

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 Pharmacol & Therapeutics* 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/SEA R	
	Hong Kong	[Australian Governmen t, 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	NS	NS	NS	NS			NS	NS	NS		NS	NS
Risk factors for variant Creutzfeldt-Jakob disease	NS	NS	NS	NS	NS		NS	NS	NS	NS	NS	
Travel (within the last 6 months) to high-risk countries with travelers' diarrhea										NS		
Recent needle stick accident				NS	NS				NS	NS		
Receiving blood products/transfusion	NS			NS	NS				NS	NS		
Gastrointestinal co-morbidities												
History of inflammatory bowel disease			NS	NS					NS		NS	
History of irritable bowel syndrome, idiopathic chronic constipation, or chronic diarrhea			NS	NS					NS		NS	

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

Chronic pain syndromes	NS	NS					NS		NS		NS	
diabetes (type I and II)	NS		NS	NS	NS				NS	NS	NS	
obese												
Depression		NS										
Eating disorders (anorexia and bulimia)	NS	NS	NS		NS		NS	NS	NS	NS	NS	NS
Schizophrenia or delusion disorder		NS										
Have you been pregnant? (Date of birth/abortion)	NS	NS	NS		NS		NS	NS	NS	NS		
Vegetarian or specific diet	NS	NS	NS	NS			NS	NS	NS	NS	NS	NS
Autism	NS	NS	NS				NS	NS		NS	NS	NS

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

Footnote:

Australian Government, Department of Health and Aged care, Fecal microbiota transplant product regulation. <https://www.tga.gov.au/products/biologicals-blood-and-tissues-and-advanced-therapies/biologicals/faecal-microbiota-transplant-products-regulation> (accessed 14December 2022)

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Seo HS, Chin HS, Kim Y-H, et al. Laboratory aspects of donor screening for fecal microbiota transplantation at a Korean fecal microbiota bank. *Anna Labo Med* 2021;41:612–. doi:10.3343/alm.2021.41.6.612

Chen J, Zaman A, Ramakrishna B, et al. Stool banking for fecal microbiota transplantation: Methods and operations at a large stool bank. Published Online First: 2020. doi:10.1101/2020.09.03.20187583

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Keller JJ, Ooijevaar RE, Hvas CL, Terveer EM, Lieberknecht SC, Högenauer C, Arkkila P, Sokol H, Gridnyev O, Mégraud F, et al. A standardised model for stool banking for faecal microbiota transplantation: A consensus report from a multidisciplinary UEG Working Group. *Uni Europ Gastroentero J* 2021; 9:229–47.

Supplementary Table 2

WHO regions	Region of America			European Region						Other regions						
References	[Staley et al.]	[Jiang et al.]	[Lynch et al.]	[Hvas et al.]	[Kachlíková et al.]	[McCuane et al.]	[Nowak et al.]	[Reigadas et al.]	[Reigada et al.]	[Rode et al.]	[Sokol et al.]	[Terveer et al.]	[Březina et al.]	[Costello et al.]	[Azimira 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		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS			NS
Known current communicable disease		NS	NS	NS	NS	NS	NS	NS	NS	2			NS			NS
Risk factors for variant Creutzfeldt-Jakob disease		NS	NS	NS	NS		NS	NS	NS	NS		NS	NS	NS		NS
Travel (within the last 6 months) to high-risk countries with travelers' diarrhea			NS			NS	NS	NS	NS	3	NS					NS
Recent needle stick accident	NS		NS	NS	NS	NS	NS	NS	NS	4	NS	NS	NS	NS	NS	NS
Receiving blood products/transfusion	NS		NS		NS	NS	NS	NS	NS			NS	NS	NS	NS	NS
Use of illicit drugs	NS		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS		
Have you or a household member had weekly or more frequent contact with	NS		NS	NS	NS	NS	NS	NS	NS		NS	NS	NS	NS	NS	NS

