

The use of faecal microbiota transplant as treatment for recurrent or refractory *Clostridioides difficile* infection and other potential indications

Mullish, Benjamin H; Merrick, Blair; Quraishi, Mohammed Nabil; Bak, Aggie; Green, Christopher A; Moore, David J; Porter, Robert J; Elumogo, Ngozi T; Segal, Jonathan P; Sharma, Naveen; Marsh, Belinda; Kontkowski, Graziella ; Manzoor, Susan E; Hart, Ailsa L; Settle, Christopher ; Keller, Josbert J; Hawkey, Peter; Iqbal, Tariq H; Goldenberg, Simon D; Williams, Horace R T

DOI:

[10.1136/gutjnl-2023-331550](https://doi.org/10.1136/gutjnl-2023-331550)

License:

Creative Commons: Attribution-NonCommercial (CC BY-NC)

Document Version

Peer reviewed version

Citation for published version (Harvard):

Mullish, BH, Merrick, B, Quraishi, MN, Bak, A, Green, CA, Moore, DJ, Porter, RJ, Elumogo, NT, Segal, JP, Sharma, N, Marsh, B, Kontkowski, G, Manzoor, SE, Hart, AL, Settle, C, Keller, JJ, Hawkey, P, Iqbal, TH, Goldenberg, SD & Williams, HRT 2024, 'The use of faecal microbiota transplant as treatment for recurrent or refractory *Clostridioides difficile* infection and other potential indications: second edition of joint British Society of Gastroenterology (BSG) and Healthcare Infection Society (HIS) guidelines', *Gut*. <https://doi.org/10.1136/gutjnl-2023-331550>

[Link to publication on Research at Birmingham portal](#)

General rights

Unless a licence is specified above, all rights (including copyright and moral rights) in this document are retained by the authors and/or the copyright holders. The express permission of the copyright holder must be obtained for any use of this material other than for purposes permitted by law.

- Users may freely distribute the URL that is used to identify this publication.
- Users may download and/or print one copy of the publication from the University of Birmingham research portal for the purpose of private study or non-commercial research.
- User may use extracts from the document in line with the concept of 'fair dealing' under the Copyright, Designs and Patents Act 1988 (?)
- Users may not further distribute the material nor use it for the purposes of commercial gain.

Where a licence is displayed above, please note the terms and conditions of the licence govern your use of this document.

When citing, please reference the published version.

Take down policy

While the University of Birmingham exercises care and attention in making items available there are rare occasions when an item has been uploaded in error or has been deemed to be commercially or otherwise sensitive.

If you believe that this is the case for this document, please contact UBIRA@lists.bham.ac.uk providing details and we will remove access to the work immediately and investigate.

Download date: 13. Nov. 2024

1 **The use of faecal microbiota transplant as treatment for recurrent or**
2 **refractory *Clostridioides difficile* infection and other potential**
3 **indications: second edition of joint British Society of**
4 **Gastroenterology (BSG) and Healthcare Infection Society (HIS)**
5 **guidelines.**

6

7 Benjamin H Mullish^{a,b,*}, Blair Merrick^{c,*}, Mohammed Nabil Quraishi^{d,e,f,*}, Aggie Bak^g,
8 Christopher A Green^{h,i}, David J Moore^j, Robert J Porter^k, Ngozi T Elumogo^{l,m}, Jonathan P
9 Segal^{n,o}, Naveen Sharma^{d,e,f}, Belinda Marsh^p, Graziella Kontkowsk^{p,q}, Susan E Manzoor^e, Ailsa
10 L Hart^{a,r}, Christopher Settle^s, Josbert J Keller^{t,u}, Peter Hawkey^{e,v}, Tariq H Iqbal^{d,e,f}, Simon D
11 Goldenberg^{c,†}, Horace R T Williams^{a,b†}

12 *Joint first authors ; †Joint senior/corresponding authors

13

14 **Affiliations:**

15 a Division of Digestive Diseases, Department of Metabolism, Digestion and Reproduction, Faculty of
16 Medicine, Imperial College London, London, UK

17 b Departments of Gastroenterology and Hepatology, St Mary's Hospital, Imperial College Healthcare
18 NHS Trust, London, UK

19 c Centre for Clinical Infection and Diagnostics Research, Guy's and St Thomas' NHS Foundation Trust,
20 King's College, London SE1 7EH, UK

21 d Department of Gastroenterology, University Hospitals Birmingham NHS Foundation Trust,
22 Birmingham, UK

23 e Microbiome Treatment Centre, University of Birmingham, Edgbaston, Birmingham, UK

24 f Institute of Cancer and Genomic Sciences, University of Birmingham, UK

25 g Healthcare Infection Society, London, UK

26 h Dept of Infectious Diseases & Tropical Medicine, University Hospitals NHS Foundation Trust,
27 Birmingham Heartlands Hospital, Bordesley Green, Birmingham B9 5SS, United Kingdom

28 i School of Chemical Engineering, University of Birmingham, Birmingham B15 2TT, United Kingdom

29 j Institute of Applied Health Research, College of Medical and Dental Sciences, University of
30 Birmingham, Birmingham, UK

31 k Department of Microbiology, Royal Devon and Exeter Hospitals, Barrack Road, United Kingdom

32 l Quadram Institute Bioscience, Norwich Research Park, Norwich, NR4 7UQ, UK.

33 m Norfolk and Norwich University Hospital, Colney Lane, Norwich, NR4 7UY, UK

34 n Department of Gastroenterology, Royal Melbourne Hospital, Melbourne, Victoria, Australia.

35 o Department of Medicine, University of Melbourne, Melbourne, Victoria, Australia.

36 p Lay representative for FMT Working Party, London, UK

37 q *C. diff* support, London, UK

FMT guidelines: main document.

38 r Department of Gastroenterology and Inflammatory Bowel Disease Unit, St Mark's Hospital and
39 Academic Institute, Middlesex, UK
40 s South Tyneside and Sunderland NHS Foundation Trust, South Shields, UK
41 t Department of Gastroenterology, Haaglanden Medisch Centrum, The Hague, the Netherlands
42 u Department of Gastroenterology and Hepatology, Leiden University Medical Center, Leiden, the
43 Netherlands
44 v Public Health Laboratory, Faculty of Medicine, University of Birmingham, Birmingham, UK

45

46 Full version of this manuscript is available in Supplementary Materials A and at:

47 (<https://his.org.uk/resources-guidelines/faecal-microbiota-transplant/>)

48 *“NICE has accredited the process used by the British Society of Gastroenterology and the*
49 *Healthcare Infection Society to produce: “The use of faecal microbiota transplant as treatment*
50 *for recurrent or refractory Clostridioides difficile infection and other potential indications: joint*
51 *British Society of Gastroenterology (BSG) and Healthcare Infection Society (HIS) guidelines.”*
52 *The NICE accreditation of HIS methodology is valid for five years from March 2020. More*
53 *information on accreditation can be viewed at [http://www.nice.org.uk/about/what-we-](http://www.nice.org.uk/about/what-we-do/accreditation)*
54 *[do/accreditation](http://www.nice.org.uk/about/what-we-do/accreditation)”*

55

56

57 **Keywords:** microbiota; faecal microbiota transplantation; Clostridioides difficile; colonic microbiome;
58 enteric bacterial infection; infective colitis; intestinal microbiology

59 1. Abstract

60 The first British Society of Gastroenterology (BSG) and Healthcare Infection Society (HIS)-endorsed
61 faecal microbiota transplant (FMT) guidelines were published in 2018. Over the past five years, there
62 has been considerable growth in the evidence base (including publication of outcomes from large
63 national FMT registries), necessitating an updated critical review of the literature and a second edition
64 of the BSG/HIS FMT guidelines. These have been produced in accordance with NICE-accredited
65 methodology, thus have particular relevance for UK-based clinicians, but are intended to be of
66 pertinence internationally. This second edition of the guidelines have been divided into
67 recommendations, good practice points, and recommendations against certain practices. With
68 respect to FMT for *Clostridioides difficile* infection (CDI), key focus areas centred around timing of
69 administration, increasing clinical experience of encapsulated FMT preparations, and optimising
70 donor screening. The latter topic is of particular relevance given the COVID-19 pandemic, and cases of
71 patient morbidity and mortality resulting from FMT-related pathogen transmission. The guidelines
72 also considered emergent literature on the use of FMT in non-CDI settings (including both
73 gastrointestinal and non-gastrointestinal indications), reviewing relevant randomised controlled trials.
74 Recommendations are provided regarding special areas (including compassionate FMT use), and
75 considerations regarding the evolving landscape of FMT and microbiome therapeutics.

76

77 **Executive summary of recommendations**

Effectiveness and safety of FMT in treating *C. difficile* infection

1.1: Offer antibiotics alone in preference to FMT as an initial treatment for *C. difficile* infection (i.e. first episode).

1.2: Consider FMT for a first recurrence of *C. difficile* infection or as an adjunct to antibiotics in refractory *C. difficile* infection.

1.3: Offer FMT to all patients with two or more recurrences of *C. difficile* infection.

1.4: Ensure that FMT is preceded by the treatment of *C. difficile* infection with appropriate antibiotics for at least 10 days.

1.5: Offer FMT to all patients, regardless of health status, except those with a known anaphylactic food allergy.

1.6: Offer one or more FMT after initial clinically assessed FMT failure.

Good practice points

GPP 1.1: Consider FMT earlier than after second *C. difficile* infection recurrence for patients with severe, fulminant or complicated *C. difficile* infection who are not responding to antibiotic therapy.

GPP 1.2: If FMT was given via endoscopy, ensure that immediate post-endoscopic management after administration is in line with any local protocols.

GPP 1.3: Inform patients about the short-term adverse events, in particular the possibility of self-limiting gastrointestinal symptoms and that serious adverse events are rare.

GPP 1.4: Inform inflammatory bowel disease patients with *C. difficile* infection about a small risk of exacerbation of their condition after FMT.

GPP 1.5: Follow-up the FMT recipients for at least eight weeks to establish its efficacy and adverse events.

GPP 1.6: Do not test for cure by absence of *C. difficile* after FMT, unless the patient has persistent *C. difficile* infection symptoms or is suspected to have relapsed.

GPP 1.7: Consider investigation for alternative causes for symptoms in patients who fail to respond to anti- *C. difficile* infection treatment including FMT.

Recipient factors influencing the outcome of FMT for patients with *C. difficile* infection

2.1: Do not refuse or delay FMT therapy due to any recipient risk factors e.g. age over 75 years old, except for patients with known anaphylactic food allergy.

Donor factors influencing the outcome of FMT for patients with *C. difficile* infection

3.1: Use FMT from universal donors in preference to related donors.

3.2: All potential donors must be screened by questionnaire or personal interview to establish risk factors for transmissible diseases and for factors that may adversely influence the gut microbiota (Box 1).

3.3: Blood and stool of all donors must be tested for transmissible diseases to ensure FMT safety (Box 2 and 3).

3.4: Discuss and agree the content of donor health questionnaire and laboratory testing at a local level, following a robust risk assessment.

