable trace-backs in the event of possible FMT-related adverse

events, and reduce the need for numerous institutions to introduce costly donor screening tests and equipment into laboratories.

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Author Contributions

S. S. Hota and S. M. Poutanen. co-led the design of the study and the development of the survey. S. S. Hota drafted the manuscript and submitted it for publication. S. Surangiwala administered the survey and completed the initial analysis of data. A. Paterson. completed additional data analysis. B. Coburn reviewed and approved the survey prior to administration. The SOFT Movement includes physician leads of FMT programs in Southern Ontario as follows: B. Coburn (University Health Network), N. Daneman (Sunnybrook Health Sciences Centre), M. Downing (St. Joseph's Health Center – Toronto), C. Graham (Trillium Health Partners), S. S. Hota (University Health Network), J. Johnstone (Public Health Ontario, St. Joseph's Health Care - Toronto), C. Lee (St. Joseph's Healthcare - Hamilton), J. McCready (Michael Garron Hospital), E. O. Petrof (Kingston General Hospital), S. M. Poutanen (Sinai Health Center, University Health Network), J. Powis (Michael Garron Hospital), D. Ricciuto (Lakeridge Health), and M. Silverman (St. Joseph's Hospital - London). All SOFT Movement leads and authors reviewed the study data for integrity, provided feedback on results, contributed to manuscript preparation and approved the final draft. All authors agree to be accountable for the data presented within the manuscript.

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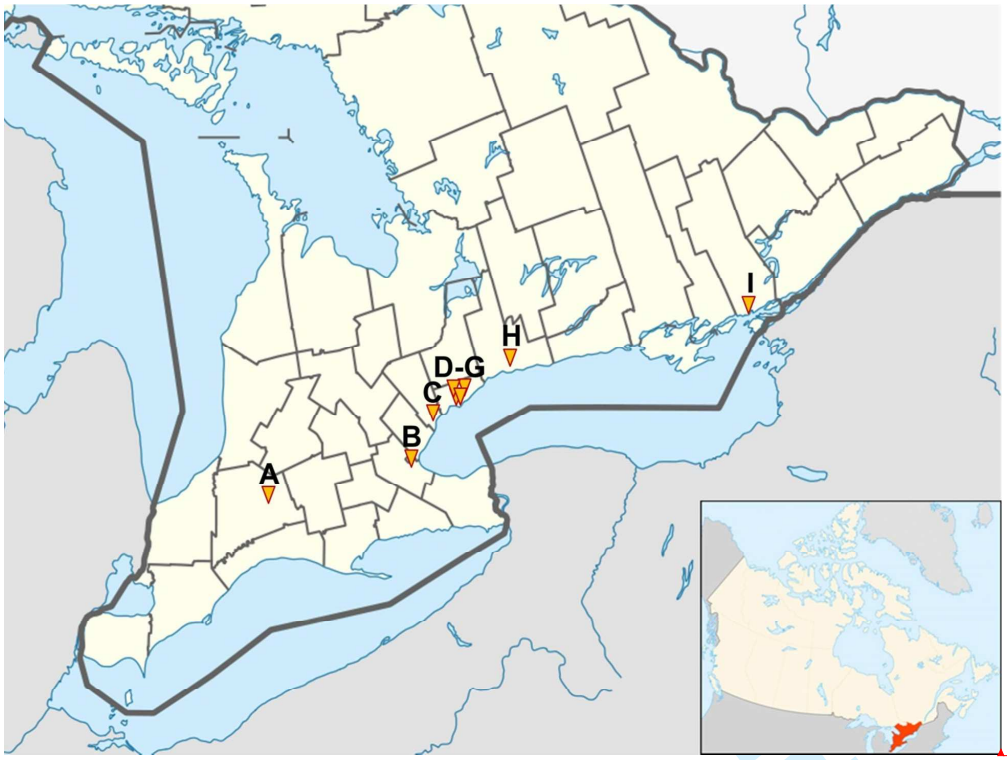
Table 1. Range of donor stool mass and diluent volume used for fecal microbiota transplantation (FMT) manufacturing within the 7 SOFT Movement institutions with finalized protocols.