live pigs in the last 6 months?																
Gastrointestinal co-morbidities																
History of inflammatory bowel disease							NS			NS			NS			
History of irritable bowel syndrome, idiopathic chronic constipation, or chronic diarrhea							NS			NS			NS			
History of gastrointestinal malignancy or known polyposis							NS			NS			NS			
Do you have 1–2 daily bowel movements?	NS	NS	NS	NS	NS	NS	NS	NS	NS		NS	NS	NS	NS	NS	NS
Is the consistency of your stool normal	NS	NS	NS	NS	NS	NS	NS	NS	NS		NS	NS	NS	NS	NS	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)		NS	NS	NS	12		NS			NS						NS
Atopic conditions (Asthma, atopic dermatitis, Eczema, eosinophils disorder)		NS	NS	NS	NS		NS			NS			NS			NS
Chronic pain syndromes		NS	NS	13	NS		NS	NS	NS	NS	NS	NS	NS			NS
diabetes (type 1 and II)		NS	NS				NS	NS	NS	NS	NS	NS	NS			
obese with body mass index (BMI) >30	NS	NS	NS	14	NS	NS	NS	NS	NS	NS			NS			
Depression	NS	NS	NS	NS	NS		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
Cardiovascular conditions (high blood pressure, cholesterol, fasting glucose, heart disease)	NS	NS	NS	NS	NS		NS	NS	NS	NS	NS	NS	NS	NS	NS	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

¹Have you ever had sexual contact with another man? (Question only for men); ²Infectious disease including MRSA or close contact with MRSA infected patient; ³Have you travel outside to Denmark, Scandinavia, and Germany?; ⁴shared a syringe or needle with others?; ⁵Antibacterials, antifungals or antivirals; ⁶Antibiotic within preceding 2 months; ⁷Antibiotics within the preceding 3 months; ⁸Including viral infection (7 days before screening) /HSV and/or papillomavirus anal lesions; ⁹Antibiotics within the preceding <6 months; ¹⁰Any kind of medication including non-steroidal anti-inflammatory drugs; ¹¹Antifungal drugs too; ¹²Systemic rheumatic diseases; ¹³Any sort of chronic disease; ¹⁴BMI >28 Kg/m²;

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
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/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. baumannii	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

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

Australian Government, Department of Health and Aged care, Fecal microbiota transplant product regulation. <https://www.tga.gov.au/products/biologicals-blood-and-tissues-and-advanced-therapies/biologicals/faecal-microbiota-transplant-products-regulation> (accessed 14December 2022)

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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 pylori	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 <i>E. coli</i>)								
<i>Listeria monocytogenes</i>	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

¹IgM immunoassay; ^{1a}Total antibody; ²Hepatitis B surface antigen test; ^{2a}Hepatitis B core antigen test; ³Anti hepatitis C immunoassay; ^{3a}Nucleic acid amplification test; ⁴IgM immunoassay; ^{4a}IgG immunoassay; ⁶HTCV I and II antibodies; ⁷CMV IgG and IgM; ⁸Viral capsid antigen (VCA IgM); ⁹Presence 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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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	Slovakia	Poland	UK	Sweden	Spain	Spain	Denmark	Netherlands	France	Netherlands	Czech
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			NS	NS			NS
Cytomegalovirus (CMV)							NS	NS						

Supplementary Table 5: WHO European region

	[Barberio et al.]	[Hvas et al.]	[Jitsumura et al.]	[Kachliková 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.]	[Tervveer 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														
<i>E. histolytica</i>				8	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
<i>T. gondii</i>		NS	NS		NS	NS	NS	NS	NS	NS	NS		NS	NS
<i>T. canis</i>		NS	NS	9	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
<i>cati and suis</i>		NS	NS	10	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
<i>S. stercoralis</i>		NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS
<i>T. spiralis</i>		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

	[Barber io et al.]	[Hvas et al.]	[Jitsum ura et al.]	[Kachlik ová et al.]	[Wierzb icka et al.]	[McCu ne et al.]	[Now ak et al.]	[Reig adas et al.]	[Reigad as et al.]	Rode et al.]	[Ross en et al.]	Sokol et al.]	[Terveer 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
<i>Stool tests</i>														
<i>Testing for viruses</i>														
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

		[Barber io et al.]	[Hvas et al.]	[Jitsum ura et al.]	[Kach liková et al.]	[Wier zbick a et al.]	[McCu ne et al.]	[Now ak et al.]	[Reig adas et al.]	[Reig adas et al.]	[Rode et al.]	[Rossen et al.]	Sokol et al.]	[Terrveer et al.]	[Brezina et al.]
NS	Parechovirus														
NS	Hepatitis A	NS													
	Testing for bacteria														
NS	Salmonella spp						13					NS			
NS	Shigella spp				NS		14					NS			
	Yersinia spp				NS		NS	NS				NS			
NS	Campylobacter spp			NS			15					NS			
	Vibrio species	NS	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		
	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