3.5: Undertake ongoing review, revision and updating of the list of pathogens for screening/testing based on local epidemiology and the latest evidence.

3.6: Blood and stool of all donors must be re-screened periodically to ensure FMT safety.

3.7: Discuss and agree on the frequency of rescreening depending on local circumstances, but do not allow the bookend periods to be longer than four months.

3.8: Health assessment which captures the donor's ongoing suitability must be completed at each stool donation.

3.9: Ensure that FMT manufactured from donors is quarantined pending post-baseline screening and test results.

Good practice points

GPP 3.1: Follow suggested recommendations in Boxes 1-4 for conditions to be included in screening and health questionnaire.

Preparation-related factors influencing the outcome of FMT for patients with *C. difficile* infection

4.1: Frozen FMT must be offered in preference to freshly processed products.

4.2: Process stools aerobically or anaerobically – both methods are acceptable.

4.3: Store prepared FMT products frozen at -70°C for up to 12 months.

4.4: Add cryoprotectant such as glycerol to frozen FMT products.

4.5: If capsules are used, these can be obtained from frozen or lyophilised faecal slurry.

Good practice points

GPP 4.1: Follow a standard protocol for stool collection.

GPP 4.2: Start processing stools within 150 minutes of defecation.

GPP 4.3: When possible, use at least 50g of stool in each FMT preparation.

GPP 4.5: Use sterile 0.9% saline as a diluent for FMT production.

GPP 4.5: Mix a minimum of 1:5 stool with diluent to make the initial faecal emulsion.

GPP 4.6: Consider homogenisation and filtration of FMT in a closed disposable system.

GPP 4.7: Consider thawing frozen FMT at ambient temperature and using it within six hours of thawing.

GPP 4.8: Avoid thawing FMT in warm water baths, due to the risks of cross contamination with *Pseudomonas species* (and other contaminants) and reduced bacterial viability.

GPP 4.9: Where glycerol is used as a cryopreservative, ensure it is at 10-15% final concentration of the prepared faecal material/slurry, with vortexing or other methods used to fully mix the cryopreservative into the material.

Route of delivery and other administration factors influencing the outcome of FMT for patients with *C. difficile* infection

5.1: Choose any route of FMT delivery but, if possible, avoid enema.

5.2: When choosing the route of delivery, consider patient preference and acceptability, cost, and the impact on environment.

5.3: Consider enema for patients in whom other FMT delivery methods are not feasible.

5.4: There is no need to administer proton pump inhibitors or other antisecretory agents as a preparation for FMT.

5.5: Do not use antimotility agents as a preparation for FMT.

5.6: Use bowel preparation/lavage as a preparation for FMT.

5.7: After upper gastrointestinal tract administration is used, remove the tube following the flushing with water.

5.8: For patients at risk of regurgitation or those with swallowing disorders, avoid administration via upper gastrointestinal tract and deliver FMT via lower gastrointestinal tract instead.

5.9: If colonoscopic administration is used, ensure that the FMT is delivered to a site that will permit its retention.

Good practice points

GPP 5.1: Use polyethylene glycol preparation as a preferred solution for bowel lavage.

GPP 5.2: Consider using prokinetics (such as metoclopramide) prior to FMT via the upper gastrointestinal tract route

GPP 5.3: Follow best practice for prevention of further transmission of *C. difficile* when administering FMT to patients.

GPP 5.4: Consider a washout period of at least 24 hours between the last dose of antibiotic and treatment with FMT.

GPP 5.5: If upper gastrointestinal tract administration is used, nasogastric, nasoduodenal or nasojejunal tube, upper GI endoscopy or a permanent feeding tube may be used for delivery.

GPP 5.6: If upper gastrointestinal administration is used, administer no more than 100 mL of FMT to the gastrointestinal tract.

Post-FMT factors influencing the outcome of FMT for patients with *C. difficile* infection

6.1: Wherever possible, avoid using non- *C. difficile* infection antibiotics for at least eight weeks after FMT.

6.2: Consult infection specialists, or other appropriate healthcare professional (e.g. gastroenterologists with experience of FMT) for advice whenever FMT recipients have an indication for long term antibiotics or have an indication for non- *C. difficile* infection antibiotics within eight weeks of FMT.

Prophylactic FMT treatment to prevent *C. difficile* infection

7.1: No recommendation

FMT for non- <i>C. difficile</i> infection indications
8.1: Do not offer FMT routinely to patients with indications other than <i>C. difficile</i> infection.
8.2: Consider FMT on case by case basis for patients with ulcerative colitis in whom licenced treatment options have failed or for those who are not suitable for currently available treatments.
Compassionate use of FMT
9.1: Consider offering compassionate use of FMT in non- <i>C. difficile</i> infection settings only when a patient cannot be entered into a clinical trial and after discussion and approval in a multidisciplinary team setting.
9.2: When offering compassionate use of FMT, the following conditions must be met: <ul style="list-style-type: none">• There is a biological rationale to justify consideration.• Patient is at risk of significant clinical compromise due to a limited alternative range of therapeutic options.• Patient understands the risks and benefits of FMT compared to other treatment options.
9.3: Prior to treatment, define what will be considered as a success or failure of FMT.
9.4: Prior to treatment, agree potential strategy for further FMTs based upon initial clinical success.
Self-banking of stool for potential future autologous FMT
10.1: Do not routinely self-bank stool from faecal material donated by patients or healthy people for potential future autologous FMT.
Regulation and oversight of FMT
11.1: Centres that manufacture and dispense FMT must adhere to any regulations applicable to the area in which they are located.

78

79 2. Patient summary

80 Faecal microbiota transplant (FMT), sometimes also known as stool or poo transplantation, can be an
81 effective treatment for patients with *Clostridioides difficile* (commonly known as *C. diff*) infection. It is
82 usually given when the infection comes back after antibiotic treatment (relapse), or occasionally if
83 antibiotics do not work (refractory). It is not fully understood how FMT helps patients with *C. diff*
84 infection, but it is thought it is partly to do with restoring beneficial gut microorganisms (e.g. bacteria)
85 and the chemicals (e.g. metabolites) they produce.

86 The first BSG/HIS guidelines on the use of FMT for *C. diff* were published in 2018, and since this time
87 new evidence has become available. This has prompted this second edition of the guidelines. Key
88 recommendations focus on which patients should be offered FMT, when it should be offered, and the
89 best ways to administer it. The guidelines also describe important considerations for screening of stool
90 donors to ensure the safety and success of FMT. Two further topics are focused on in this second
91 edition. One is the evidence for the use of FMT for conditions other than *C. diff* infection, including

FMT guidelines: main document.

92 irritable bowel syndrome, ulcerative colitis and Crohn’s disease, as well as conditions outside of the
93 gut, such as obesity and metabolic syndrome. The second topic considers patients with conditions in
94 which there are no other treatment options available to them, and if they can be offered FMT: this is
95 called compassionate use.

96 3. Introduction

97 Faecal microbiota transplant (FMT; sometimes referred to by other names, including ‘intestinal
98 microbiota transplant/transfer [1]) describes the transfer of minimally manipulated faeces from a
99 healthy screened donor to a patient for the treatment of disease. FMT is now entering its second
100 decade of use in modern mainstream medicine, with the first randomised trial reporting its utility
101 following antibiotic treatment in recurrent *Clostridioides difficile* infection (CDI) in 2013 [2]. The first
102 BSG/HIS-endorsed FMT guidelines were published in 2018 [2], and the interest continues to grow in
103 the use of FMT, both for CDI and for its potential in the management of non-CDI conditions [3].

104 Since the first BSG/HIS FMT guidelines in 2018, there has been publication of European and North
105 American CDI-related guidelines [4] that have also addressed FMT, consensus reports relating to
106 aspects of FMT service design and delivery [5], and other BSG guidelines that have made consideration
107 of a role for FMT in a non-CDI setting, e.g. for inflammatory bowel disease [6]. More recently, National
108 Institute for Health and Care Excellence (NICE) medical technologies guidance summarised the clinical
109 and cost effectiveness of FMT, from a UK National Health Service (NHS) perspective [7]. Despite these
110 publications, the BSG and HIS advocated for a second edition of the UK FMT guidelines (with the
111 focused version presented here, and full version available in Supplementary Materials file A) for a
112 number of reasons. Firstly, the high levels of clinical interest within this field mean that this has been
113 a fast-moving area with a rapidly-growing literature base. Particular areas of evolution since the last
114 guideline iteration have included randomised trials in both CDI and non-CDI settings, the reporting of
115 data from regional and national FMT registries (with longer periods of follow-up and larger numbers
116 of patients than were previously described), and concerns related to donor screening (relating both
117 to the COVID-19 pandemic, and high profile reports of FMT-related pathogen transmission with
118 adverse patient outcomes). Secondly, while the NICE medical technologies guidance presented a
119 general evaluation of the clinical use of FMT, its remit did not include guidance as to many of the more
120 specific areas related to FMT provision and administration that are of greatest relevance to practising
121 clinicians in this field, including donor selection and screening and material preparation, or consider
122 non-CDI indications. As such, there was a compelling case to apply NICE-accredited methodology to
123 the current evidence base and provide clinicians with the highest quality recommendations and
124 guidance on which to base their practice of FMT use in adults.

125 The focus of these guidelines was on the use of ‘conventional’ FMT, to inform use in healthcare
126 settings (primarily the NHS), and in academia. As such, as per the prior guidelines, studies were
127 considered only if they explored the administration of whole stool, and not modified products, such
128 as cultured microorganisms (or their proteins, metabolites or other components), or microbiota
129 suspensions. The guideline development team (referred to as Working Party) are aware of
130 developments in the United States in this space, particularly the recent FDA approval of ‘next
131 generation’ FMT products, including RBX2660/Rebyota (Ferring; a rectally-administered FMT-type
132 product [8]), and SER-109/ Vowst (Seres/Nestle; a purified spore-based product [9]) for preventing
133 CDI relapses. Clinical trials that contributed to the licensing of these products investigated the

FMT guidelines: main document.

134 performance of these agents compared to standard-of-care anti-CDI antibiotics. None explored
135 efficacy compared to 'conventional' FMT. At the time of writing, no such products were licensed for
136 use within the UK or European Union, and none have been licensed in any region as part of
137 management of a non-CDI indication.

138 Glossary of terms used is provided in Supplementary Materials file B.

Box 5: Commonly accepted CDI definitions*

Recurrent CDI: infection symptoms resolved after treatment but recurred within eight weeks. It is currently difficult to establish a difference between a relapse of the disease or the occurrence of a new infection.

Refractory CDI: CDI which is not responding to antibiotic treatment. This type of CDI may or may not be considered fulminant CDI.

Severe CDI: when fever, leucocytosis, and rise in serum creatinine are present, which may also be supported by further diagnostic abnormalities, e.g. distension of the large intestine seen at imaging.

Fulminant CDI: also known as severe-complicated, occurs when one of the following CDI-related factors are present: hypotension, septic shock, elevated serum lactate, ileus, toxic megacolon, bowel perforation or a fulminant course of disease.

