# Revisiting the donor screening protocol of faecal microbiota transplantation (FMT): a systematic review

We read with interest the recent work by Haifer *et al*,[1] which highlighted the importance of donor selection in determining the clinical efficacy of treating ulcerative colitis (UC) using faecal microbiota transplantation (FMT), with one donor having 100% efficacy compared with a second donor (36% efficacy). Considering the impact of COVID-19 pandemic on FMT, updated guidance including patient selection, donor recruitment and selection, FMT procedures and stool manufacturing was provided by worldwide FMT experts in international guideline by Ianiro *et al*.[2] The US Food and Drug Administration (FDA) has recommended that FMT donor screening must include a questionnaire specifically addressing risk factors for colonisation with multidrug-resistant organisms (MDROs) and stool testing for MDROs, including extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae, vancomycin-resistant enterococci (VRE), carbapenem-resistant Enterobacteriaceae (CRE) and methicillin-resistant *Staphylococcus aureus* (MRSA) at minimum.[3] The evolution of FMT and the introduction of essential donor screening requirements by the FDA are listed in figure 1A. However, little is known on the differences in donor screening protocols in different FMT centres. Therefore, we aim to provide an update on the screening strategy for faecal donors based on emerging trends in diseases as well as to propose a set of blood and stool tests to ensure safety of the FMT procedure via systematically reviewing the existing data and with our own experience in the centre of FMT at The Chinese University of Hong Kong.

We thus systematically reviewed (INPLASY2021120063)[4] the published literature (Embase and MEDLINE through PubMed and Web of Science) and consensus documents on donor screening procedures from FMT units worldwide. Thirty-three (n=33) clinical studies (Preferred Reporting Items for Systematic Reviews and Meta-Analyses flowchart, figure 1B) and 11 (n=11) consensus documents in different WHO regions (figure 1C) were compared along with our local donor screening procedure (see online supplemental appendix)

The consensus documents and national guidelines published in all WHO regions supported screening of MDROs, including ESBL, VRE, CRE and MRSAs, in potential stool donors, except the Austrian[5] and Taiwan guidelines.[6] There was one European study testing for other MDROs, MDR *Acinetobacter baumannii*.[7] Considering the high prevalence of MDROs in Hong Kong, with ESBL and MRSA being 52.8% and 2.5%, respectively,[8] our FMT centre is currently screening ESBL, VRE, CRE, MRSA and MDR *A. baumannii*. Equally, a controversy is to what limits detecting ESBL–Enterobacteriaceae in the donor, for example, in India, where >70% of the population is already colonised.[9]

Different practices of SARS-CoV-2 testing for potential stool donors were adopted by different stool bank centres

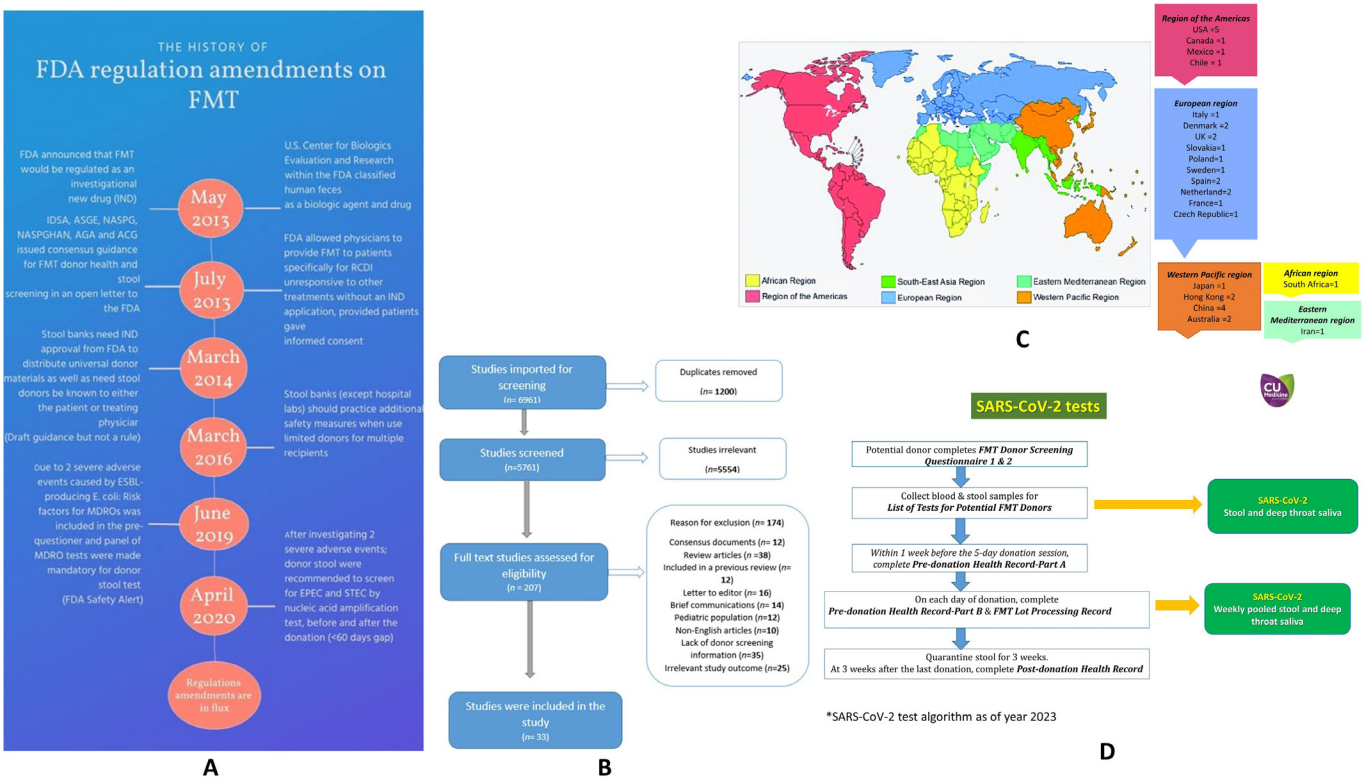


**Figure 1** (A) FDA regulation amendments and safety alerts on FMT. (B) PRISMA flow diagram for the study selection. (C) Included study stratification according to the WHO regions. (D) SARS-CoV-2 testing time points. ACG, American College of Gastroenterology; AGA, American Gastroenterological Association; ASGE, American Society for Gastrointestinal Endoscopy; EPEC, enteropathogenic *Escherichia coli*; ESBL, extended-spectrum β-lactamase; FDA, Food and Drug Administration; FMT, faecal microbiota transplantation; IDSA, Infectious Disease Society of America; IND, investigational new drug; MDRO, multidrug-resistant organism; RNASPG, North American Society for Paediatric Gastroenterology; NASPGHAN, North American Society For Paediatric Gastroenterology, Hepatology & Nutrition; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RCDI, Recurrent Clostridiodes difficile infections; STEC, Shiga toxin-producing *Escherichia coli*.

since the COVID-19 pandemic. Currently, our biobank is following a stepwise procedure to detect SARS-CoV-2 in donors (figure 1D).

The repertoire of the optimal testing methods for infective agents is rapidly changing due to the advancement of technology and our increased understanding of the risks associated with FMTs. For example, increasingly more national consensus guidelines, including the American guideline,[10] recommend the detection of Shiga toxin in *Escherichia coli* with PCR, which is a more sensitive method as compared with enzyme immunoassays (EIA), but with a higher cost. In addition, the detection of specific MDROs in stool samples of potential donors depends on their local prevalence and risk assessment. With the rapidly increasing numbers of FMT biobanks established worldwide, there is a need for a working consensus perhaps of a minimal set of screening questionnaire and laboratory test requirements. Here we propose (table 1) a minimum but essential set of screening questionnaire and laboratory tests in donor selection. Additional consideration made to specific conditions and tests will be based, according to a risk-based assessment, depending on the geographical prevalence of disease and other cultural and medicine licensing requirements and risk–benefit factors in their region.

**Table 1** Recommended minimum list of questionnaire, blood and stool test for rigorous FMT donor screening procedure

| Prescreening data | Test method |
|---|---|
| Risk of infectious agents | |
| Known HIV, hepatitis B or C infections | Questionnaire |
| High-risk sexual behaviours | Questionnaire |
| Use of illicit drugs | Questionnaire |
| Travel (within the last 6 months) to high-risk countries with travellers' diarrhoea | Questionnaire |
| Recent needle stick accident | Questionnaire |
| GI comorbidities | |
| History of IBD | Questionnaire |
| History of IBS, idiopathic chronic constipation or chronic diarrhoea | Questionnaire |
| History of GI malignancy or known polyposis | Questionnaire |
| Factors that could affect the composition of gut microbiota | |
| Antibiotics within the preceding 3 months | Questionnaire |
| Major immunosuppressive medications | Questionnaire |
| Other factors | |
| History of major GI surgery | Questionnaire |
| Metabolic syndrome | Questionnaire |
| Systemic autoimmunity (multiple sclerosis and connective tissue disease) | Questionnaire |
| Atopic conditions (asthma, atopic dermatitis and eczema) | Questionnaire |
| Obesity | Questionnaire |
| Depression | Questionnaire |
| Schizophrenia or delusion disorder | Questionnaire |
| Blood tests | Test method |
| Testing for viruses | |
| Hepatitis A (HAV) | HAV-IgM |
| Hepatitis B | Hepatitis B surface antigen (HBsAg), anti-Hbc |
| Hepatitis C (HCV) | Anti-HCV |
| Hepatitis E (HEV) | Anti-HEV IgM |
| HIV I and II | Anti-HIV |
| Human T-cell lymphotropic virus | Anti-HTLV |
| Testing for bacteria | |
| *Treponema pallidum* | Screening test (eg, Rapid Plasma Reagin (RPR), Venereal Disease Research Laborotory test (VDRL) and EIA) |
| Other tests | |
| Complete blood count | NA |
| C reactive protein | NA |
| Renal function test | NA |
| Liver function test | NA |
| Stool tests | Test method |
| Testing for viruses | |
| Rotavirus | EIA |
| Norovirus | PCR |
| Testing for bacteria | |
| *Salmonella* sp | Culture±PCR |
| *Shigella* sp | Culture±PCR |
| *Campylobacter* sp | Culture±PCR |
| *Vibrio* sp | Culture±PCR |
| *Clostridium difficile* | PCR |
| *Helicobacter pylori* | Stool antigen |
| MDR bacteria | |
| ESBL-producing Enterobacteriaceae | Culture |
| VRE | Culture |
| CRE (KPC, NDM and OXA 48) | Culture |