[Brezina et al.]		[Barberio et al.]	[Hvas et al.]	[Jitsumura et al.]	[Kachliková 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.]	[Terveer et al.]
	Enterotoxigenic <i>E. coli</i> (ETEC)	NS	NS	NS	NS	NS	NS	NS	NS	NS		NS	NS	NS
NS	Enteroinvasive <i>E. coli</i> (EIEC)			NS	NS	NS	NS	NS	NS	NS		NS	NS	NS
NS	Attaching and Effacing <i>E. coli</i> (A/EEC)	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS		NS	NS
NS	Verotoxin-producing <i>E. coli</i>	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS	NS		NS
NS	MDR Bacteria													
NS	ESBL producing enterobacterae (Enrichment culture)			NS	NS		18	NS				NS		
NS	VRE				NS							NS		
NS	CPE (CRE/KPC/NDM,OXA 48)		#	##	NS	###	19	#				NS		
	MRSA	NS	NS		NS		NS	NS			NS	NS	NS	
	MDR <i>A. baumannii</i>	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	

¹IgM immunoassay; ^{1a}Total antibody; ²Hepatitis B surface antigen test; ^{2a}Hepatitis B core antigen test; ^{2b}Nucleic acid amplification test; ³Anti hepatitis C immunoassay; ^{3a}Nucleic acid amplification test; ⁴IgM immunoassay; ⁵4th generation immunoassay; ^{5a}Nucleic acid amplification test; ⁶HTCV I and II antibodies; ⁷Wassermann's reaction; ^{7a}Rapid plasma regain test; ^{8,9,10}antibody test; ¹¹PCR; ¹²Adenovirus 40/41/52

	[Barberio et al.]	[Hvas et al.]	[Jitsumura et al.]	[Kachliková et al.]	[Wierzbička et al.]	[McCune et al.]	[Nowak et al.]	[Reigadas et al.]	[Reigadas et al.]	Rode et al.]	[Rossen et al.]	Sokol et al.]	[Tervveer 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	

multiplex PCR; ^{13,14,15}Culture; ¹⁶Presence of toxins and antigens; ^{16a}Culture and PCR; ¹⁷Stool antigen test; ¹⁸Enrichment culture; ¹⁹Selective chromogenic culture; ²⁰Fecal Giardia antigen; ^{20a}Enzyme immunoassay; ²¹Antigen and/or acid fast staining; ^{21a}Enzyme immunoassay; ²²Strongyloides ELISA; ²³Antibody 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

<i>Paragonimus</i>	NS		NS	NS	NS	NS	NS	NS	NS	NS	NS
<i>westermanii</i>	NS		NS	NS	NS	NS	NS	NS	NS	NS	NS
<i>Paragonimus miyazakii</i>	NS		NS	NS	NS	NS	NS	NS	NS	NS	NS
<i>Fasciola spp.,</i>	NS		NS	NS	NS	NS	NS	NS	NS	NS	NS
<i>Sparganosis mansoni,</i>	NS		NS	NS	NS	NS	NS	NS	NS	NS	NS
<i>Cysticercus cellulosae</i>	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. pylori	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

<i>Giardia lamblia</i>	NS	NS				NS	NS		NS	NS	NS	¹ total
<i>Entamoeba histolytica</i>	NS	NS	NS			NS	NS		NS	NS	NS	antibody
<i>Microsporidia,</i>	NS	NS	NS	NS		NS	NS		NS	NS	NS	test (IgM
<i>Cyclospora</i>	NS	NS	NS	NS		NS	NS		NS	NS	NS	and
<i>Isospora</i>	NS	NS	NS	NS		NS	NS		NS	NS	NS	IgG); ^{1a} HAV
<i>blastocystis</i>	NS	NS		NS	NS	NS	NS	NS	NS	NS	NS	IgM; ²
<i>dientamoeba</i>	NS	NS		NS	NS	NS	NS	NS	NS	NS	NS	hepatitis B
Other tests												surface
fragilis and entamoeba	NS	NS	NS		NS	NS	NS	NS	NS	NS	NS	antigen;
histolytica PCR												^{2a} antibody
light microscopy for the												to hepatitis
presence of ova, cysts,												B core
and parasites												antigen;
												^{2b} total

antibody test; ^{2c}PCR; ³antibody; ^{3a}PCR; ⁴HAE IgM; ⁵HIV Elisa; ⁶HTLV antibody; ⁷CMV IgM, IgG; ⁸EBV IgM, IgG; ⁹*H. pylori* serology; ¹⁰Syphilis rapid plasma regain test; ¹¹Strongyloides serology; ¹²toxins A and B by EIA; ^{12a}Glutamate dehydrogenase gene + polymerase chain reaction; ¹³Anti-*H. pylori* IgG; ⁴⁷antigen; ⁴⁸Fecal Giardia antigen; ⁵¹Acid-fast stain for *Cyclospora*; ⁵²Acid-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