Route of Administration	**Range of mass of stool used (g)**		**Range of diluent used (mL)**	
	Min	Max	Min	Max
Enema	20	100	25	300
Colonoscopy	30	150	200	300
ND/NJ	30	100	70	250

Figure 1. Location of fecal microbiota transplantation (FMT) programs in SOFT Movement, 2016



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FMT programs included:

A. St. Joseph's Hospital, London

B. St. Joseph's Healthcare, Hamilton

C. Trillium Health Partners, Mississauga

D. University Health Network/Sinai Health System, Toronto

E. Michael Garron Hospital, Toronto

F. St. Joseph's Health Centre, Toronto*

G. Sunnybrook Health Science Centre, Toronto*

H. Lakeridge Health, Oshawa

I. Kingston General Hospital, Kingston

*Sunnybrook Health Sciences Centre and St. Joseph's Health Centre (Toronto) were not operating at the time of the survey

Figure 2. Proportion of the 7 operating SOFT Movement programs providing FMT to each of the following subgroups of patient *Clostridium difficile* infection (CDI) or recurrent CDI (rCDI)

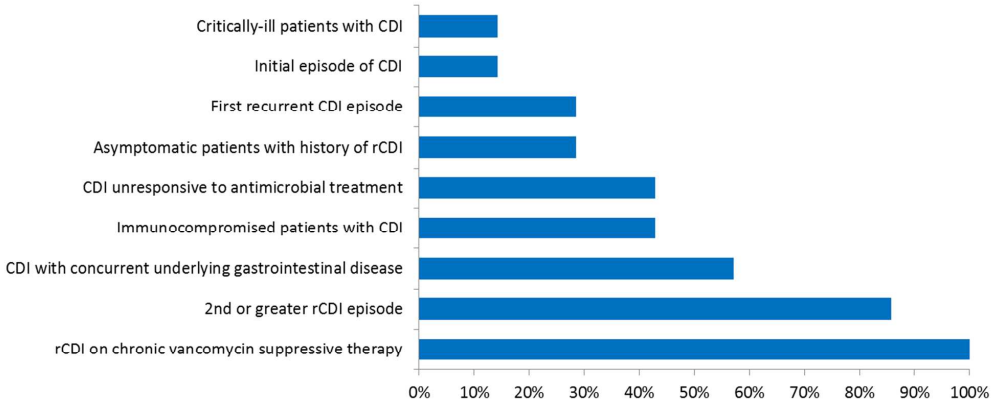
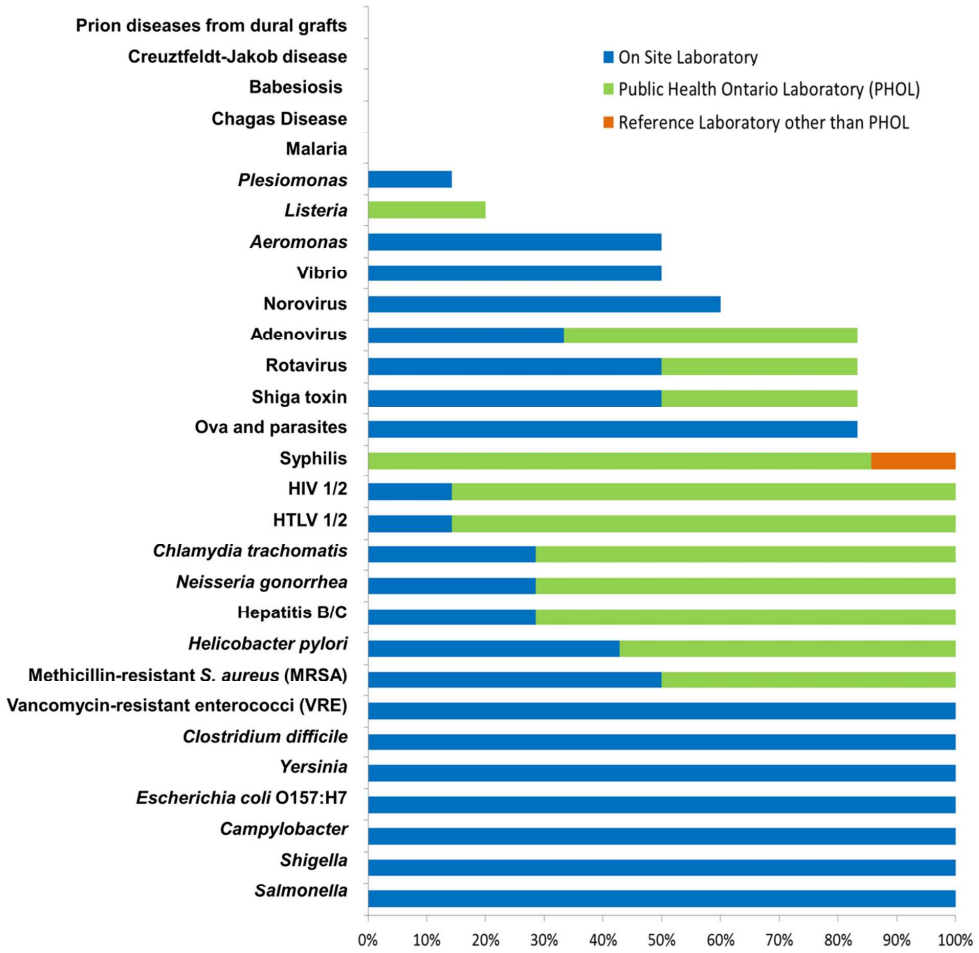