Please note that clinically, many of these definitions overlap and it is not always possible to clearly group patients into these categories. Additionally, over the disease course this may change, e.g. refractory CDI may become fulminant. *Taken from ESCMID guidelines [https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X\(21\)00568-1/fulltext#secsectitle0070](https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(21)00568-1/fulltext#secsectitle0070)

139

140 **3.1 Aims and Scope**

141 The main purpose of this second edition of the guidelines was to set recommendations and best
142 practice for the optimal provision of effective and safe FMT for recurrent or refractory CDI (defined in
143 Box 5) in adult (≥ 18 years) patients. The secondary purpose was to provide guidance for using FMT in
144 conditions other than CDI in the adult population. These recommendations focused on the provision
145 of FMT in the UK, although many aspects are also relevant internationally. The focus was on 'minimally
146 manipulated' stool, and not the 'next generation' FMT products (i.e. defined microbial communities
147 'microbiome therapeutics'). The diagnosis and management of CDI in general were considered outside
148 the scope of these guidelines.

149

150 **3.2 Methodology**

151 Topics for these guidelines were derived from the initial discussions of the Working Party during the
152 stakeholder meeting. The included questions (Appendix 1) were adapted from those in the previous

FMT guidelines: main document.

153 version of the guidelines published in 2018 [1]. Methods were followed in accordance with the NICE
154 manual for conducting evidence syntheses (Supplementary file C).

155 **Data sources and search strategy**

156 Three electronic databases (MEDLINE, Embase, Cochrane Central Register of Controlled Trials) were
157 searched with the last search date in July 2023. Search terms were constructed using relevant index
158 and free text terms (Appendix 1). Reference lists of identified relevant articles were scanned for
159 additional studies and forward reference searching (identifying articles which cite relevant articles)
160 was performed. The searches were restricted to primary articles published in the English language.

161 **Study eligibility and selection criteria**

162 Search results were downloaded to Covidence software and screened for relevance. Two reviewers
163 discussed their disagreements first and the third reviewer was available to arbitrate but was not
164 needed. The results of study selection and the list of excluded studies for all questions are available in
165 Appendix 2.

166 **Data extraction and quality assessment**

167 Included epidemiological studies were appraised for quality using checklists (links available in
168 Appendix 3a). The results of quality appraisal are available in Appendix 3b.

169 Data were extracted by one reviewer and checked by other reviewers. For each question, the data
170 from the included studies were extracted to create the tables of study description and summary of
171 findings tables (Appendix 4).

172 **Rating of evidence and recommendations**

173 The strength of the evidence was defined by GRADE (Grading of Recommendations Assessment,
174 Development and Evaluation) tables (Appendix 5) and using the ratings 'high', 'moderate', 'low' and
175 'very low' to construct the evidence statements, which reflected the Working Party's confidence in
176 the evidence. The strength of recommendation was adopted from GRADE and reflects the strength of
177 each evidence statement.

178 **Consultation process**

179 Feedback on draft guidelines was received from the participating organisations and through
180 consultation with relevant stakeholders. The Working Party reviewed stakeholder comments, and
181 collectively agreed revisions (Supplementary Materials file D).

182

183 **3.3 Guideline development team and Conflicts of Interest**

184 Members of the Working Party represent professional societies i.e. British Society of Gastroenterology
185 (BSG) and Healthcare Infection Society (HIS) as well as clinical microbiologists, gastroenterologists,
186 infection prevention and control (IPC) doctors, clinical and academic researchers, FMT production
187 manager, methodologists, and two lay members. Individual members were mostly UK-based but some
188 international experts were also chosen to ensure that the guidelines are also relevant to an

189 international audience. BSG and HIS commissioned the authors to undertake this Working Party
190 report. The authors received no specific funding for this work. Financial support for the time required
191 to obtain the evidence and write the manuscript was provided by the authors' respective employing
192 institutions. B.H.M. was the recipient of an NIHR Academic Clinical Lectureship (CL-2019-21-002). The
193 Division of Digestive Diseases at Imperial College London receives financial and infrastructure support
194 from the NIHR Imperial Biomedical Research Centre based at Imperial College Healthcare NHS Trust
195 and Imperial College London. The authors would like to thank Dr Rohma Ghani for her assistance on
196 the topic of donor screening, Dr Bin Gao for reviewing the studies related to FMT given to patients
197 with functional constipation, Dr Andrew Flatt for advice on donor screening, Prof Mark Gilchrist for
198 advice on medical product regulation, and Professor Jessica Allegretti, Professor Christian Lodberg
199 Hvas and Dr Simon Baunwall for providing additional data from the included studies. The views
200 expressed in this publication are those of the authors and have been endorsed by BSG and HIS and
201 approved following a consultation with external stakeholders. Authors declared no substantial
202 conflicts of interest which would prevent them from being the members of the guidelines panel. All
203 conflicts of interest are disclosed in Supplementary Materials file C.

204 **Contributions**

205 DJM helped design literature strategy. BHM, BM (Merrick), MNQ and AB screened the
206 literature. AB conducted searches, performed initial data extraction and evidence syntheses,
207 which was checked by BHM, BM (Merrick) and MNQ. All authors except AB also provided
208 advice. BHM, BM (Merrick), MNQ and AB wrote the first draft. BHM, BM (Merrick), MNQ, AB,
209 CAG, DJM, RJP, NTE, JPS, NS, BM (Marsh), GK, SEM, ALH, CS, JJK, PH, THI, SDG and HRTW all
210 attended Working Party meetings and contributed to rating of evidence and
211 recommendations. BHM, BM (Merrick), MNQ, AB, CAG, DJM, RJP, NTE, JPS, NS, BM (Marsh),
212 GK, SEM, ALH, CS, JJK, PH, THI, SDG and HRTW all read, reviewed, contributed to the writing
213 of and approved the final documents.

214 **3.4 Scheduled Review**

215 The guidelines will be reviewed at least every four years and updated if change(s) are necessary or if
216 evidence emerges that requires a change in practice.

217 **3.5 Implementation**

218 The Working Party agreed that there is no anticipated additional cost associated with implementation
219 of these guidelines unless existing practice falls well below currently accepted standards. Assessing
220 the cost-effectiveness of different treatments is not within the scope of this guidance. The practices
221 recommended by these guidelines are currently used in most centres offering FMT in the UK. There is
222 a potential cost saving and other benefits (e.g. reducing the carbon footprint) when certain
223 recommendations are followed (e.g. donor screening or using aerobic processes for FMT preparation).
224 Lay materials and continuing professional development questions (CPD) are available in the
225 Supplementary Materials (files E and F).

226 4. Rationale for recommendations

227 4.1 Effectiveness and safety of FMT in treating CDI

228 There is clear evidence of the growing use of FMT globally. With the availability of randomised trial
229 outcome data, FMT has become an accepted treatment for recurrent and refractory CDI. A recent pan-
230 European survey suggested a disparity in access to FMT between countries (or even between regions
231 within countries), suggesting ongoing significant underutilisation in patients who may stand to benefit
232 from FMT [10]. Previous BSG/HIS guidelines [3] recommended that FMT should be offered to patients
233 with refractory CDI, or those with risk factors for recurrence, but not as first line treatment. At the
234 time of their publication, there were fewer randomised trials and comparison treatment was limited
235 to vancomycin. Due to a small number of studies conducted before the first edition of the guidelines
236 was published, meta-analyses were not possible and the evidence for effectiveness was not well-
237 established. Additionally, effectiveness and, more importantly, safety of FMT for some patient
238 populations including those who were immunocompromised or immunosuppressed, frail and older
239 patients, and patients with certain comorbidities, was unknown.

240 Of note, FMT use in the context of CDI is predominantly described as being administered after a course
241 of anti-CDI antibiotics. Depending upon the study reviewed, FMT may be either viewed as a direct part
242 of the treatment of an episode of CDI (i.e. consolidation of therapy after anti-CDI antibiotics), or that
243 the anti-CDI antibiotics are the central therapy and that the role of FMT is primarily prevention of
244 further recurrence. Growing understanding about mechanisms of efficacy of FMT in CDI – including
245 FMT's roles in both direct inhibition of the growth of *C. difficile*, as well as prevention of spore
246 germination [11] mean that both interpretations merit consideration. Reflecting this view, FMT in CDI
247 will interchangeably be referred to as a modality of treatment and intervention to prevention of
248 recurrence within this guideline, with the assumption that FMT has been administered only after a
249 preceding course of anti-CDI antibiotics unless otherwise stated.

250

251 **General population with CDI**

252 *Effectiveness of FMT vs standard care or placebo:* There was strong evidence which suggested that
253 FMT is more effective than standard care or placebo for preventing CDI recurrence in general
254 population [2,12-16].

255 *Adverse events following FMT vs standard care or placebo:* There was strong evidence which
256 suggested no negative effect of FMT [2,12-16].

257 **Patients with severe, complicated or fulminant CDI**

258 *Effectiveness of FMT in patients with severe CDI:* There was weak evidence which suggested that FMT
259 is beneficial in this patient group [17].

260 *Effectiveness of FMT in patients with severe CDI compared to patients with mild/moderate CDI:* There
261 was moderate evidence which suggested there was no difference between these two patient groups
262 [18-24].

263 *Effectiveness of FMT in patients with refractory or fulminant CDI vs recurrent CDI:* There was
264 inconsistent evidence which suggested no difference in effect for these patient groups [25-29].

FMT guidelines: main document.

265 *Effectiveness of FMT in patients with pseudomembranous colitis compared to other patients:* There
266 was weak evidence, and it is not clear whether in these patients FMT may be less successful [19,22].

267 *Adverse events in patients with severe, refractory or fulminant CDI:* There was weak evidence which
268 suggested there was no increased risk associated with FMT for these types of patients [17,18,25].

269 *Adverse events in patients with pseudomembranous colitis:* There were no studies.

270 **First episode of CDI**

271 *Effectiveness of FMT:* There was moderate evidence which suggested that FMT is effective in these
272 patients [13,30].

273 *Adverse events:* There was moderate evidence which suggested no negative effect [13].

274 **Patients with co-existing Inflammatory Bowel Disease (IBD) and CDI**

275 *Effectiveness of FMT:* There was weak evidence that suggested FMT was effective in treating CDI in
276 patients with IBD [31-35].

277 *Effectiveness of FMT in IBD patients with CDI compared to patients without IBD:* There was moderate
278 evidence which suggested that FMT for CDI is equally successful in patients who have IBD and those
279 who do not [18,22,23,25,27,36-41].

280 *Effect on adverse events:* There was weak evidence, but it suggested that FMT is safe in patients with
281 IBD treated for CDI [28,31,33,34,36]. However, two studies also highlighted that some IBD patients
282 may experience a flare following FMT [31,36].

283 **Immunocompromised or immunosuppressed patients with CDI**

284 *Effectiveness of FMT:* There was weak evidence which suggested that FMT is effective in treating CDI
285 in patients who are immunocompromised or immunosuppressed [42,43].

286 *Effectiveness in immunocompromised/immunosuppressed patients compared to immunocompetent*
287 *patients:* There was moderate evidence which suggested that there was no difference in effectiveness
288 between these two patient groups [19,21-23,26,28,37-41,44].