Continued

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**Supplemental material** This content has been supplied by the author(s). It has not been vetted by

**Table 1** Continued

| Prescreening data | Test method |
|---|---|
| MRSA | Culture |
| Testing for parasites | |
| *Cyclospora* sp | Microscopy±antigen |
| *Isospora* sp | Microscopy±antigen |
| *Giardia* sp | Microscopy±antigen |
| *Cryptosporidium* sp | Microscopy±antigen |
| *Entamoeba histolytica* | Microscopy±antigen |
| Light microscopy for ova and cysts | Microscopy |

CRE, carbapenem-resistant Enterobacteriaceae; ESBL, extended-spectrum β-lactamase; FMT, faecal microbiota transplantation; MDR, multidrug resistant; MRSA, methicillin-resistant *Staphylococcus aureus*; NA, not applicable; NA, not available; VRE, vancomycin-resistant enterococci .



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**Supplementary Information**

# Revisiting the donor screening protocol of fecal microbiota transplantation (FMT): A systematic review

## Supplementary Materials and Methods

### Protocol development

This systematic review was carried out according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis PRISMA statement and the published International Platform of Registered Systematic Review and Meta-analysis Protocols (INPLASY) with registration number INPLASY2021120063.

### Search strategy

A comprehensive search and systematic literature review were performed using 3 bibliographic databases namely, EMBASE and MEDLINE through PubMed and WEB of SCIENCE for the last decade, using the search terms, ("Faecal microbiota transplantation" OR "FMT" OR "bacteriotherapy" OR "gut microbiota transplantation" OR "fecal transplantation" OR "intestinal microbiota transfer") along with the term "AND" separately with ("Clostridioides difficile" OR "C. difficile"), and ("Inflammatory bowel disease" OR "IBD" OR "Crohn's disease" OR "Ulcerative colitis" OR "UC"). The same search term was used in all databases to retrieve the data for this review. Additionally, we have reviewed all international consensus documents and local guidelines published in English, on the topic of interest.

### Eligibility criteria

The PICOS (Population, Intervention, Comparator, Outcomes, and Study Design) approach was used to guide the determination of the eligibility criteria.

Population**:** The current study intended to review three major adult population (> 18 years) categories (1) laboratory-confirmed diagnosis of *C. difficile* colitis (severe or complicated CDI), (2) ≥2 laboratory-confirmed relapses of *C. difficile* colitis after receipt of initial specific antimicrobial treatment, (3) Ulcerative colitis and inflammatory bowel disease was diagnosed based on clinical, endoscopic, and histological criteria

Interventions**:** Single or multiple FMT in patients/populations with the above underline medical conditions were included. All FMT administration routes were considered including; colonoscopy, oral gavage, naso-duodenal tube, and enema. The fresh, frozen or encapsulated samples that were used in FMT along with related or unrelated donors were also included where adequate information was disseminated in the donor screening procedure.

Comparator**:** Since this is a qualitative analysis and the primary objective is to analyze donor screening procedures, the presence of a comparator is not applicable.

Outcomes**:** Primary outcome of this review is to rationalize rigorous donor screening procedures suitable for the Western-pacific region including assessing the optimal strategy to detect ESBL-producing bacteria due to their high prevalence rates in the region, including other MDROs.

Study design**:** The review included all types of observational (retrospective and prospective) and clinical (randomized control, interventional, cohorts, case reports, and case series studies) studies on FMT against aforementioned (*C. difficile*, UC, and IBD) gut-related diseases.

Excluding criteria**:** We excluded reviews, editorials, and letters to the editor or commentaries that did not provide precise and sufficient information for the donor screening analysis. Furthermore, the FMT applications for pediatric patients were also excluded due to the inability to compare the outcomes with the adult's stable gut microbiota. Non-English articles and FMT applications other than *C. difficile*, ulcerative colitis, and Inflammatory bowel disease were also excluded, as our research group already published a systematic review and meta-analysis for the application of FMT in AMR remission and lack of evidence for other applications of FMT. Additionally, we refrain from including the relevant articles already reviewed by Lai et al [Lai CY, Sung J, Cheng F, et al. Systematic review with Meta-analysis: Review of donor features, procedures and outcomes in 168 clinical studies of Faecal Microbiota Transplantation. Aliment Pharmaco & Therapeu 2019;49:354–63. doi:10.1111/apt.15116], as this manuscript is an update and extension of the dynamically evolving donor screening procedures.

**Assessment of risk of bias for the included studies**

Two reviewers (RN, and PD) independently assessed the eligibility of all articles and this was performed using the https://www.covidence.org online platform. The article selection process included two stages. At stage 1, the, titles and abstracts were reviewed by one research staff (PD) and one supervisor (RN). At this stage, two reviewers met to discuss the uncertainties of the citations. Thereafter, the full-text articles were reviewed to judge the entitlement by two reviewers at stage 1 (PD and RN) and by a senior supervisor MI. Each study was read in full by each reviewer and assessed for inclusion. Full texts that did not fulfill the priori-defined inclusion criteria were excluded. Disagreements regarding inclusion in the final review were resolved through discussion with senior reviewer MI.

The quality of the randomized control trials, case series, cohorts, and case studies was assessed using the JBI critical appraisal checklist which looks at 13, 10, 11, and 8 critical aspects, respectively for the possibility of bias in its design, conduct, and analysis [Critical appraisal tools. JBI. https://jbi.global/critical-appraisal-tools (accessed 12 Nov2022)]. The studies with the selection "No" (Red color boxes) for at least 3 questions in the appraisal form were considered to pose a lack of integrity in the study design, hence excluded from data abstraction and reviewing. Decisions regarding study eligibility and quality were made by two reviewers, and any disagreements were resolved by discussion.