Figure 3. Proportion of the 7 operating SOFT Movement programs completing laboratory testing for the infectious disease agents recommended by Health Canada



SOFT Movement Survey of FMT Programs

Part 1: General Information about your Fecal Microbiota Transplant (FMT) Program

1) Please fill out the information below:

First Name: _____

Last Name: _____

Title: _____

Please enter an email address we can use to communicate with you.:

_____

Please fill out the start date of this survey below.:

_____

2) Please enter the name of the institution and city where your FMT program is based:

Institution name: _____

City: _____

3) Have you begun performing FMTs at your location?

( ) Yes

( ) No

4) Approximately what year did you start performing FMT? If you have not, what year do you anticipate you will be starting to perform FMTs?

( ) Please enter year: _____

( ) Not applicable

5) If applicable, please enter the number of FMTs performed since the program started? If not applicable, please enter 0 (zero).

_____

6) Have you performed FMT in the context of a research study, for clinical care or both?

( ) Research only

( ) Clinical care only

( ) Both

7) Which approvals or endorsements did you require before starting your FMT program (check all that apply):

[ ] Medical Advisory Committee

[ ] Hospital Senior Administrators

[ ] Research Ethics Board

[ ] Other (please specify): _____

8) Approximately how long does it take for a patient to get a FMT from initial clinical assessment to first administration?

( ) < 1week

( ) 1-4 weeks

( ) 4-12 weeks

( ) >12 weeks

9) Aside from the persons who manufacture and administer FMT, who else supports the program and in what capacity (select all that apply and please list duties below)?

[ ] Coordinator: _____

[ ] Clinical nurse: _____

[ ] Research nurse: _____

[ ] Trainee MD: _____

[ ] Students: _____

[ ] Volunteers: _____

[ ] Other (please specify): _____

[ ] Not applicable

Part 2: Donor Selection and Screening

10) Please attach your Standard Operating Procedures for FMT donor screening (if available) below.