289 *Adverse events:* There was weak evidence which suggested that FMT is safe in this patient group
290 [42,43].

291 **Cancer patients with CDI**

292 *Effectiveness of FMT:* There was weak evidence which suggested that FMT is effective in this patient
293 group [45,46].

294 *Effectiveness in cancer patients compared to patients with no cancer:* There was weak evidence, but
295 it suggested that there was no difference in the effectiveness between these two patient groups
296 [19,21,40].

297 *Adverse events:* There was weak evidence which suggested that FMT was safe in this patient group
298 [45,46].

299 **Post solid organ-transplant patients with CDI**

300 *Effectiveness of FMT:* There was weak evidence which suggested that FMT is effective in this patient
301 group [47].

302 *Effectiveness in solid organ transplant patients compared to patients with no solid organ transplant:*
303 There were no studies.

FMT guidelines: main document.

304 *Adverse events:* There was weak evidence which suggested that FMT is safe in this patient group [47].

305 **Patients with liver disease and CDI**

306 *Effectiveness of FMT:* There was weak evidence which suggested FMT is effective in this patient group
307 [48].

308 *Effectiveness in patients with liver disease compared to patients without liver disease:* There was weak
309 evidence which suggested no difference in the effectiveness of FMT between these two groups of
310 patients [38,40,49].

311 *Adverse events:* There was weak evidence which suggested that FMT was safe in this patient group
312 [48].

313 **Patients with kidney disease and CDI**

314 *Effectiveness of FMT:* There were no studies.

315 *Effectiveness in patients with kidney disease compared to patients without kidney disease:* There was
316 weak evidence which suggested that there is no difference in the effectiveness of FMT between these
317 patient groups [19,23,38,40].

318 *Adverse events:* There were no studies.

319 **Patients with diabetes mellitus and CDI**

320 *Effectiveness of FMT:* There were no studies.

321 *Effectiveness in patients with DM compared to patients without DM:* There was weak evidence which
322 suggested that there is no difference in the effectiveness of FMT between these patient groups
323 [19,39,40].

324 *Adverse events:* There were no studies.

325 **Patients with cardiovascular disease and CDI**

326 *Effectiveness of FMT:* There were no studies.

327 *Effectiveness in patients with CVD compared to patients without CVD:* There was weak evidence, which
328 suggested that there is no difference in the effectiveness of FMT between these patient groups [39].

329 *Adverse events:* There were no studies.

330 **Patients with recurrent urinary tract infections and CDI**

331 *Effectiveness of FMT:* There were no studies.

332 *Effectiveness in patients with UTI compared to patients without UTI:* There was weak evidence, which
333 suggested that there is no difference in the effectiveness of FMT between these patient groups [23].

334 *Adverse events:* There were no studies.

335 **Patients with COVID-19 infection and CDI**

336 *Effectiveness of FMT:* There was weak evidence which suggested that FMT is effective in this patient
337 group [50].

338 *Effectiveness in patients with COVID-19 compared to patients without COVID-19:* There were no
339 studies.

340 *Adverse events:* There was weak evidence which suggested FMT is safe in this patient group [50].

FMT guidelines: main document.

341 **Patients with CDI and other conditions**

342 *Effectiveness of FMT:* There were no studies.

343 *Effectiveness in patients with other conditions compared to patients without these conditions:* There
344 was weak evidence, which suggested that there is no difference in the effectiveness of FMT between
345 these patient groups [19,22,38,39].

346 *Adverse events:* There were no studies.

347 **Patients with CDI and multiple comorbidities**

348 *Effectiveness of FMT:* There were no studies.

349 *Effectiveness in patients with multiple comorbidities compared to patients without comorbidities:*
350 There was weak evidence which suggested that FMT may be less successful in patients with multiple
351 comorbidities [20,27,37,44,51,52].

352 *Adverse events:* There were no studies.

353 **Additional data from excluded studies**

354 *Quality of life*

355 One study [53], reported improved quality of life after the patients underwent FMT for CDI.

356 *Mortality*

357 Two studies [54,55] reported no difference in mortality rates, one [56] reported that the incidence of
358 CDI-related mortality decreased when FMT programme was introduced, one [23] reported that early
359 FMT reduced mortality in severe cases and one study [57] reported that patients who received FMT
360 had a 77% decrease in odds for mortality.

361 *Long-term effectiveness*

362 Six studies [23,58-62] which reported that at long-term follow-up (up to one year), FMT was still
363 effective.

364 *Asymptomatic carriage after FMT*

365 One study [63] reported that asymptomatic carriage of *C. difficile* after FMT is rare.

366 *New or worsening symptoms following FMT*

367 One study [23] reported that one year after follow-up nausea was present in 18% of the patients,
368 abdominal pain in 21% and diarrhoea in 33%, but that no serious events related to FMT occurred. One
369 study [59] reported that within a year after FMT, the prevalence of constipation increased, but that
370 most of the cases did not need treatment. Other symptoms included urgency, cramping and an
371 increased incidence of IBS. Two years after FMT, new conditions included weight gain, diabetes
372 mellitus, dyslipidaemia, thyroid problems, GI problems, and serious infections. These conditions were
373 not considered directly linked to FMT. Other studies reported the onset of the following new issues
374 [36,54,60,62], but none of these conditions were assessed for causality. One study reported worsening
375 pre-existing chronic IBD and rheumatoid arthritis [60]. One study [64] that there was a slightly higher
376 incidence of myocardial infarction in FMT group compared to non-FMT at one year follow-up, but that
377 the incidence of other conditions was similar. At ten-year follow-up, one study [65] reported that there
378 were no new diagnoses of autoimmune diseases, GI disorders or malignancies and that there were no
379 deaths which were attributed to FMT.

380 *Resolution or improvement of conditions following FMT*

381 Three studies reported resolution or improvement of existing conditions following FMT [54,60,62],
382 including eradication of multi-drug resistant micro-organisms [54], improvement of undifferentiated
383 colitis, Crohn's disease, ulcerative colitis, diabetes mellitus and Parkinson's disease [62] and
384 improvement of IBS, IBD, and alopecia areata [60]. None of these studies investigated whether these
385 improvements were directly associated with FMT.

386 *The Working Party discussed the above evidence and concluded that FMT administered after CDI*
387 *treatment with appropriate antibiotics appears to be more effective than placebo, or additional doses*
388 *of vancomycin or fidaxomicin in prevention of CDI recurrence. However, the sensitivity analyses*
389 *performed due to high heterogeneity suggest that its effectiveness depends on many factors, including*
390 *the route of FMT administration, the number of FMTs given, type of the patient and the length of*
391 *follow-up. It is also important to highlight that the high heterogeneity was also a result of different*
392 *types of comparisons, which are typically used in clinical practice and constitute standard care, e.g. in*
393 *some studies, participants were given initial antibiotics to treat CDI and received placebo as a part of*
394 *standard care while in other studies participants received the initial antibiotics for treatment as well*
395 *as additional doses of vancomycin or fidaxomicin as a comparison to FMT. In either case, FMT was*
396 *more effective than any of these standard regimens. The results of one RCT⁵ support previous*
397 *observational reports that retention enema is not an efficient route of administration.*

398 *Additionally, FMT seems to be beneficial for patients with different types of comorbidity regardless of*
399 *the severity or phenotype of CDI and the number of CDI episodes preceding FMT. The Working Party*
400 *acknowledged that some types of comorbidities and multiple comorbidities may make the FMT less*
401 *effective, and that for these patients, more than one FMT may be required. Clinically, this would be*
402 *similar for all patients because subsequent FMT, preferably from a different donor, should be offered*
403 *if the first FMT fails. One dose of FMT may be less effective in patients with severe or*
404 *pseudomembranous colitis and to achieve a desired effect, these patients could benefit from additional*
405 *doses. However, clinically, this issue may not be relevant because in practice CDI patients are not*
406 *routinely assessed for the presence of pseudomembranous colitis. Therefore, the clinical pathway for*
407 *these patients would remain similar to patients with other CDI types. Nevertheless, FMT in these*
408 *patients still appears to be better than placebo or antibiotics alone. Thus, FMT should be given for*
409 *different types of patients, regardless of their comorbidities or the type of CDI. As per the previous*
410 *iteration of the guidelines, the Working Party discussed that the only absolute contraindication for FMT*
411 *is the presence of anaphylactic food allergy.*

412 *In previous guidelines, there was a concern that FMT may cause harm in some types of patients,*
413 *including those who are immunocompromised or immunosuppressed, those with liver or kidney*
414 *disease or those with IBD. However, the evidence now suggests that the incidence of adverse events,*
415 *regardless of their severity, appears to be similar in different types of patients. Thus, the Working Party*
416 *agreed that FMT should still be considered as a treatment option for patients with comorbidities based*
417 *on its safety. Moreover, in the general population, the incidence of adverse events in patients who*
418 *receive FMT does not appear to be different when compared to patients who receive placebo or anti-*
419 *CDI antibiotics. The Working Party would also like to stress that, due to the similar incidence of*
420 *occurrence in different treatment groups, GI events such as diarrhoea, nausea or bloating are probably*
421 *more likely to be associated with CDI itself and possibly some co-interventions (e.g. bowel preparation)*
422 *rather than with FMT treatment. Based on clinical experience of the Working Party members, adverse*

423 *events, none of which were captured by the included studies, may occasionally occur but their incidence*
424 *is very rare. A recent systematic review [66], which investigated the occurrence of adverse events after*
425 *FMT, reported that the overall rate of severe adverse events was 0.65% [95% CI 0.45-0.89]. The*
426 *population in this study included patients with IBD (4.8%) as well as*
427 *immunosuppressed/immunocompromised patients (8%). For specific adverse events, the incidence*
428 *was 0.19% [95% CI 0.09-0.31] for sepsis or sepsis-like conditions, 0.27% [95% CI 0.15-0.43] for*
429 *aspiration pneumonia and 0.20% [95% CI 0.09-0.34] for bowel perforation. Mild adverse events were*
430 *also relatively rare, with constipation reported in 1.03% [95% CI 0.77-1.33] of the patients, abdominal*
431 *pain in 1.66% [95% CI 1.33-2.03], nausea in 0.92% [95% CI 0.67-1.20], vomiting in 0.34% [95% CI 0.20-*
432 *0.52], flatulence in 0.70% [95% CI 0.49-0.94], and febrile episodes in 0.33% [95% CI 0.19-0.50] of*
433 *patients following FMT. In general, the majority of adverse events seem to occur either due to unsafe*
434 *FMT products or unsafe practice of administration, both of which are avoidable when careful donor*
435 *screening is in place and appropriate care is given to FMT recipients. Other events may be*
436 *unpreventable, e.g. diarrhoea due to glycerol being used as cryoprotectant, but these are relatively*
437 *minor and self-limiting.*

438 *The data from the excluded studies point out that the desired effects of FMT are generally long-lasting*
439 *with many patients experiencing no recurrence of CDI and no evidence of adverse events occurring*
440 *months to years after FMT. There are some patients who experience recurrence or relapse and the*
441 *Working Party discussed how these patients should be managed. It was concluded that current*
442 *evidence [23] and clinical practice support the treatment of these patients with either further FMT or*
443 *anti-CDI antibiotic therapy.*

444 *The Working Party discussed whether, due to an apparent benefit, FMT should be offered as a*
445 *treatment for patients with the first episode of CDI. The effectiveness for patients experiencing the first*
446 *or second CDI has recently been established in one RCT [13]. However, due to the fact that FMT is more*
447 *invasive, appears to be more expensive, grapples with challenges in donor recruitment, and that a*
448 *relatively high success rate can be achieved with anti-CDI antibiotics alone, this is not currently*
449 *recommended. Instead, this issue can be investigated in the future studies.*

450

Recommendations

1.1: Offer antibiotics alone in preference to FMT as an initial treatment for *C. difficile* infection (i.e. first episode).