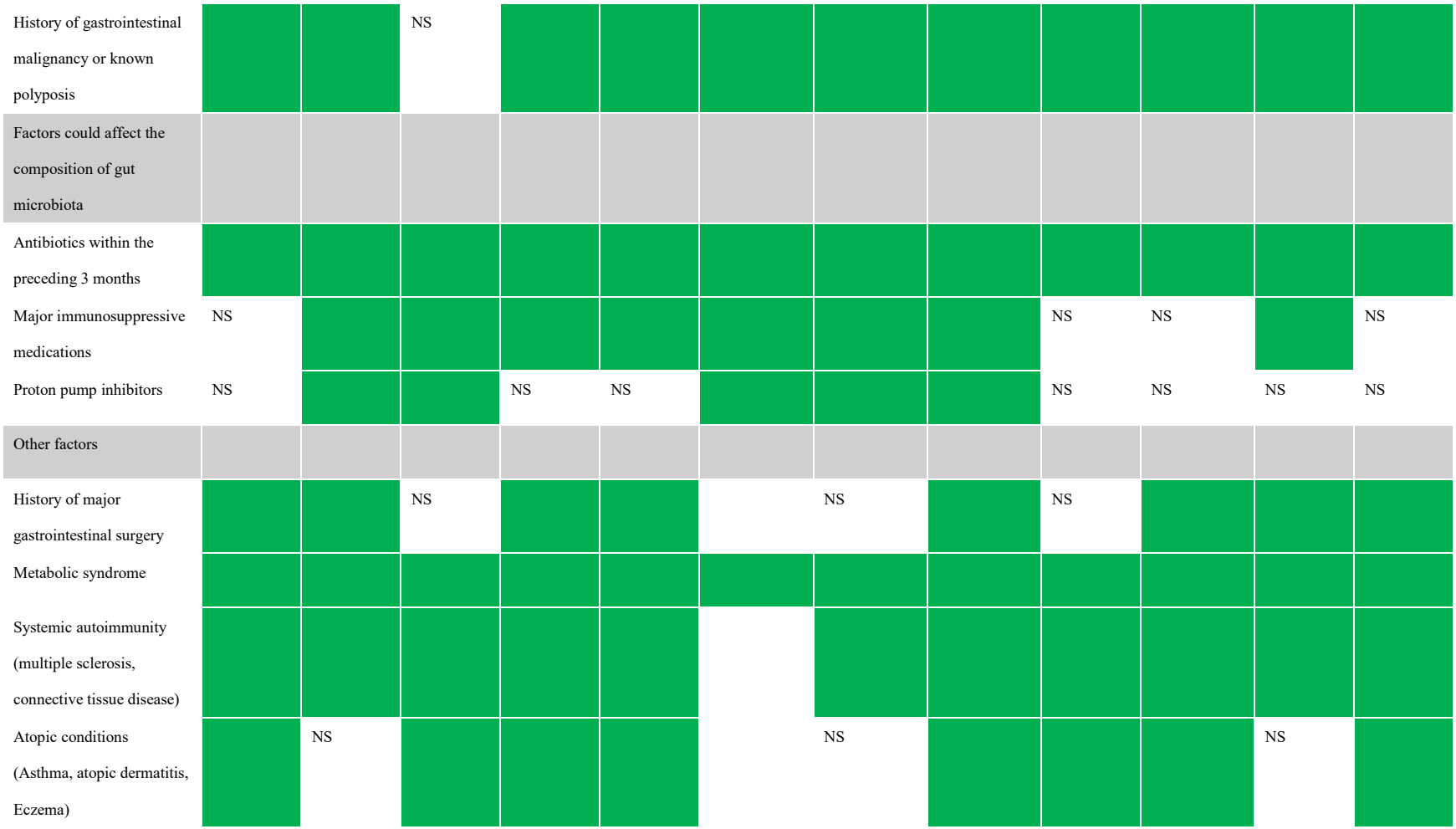
**Data extraction**

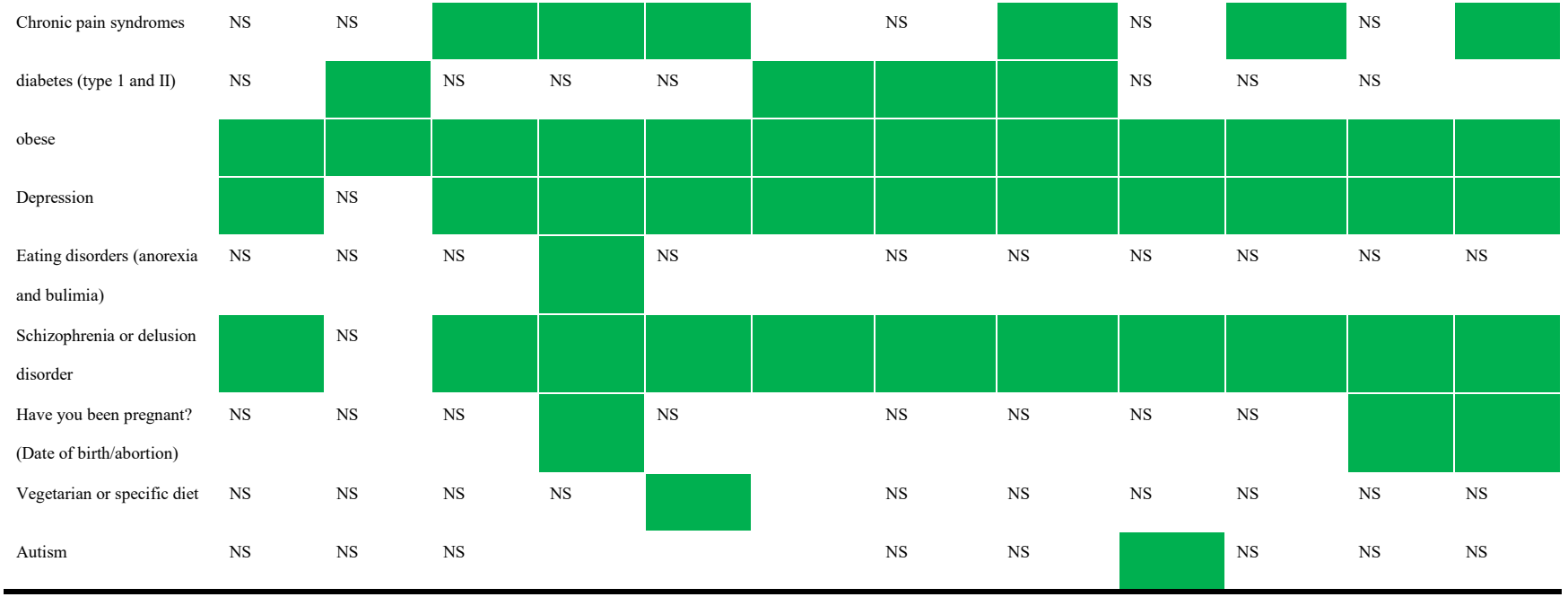
Two researchers (RN and PD) developed an individual data abstraction spreadsheet using Excel version 2016 (Microsoft Corporation, Redmond, Washington, USA) and conducted the data abstraction for the included full-text articles and the consensus documents. After this, the data were independently assessed by the review authors. We gathered the following information: type of study, period, place of conduct, type of donor, donor screening timeline (where applicable), pre-screening questionnaire, and list of blood and stool tests.

## Supplementary Table 1

| **WHO Regions** | WPR | | | | AMR | | AMR/EUR | EUR | | | | EUR/AMR/WPR/SEAR |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Hong Kong | [Australian Government, FMT product regulation] | [Lin et al.] | [Seo et al.] | [Chen et al.] | [Government of Canada] | [Cammarota et al.] | [Mullish et al.] | [Terveer et al.] | [Kump et al.] | [Nakov et al.] | [Keller et al.] |
| Risk of infectious agents | | | | | | | | | | | | |
| Known HIV, Hepatitis B, or C infections | | | | NS | NS | | | | | | | |
| Known exposure to HIV or viral hepatitis (within the previous 12 months.) | NS | | NS | NS | | | NS | NS | | NS | | NS |
| High-risk sexual behaviors | | | | | | | | | NS | NS | | |
| Use of illicit drugs | | NS | | NS | NS | | | | NS | | | |
| Tattoo or body piercing within 6 months | NS | | | | | | | | NS | NS | | |
| Incarceration or history of incarceration | NS | | | | NS | | NS | NS | NS | NS | NS | |


Known current communicable disease
Risk factors for variant Creutzfeldt-Jakob disease
Travel (within the last 6 months) to high-risk countries with travelers' diarrhea
Recent needle stick accident
Receiving blood products/transfusion
Gastrointestinal co-morbidities
History of inflammatory bowel disease
History of irritable bowel syndrome, idiopathic chronic constipation, or chronic diarrhea
NS


History of gastrointestinal malignancy or known polyposis
Factors could affect the composition of gut microbiota
Antibiotics within the preceding 3 months
Major immunosuppressive medications
Proton pump inhibitors
Other factors
History of major gastrointestinal surgery
Metabolic syndrome
Systemic autoimmunity (multiple sclerosis, connective tissue disease)
Atopic conditions (Asthma, atopic dermatitis, Eczema)
NS




WHO regions: AMR (Regions of the Americas); SEAR (South-East Asian Region); EUR (European Region); WPR (Western Pacific Region); NS: Not stated

Footnote:

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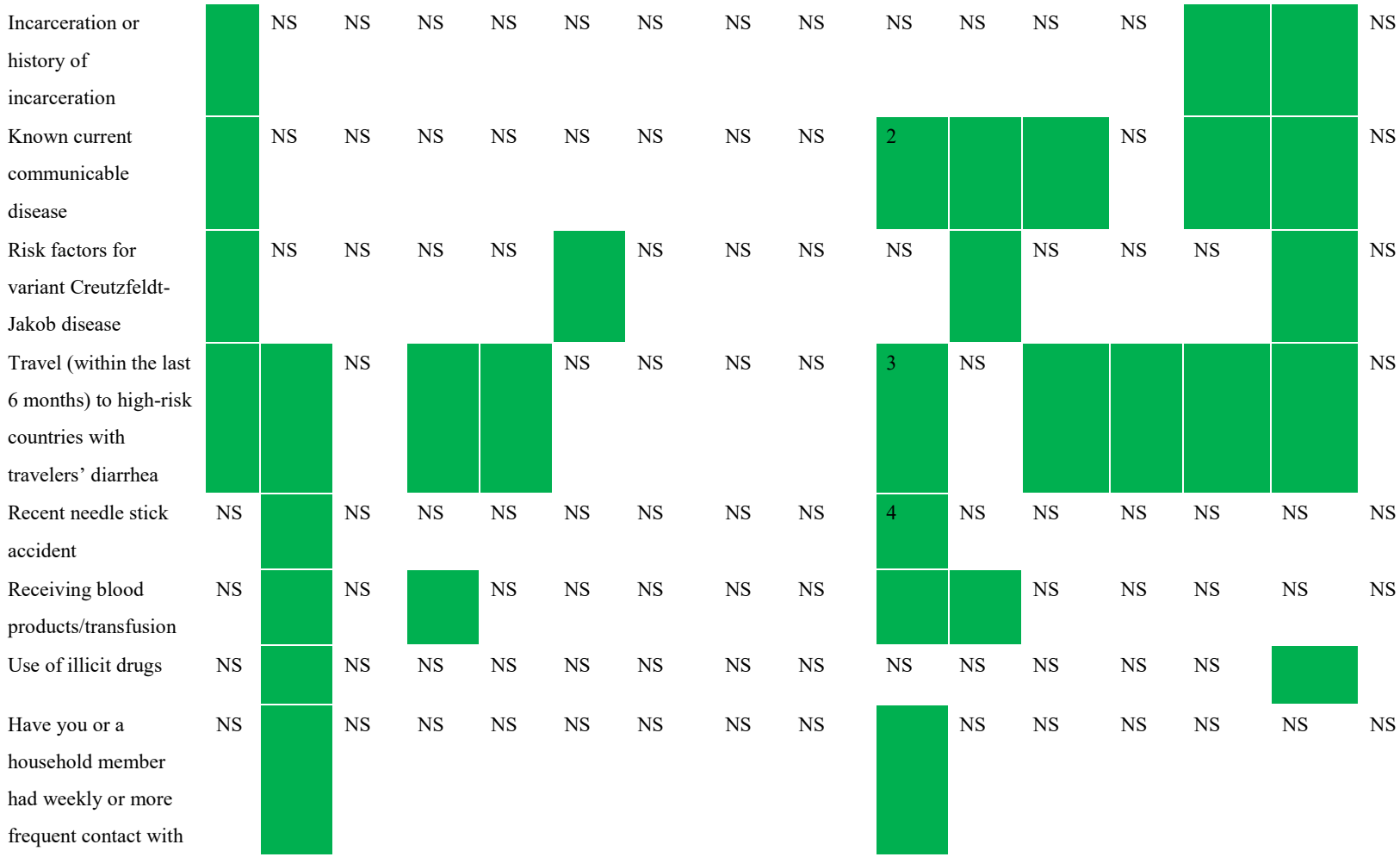
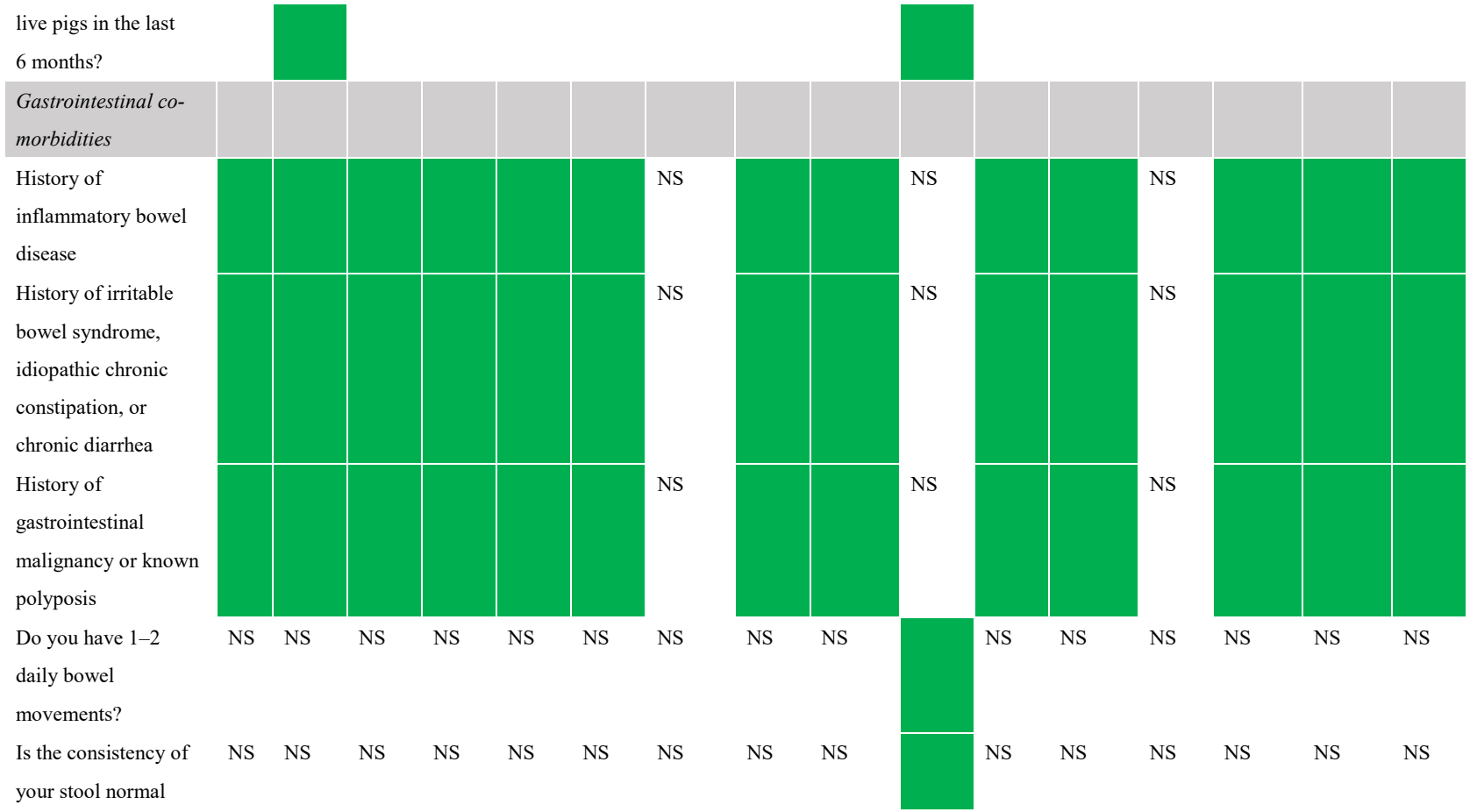
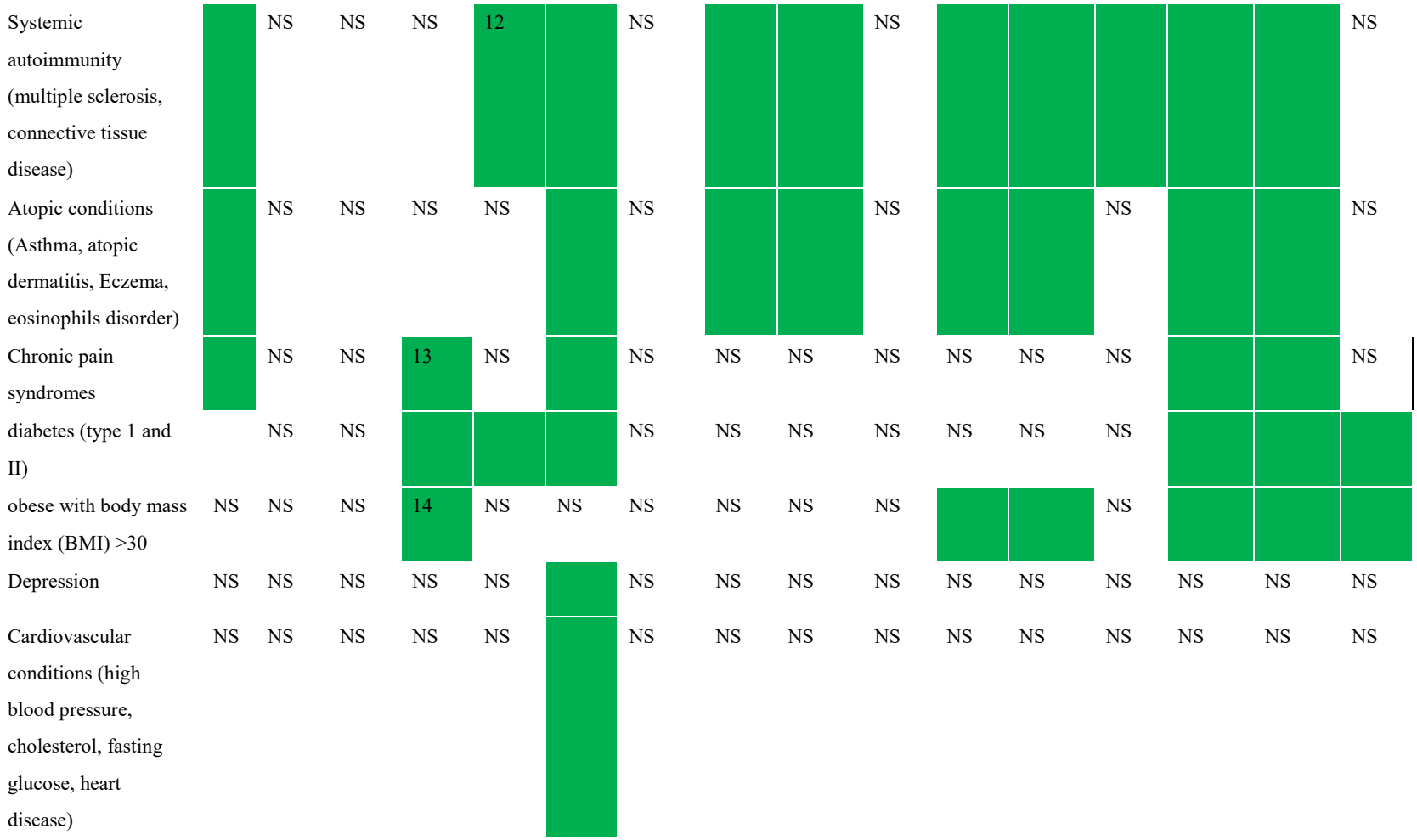
## Supplementary Table 2

| WHO regions | Region of America | | | European Region | | | | | | | | | | Other regions | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| References | [Stal ey et al.] | [Jiang et al.] | [Lynch et al.] | [Hvas et al.] | [Kachlí ková et al.] | [McCu ne et al.] | [Nowak et al.] | [Reiga das et al.] | [Reigada et al.] | [Rode et al.] | [Sokol et al.] | [Terveer et al.] | [Březin a et al] | [Costello et al.] | [Azimira d et al.] | [Lee et al.] |
| Risk of infectious agents | | | | | | | | | | | | | | | | |
| Known HIV, Hepatitis B, or C infections | | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS | NS | NS | NS | NS |
| Known exposure to HIV or viral hepatitis (within the previous 12 months.) | | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS | NS | NS | NS | NS |
| High-risk sexual behaviors | | | NS | | | | NS | NS | NS | 1 | NS | NS | NS | | | |
| Use of illicit drugs | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | | NS |
| Tattoo or body piercing within 6 months | | | NS | NS | | NS | NS | NS | NS | | NS | NS | NS | NS | | |