Please attach on web survey

11) Do you use universal FMT donors?

( ) Yes

( ) No

12) If you use universal FMT donors, how often do you screen them?

( ) Every month

( ) Every 2 months

( ) Every 3 months

( ) Every 4 months

( ) Every 5 months

( ) Every 6 months

( ) I do not use universal donors

( ) Other (please specify): _____

13) If you do not use universal FMT donors, when do you perform donor screening?

( ) Within 2 weeks of donation for FMT

( ) Within 4 weeks of donation for FMT

( ) Within 3 months of donation for FMT

( ) Within 6 months of donation for FMT

( ) Other (please specify): _____

14) Do you perform microbiota analysis of donor feces?

( ) Yes

( ) No

15) If you perform microbiota analysis of donor feces, do you use this as part of your selection criteria for choosing donors?

( ) Yes

( ) No

( ) Not applicable

16) Which of the following agents suggested by Health Canada do you use as exclusion criteria when screening donors for FMT?

[ ] Systemic immunosuppressive or biological agents

[ ] Systemic antineoplastic agents

[ ] Exogenous glucocorticoids

[ ] Anti-diarrheal drugs

[ ] Mineral oil

[ ] Bismuth

[ ] Magnesium

[ ] Kaolin

[ ] Recent use of antibiotics (if yes, please specify your definition of recent use):
_____

[ ] All of the above

17) Do you screen for additional agents not included in Health Canada's suggestions?

( ) Yes (please specify): _____

( ) No

18) Which of the following microorganisms or diseases suggested by Health Canada do you use as exclusion criteria routinely in FMT donors? (Enter all that apply)

[ ] Cancer

[ ] *Salmonella* species

[ ] *Shigella*

[ ] *Campylobacter*

[ ] Sorbitol-negative *Escherichia coli* 0157-H7

[ ] Shiga toxin

[ ] *Yersinia*

[ ] *Plesiomonas*

[ ] *Aeromonas*

[ ] *Vibrio*

[ ] *Listeria*

[ ] *Helicobacter pylori*

[ ] *Clostridium difficile*

[ ] Vancomycin-resistant *enterococci* (VRE)

[ ] Methicillin-resistant *Staphylococcus aureus* (MRSA)

[ ] Syphilis

[ ] *Neisseria gonorrhea*

[ ] *Chlamydia trachomatis*

[ ] Norovirus

[ ] Rotavirus

[ ] Adenovirus

[ ] HIV 1/2

[ ] HTLV-I/II

[ ] Hepatitis B/C

[ ] Ova and parasites

[ ] Malaria

[ ] Chagas disease

[ ] Babesiosis

[ ] Creuztfeldt-Jakob disease

[ ] Prion-related diseases from dural mater grafts

[ ] All of the above

19) What screening modality do you use to screen for the above microorganisms/diseases?

	Risk factors	Medical assessment	Laboratory test			Test type (please enter below if applicable)
	Risk factors	Medical assessment	Test performed at your site	Test performed at PHL	Test performed at site other than PHL	
Salmonella species	[ ]	[ ]	___	___	___	___
Shigella	[ ]	[ ]	___	___	___	___
Campylobacter	[ ]	[ ]	___	___	___	___
Sorbitol-negative *Escherichia coli* 0157-H7	[ ]	[ ]	___	___	___	___
Shiga toxin	[ ]	[ ]	___	___	___	___
Yersinia	[ ]	[ ]	___	___	___	___
Plesiomonas	[ ]	[ ]	___	___	___	___
Aeromonas	[ ]	[ ]	___	___	___	___
Vibrio	[ ]	[ ]	___	___	___	___
Listeria	[ ]	[ ]	___	___	___	___
Helicobacter pylori	[ ]	[ ]	___	___	___	___
Clostridium difficile	[ ]	[ ]	___	___	___	___
Vancomycin-resistant *enterococci* (VRE)	[ ]	[ ]	___	___	___	___
Methicillin-resistant *Staphylococcus aureus* (MRSA)	[ ]	[ ]	___	___	___	___