1.2: Consider FMT for a first recurrence of *C. difficile* infection or as an adjunct to antibiotics in refractory *C. difficile* infection.

1.3: Offer FMT to all patients with two or more recurrences of *C. difficile* infection.

1.4: Ensure that FMT is preceded by the treatment of *C. difficile* infection with appropriate antibiotics for at least 10 days.

1.5: Offer FMT to all patients, regardless of health status, except those with a known anaphylactic food allergy.

1.6: Offer one or more FMT after initial clinically assessed FMT failure.

Good practice points

GPP 1.1: Consider FMT earlier than after second *C. difficile* infection recurrence for patients with severe, fulminant or complicated *C. difficile* infection who are not responding to antibiotic therapy.

GPP 1.2: If FMT was given via endoscopy, ensure that immediate post-endoscopic management after administration is in line with any local protocols.

GPP 1.3: Inform patients about the short-term adverse events, in particular the possibility of self-limiting gastrointestinal symptoms and that serious adverse events are rare.

GPP 1.4: Inform Inflammatory Bowel Disease patients with *C. difficile* infection about a small risk of exacerbation of their condition after FMT.

GPP 1.5: Follow-up the FMT recipients for at least eight weeks to establish its efficacy and adverse events.

GPP 1.6: Do not test for cure by absence of *C. difficile* after FMT, unless the patient has persistent *C. difficile* infection symptoms or is suspected to have relapsed.

GPP 1.7: Consider investigation for alternative causes for symptoms in patients who fail to respond to anti- *C. difficile* infection treatment including FMT.

451

452 **4.2 Recipient factors influencing the outcome of FMT for patients with CDI**

453 The evidence above demonstrates that FMT is generally effective in the majority of individuals
454 regardless of their health status. Despite this, there are still patients in whom FMT fails. Risk factors
455 for CDI recurrence after FMT are poorly understood, but certain patient characteristics such as
456 advanced age, female sex and some medications have been proposed as potential predictors for
457 failure [67]. There may also be some additional modifiable factors which could be optimised before
458 FMT is given and these have not yet been explored. Despite some studies reporting some patient
459 characteristics as risk factors, the results have been mostly inconsistent. Additionally, there remain
460 concerns about the safety of FMT for some patients. Underlying vulnerabilities such as older age and
461 the effect of some medications could potentially increase individual's risk of severe adverse events
462 associated with FMT. Previous BSG/HIS guidelines [3] did not identify any risk factors for CDI
463 recurrence other than post-FMT antibiotics. The guidelines also found very little evidence that would
464 demonstrate the safety of FMT in more vulnerable populations. As a result, the guidelines
465 recommended caution when administering FMT to people with certain conditions such as
466 immunosuppression or liver disease and suggested that antibiotic therapy should be avoided or
467 delayed when possible.

468 **Demographic factors**

469 *Age*

470 *Effect on success rates:* There was moderate evidence which suggested that this does not influence
471 the effectiveness of FMT [19-23,26-28,37-40,44,68,69].

472 *Effect on adverse events:* There was weak evidence which suggested that adverse events are similar
473 across all age groups [68].

474 *Sex*

475 *Effect on success rates:* There was moderate evidence which suggested that this does not influence
476 the effectiveness of FMT [19-21,23,26-28,37-40,44].

477 *Effect on adverse events:* There were no studies.

478 *Body mass index*

479 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
480 effectiveness of FMT [19,39].

481 *Effect on adverse events:* There were no studies.

482 **Factors associated with CDI**

483 *Number of CDI episodes before FMT*

484 *Effect on success rates:* There was moderate evidence which suggested that this does not influence
485 the effectiveness of FMT [19-21,23,28,38,44,69].

486 *Effect on adverse events:* There were no studies.

487 *Hospitalisation due to CDI*

488 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
489 effectiveness of FMT [19,38].

490 *Effect on adverse events:* There were no studies.

491 *Antibiotics used for treatment of CDI before FMT*

492 *Effect on success rates:* There was weak evidence which suggested that these do not influence the
493 effectiveness of FMT [19,22,39,40,69].

494 *Effect on adverse events:* There were no studies.

495 *C. difficile strain*

496 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
497 effectiveness of FMT [21,23,41].

498 *Effect on adverse events:* There were no studies.

499 *Healthcare-acquired CDI*

500 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
501 effectiveness of FMT [20].

502 *Effect on adverse events:* There were no studies.

FMT guidelines: main document.

503 **Other risk factors**

504 *Use of Proton Pump Inhibitors and other anti-secretory medications*

505 *Effect on success rates:* There was moderate evidence which suggested that these do not influence
506 the effectiveness of FMT [19,20,22,23,26,28,37,38,40,41].

507 *Effect on adverse events:* There were no studies.

508 *Use of corticosteroids preceding the administration of FMT*

509 *Effect on success rates:* There was weak evidence which suggested that these do not influence the
510 effectiveness of FMT [40].

511 *Effect on adverse events:* There were no studies.

512 *Use of lactulose preceding the administration of FMT*

513 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
514 effectiveness of FMT [40].

515 *Effect on adverse events:* There were no studies.

516 *Probiotic use preceding the administration of FMT*

517 *Effect on success rates:* There was weak evidence which suggested that these do not influence the
518 effectiveness of FMT [19,22].

519 *Effect on adverse events:* There were no studies.

520 *Non-CDI antibiotic use preceding the administration of FMT*

521 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
522 effectiveness of FMT [23,26,40].

523 *Effect on adverse events:* There were no studies.

524 *Use of narcotics preceding the administration of FMT*

525 *Effect on success rates:* There was weak evidence which suggested that these do not influence the
526 effectiveness of FMT [39].

527 *Effect on adverse events:* There were no studies.

528 *Hospitalised at or before FMT*

529 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
530 effectiveness of FMT [22,26,28,39].

531 *Effect on adverse events:* There were no studies.

532 *Blood biomarkers*

533 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
534 effectiveness of FMT [20,28,51]. However, one study [51] reported a higher risk of recurrence of CDI
535 in patients with zinc deficiency as well as a beneficial effect for zinc-deficient patients who were given
536 zinc supplements.

537 *Effect on adverse events:* There were no studies.

538 *Other risk factors*

539 *Effect on success rates:* There was weak evidence which suggested that these do not influence the
540 effectiveness of FMT [27,38,41,69].

541 *Effect on adverse events:* There were no studies.

542 *Upon reviewing the above evidence, the Working Party agreed that there are currently no identified*
543 *factors which affect the effectiveness of FMT. There may be some characteristics of CDI infection that*
544 *may result in FMT being less effective; however, as was highlighted in a previous section, FMT is still*
545 *more effective than standard antibiotics and placebo. Adverse events were assessed only for patients’*
546 *age and the evidence suggested that age had no effect. The Working Party agreed that the paucity of*
547 *studies reporting adverse events for patients with different characteristics likely represent the lack of*
548 *effect of these characteristics on the incidence and severity of adverse events. Based on these*
549 *conclusions, the Working Party agreed that FMT should not be declined or delayed based on any*
550 *patient- or CDI-related characteristic.*

551 *Additionally, the Working Party agreed that further studies investigating the effect of non-modifiable*
552 *risk factors (e.g. age, sex, etc.) are not necessary because the existing studies suggest that these factors*
553 *are not likely to influence the effectiveness or adverse events of FMT to the point where antibiotics*
554 *and/or other therapies should be considered as an alternative. As such, future studies should focus on*
555 *investigating modifiable risk factors which can be corrected before FMT is given so that its outcomes*
556 *are optimised. A recent review [70] identified possible recipient factors which facilitated donor*
557 *microbiota engraftment, including genetics, inflammation status and environmental factors (e.g. diet).*
558 *Further studies are needed to identify if these factors can influence clinical outcomes of FMT.*

Recommendations
2.1: Do not refuse or delay FMT therapy due to any recipient risk factors e.g. age over 75 years old, except for patients with known anaphylactic food allergy.
Good practice points
GPP 2.1: none

559

560 **4.3 Donor factors influencing the outcome of FMT for patients with CDI**

561 A robust donor screening programme is an essential part of FMT services to ensure safety for FMT
562 recipients. Donor recruitment is challenging; using standard criteria applied in many FMT services to
563 ensure safety and efficacy, one recent study reported that only 1.7% of prospective candidates
564 qualified as suitable donors [71]. Moreover, the study reported that due to a lengthy screening process
565 as many as 39% of the candidates were lost to follow-up even before their suitability was established.
566 The reluctance of the public to donate their stool is also well documented and seems to stem from
567 the social perception of stool, the lack of awareness of the importance of donation, and the logistic
568 difficulties in collection and transport of the stool [72]. Evidently, there is a need for a pragmatic
569 approach for the recruitment and screening of potential donors.

570 The primary aim of donor screening is mitigating risk of pathogen transmission via FMT. A secondary
571 aim of donor screening is to exclude potential donors who may have an ‘aberrant/adverse’ gut
572 microbiome. While the complexity and relative novelty of exploration of the gut microbiome means
573 that there is no clear agreed definition of what a ‘healthy’ or ‘unhealthy’ gut microbiome is [73], either
574 compositionally or functionally, there is the theoretical potential for transmission of gut microbiome
575 traits (and therefore potential for transmission of risk for diseases with a link to the gut microbiome)
576 via FMT. There are also some studies that include microbiome sequencing and other approaches to

577 try and find which bacteria transplanted from donor to recipient are associated with success [74,75].
578 So far, it has been difficult to define a core set of bacteria or functions underlying a good donor or
579 successful FMT. At the moment, there is little evidence which allows FMT services to define a healthy
580 microbiome which is most optimal for donation. Previous BSG/HIS guidelines [3] acknowledged that
581 research into donor factors is lacking. Therefore, the guidelines recommended a general approach
582 that all healthy adults under 60 years of age with BMI under 30kg/m² could be potential candidates
583 for donor screening. The recommendations then focused on an initial screening using a health and
584 travel questionnaire, followed up by a battery of laboratory testing of blood and stools to further
585 ensure the safety of FMT material. The guidelines also recommended regular re-assessment of donors
586 to ensure continuing safety. Since the guidelines were published, more evidence has become
587 available, especially around the experience of donor screening and the retention of possible donors.
588 The emergence of the COVID-19 pandemic also raised questions whether prospective donors should
589 be tested for other, non-gastrointestinal pathogens, to ensure the safety of recipients.