Incarceration or history of incarceration
Known current communicable disease
Risk factors for variant Creutzfeldt-Jakob disease
Travel (within the last 6 months) to high-risk countries with travelers' diarrhea
Recent needle stick accident
Receiving blood products/transfusion
Use of illicit drugs
Have you or a household member had weekly or more frequent contact with
NS
2
3
4


live pigs in the last 6 months?
Gastrointestinal co-morbidities
History of inflammatory bowel disease
History of irritable bowel syndrome, idiopathic chronic constipation, or chronic diarrhea
History of gastrointestinal malignancy or known polyposis
Do you have 1–2 daily bowel movements?
Is the consistency of your stool normal
NS

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| (smooth and shaped like a sausage)? | | | | | | | | | | | | | | | | |
| Factors could affect the composition of gut microbiota | | | | | | | | | | | | | | | | |
| Antibiotics within the preceding 3 months | | NS | | 5 | | NS | 6 | NS | NS | 7 | 8 | 9 | | | | NS |
| Major immunosuppressive medications | | NS | NS | 10 | NS | NS | NS | NS | NS | NS | 11 | NS | NS | NS | NS | NS |
| Systemic antineoplastic agents | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Proton pump inhibitors | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS | NS |
| Other factors | | | | | | | | | | | | | | | | |
| Allergies | | NS | NS | | NS | NS | NS | | | NS | | | NS | | | NS |
| History of major gastrointestinal surgery | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Metabolic syndrome | | NS | NS | NS | | NS | NS | | | NS | NS | | NS | NS | | NS |


Systemic autoimmunity (multiple sclerosis, connective tissue disease)
Atopic conditions (Asthma, atopic dermatitis, Eczema, eosinophils disorder)
Chronic pain syndromes
diabetes (type 1 and II)
obese with body mass index (BMI) >30
Depression
Cardiovascular conditions (high blood pressure, cholesterol, fasting glucose, heart disease)
12
13
14
NS

| | | | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Actively smoke | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS |
| Eating disorders (anorexia and bulimia) | NS | NS | NS | NS | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Schizophrenia or delusion disorder | NS | NS | NS | NS | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| Have you been pregnant? (Date of birth/abortion) | NS | NS | NS | NS | NS | NS | NS | NS | NS | | | NS | NS | NS | NS | NS |
| Hemorrhoid disease | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS | NS | NS | NS |
| History of typhoid fever infection | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS | NS | NS | NS |
| Vegetarian or specific diet | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS | NS | NS | NS |
| Autism | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS | | NS | NS |

[1]Have you ever had sexual contact with another man? (Question only for men); [2]Infectious disease including MRSA or close contact with MRSA infected patient; [3]Have you travel outside to Denmark, Scandinavia, and Germany?; [4]shared a syringe or needle with others?; [5]Antibacterials, antifungals or antivirals; [6]Antibiotic within preceding 2 months; [7]Antibiotics within the preceding 3 months; [8] Including viral infection (7 days before screening) /HSV and/or papillomavirus anal lesions; [9]Antibiotics within the preceding <6 months; [10]Any kind of medication including non-steroidal anti-inflammatory drugs; [11]Antifungal drugs too; [12]Systemic rheumatic diseases; [13]Any sort of chronic disease; [14]BMI >28 Kg/m$^2$;

Footnote:

Staley C, Halaweish H, Graiziger C, Hamilton MJ, Kabage AJ, Galdys AL, Vaughn BP, Vantanasiri K, Suryanarayanan R, Sadowsky MJ, et al. Lower endoscopic delivery of freeze-dried intestinal microbiota results in more rapid and efficient engraftment than oral administration. *Scient Repo*2021; 11

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## Supplementary Table 3. National consensus (Laboratory tests)

| EUR | EUR/AMR | AMR | EUR/AMR/WPR | WPR | WPR |
|---|---|---|---|---|---|

| | | | | | | | | /SEAR | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | [Mullish et al.] | [Terveer et al.] | [Kump et al.] | [Nakov et al.] | [Cammarota et al.] | [Chen et al.] | [Government of Canada] | [Keller et al.] | Hong Kong | [Australian Government, FMT product] | [Lin et al.] | [Seo et al.] |
| **Blood Tests** | | | | | | | | | | | | |
| ***Testing for viruses*** | | | | | | | | | | | | |
| **Hepatitis A** | 1 | 1 | 1 | 1 | | 1 | NS | 1 | 1 | | 1 | 1 |
| **Hepatitis B** | 2, 2a | 2, 2a | 2a | 2a | | 2a, 2b | | 2 | 2, 2a | 2c | 2, 2a, 2b | 2 |
| **Hepatitis C** | 3 | 3 | 3 | 3 | | 3 | | 3 | 3 | 3a | 3 | 3 |
| **Hepatitis E** | 4 | 4 | NS | 4 | | NS | NS | | 4 | NS | NS | NS |
| **HIV I and II** | | | | | | | | | | | | |
| **Human T-cell lymphoma virus** | NS | | NS | NS | NS | | | NS | | | | NS |
| **Cytomegalovirus (CMV)** | 5* | 5a | * | | NS | NS | NS | | NS | NS | 5a | |
| **Epstein-Barr virus** | * | | NS | | NS | NS | NS | NS | NS | NS | | |
| **Testing for bacteria** | | | | | | | | | | | | |
| **Treponema pallidum** | | | | | | 6 | | | | | 6 | 6 |
| **Test for parasites** | | | | | | | | | | | | |
| **Entamoeba histolytica,** | | NS | NS | NS | NS | | NS | NS | NS | NS | | NS |
| **Toxoplasma gondii** | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Strongyloides stercoralis** | | | NS | NS | | | NS | NS | NS | | NS | NS |
| **Other testes** | | | | | | | | | | | | |
| **Complete blood count** | | NS | NS | | | | NS | | | | | |
| **C-reactive proteins** | | NS | NS | | NS | NS | NS | | | | | |
| **Erythrocyte sedimentation rate** | | NS | NS | | NS | NS | NS | NS | | NS | | |
| **Renal function test** | | NS | NS | | | NS | NS | | | NS | | |
| **Liver function test** | | NS | NS | | | | NS | | | | | |
| ***Stool tests*** | | | | | | | | | | | | |
| ***Testing for viruses*** | | | | | | | | | | | | |
| **Rotavirus** | | | | | | | | | | | | |
| **Norovirus** | 7 | 7 | 7 | | | 7 | | 7 | 7 | | 7 | 7 |
| **Adenovirus** | NS | | NS | | | | | NS | NS | NS | | |
| **Astrovirus** | NS | | NS | | NS | NS | NS | NS | NS | NS | NS | |
| **Sapovirus** | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| **Enterovirus** | NS | | NS | | NS | NS | NS | NS | NS | NS | NS | NS |
| **Parechovirus** | NS | | NS | | NS | NS | NS | NS | NS | NS | NS | NS |
| ***Testing for bacteria*** | | | | | | | | | | | | |
| ***Salmonella* spp** | 8 | 8, 8a | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8 | 8a |
| ***Shigella* spp** | 9 | 9, 9a | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9 | 9a |
| ***Yersinia* spp** | | | | | | NS | | | NS | NS | | |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Campylobacter* spp** | 10 | 10, 10a | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10 | 10a |
| **Vibrio species** | NS | NS | NS | NS | | | | | | NS | | |
| ***C. difficile*** | 11 | 11 | | | | | NS | | 11 | | | NS |
| ***H. pylori*** | 12 | 12 | NS | | | | | | 12 | | | 12a |
| **Aeromonas spp.,** | NS | | NS | NS | NS | | | NS | NS | NS | NS | |
| ***E.coli* 0157 (Shiga toxin-producing E. coli (STEC)** | NS | NS | NS | NS | NS | | | NS | | NS | NS | NS |
| **Verotoxin-producing/Shiga toxin-producing *E. coli*** | | | NS | | | | | | NS | NS | NS | NS |
| **MDR Bacteria** | | | | | | | | | | | | |
| **ESBL producing Enterobacteriaceae** | | | NS | | | | | | | | NS | |
| **VRE** | ** | ** | NS | | | | | | | | | |
| **CPE (CRE/KPC/NDM,OXA 48)** | | ** | NS | | | | | | | | | |
| **MRSA** | ** | ** | NS | | | NS | | | | | NS | |
| **MDR *A. baumanni*** | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS | NS |
| **aminoglycoside and quinolone resistant** | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Enterobacterales** | | | | | | | | | | | | |
| **Testing for parasites** | | | | | | | | | | | | |
| **Cyclospora** | 13 | NS | NS | | NS | | NS | | 13 | NS | NS | NS |
| **Isospora** | | NS | NS | | | | NS | 14 | | NS | NS | NS |
| **Giardia spp** | 15 | 15b*** | 15 | | | 15a | NS | | 15 | | | 15b |
| **Cryptosporidium spp** | | 16*** | | | | | NS | | | | NS | 16 |
| **Strongyloides** | NS | *** | NS | NS | NS | NS | NS | 17 | NS | NS | NS | 17 |
| **Microsporidium spp,** | | *** | NS | | | | NS | NS | | NS | NS | NS |
| **Entamoeba histolytica** | NS | | NS | | NS | NS | NS | | | | | |
| **Llight microscopy for ova, cysts** | | | | NS | | | | NS | | NS | | NS |
| **Other tests** | | | | | | | | | | | | |
| **Feacal occult blood testing** | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS | |
| **Calprotectin** | NS | NS | NS | | NS | NS | NS | NS | NS | NS | NS | NS |

[1]lgM immunoassay; [2]Hepatitis B surface antigen test; [2a]Hepatitis B core antibody test; [2b]Hepatitis B antibody; [2c]Nucleic acid amplification test; [3]Anti hepatitis C immunoassay; [3a]Nucleic acid amplification test; [4]lgM immunoassay; [5]CMV lgG and lgM; [5a]CMV IgM only; [6]Rapid plasma regain test; [7]PCR; [8]Culture; [8a]Salmonella PCR; [9]Culture; [9a] Shigella PCR; [10]Culture;[10a]Campylobacter PCR; [11]PCR; [12]Stool antigen test, [12a]nested PCR; [13,14]Acid fast staining; [15]Fecal Giardia antigen; [15a]Enzyme immunoassay; [15b] PCR; [16] PCR; [17]Strongyloides ELISA.