Syphilis	[ ]	[ ]	___	___	___	___
Neisseria gonorrhea	[ ]	[ ]	___	___	___	___
Chlamydia trachomatis	[ ]	[ ]	___	___	___	___
Norovirus	[ ]	[ ]	___	___	___	___
Rotavirus	[ ]	[ ]	___	___	___	___
Adenovirus	[ ]	[ ]	___	___	___	___
HIV 1/2	[ ]	[ ]	___	___	___	___
HTLV-I/II	[ ]	[ ]	___	___	___	___
Hepatitis B/C	[ ]	[ ]	___	___	___	___
Ova and parasites	[ ]	[ ]	___	___	___	___
Malaria	[ ]	[ ]	___	___	___	___
Chagas disease	[ ]	[ ]	___	___	___	___
Babesiosis	[ ]	[ ]	___	___	___	___
Creuztfeldt-Jakob disease	[ ]	[ ]	___	___	___	___
Prion-related diseases from dural mater grafts	[ ]	[ ]	___	___	___	___
Cancer	[ ]	[ ]	___	___	___	___

20) Do you screen for any additional microorganisms or diseases not included by Health Canada suggestions?

( ) Yes (please specify): _____

( ) No

21) Do you collect a dietary history of FMT donors in the event recipients have food allergies?

( ) Yes

( ) No

Part 3: FMT Manufacturing

22) Please attach your Standard Operating Procedures for FMT manufacturing (if available) below.

Please attach on web survey

23) Where is FMT manufactured in your centre (select more than one if applies)?

[ ] Clinical microbiology laboratory

[ ] Research laboratory

[ ] Pharmacy

[ ] Clinic

[ ] Other (please specify)

24) Who manufactures FMT (select all that apply)?

[ ] MD

[ ] Trainee MD

[ ] Clinical nurse

[ ] Research nurse

[ ] Laboratory technologist

[ ] Clinical microbiology technologist/technician

[ ] Research technologist/technician

[ ] Other (please specify): _____

25) Approximately what mass of donor stool do you use for each FMT (please select all that apply)?

	10g	20g	30g	40g	50g	100g	150g	Other amount (please enter below)
Enema	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	___
Colonoscopy	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	___
Nasogastric/nasojejunal	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	___

26) Approximately what volume of diluent do you use for each FMT (check all that apply if more than one route of administration at your center)?

	25mL	50mL	100mL	150mL	200mL	300mL	400mL	500mL	Other amount (please enter below)
Enema	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	___
Colonoscopy	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	___
Nasogastric/nasojejunal	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	[ ]	___

27) What type of diluent do you use for FMT?

[ ] Tap water

[ ] Sterile water

[ ] Sterile normal saline

[ ] Other (please specify): _____

28) What form of FMT do you manufacture (select all that apply)?

[ ] Fresh

[ ] Frozen

[ ] Capsules

[ ] Lyophilized (freeze-dried)

[ ] Other (please specify): _____

29) What are your recommended storage conditions for donor feces prior to FMT manufacturing?

( ) Household freezer

( ) Household fridge

( ) Room temperature

( ) Other (please specify): _____

30) How long do you allow donor feces to be stored prior to delivery to your unit for FMT manufacturing?

( ) Up to 24 hour

( ) Up to 48 hour

( ) Up to 72 hour

( ) Other (please specify): _____

31) What storage conditions for donor feces do you use after receiving donor feces for FMT manufacturing?

( ) Room temperature

( ) 4-5C

( ) -20C

( ) -80C

( ) Other (please specify): _____

32) How long do you allow donor feces to be stored in your unit before manufacturing for FMT?

( ) A few hours

( ) A few hours to 24 hours

( ) 24-48 hours

( ) 48-72 hours

( ) Other (please specify): _____

33) If you use frozen FMT, which cryoprotectant do you use?