590 *Related vs not related donor*

591 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
592 effectiveness of FMT [22,24,52].

593 *Effect on adverse events:* There were no studies.

594 *Age of the donor*

595 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
596 effectiveness of FMT [23,27].

597 *Effect on adverse events:* There were no studies.

598 *Sex of the donor*

599 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
600 effectiveness of FMT [23].

601 *Effect on adverse events:* There were no studies.

602 *Amount of stool produced*

603 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
604 effectiveness of FMT [27].

605 *Effect on adverse events:* There were no studies.

606 *Microbiome composition of the donor*

607 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
608 effectiveness of FMT [27].

609 *Effect on adverse events:* There were no studies.

610 *The Working Party reviewed the above evidence and concluded that it is likely that routinely measured*
611 *donor factors do not influence the effectiveness of FMT for treatment of CDI. The Working Party agreed*
612 *that the use of universal donors is the most practical and cost-effective way to obtain donor stools. The*
613 *previous practice of using related donors, which in early days before stools banks existed were the*
614 *most reliable source of donor stools, is now outdated and should be avoided. There is no established*
615 *evidence that stools from a related donor influences the effectiveness of the FMT, but there may be*
616 *logistical difficulties and potentially additional costs related to donor screening. There is also a concern*
617 *that stool microbiota may be less diverse in these donors. As a related donor may cohabit with a*

618 *recipient, the overlap of environmental factors with the patient (e.g. diet) may affect their gut*
619 *microbiome and the success of FMT.*

620 *There were no studies which investigated whether the donor factors affected the incidence or severity*
621 *of adverse events, but the members agreed that, apart from the composition of the microbiota, they*
622 *are not likely to influence the effectiveness of FMT. As mentioned above, some studies demonstrate*
623 *that the composition of microbiota of the donor stool may predict the success or failure of FMT [74,75],*
624 *but none of these studies met the inclusion criteria for these guidelines. The Working Party stressed*
625 *that wherever donor factors have been investigated, this was done in situations in which all donors*
626 *were screened for possible transmissible diseases and where safety of FMT material was established.*
627 *Therefore, they stated that screening of all donors must remain in place to ensure the safety of FMT*
628 *recipients. All donors should also be re-screened regularly to ensure ongoing safety.*

629 **Rationale for recommendations on overall approach to donor screening**

630 The Working Party agreed a robust donor screening procedure remains mandatory. As per the original
631 version of these guidelines, the screening should continue to comprise a questionnaire, to identify risk
632 factors for an aberrant microbiome and pathogen carriage, and laboratory-based testing for pathogen
633 detection. This should be an ongoing process that is repeated at appropriate intervals.

634 The Working Party discussed the reported FMT complications since the last guidelines which might
635 influence updates in the recommended donor screening protocols. From one perspective, there have
636 been a number of reported cases of infection post-FMT apparently related to pathogen transmission
637 which may have been mitigated by additional donor screening processes, including *C. perfringens* [76],
638 atypical enteropathogenic *E. coli* [77], and Shiga toxin-producing *E. coli* [78]. It is also important to
639 highlight the well-publicised case of FMT-related infection transmission in two immunosuppressed
640 patients who developed bloodstream infection after transmission of *E. coli* carrying an extended-
641 spectrum beta-lactamase (ESBL) via FMT, leading to one death [79,80]. There had been considerable
642 concern since the emergence of SARS-CoV-2 regarding its potential for transmission via FMT
643 (particularly related to its potential route of entry via the luminal tract, and well-described GI
644 symptoms related to infection), and rapid consensus updates to donor screening were introduced to
645 mitigate risk [81]. However, despite this theoretical risk, there are no reported cases of FMT-related
646 SARS-CoV-2 transmission described, to the knowledge of the Working Party. Since the last guideline,
647 there has been an increased period of time for reporting of registry data and of prospective case series.
648 Overall, FMT for rCDI appears safe with several years of follow-up post-treatment; there have been
649 very few cases of infection potentially attributable to FMT, and very low rates of new diseases which
650 might feasibly be attributable to FMT [23,36,54,58-62,64-66]. There is a need to strike an appropriate
651 balance between screening practices that are robust enough to mitigate the potential risks of
652 providing FMT, whilst allowing sufficient pragmatism. Overly stringent screening focused on
653 theoretical risk of every possible pathogen risks making the process impossible to comply with.

654 Regarding the recommended donor history/questionnaire, the Working Party provided some updates
655 to this compared to the original version of this guideline (Box 1). For instance, the assessment for risk
656 factors for blood-borne viruses has been updated to be consistent with those from UK Blood and
657 Transplant. The Working Party noted that FMT services in certain settings aimed to recruit donors
658 from within blood donation services, given the degree of overlap in assessment between blood and
659 stool donation, although no such approach was currently being undertaken within the UK. Additional
660 assessments have now been recommended, e.g. enquiring about recent cold sores, anal ulcers and/or

661 persistent pruritus ani, to screen for organisms that colonise the oral, rectal or perineal mucosa,
662 including Herpes simplex virus, pinworm and Mpox (previously monkeypox) virus. Of note, the
663 Working Party discussed that while a health questionnaire assessment is mandatory, it is beyond the
664 scope of the committee to mandate specific content or specific exclusion criteria, and Box 1 represents
665 recommendations based upon suggested best practice rather than compulsory questions.
666 Questionnaire content and clinical interpretation of responses should be discussed and agreed at a
667 local level following a robust risk assessment.

668 Laboratory-based blood screening of potential donors remains mandatory (Box 2). The Working Party
669 discussed that while a number of the pathogens listed in Box 2 are not recognised to transmit via the
670 faeco-oral route (being predominantly blood-borne pathogens), and the theoretical risk of them being
671 transmitted via FMT being therefore low, there was still justification to screen for them out of a
672 principle of caution. The Working Party again discussed and upheld their recommendation regarding
673 Epstein-Barr virus (EBV) and Cytomegalovirus (CMV) testing being only recommended where there is
674 the potential that the FMT prepared from that donor will be administered to immunosuppressed
675 patients at risk of severe infection. Of interest, recent evidence suggests that only a very small
676 proportion (approximately 1%) of CMV IgG or IgM positive donors have detectable stool CMV DNA on
677 PCR, and no CMV IgM positive donors or those with stool CMV DNA have infectious virus on cell culture
678 [82]. Nevertheless, this recommendation has also been upheld on the principle of an abundance of
679 caution. While the Working Party recommended consideration of a set of general/metabolic blood
680 tests for donors, they did not set specific limits/thresholds for values. The examples were discussed
681 of a donor with, for instance, incidental marked anaemia or raised CRP as being at high risk of having
682 significant undiagnosed disease which may impact the gut microbiome, and therefore being
683 unsuitable for material donation.

684 The Working Party discussed the need to update stool pathogen screening compared to the last
685 version of the guideline (Box 3). In one respect, they acknowledged the need to recommend additional
686 screening, with faecal SARS-CoV-2 being of relevance given its potential for faecal-oral transmission,
687 as discussed above. The Working Party recognised that a global consensus document designed for
688 European practice developed at the height of the COVID-19 pandemic had recommended SARS-CoV-
689 2 screening of each donated stool sample [81]. The Working Party concluded that while an argument
690 could be made for continuing with this approach based on risk assessment at present, the currently
691 evolving risk landscape related to SARS-CoV-2 (related to a number of factors, including national
692 COVID-19 vaccination roll out) may mean that a modified protocol for SARS-CoV-2 screening may
693 become appropriate over the lifetime of this guideline. Similarly, the Working Party noted a report of
694 atypical enteropathogenic *E. coli* transmission related to FMT, and as such felt that more considered
695 screening for this in donors was justified [77]. The Working Party also discussed that new evidence
696 had emerged since the last version of the guidelines that suggested against certain GI pathobionts
697 being transmitted via FMT. In particular, a Danish FMT service recently described 13 out of 40 donors
698 as being *H. pylori* stool antigen positive, but that 26 FMTs administered from five positive donors had
699 not resulted in any recipients becoming *H. pylori* stool antigen positive at a median of 59 days [83].
700 While these data do not support the need for *H. pylori* stool antigen being part of screening, the
701 Working Party also discussed the different risk burden that theoretical *H. pylori* transmission might
702 have in the UK versus in the Far East, given its association with gastric cancer. It was noted that there
703 are recent data demonstrating transmission of *Blastocystis* via FMT, but that this did not influence
704 success of FMT as treatment for rCDI, and it was not associated with any gastrointestinal

705 symptomatology over months of follow-up, suggesting no need to intensify donor screening for this
706 organism [84].

707 The Working Party noted recent literature exploring the impact of FMT upon the gut microbiota
708 dynamics of potentially pro-carcinogenic bacteria. This topic first came to light from a study of 11
709 paediatric rCDI patients (of whom six had underlying IBD), in whom four patients were found to have
710 sustained acquisition of procarcinogenic bacteria post-FMT, after transmission from colonised donors.
711 It was also noted that two patients experienced clearance of such bacteria after FMT from a negative
712 donor [85]. Using full genome sequencing, one of these patients acquiring pro-carcinogenic bacteria
713 was shown to have durable donor-to-recipient transmission of *E. coli* with the colibactin gene (*clbB*),
714 which has been associated with colonic tumours [86]. A further retrospective study [87] analysed stool
715 metagenomes of matched pre- vs post-FMT samples from 49 rCDI patients, together with their
716 matched donors. This showed higher prevalence and abundance of potentially pro-carcinogenic
717 polyketide synthase-positive (pks+) *E. coli* in the gut microbiome of rCDI patients compared to their
718 healthy donors, and that the pks status of the post-FMT gut microbiome related to the pks status of
719 the donor being used (with pks being negative in five out of eight of their donors at all time points
720 sampled and detected in overall low levels otherwise). More specifically, persistence (eight out of nine
721 patients) or clearance (13/18 patients) of pks+ *E. coli* in pks+ patients correlated to pks in the donor
722 ($p = 0.004$). While these data are of interest, the Working Party concluded that the small number of
723 publications on this topic, unclear understanding of the true potential causative procarcinogenic
724 nature of the bacteria being studied, and overall reassuring safety profile of FMT meant that there
725 was no current clinical indication for routine metagenome screening for such bacteria or their genes
726 as part of donor screening. Additionally, since the durability of engraftment of donor strains after a
727 single FMT is variable but may be only several months in the case of a reasonable proportion of taxa
728 [88], the real procarcinogenic risk could be even lower than previously suggested, should bacteria with
729 these gene cassettes be those with limited colonisation duration. Further studies within this field
730 should be undertaken and results monitored. The Working Party noted that FMT for rCDI is often being
731 used in an older and frail population for whom the risk-to-benefit ratio of FMT is being considered
732 over a fairly short period, i.e. patients with limited alternate therapeutic options, with the aim of
733 minimising further hospital admissions. This ratio would be different in the context of younger
734 patients, where FMT was used on a more exploratory basis, and this may influence the importance of
735 considering the potential future role for screening for such bacteria.