*Immunocompromised only

** optional, based on risk assessment

*** if travel history to Middle and South America, Africa, or Asia

**** recommended for indication of IBD

WHO regions: AMR (Regions of the Americas); SEAR (South-East Asian Region); EUR (European Region); WPR (Western Pacific Region)

Footnote:

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## Supplementary Table 4: WHO region of the Americas

| | [Aas et al.] | [Jiang et al.] | [Lynch et al.] | [Walton et al.] | [Staley et al.] | [Dubberke et al.] | [Espinoza et al.] | [González et al.] |
|---|---|---|---|---|---|---|---|---|
| **Time period** | 1994 -2002 | NS | 2012-2017 | NS | 2018-2019 | 2014-2015 | NS | NS |
| **Type of Study** | CS | RCT | CS | CS | CS | RCT | CSt | RCT |
| **Country** | USA | USA | USA | USA | USA | Canada | Chile | Mexico |
| **Donor** | R and UR | NS | NS | NS | NS | NS | NS | NS |
| **GI disorder** | *C. difficile* | NS | NS | NS | NS | *C. difficile* | NS | NS |
| **Blood Tests** | | | | | | | | |
| ***Testing for viruses*** | | | | | | | | |
| **Hepatitis A** | 1 | 1, 1a | | | | | 1 | NS |
| **Hepatitis B** | 2, 2a | **2, 2a** | | | | | 2, 2a | NS |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Hepatitis C** | 3 | **3a** | | | NS | | 3a | NS |
| **HIV I and II** | 4 | 4a | | | | | 4a | NS |
| **Cytomegalovirus (CMV)** | NS | 6 | NS | NS | NS | NS | 6 | NS |
| **Epstein-Barr virus** | NS | 7 | NS | NS | NS | NS | 7 | NS |
| **Human T-cell lymphoma virus antibody (HTLV)** | NS | 8 | NS | NS | NS | NS | 8 | NS |
| ***Testing for bacteria*** | | | | | | | | |
| ***Treponema pallidum* (Syphilis)** | | | | NS | | NS | NS | NS |
| ***Testing for parasites*** | | | | | | | | |
| *Entamoeba histolytica* | NS | 17 | NS | NS | NS | NS | NS | NS |
| ***Strongyloides stercoralis*** | NS | 18 | NS | NS | NS | NS | NS | NS |
| ***Other testes*** | | | | | | | | |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **Complete blood count** | NS | NS | NS | NS | NS | NS | NS | |
| **Liver enzymes** | NS | NS | NS | NS | NS | NS | NS | |
| ***stool tests*** | | | | | | | | |
| ***Testing for viruses*** | | | | | | | | |
| **Norovirus** | NS | NS | NS | NS | NS | | NS | NS |
| **Adenovirus** | NS | NS | NS | NS | NS | | NS | NS |
| **Rotavirus** | NS | NS | NS | NS | NS | | NS | NS |
| ***Testing for bacteria*** | | | | | | | | |
| ***Salmonella* spp** | NS | | NS | | | | NS | NS |
| ***Shigella* spp** | NS | | NS | | | | NS | NS |
| ***Yersinia* spp** | NS | | NS | | | | NS | NS |
| ***Campylobacter* spp** | NS | | NS | | | | NS | NS |
| ***C. difficile*** | NS | 9, 9a | | | | | | NS |
| ***Helicobacter pyroli*** | NS | | NS | NS | | NS | | NS |
| **Vibrio species** | NS | NS | NS | | NS | | NS | NS |
| ***E. coli* 0157 (Shiga like toxin** | NS | NS | NS | | NS | NS | NS | NS |

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| **producing *E. coli*)** | | | | | | | | |
| ***Listeria monocytogenes*** | NS | NS | NS | NS | NS | | NS | NS |
| **Test for parasites** | | * | | | | | | |
| **Cyclospora spp** | **NS** | NS | NS | NS | | NS | NS | NS |
| **Isospora** | NS | NS | NS | NS | | NS | NS | NS |
| **Giardia spp** | NS | NS | NS | NS | | NS | | NS |
| **Cryptosporidium parvum** | NS | NS | NS | NS | | NS | NS | NS |
| **light microscopy for presence of ova, cysts, and parasites** | | NS | | | | NS | | NS |

[1]lgM immunoassay; [1a]Total antibody; [2]Hepatitis B surface antigen test; [2a]Hepatitis B core antigen test; [3]Anti hepatitis C immunoassay; [3a]Nucleic acid amplification test; [4]lgM immunoassay; [4a]lgG immunoassay; [6]HTCV I and II antibodies; [7]CMV lgG and lgM; [8]Viral capsid antigen (VCA lgM); [9]Presence of toxins and antigens; [9a]Culture and PCR

NS: Not stated; CS: Case series: RCT: Randomized control trial; Cst: Case studies

Footnote:

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Jiang Z-D, Jenq RR, Ajami NJ, et al. Safety and preliminary efficacy of orally administered lyophilized fecal microbiota product compared with frozen product given by enema for recurrent clostridium difficile infection: A randomized clinical trial. PLOS ONE 2018;13. doi:10.1371/journal.pone.0205064

Lynch SM, Mu J, Grady JJ, Stevens RG, Devers TJ. Fecal microbiota transplantation for clostridium difficile infection: A one-center experience. Digestive Dis 2019; 37:467–72.

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**Supplementary Table 5: WHO European region**

| | [Barberio et al.] | [Hvas et al.] | [Jitsumura et al.] | [Kachlíková et al] | [Wierzbicka et al.] | [McCune et al.] | [Nowak et al.] | Reigadas et al.] | Reigadas et al.] | Rode et al.] | [Rossen et al.] | [Sokol et al.] | [Terrveer et al.] | [Brezina et al.] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Time period** | 2016-2019 | 2016-2018 | | 2017-2019 | 2018-2019 | | 2013-2017 | NS | 2014-2017 | NS | NS | 2014-2017 | 2016-2019 | |
| **Type of study** | POS | RCT | RCT | POS | CT | CT | CoS | CS | CT | CT | RCT | RCT | OS | RCT |
| **Country** | Italy | Denmark | UK | Solvakia | Poland | UK | Sweden | Spain | Spain | Denmark | Netherland | France | Netherland | Czeck |
| **Donor** | UR | | UR | UR | UR | NS | R | NS | NS | NS | R- | UR | UR | UR |
| **GI disorder** | Cd | Cd | UC | **Cd** | **UC** | NS | NS | NS | NS | NS | UC | CD | Cd | UC |
| **Blood Tests** | | | | | | | | | | | | | | |
| ***Testing for*** | | | | | | | | | | | | | | |
| **Hepatitis A** | | NS | | | 1 | | NS | | | 1 | | | 1a | |
| **Hepatitis B** | | | | | 2, 2a | | | | | 2, 2a, 2b | | | 2, 2a | |
| **Hepatitis C** | | | | | 3 | 3 | | | | 3, 3a | | | 3 | |
| **Hepatitis E** | | | NS | NS | NS | 4 | NS | NS | NS | NS | NS | NS | NS | NS |
| **HIV I and II** | | | | | | 5 | | | | 5a | | | | |
| **Human T-cell lymphoma virus antibody (HTLV)** | | NS | | NS | NS | 6 | NS | | | SN | SN | | | NS |
| **Cytomegalovirus (CMV)** | | | | | | | NS | NS | | | | | | |

| | [Barberio et al.]] | [Hvas et al.] | [Jitsumura et al.] | [Kachlíková et al] | [Wierzbicka et al.] | [McCune et al.] | [Nowak et al.] | [Reigadas et al.] | [Reigadas et al.] | Rode et al.] | [Rossen et al.] | Sokol et al.] | [Terrveer et al.] | [Brezina et al.] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Epstein-Barr virus** | | | | | | NS | NS | NS | | NS | NS | NS | | |
| **Testing for bacteria** | | | | | | | | | | | | | | |
| NS | | NS | NS | | | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| **Treponema pallidum** | | NS | | | | | | | | 7, 7a | | | | |
| **Test for parasites** | | | | | | | | | | | | | | |
| ***E. histolytica*** | | | | 8 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| ***T. gondii*** | | NS | NS | | NS | NS | NS | NS | NS | NS | NS | | NS | NS |
| ***T. canis*** | | NS | NS | 9 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| **cati and suis** | | NS | NS | 10 | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| ***S. stercoralis*** | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| **T. spiralis** | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS |
| **Other testes** | | | | | | | | | | | | | | |
| **Complete blood count** | | | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| **C-reactive proteins** | | | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |

| | [Barberio et al.] | [Hvas et al.] | [Jitsumura et al.] | [Kachlíková et al] | [Wierzbicka et al.] | [McCune et al.] | [Nowak et al.] | [Reigadas et al.] | [Reigadas et al.] | Rode et al.] | [Rossen et al.] | Sokol et al.] | [Terrveer et al.] | [Brezina et al.] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Erythrocyte sedimentation rate (ESR)** | | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| **Albumin** | | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| **Renal function test** | | | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| **Liver function test** | | | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| ***Stool tests*** | | | | | | | | | | | | | | |
| ***Testing for viruses*** | | | | | | | | | | | | | | |
| **Rotavirus** | | NS | NS | NS | NS | NS | NS | | | | | | | NS |
| **Norovirus** | | NS | | NS | NS | 11 | NS | | | | | | * | NS |
| **Adenovirus** | | | NS | NS | NS | NS | NS | | | | | | 12** | NS |
| **Astrovirus** | | NS | NS | NS | NS | NS | NS | NS | NS | | | | | NS |
| **Sapovirus** | | NS | NS | NS | NS | NS | NS | NS | NS | | | | | NS |
| **Enterovirus** | | | NS | NS | NS | NS | NS | NS | NS | NS | NS | | | NS |
| **Poliovirus** | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS |
| **Aichi virus** | | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS |

| | [Barberio et al.] | [Hvas et al.] | [Jitsumura et al.] | [Kachlíková et al] | [Wierzbicka et al.] | [McCune et al.] | [Nowak et al.] | [Reigadas et al.] | [Reigadas et al.] | [Rode et al.] | [Rossen et al.] | Sokol et al.] | [Terrveer et al.] | [Brezina et al.] | [Brezina et al.] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Parechovirus** | | | | | | | | | | | | | | | NS |
| **Hepatitis A** | | **NS** | | | | | | | | | | | | | NS |
| ***Testing for bacteria*** | | | | | | | | | | | | | | | |
| ***Salmonella* spp** | | | | | | 13 | | | | | NS | | | | NS |
| ***Shigella* spp** | | | | NS | | 14 | | | | | NS | | | | NS |
| ***Yersinia* spp** | | | | NS | | NS | NS | | | | NS | | | | |
| ***Campylobacter* spp** | | | NS | | | 15 | | | | | NS | | | | NS |
| **Vibrio species** | NS | NS | NS | NS | NS | NS | NS | | | NS | NS | | | NS | |
| **C. difficile** | | | NS | 16 | | 16a | | | | NS | NS | | | | NS |
| **H. pylori** | NS | NS | NS | | | 17 | NS | | | | NS | NS | | | NS |
| **Aeromonas spp.,** | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS |
| | | | | | | | | | | | | | | | |
| ***E. coli* 0157 (Shiga toxin-producing *E. coli* (STEC)** | | NS | | NS | NS | | NS | | | | NS | NS | | NS | NS |
| **Enteropathogenic *E. coli* (EPEC)** | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS | NS | NS | NS |

| | [Barberio et al.] | [Hvas et al.] | [Jitsumura et al.] | [Kachlíková et al] | [Wierzbicka et al.] | [McCune et al.] | Nowk et al.] | [Reigadas et al.] | [Reigadas et al.] | Rode et al.] | [Rossen et al.] | Sokol et al.] | [Terrveer et al.] | [Brezina et al.] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Enterotoxigenic *E. coli* (ETEC)** | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS | NS | |
| **Enteroinvasive *E. coli* (EIEC)** | | | NS | NS | NS | NS | NS | NS | NS | | NS | NS | NS | NS |
| **Attaching and Effacing *E. coli* (A/EEC)** | **NS** | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS | NS |
| **Verotoxin-producing *E. coli*** | **NS** | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS |
| **MDR Bacteria** | | | | | | | | | | | | | | |
| **ESBL producing enterobacteraecae (Enrichment culture)** | | | NS | NS | | 18 | NS | | | | NS | | | NS |
| **VRE** | | | | NS | | | | | | | NS | | | NS |
| **CPE (CRE/KPC/NDM,OXA 48)** | | # | ## | NS | ### | 19 | # | | | | NS | | | NS |
| **MRSA** | NS | NS | | NS | | NS | NS | | | NS | NS | NS | | NS |
| **MDR *A. baumanni*** | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS |
| **aminoglycoside and quinolone resistant Enterobacterales** | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS |

| | [Barberio et al.] | [Hvas et al.] | [Jitsumura et al.] | [Kachlíková et al] | [Wierzbicka et al.] | [McCune et al.] | [Nowak et al.] | [Reigadas et al.] | [Reigadas et al.] | Rode et al.] | [Rossen et al.] | Sokol et al.] | [Terrveer et al.] |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Testing for parasites** | | | | | | | | | | | | | |
| **Cyclospora** | | | NS | NS | NS | NS | NS | NS | NS | NS | NS | | |
| **Isospora** | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS |
| **Giardia spp** | | | 20 | | NS | 20a | NS | NS | NS | | | | |
| **Cryptosporidium spp** | **NS** | **NS** | 21 | | NS | 21a | NS | NS | NS | | | | |
| **Strongyloides** | **NS** | NS | NS | NS | NS | NS | NS | NS | NS | NS | 22 | | |
| **Cystoisospora belli** | **NS** | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | |
| **Microsporidium spp,** | **NS** | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | |
| **Entamoeba histolytica** | **NS** | | NS | | NS | NS | NS | NS | NS | | 23 | | |
| **Protozoa and helminths** | NS | NS | | | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| **Other tests** | | | | | | | | | | | | | |
| **Fecal occult blood testing** | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| **Calprotectin** | **NS** | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| **light microscopy for the presence of ova, cysts and** | | | NS | NS | | | NS | | | NS | | NS | |

[1]IgM immunoassay; [1a]Total antibody; [2]Hepatitis B surface antigen test; [2a]Hepatitis B core antigen test; [2b]Nucleic acid amplification test; [3]Anti hepatitis C immunoassay; [3a]Nucleic acid amplification test; [4]IgM immunoassay; [5]4th generation immunoassay; [5a]Nucleic acid amplification test; [6]HTCV I and II antibodies; [7]Wassemann's reaction; [7a]Rapid plasma regain test; [8,9,10]antibody test; [11]PCR; [12]Adenovirus 40/41/52

multiplex PCR; [13,14,15]Culture; [16]Presence of toxins and antigens; [16a]Culture and PCR; [17]Stool antigen test; [18]Enrichment culture; [19]Selective chromogenic culture; [20]Fecal Giardia antigen; [20a]Enzyme immunoassay; [21]Antigen and/or acid fast staining; [21a]Enzyme immunoassay; [22]Strongyloides ELISA; [23]Antibody test
[#]CRE alone; [##]NDM alone; [###]NDM, KPC and OXA48 all three genes; POS:Prospective observational cohort study; CoS: Cohort study; CT: Clinical Trial

Footnote:

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**Supplementary Table 6: WHO Western-Pacific region**

| | Western Pacific region | | | | | | | | | African region | Eastern Mediterranean region |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | [Cui et al.] | [Bamba et al.] | [Chauhan et al.] | [Costello et al.] | [Yau et al.] | [Zhang et al.] | [He et al.] | [Lui et al.] | [Ren et al.] | [Lee et al] | [Azimirad et al.] |
| **Time period** | 2012-2014 | 2013-2017 | 2014-2019 | 2013-2016 | 2017-2019 | 2012-2014 | 2012-2014 | 2013-2018 | NS | 2018-2019 | 2012-2016 |
| **Type of Study** | OS | CS | CS | RCT | CoS | CS | CS | RS | CoS | CS | CS |
| **Country** | China | Japan | Australia | Australia | Hong Kong | China | China | Hong Kong | China | South Africa | Iran |
| **Donor** | R | R-UR | R | UR | UR | UR | UR | NS | UR | R | |
| **GI disorder** | UC | Cd | Cd | UC | NS | Cd | UC | Cd | UC | | |
| Blood Tests | | | | | | | | | | | |
| ***Testing for viruses*** | | | | | | | | | | | |
| **Hepatitis A** | | | 1 | | | 1a | 1a | 1a | | | |
| **Hepatitis B** | | | 2, 2a, 2b | 2c | | 2, 2a, 2b | 2, 2a, 2b | 2, 2a | | | |
| **Hepatitis C** | | | 3 | 3a | | 3 | 3 | 3 | | NS | |
| **Hepatitis E** | NS | NS | NS | NS | | NS | NS | 4 | | NS | NS |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **HIV I and II** | | | 5 | | | | | | | | |
| **Human T-cell lymphoma virus antibody** | NS | NS | 6 | | | NS | NS | | NS | NS | NS |
| **Cytomegalovirus (CMV)** | NS | NS | 7 | | NS | NS | NS | NS | | NS | NS |
| **Epstein-Barr virus** | NS | NS | 8 | | NS | NS | NS | NS | | NS | NS |
| **Rotavirus** | NS | NS | NS | NS | NS | NS | NS | NS | | NS | NS |
| **Testing for bacteria** | | | | | | | | | | | |
| ***Helicobacter pylori*** | | NS | 9 | | | NS | NS | NS | NS | NS | NS |
| ***Treponema pallidum* (Syphilis)** | | NS | 10 | NS | | | | NS | NS | NS | NS |
| **Testing for parasites** | | | | | | | | | | | |
| ***Entamoeba histolytica*** | NS | NS | NS | | NS | NS | NS | | NS | NS | NS |
| ***Dirofilaria immitis*** | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| ***Toxocara canis*** | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| ***Ascaris suum*** | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| ***Anisakis*** | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| ***Gnathostoma*** | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| ***Strongyloides stercoralis*** | NS | | 11 | | NS | NS | NS | NS | NS | NS | NS |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Paragonimus*** | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| ***westetrmanii*** | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| ***Paragonimus miyazakii*** | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| ***Fasciola spp.,*** | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| ***Sparganosis mansoni,*** | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| ***Cysticercus cellulosae*** | NS | | NS | NS | NS | NS | NS | NS | NS | NS | NS |
| **Other tests** | | | | | | | | | | | |
| **Complete blood count** | | NS | NS | | | | | | NS | | NS |
| **Fasting lipid and blood sugar levels** | NS | NS | NS | | | NS | NS | NS | NS | NS | NS |
| **C-reactive protein (CRP)** | | NS | NS | | | | | | NS | | NS |
| **Erythrocyte sedimentation rate (ESR)** | | NS | NS | | | | | | NS | | NS |
| **Renal function test** | NS | NS | NS | | NS | NS | NS | NS | NS | NS | NS |
| **Liver function test** | NS | NS | NS | | NS | NS | NS | NS | NS | NS | NS |
| **Stool tests** | | | | | | | | | | | |
| **Testing for viruses** | | | | | | | | | | | |
| **Norovirus** | NS | NS | NS | NS | NS | NS | NS | | NS | NS | NS |

| | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **Rotavirus** | NS | NS | NS | NS | NS | NS | NS | | NS | NS | NS |
| **Testing for bacteria** | | | | | | | | | | | |
| ***Salmonella* spp** | NS | | NS | NS | NS | NS | NS | | NS | | NS |
| ***Shigella* spp** | NS | | NS | NS | NS | NS | NS | | NS | | NS |
| ***Yersinia* spp** | NS | NS | NS | NS | NS | NS | NS | NS | NS | | NS |
| ***Campylobacter* spp** | NS | | NS | NS | NS | NS | NS | | NS | | NS |
| **Vibrio species** | NS | | NS | NS | NS | NS | NS | | NS | NS | NS |
| ***C. difficile*** | NS | | 12 | | NS | NS | NS | 12a | NS | NS | |
| ***E. coli* 0157 (Shiga like toxin-producing *E. coli*)** | NS | | | | NS | NS | NS | | NS | NS | |
| **MDR Bacteria** | | | | | | | | | | | |
| **VRE** | NS | | | NS | | NS | NS | | NS | NS | NS |
| **CPE** | NS | | | NS | | NS | NS | NS | NS | NS | NS |
| **CRE** | NS | NS | NS | NS | | NS | NS | | NS | NS | NS |
| **MRSA** | NS | NS | NS | NS | | NS | NS | | NS | NS | NS |
| **MDR *Acinetobacter*** | NS | NS | NS | NS | | NS | NS | | NS | NS | NS |
| ***H. pyroli*** | NS | NS | NS | NS | | NS | NS | 13 | NS | NS | NS |
| **Testing for parasites** | | | | | | | | | | | |
| ***Clonorchis sinensis*** | NS | NS | NS | NS | | NS | NS | | NS | NS | NS |
| ***Cryptosporidium parvum*** | NS | NS | NS | | | NS | NS | | NS | NS | NS |

| | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ***Giardia lamblia*** | NS | NS | | | | NS | NS | | NS | NS | NS | |
| ***Entamoeba histolytica*** | NS | NS | NS | | | NS | NS | | NS | NS | NS | |
| ***Microsporidia,*** | NS | NS | NS | NS | | NS | NS | | NS | NS | NS | |
| ***Cyclospora*** | NS | NS | NS | NS | | NS | NS | | NS | NS | NS | |
| ***Isospora*** | NS | NS | NS | NS | | NS | NS | | NS | NS | NS | |
| ***blastocystis*** | NS | NS | | NS | NS | NS | NS | NS | NS | NS | NS | |
| ***dientamoeba*** | NS | NS | | NS | NS | NS | NS | NS | NS | NS | NS | |
| **Other tests** | | | | | | | | | | | | |
| **fragilis and entamoeba histolytica PCR** | NS | NS | NS | | NS | NS | NS | NS | NS | NS | NS | |
| **light microscopy for the presence of ova, cysts, and parasites** | | | | | | | | | | | | |

[1]total antibody test (IgM and IgG);[1a]HAV lgM; [2] hepatitis B surface antigen; [2a]antibody to hepatitis B core antigen; [2b]total antibody test; [2c]PCR; [3]antibody; [3a]PCR; [4]HAE lgM; [5]HIV Elisa; [6]HTLV antibody; [7]CMV IgM, IgG; [8]EBV IgM, IgG; [9]*H. pylori* serology; [10]Syphilis rapid plasma regain test; [11]Strongyloides serology; [12]toxins A and B by EIA; [12a]Glutamate dehydrogenase gene + polymerase chain reaction; [13]Anti–H. pylori lgG; [47]antigen; [48]Fecal Giardia antigen; [51]Acid-fast stain for *Cyclospora*; [52]Acid-fast stain for *Isospora*

OS: Observational study; CS: Case series study; RCT: Randomized Control study; CoS: Cohort Study; UC: Ulcerative Colitis; R: Resistance; UR: Un-related; NS: Not Stated

Footnote:

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**Appendix 1**

**JBI critical appraisal checklist for randomized clinical trials**

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | Overall appraisal |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Jiang et al. | | | | | | | | | | | | | | Include |
| Dubberke et al. | | | | | | | | | | | | | | Include |
| González et al. | | | | | | | | | | | | | | Include |
| Hvas et al. | | | | | | | | | | | | | | Include |
| Jitsumura et al. | | | | | | | | | | | | | | Include |
| Rossen et al. | | | | | | | | | | | | | | Include |
| Sokol et al. | | | | | | | | | | | | | | Include |
| Brezina et al. | | | | | | | | | | | | | | Include |
| Costello et al. | | | | | | | | | | | | | | Include |

1: Was true randomization used for the assignment of participants to treatment groups?; 2: Was allocation to treatment groups concealed?; 3: Were treatment groups similar at the baseline?; 4: Were participants blind to treatment assignment?; 5: Were those delivering treatment blind to treatment assignment?; 6: Were outcomes assessors blind to treatment assignment?; 7: Were treatment groups treated identically other than the intervention of interest?; 8: Was follow-up complete and if not, were differences between groups in terms of their follow-up adequately described and analyzed?; 9: Were participants analyzed in the groups to which they were randomized?; 10: Were outcomes measured in the same way for treatment groups?; 11: Were outcomes measured in a reliable way?; 12: Was appropriate statistical analysis used?; 13: Was the trial design appropriate, and were any deviations from the standard RCT design (individual randomization, parallel groups) accounted for in the conduct and analysis of the trial?

Following the criteria

Not following the criteria

**JBI critical appraisal checklist for case series**

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Overall appraisal |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Aas et al. | | | | | | | | | | | Include |
| Walton et al. | | | | | | | | | | | Include |
| Bamba et al. | | | | | | | | | | | Include |
| Chauhan et al. | | | | | | | | | | | Include |
| Zhang et al. | | | | | | | | | | | Include |
| He et al. | | | | | | | | | | | Include |
| Lee et al. | | | | | | | | | | | Include |
| Azimirad et al. | | | | | | | | | | | Include |
| Staley et al. | | | | | | | | | | | Include |
| Wierzbicka et al. | | | | | | | | | | | Include |
| McCune et al. | | | | | | | | | | | Include |
| Reigadas et al. | | | | | | | | | | | Include |
| Reigadas et al. | | | | | | | | | | | Include |
| Rode et al. | | | | | | | | | | | Include |

1: Were there clear criteria for inclusion in the case series?; 2: Was the condition measured in a standard, reliable way for all participants included in the case series?; 3: Were valid methods used for identification of the condition for all participants included in the case series?; 4: Did the case series have consecutive inclusion of participants?; 5: Did the case series have complete inclusion of participants?; 6: Was there clear reporting of the demographics of the participants in the study?; 7: Was there clear reporting of clinical information of the participants?; 8: Were the outcomes or follow-up results of cases clearly reported?; 9: Was there clear reporting of the presenting site(s)/clinic(s) demographic information?; 10: Was statistical analysis appropriate?

Following the criteria
Not following the criteria
Unclear

**JBI critical appraisal checklist for cohort series**

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | Overall appraisal |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Ren et al. | | | | | | | | | | | | Include |
| Yau et al. | | | | | | | | | | | | Include |
| Barberio et al. | | | | | | | | | | | | Include |
| Kachlíková et al. | | | | | | | | | | | | Include |
| Nowak et al. | | | | | | | | | | | | Include |

1: Were the two groups similar and recruited from the same population?; 2: Were the exposures measured similarly to assign people to both exposed and unexposed groups?; 3: Was the exposure measured in a valid and reliable way?; 4: Were confounding factors identified?; 5: Were strategies to deal with confounding factors stated?; 6: Were the groups/participants free of the outcome at the start of the study (or at the moment of exposure)?; 7: Were the outcomes measured in a valid and reliable way?; 8: Was the follow-up time reported and sufficient to be long enough for outcomes to occur?; 9: Was follow-up complete, and if not, were the reasons to lose to follow-up described and explored?; 10: Were strategies to address incomplete follow-up utilized?; 11: Was appropriate statistical analysis used?

Following the criteria

Not following the criteria

**JBI critical appraisal checklist for case studies**

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | Overall appraisal |
|---|---|---|---|---|---|---|---|---|---|
| Espinoza et al. | | | | | | | | | Include |

1: Were patient's demographic characteristics clearly described?; 2: Was the patient's history clearly described and presented as a timeline?; 3: Was the current clinical condition of the patient on presentation clearly described?; 4: Were diagnostic tests or assessment methods and the results clearly described?; 5: Was the intervention(s) or treatment procedure(s) clearly described?; 6: Was the post-intervention clinical condition clearly described?; 7: Were adverse events (harms) or unanticipated events identified and described?; 8: Does the case report provide takeaway lessons?

Following the criteria

Not following the criteria