( ) Glycerol (please enter concentration in final FMT):

_____

( ) Other (please specify): _____

( ) No cryoprotectant

( ) Not applicable

34) If you use frozen FMT, at what temperature is the sample frozen?

( ) -20C

( ) -80C

( ) Other (please specify): _____

( ) Not applicable

35) What is the maximum acceptable time from FMT donation to patient administration in your institution?

( ) 3 hours

( ) 6 hours

( ) 12 hours

( ) 24 hours

( ) 48 hours

( ) 96 hours

( ) >96 hours

( ) Not applicable

36) Did you undertake any manufacturing validation studies prior to starting your FMT program?

( ) Yes

( ) No

37) What are your rejection criteria for donor stools at the time of donation (select all that apply)?

[ ] Clinical criteria only (donor has active fever, diarrhea etc.)

[ ] Unformed stool provided for donation

[ ] Urine mixed in donated stools

[ ] Mucous in donated stools

[ ] Insufficient quantity of donated stools

[ ] Blood in donated stools (if so, do you do Fecal Occult Blood Testing?): _____

[ ] Other (please specify): _____

Part 4: Good Manufacturing/Biosafety Procedures

38) Do you manufacture FMT in a biosafety cabinet?

( ) Yes

( ) No

39) How do you disinfect your manufacturing equipment (select all that apply)?

[ ] Disinfect with sporicidal agent pre- and post-FMT

[ ] Disinfect with non-sporicidal disinfectant pre- and post-FMT

[ ] Use only disposable equipment for all manufacturing steps

[ ] Other (please specify)

40) What personal protective equipment is used by the FMT manufacturer (select all that apply)?

[ ] Single pair of gloves

[ ] Double gloves

[ ] Fluid-resistant gown

[ ] Non-fluid-resistant gown

[ ] Procedure mask

[ ] Face shield

[ ] Hair coverings

[ ] Shoe protection

[ ] Other (please specify): _____

Part 5: Patients

41) For which of the follow conditions do you administer FMT?

[ ] *Clostridium difficile infection*

[ ] Inflammatory bowel disease

[ ] Irritable bowel syndrome

[ ] Other (please specify): _____

42) To which of the following subgroups of *Clostridium difficile* infection (CDI) do you administer FMT (select all that apply)?

[ ] Initial episode of CDI as part of treatment for acute disease or immediately thereafter (ie. within 2 weeks of symptom-onset)

[ ] First recurrent CDI episode as part of treatment for acute disease or immediately thereafter (ie. within 2 weeks of symptom-onset)

[ ] Second or greater recurrent CDI episode(s) as part of treatment for acute disease or immediately thereafter (ie. within 2 weeks of symptom-onset)

[ ] Patients with a history of recurrent CDI after they have been treated and are asymptomatic off therapy (i.e. beyond 2 weeks of symptom onset)

[ ] Patients with a history of recurrent CDI on chronic suppressive oral vancomycin

[ ] Patients with CDI who are unresponsive to antimicrobial treatment

[ ] Critically-ill patients with CDI

[ ] Immunocompromised patients with CDI

[ ] Those with concurrent underlying GI disease with CDI

[ ] Other (please specify): _____

[ ] Not applicable

43) What are your major exclusion criteria for FMT receipt (select all that apply)?

[ ] Age over 90 years

[ ] Immunocompromised status

[ ] Bleeding disorder (i.e. irreversible)

[ ] Severe, uncontrollable diarrhea

[ ] Bloody diarrhea

[ ] Other (please specify): _____

Part 6: Clinical Procedures for FMT Administration

44) Please attach your Standard Operating Procedures for FMT administration (if available) below.

Please attach on web survey

45) Where do you perform FMT (select all that apply)?

[ ] Clinic room

[ ] Day unit

[ ] Inpatient room

[ ] Outside of hospital

[ ] Other (please specify): _____

46) Who administers FMT to patients (select all that apply)?