736 The Working Party also noted that a number of studies had proposed using stool metagenomics as a
737 tool to assess stool donors, and proposed a variety of ecological or taxonomy-based metrics to select
738 out and stratify potentially 'ideal' donors [89]. Discussions within the Working Party concluded that
739 while this was of research interest, there was no justification for use of any assessment of this nature
740 as part of the donor screening/selection process at present. It was also observed that a small number
741 of studies had suggested a potential role for additional modalities of laboratory assessment as part of
742 donor screening; for instance, one study observed a trend towards increased gastrointestinal
743 symptoms post-FMT for rCDI after receipt of FMT from a donor with positive small intestinal bacterial
744 overgrowth, as assessed by positive lactulose breath test [90]. Again, the Working Party felt that while
745 this was of interest and supported future research, there was no current justification for this to be
746 incorporated into the donor screening process.

747 As per their discussions regarding the health questionnaire, the Working Party felt that it was beyond
748 the scope to mandate or exclude specific laboratory tests. Thus, the lists given in Boxes 2 and 3 reflect
749 suggested best practice but not compulsory testing. Laboratory-based testing and clinical
750 interpretation of results should be performed and agreed at a local level following a robust risk
751 assessment. Consistent with this, the Working Party noted the differences in laboratory donor
752 screening approaches that are reported in different regions globally. These are consistent with the
753 different prevalence and risk profile of different pathogens within each region [91]. As highlighted by
754 the case of COVID-19, the list of pathogens for which testing is undertaken needs to be constantly
755 reviewed, revised, and updated, based on local epidemiology and the latest evidence base. One area
756 that may require particular focus in this regard is the potential for emergence of new viral pathogens,
757 or rise in population prevalence of known viral pathogens with established faecal-oral transmission
758 e.g. poliovirus; the pertinence of this is highlighted by its detection within sewage water in London in
759 2022 [92,93].

760 The Working Party no longer supports the use of fresh FMT, because this approach does not allow for
761 direct testing of the donor stool used to manufacture FMT prior to administration and does not allow
762 for a period of quarantine in the case where additional donor testing may be required. Stool may be
763 processed into FMT immediately from donors who have passed baseline screening, but the Working
764 Party agreed that it should initially be quarantined. The Working Party also agreed that post-baseline
765 screening is required prior to release of FMT from quarantine to further mitigate the risk of pathogen
766 transmission. This post-baseline donor screening needs to take a safe but pragmatic approach, and
767 should cover two aspects:

- 768 • Bookend testing (Box 4) on donated stool to pick up acquisition of asymptomatic,
769 transmissible enteric pathogens during the donation period. Again, exact framework should
770 be defined by local policies and donation schedules, ideally following a robust risk assessment.
771 However, the Working Party recognised that there is a need to define the longest period the
772 donor can donate without testing to ensure that safety of the recipient is not compromised.
773 The Working Party agreed that this period should be no longer than four months. Bookend
774 testing could include testing of pooled aliquots of donor stool used for manufacturing FMT.
775 FMT could only be considered for release from quarantine once results have been
776 demonstrated to be clear.
- 777 • Bookend assessment and/or testing of donor to identify risk factors for pathogen acquisition
778 since baseline screening. The exact framework should be defined by local policies and
779 donation schedules, ideally following a robust risk assessment. It could involve a donor
780 questionnaire at each donation. FMT could only be considered for release from quarantine if
781 no specific risks were identified. FMT manufactured from donors identified as having acquired
782 risk factors during the donation period (such as unprotected sex with a new partner) would
783 need to undergo continued quarantine, and only be considered from release once the
784 appropriate repeat blood testing had been performed, and results were demonstrated to be
785 clear, ensuring that there had been a sufficient time period to allow for seroconversion.
786

Recommendations
3.1: Use FMT from universal donors in preference to related donors.

3.2: All potential donors must be screened by questionnaire or personal interview to establish risk factors for transmissible diseases and for factors that may adversely influence the gut microbiota (Box 1).

3.3: Blood and stool of all donors must be tested for transmissible diseases to ensure FMT safety (Box 2 and 3).

3.4: Discuss and agree the content of donor health questionnaire and laboratory testing at a local level, following a robust risk assessment.

3.5: Undertake ongoing review, revision and updating of the list of pathogens for screening/testing based on local epidemiology and the latest evidence.

3.6: Blood and stool of all donors must be re-screened periodically to ensure FMT safety.

3.7: Discuss and agree on the frequency of rescreening depending on local circumstances, but do not allow the bookend periods to be longer than four months.

3.8: Health assessment which captures the donor's ongoing suitability must be completed at each stool donation.

3.9: Ensure that FMT manufactured from donors is quarantined pending post-baseline screening and test results.

Good practice points

GPP 3.1: Follow suggested recommendations in Boxes 1-4 for conditions to be included in screening and health questionnaire.

787

788

Box 1: Recommended donor history questionnaire

Positive response to any of these questions may exclude further consideration regarding donation at that time, it may be appropriate to rescreen and consider for donation at a later time point based upon the particular scenario.

- Receipt of antibiotics and/or other medications potentially associated with gut microbiome perturbation, to include (but not limited to) proton pump inhibitor, statin, immunosuppression, chemotherapy, within the past three months.
- Known prior exposure to HIV and/or viral hepatitis, within the past three months.
- Known previous or latent tuberculosis.
- Use of illicit drugs, any tattoo, body piercing, needlestick injury, blood transfusion, acupuncture (outside of licensed or approved UK facilities), all within the previous four months.
- New or multiple (more than one) sexual partners within the past three months.
- Sex with somebody diagnosed with HTLV-1 and -2*.
- Previously living in areas with high prevalence of HTLV-1 and -2*.
- Receipt of a live attenuated vaccine within the past six months.
- Cold sores, anal ulcers, anal sores, pruritus ani within the past three months.
- Underlying gastrointestinal conditions/symptoms (e.g. history of IBD, IBS, chronic diarrhoea, chronic constipation, coeliac disease, bowel resection or bariatric surgery).
- Acute diarrhoea/gastrointestinal symptoms within the past two weeks.
- Family history of any significant gastrointestinal conditions (e.g. family history of IBD, or colorectal cancer).
- History of atopy (e.g. asthma, eosinophilic disorders).
- Any systemic autoimmune conditions.
- Any metabolic conditions, including diabetes and obesity.
- Any neurological or psychiatric conditions.
- History of chronic pain syndromes, including chronic fatigue syndrome and fibromyalgia.
- History of any malignancy.
- History of receiving growth hormone, insulin from cows, or clotting factor concentrates, or known risk of prion disease.
- History of receiving an experimental medicine (including vaccines) within the past six months.
- History of travel to tropical countries within the past six months.

*This question to be asked in centres where laboratory screening for HTLV-1 and -2 may be difficult; areas to focus on, but not limited to: Japan, the Caribbean, and South America.

Box 2: Recommended blood screening for donors

Pathogen Screening:

- Hepatitis A IgM
- Hepatitis B (HBsAg And HBcAb)
- Hepatitis C antibody
- Hepatitis E IgM
- HIV -1 and -2 antibodies
- HTLV-1 and -2 antibodies
- *Treponema pallidum* antibodies (TPHA, VDRL)
- Epstein-Barr virus IgM and IgG*
- Cytomegalovirus IgM and IgG*
- *Strongyloides stercoralis* IgG
- *Entamoeba histolytica* serology
- Cysticercal serology.

General/Metabolic Screening:

- Full blood count with differential
- Creatinine and electrolytes
- Liver enzymes and liver function tests.
- C-reactive protein

*EBV and CMV testing is recommended where there is the potential that the FMT prepared from that donor will be administered to immunosuppressed patients at risk of severe infection if exposed to CMV and EBV.

790

Box 3: Recommended stool screening for donors

- *Clostridioides difficile tcdB (toxin B) by PCR**
- *Campylobacter, Salmonella and Shigella, preferably by PCR*
- *Shiga toxin-producing Escherichia coli by PCR*
- *Other enteropathogenic E. coli, including, but not limited to Enteropathogenic E. coli (EPEC), by PCR*
- *Multi-drug resistant bacteria, including but not limited to, carbapenemase-producing Enterobacterales (CPE), extended-spectrum beta-lactamases (ESBL), and vancomycin resistant Enterococci (VRE) **.*
- *Stool ova, cysts and parasite analysis, including:*
- *Cryptosporidium and Giardia antigen or PCR*
- *Acid fast staining for Cyclospora, Isospora and Microsporidia.*
- *Norovirus and rotavirus PCR.*
- *SARS-CoV-2****
- *H. pylori stool antigen*****

* Glutamate Dehydrogenase (GDH) screening for possible *C. difficile* is not required or recommended; where performed, a positive GDH would not be sufficient to exclude a donor on the grounds of "positive *C. difficile* status".

**Methicillin-resistant *Staphylococcus aureus* (MRSA) is primarily recognised as a skin rather than a gastrointestinal organism; therefore screening is not universally recommended.

***Based upon current prevalence and laboratory expertise, a broader viral screen may be appropriate, ideally via multiplex panel, which may include e.g. sapovirus and poliovirus.

****Consider testing but not necessarily to exclude as a donor; may potentially wish to consider informing any recipients of *H. pylori* stool antigen-positive material, especially if recipients do not have a background of/are not currently *H. pylori* stool antigen positive.

791

Box 4: Post-baseline bookend screening stool microbiology

- *Clostridioides difficile tcdB (toxin B)*
- *Campylobacter, Salmonella and Shigella*
- *Shiga toxin-producing Escherichia coli*
- *Other enteropathogenic E. coli, including, but not limited to Enteropathogenic E. coli (EPEC)*
- *Microsporidia*
- *Norovirus and rotavirus PCR*
- *Cryptosporidium*
- *SARS-CoV-2*
- *Cyclospora*

792

793

794 **4.4 Preparation-related factors influencing the outcome of FMT for patients with CDI**

795 The effectiveness of FMT is presumed to depend upon transferred commensal microbiota being able
796 to engraft and proliferate in the recipient's colon. Thus, preservation of viability of relevant bacteria
797 during processing and storage is considered an important factor for FMT effectiveness. At the
798 moment, there is no standard approach to how donated stools are processed and stored, although it
799 has been suggested that variations in processing seem to have little influence on FMT effectiveness
800 for rCDI [94]. Due to the difficulties with donor recruitment, as well as an additional benefit of
801 quarantine of the donor stools, the desire is to keep FMT product for as long as possible. Longer
802 storage is also helpful if an interruption of donor supply or manufacturing process occurs, an example
803 of which was observed during the recent pandemic. There is a need for studies to determine the time
804 thresholds and optimal conditions in which FMT products need to be processed and used. The
805 determination of appropriate storage temperatures is also important for cost-effectiveness and
806 environmental considerations. Previous BSG/HIS guidelines [3] found mostly low-quality evidence in
807 relation to stool processing and storage. Based on standard practice, they recommended that stools
808 should be processed within six hours of defecation, stored at -80°C and used within six months of
809 processing.