[ ] MD

[ ] Trainee MD

[ ] Nurse

[ ] Other (please specify): _____

47) How long before FMT do you stop oral vancomycin (or other antibiotic) if a patient is on treatment/suppression?

( ) <24 hours

( ) 24-48 hours

( ) 48-96 hours

( ) >96 hours

( ) Not applicable

48) What route(s) of administration do you use for FMT?

[ ] Enema

[ ] Colonoscopy

[ ] Nasogastric/nasojejunal tube

[ ] Other (please specify): _____

49) On average, how long does the FMT procedure take?

	<10minutes	**10-30 minutes**	**30-60 minutes**	**>60 minutes**	**Not applicable**
Enema	[ ]	[ ]	[ ]	[ ]	[ ]
Colonoscopy	[ ]	[ ]	[ ]	[ ]	[ ]
Nasogastric/nasojejunal	[ ]	[ ]	[ ]	[ ]	[ ]

50) How many FMTs do you perform per patient?

	Only 1	**Up to 3**	**Up to 5**	**>5 if necessary**	**Not applicable**
Enema	[ ]	[ ]	[ ]	[ ]	[ ]
Colonoscopy	[ ]	[ ]	[ ]	[ ]	[ ]
Nasogastric/nasojejunal	[ ]	[ ]	[ ]	[ ]	[ ]

51) If you administer multiple FMTs per patient, what is the frequency of FMT?

	Daily	Every 2-4 days	Every 4-7 days	Weekly	Every 10-14 days	Other (please enter a value below)	Not applicable
Enema	[ ]	[ ]	[ ]	[ ]	[ ]	___	( )
Colonoscopy	[ ]	[ ]	[ ]	[ ]	[ ]	___	( )
Nasogastric/nasojejunal	[ ]	[ ]	[ ]	[ ]	[ ]	___	( )

52) What are your criteria for failure of FMT?

( ) Return of CDI symptoms

( ) Return of CDI symptoms and laboratory confirmation

( ) Other (please specify): _____

53) What is your routine follow-up post-FMT?

( ) I only see post-FMT patient's as needed, if they have concerns

( ) I see post-FMT patients regularly, at the following time points (other please specify)::
_____

54) Do you perform microbiota analysis of FMT recipient feces prior to FMT administration?

( ) Yes

( ) No

55) Do you perform microbiota analysis of FMT recipient feces following FMT administration?

( ) Yes (please specify frequency): _____

( ) No

Part 7: Infection Control Procedures

56) What personal protective equipment is worn by the individual administering FMT (select all that apply)?

[ ] Single pair of gloves

[ ] Double gloves

[ ] Fluid-resistant gown

[ ] Non-fluid-resistant gown

[ ] Procedure mask

[ ] Face shield

[ ] Hair coverings

[ ] Shoe protection

[ ] Other (please specify): _____

57) How is the FMT procedure room/area disinfected between FMTs, if multiple FMTs are scheduled back to back?

( ) I never have more than one FMT in a day

( ) Wipe down with non-sporicidal hospital disinfectant by FMT team

( ) Wipe down with sporicidal disinfectant by FMT team

( ) Cleaning by housekeeping staff using non-sporicidal hospital disinfectant

( ) Cleaning by housekeeping staff using sporicidal disinfectant

( ) Other (please specify): _____

58) How is the FMT procedure room/area disinfected after FMT procedures are done for the day?

( ) Wipe down with non-sporicidal disinfectant by FMT team

( ) Wipe down with sporicidal disinfectant by FMT team

( ) Cleaning by housekeeping staff using non-sporicidal disinfectant

( ) Cleaning by housekeeping staff using sporicidal disinfectant

( ) Other (please specify): _____

Remarks

59) Do you have any other questions/comments/concerns to share?

_____

_____

_____

_____

Thank You!