810 *Fresh vs frozen stool*

811 *Effect on success rates:* There was moderate evidence which suggested that fresh and frozen stools
812 are equally effective [19,21,27,28,69].

813 *Effect on adverse events:* There was weak evidence which suggested that this does not influence the
814 effectiveness of FMT [29].

815 *Stool frozen at -20°C vs -80°C*

816 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
817 effectiveness of FMT [95].

818 *Effect on adverse events:* There were no studies.

819 *Lyophilised stool*

820 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
821 effectiveness of FMT [96-98].

FMT guidelines: main document.

822 *Effect on adverse events:* There was weak evidence which suggested FMT from lyophilised stools is
823 safe [97].

824 *Type of capsule*

825 *Effect on success rates:* There was weak evidence which suggested that this does not influence the
826 effectiveness of FMT [99].

827 *Effect on adverse events:* There were no studies.

828 *Processing time*

829 *Effect on success rates:* There was weak evidence which suggested that processing time for 150
830 minutes or longer does not influence the effectiveness of FMT [23,100].

831 *Effect on adverse events:* There were no studies.

832 *Storage time*

833 *Effect on success rates:* There was weak evidence which suggested that storing frozen products for
834 more than a year may not influence the effectiveness of FMT [23,95,100].

835 *Effect on adverse events:* There were no studies.

836 **Additional data from excluded studies**

837 *Anaerobic vs aerobic processing*

838 Two studies [94,101] reported that processing the stool samples under anaerobic conditions helps to
839 preserve microbial diversity [94] and viability [101]. On the other hand, one study [102] reported that
840 oxygen-free atmosphere was not necessary as long as the air above collected samples was removed.

841 *Effect of freezing*

842 Two studies [94,103] reported that freezing resulted in the loss of microbial diversity of the processed
843 stool samples. One study [103] reported that preparation in maltodextrin-trehalose solutions, storage
844 at -80°C standard freezer and rapid thawing at 37°C, provided the best results for the samples to retain
845 their revivification potential. The same solution was also reported to be effective in preserving
846 lyophilized samples [102].

847 *Emulsion process*

848 One study [104] showed that magnet plate emulsion (MPE) and Seward Stomacher Emulsion (SSE)
849 were similar in terms of maintaining microbial load.

850 *The Working Party concluded that there is currently no evidence to suggest that any preparation*
851 *factors in particular have an effect on the effectiveness or the incidence and severity of adverse events*
852 *of FMT for CDI. The literature from the excluded studies suggests that anaerobic process and freezing*
853 *the products has an effect on the viability of the microbiota, but there still seems to be an adequate*
854 *clinical effect regardless of these findings. In terms of efficacy, it is currently not known how long fresh*
855 *stools can be kept before they are processed and how long the FMT products can stored frozen.*
856 *However, the literature suggests that up to 180 minutes before processing starts and up to 12 months*
857 *of storage time is acceptable. Due to a relatively low impact on effectiveness, the Working Party*
858 *suggested that other factors such as overall safety, cost-effectiveness, convenience and environmental*
859 *concerns should be considered when preparing and storing FMT products. It is preferred that the*
860 *products are stored frozen because this provides convenience and additional safety as the delay in*
861 *administration allows more time to withdraw faeces if a donor becomes ill or tests positive for a*

862 *transmissible pathogen. Current practice in the UK is to start the processing of the stools as soon as*
863 *possible and no longer than within 150 minutes from the time of defecation to freezing. The Working*
864 *Party stated that there is no reason to challenge this practice. A threshold of 150 minutes is used with*
865 *in a number of studies, reflecting a balance between enough time to pragmatically transfer stool from*
866 *production by donor to an FMT laboratory, and yet a short enough time to mitigate alterations to*
867 *microbiome composition and functionality [105]. Either aerobic or anaerobic process is acceptable,*
868 *and in line with standard practice, cryoprotectant needs to be added. Additionally, the Working Party*
869 *reported that many centres in the UK and in mainland Europe have successfully used older products*
870 *and they concluded that the storage time of the frozen FMT products can be extended from six to 12*
871 *months and that the temperature of the freezer can be increased to -70°C to minimise the*
872 *environmental impact. It is currently not known whether the products could be stored at -20°C for up*
873 *to 12 months. The Working Party expressed concerns that storage at this temperature could result in*
874 *the loss of bacterial count and therefore recommended that this practice should be avoided until there*
875 *is more evidence to support it. Since the FMT needs time to be thawed, and there is a concern that the*
876 *microbial cultures will start to deteriorate, the Working Party recommended that this is done in an*
877 *ambient temperature and used within six hours of thawing. The Working Party also agreed that*
878 *thawing in water baths should be avoided because this may lead to contamination of FMT with*
879 *waterborne pathogens. The decision whether and how stools should be encapsulated or lyophilised*
880 *can be left to individual laboratories and will depend on the availability of the equipment.*

881 *The Working Party agreed to provide the advice in line of the recommendations from the previous*
882 *edition of the guidelines [3], which suggested, based on data from two systematic reviews, that 50g of*
883 *stool should be used for FMT. Previous edition of the guidelines also recommended that stools should*
884 *be mixed with 1:5 proportion to a diluent. However, the Working Party also agreed that these should*
885 *be considered as arbitrary figures, not currently supported by the evidence. Thus, FMT processing*
886 *facilities may choose to adjust this volume and proportion depending on a clinical need and the*
887 *availability of the donor stools. While the bottom limit for the volume of the stool to be used has not*
888 *yet been established, it has been acknowledged that some FMT centres use 30g of stools diluted to 1:6*
889 *ratio and this is still clinically effective.*

Recommendations
<p>4.1: Frozen FMT must be offered in preference to freshly processed products.</p> <p>4.2: Process stools aerobically or anaerobically – both methods are acceptable.</p> <p>4.3: Store prepared FMT products frozen at -70°C for up to 12 months.</p> <p>4.4: Add cryoprotectant such as glycerol to frozen FMT products.</p> <p>4.5: If capsules are used, these can be obtained from frozen or lyophilised faecal slurry.</p>
Good practice points
<p>GPP 4.1: Follow a standard protocol for stool collection.</p> <p>GPP 4.2: Start processing stools within 150 minutes of defecation.</p>

GPP 4.3: When possible, use at least 50g of stool in each FMT preparation.

GPP 4.5: Use sterile 0.9% saline as a diluent for FMT production.

GPP 4.5: Mix a minimum of 1:5 stool with diluent to make the initial faecal emulsion.

GPP 4.6: Consider homogenisation and filtration of FMT in a closed disposable system.

GPP 4.7: Consider thawing frozen FMT at ambient temperature and using it within six hours of thawing.

GPP 4.8: Avoid thawing FMT in warm water baths, due to the risks of cross contamination with *Pseudomonas species* (and other contaminants) and reduced bacterial viability.

GPP 4.9: Where glycerol is used as a cryopreservative, ensure it is at 10-15% final concentration of the prepared faecal material/slurry, with vortexing or other methods used to fully mix the cryopreservative into the material.

890

891 **4.5 Route of delivery and other administration factors influencing the outcome of** 892 **FMT for patients with CDI**

893 FMT can be delivered via upper and lower GI tract allowing it to reach different parts of the digestive
894 tract. Different delivery routes may have different rates of success but are also associated with
895 different risk and adverse events and may therefore not be suitable for all patients. There are also
896 other factors to consider during FMT administration. It is still not clear whether taking certain
897 medications or undergoing bowel preparation shortly before FMT could influence its outcome.
898 Previous BSG/HIS guidelines³ acknowledged that lower and upper GI administration have similar
899 success rates and adverse events and that both could be used if clinically appropriate. However, due
900 to the evidence suggesting lower efficacy associated with enema administration, this route of delivery
901 was only recommended when neither upper GI endoscopy, nor colonoscopy, would be considered
902 appropriate. Additionally, at the time of publication, there was a paucity of evidence regarding
903 encapsulated FMT, thus no recommendations were made regarding its use. Regarding other factors,
904 the evidence was low, but the guidelines suggested the use of bowel lavage and a single dose of
905 antimotility agent if FMT was to be delivered via lower GI route and the use of PPI and prokinetics
906 when FMT was via upper GI tract.

907 **Route of delivery**

908 *Colonoscopy vs other methods*

909 *Effect on success rates:* There was moderate evidence which suggested that a colonoscopic route may
910 be slightly more effective when compared to other administration routes combined
911 [19,21,25,26,38,39,96,106,107].

912 *Effect on adverse events:* There was weak evidence which suggested colonoscopic delivery has no
913 effect on adverse events [25,38,107].

FMT guidelines: main document.

914 *Enema vs other methods*

915 *Effect on success rates:* There was inconsistent evidence but it suggested that enema may be less
916 effective than other methods [26,108,109].

917 *Effect on adverse events:* There was very weak evidence which suggested that delivery via enema had
918 no effect on adverse events when compared to other administration routes,[42,109].

919 *Lower GI (unspecified) vs other methods*

920 *Effect on success rates:* There was very weak evidence which suggested no difference in effect when
921 comparing lower GI administration to other methods when combined [23,27,110].

922 *Effect on adverse events:* There was very weak evidence which suggested that delivery via lower GI
923 route had no effect on adverse events when compared to other administration routes [110].

924 *Upper GI vs other methods*

925 *Effect on success rates:* There was weak evidence which suggested no difference in effect when
926 comparing upper GI administration to other methods when combined [19,21,23,25-27,106,107,110].

927 *Effect on adverse events:* There was weak evidence which suggested that upper GI had no effect on
928 adverse events when compared to other administration routes [25,106,107,110].

929 *Oral capsules vs other methods*

930 *Effect on success rates:* There was weak evidence which suggested no difference in effect when
931 comparing oral capsules to other delivery methods when combined [21,26,38,96,106-110].

932 *Effect on adverse events:* There was weak evidence which suggested that oral capsules had no effect
933 on adverse events when compared to other administration routes [38,43,44,106,107,110].

934 *Bidirectional (upper and lower GI simultaneously) vs other methods*

935 *Effect on success rates:* There was very weak evidence which suggested a potential benefit when
936 comparing bidirectional method of FMT administration to other routes when combined [106].

937 *Effect on adverse events:* There was very weak evidence which suggested that bi-directional method
938 had no effect on adverse events when compared to other administration routes [106].

939 **Other factors**

940 *Location of delivery*

941 *Effect on success rates:* There was very weak evidence which suggested this did not influence the
942 effectiveness of FMT [39].

943 *Effect on adverse events:* There were no studies.

944 *Volume of FMT infused*

945 *Effect on success rates:* There was very weak evidence which suggested this did not influence the
946 effectiveness of FMT [26,39].

947 *Effect on adverse events:* There were no studies.

948 *PPI use*

949 *Effect on success rates:* There was very weak evidence which suggested this did not influence the
950 effectiveness of FMT [21].

FMT guidelines: main document.

951 *Effect on adverse events:* There were no studies.

952 *Antimotility agents used*

953 *Effect on success rates:* There was very weak evidence which suggested this did not influence the
954 effectiveness of FMT [21,39].

955 *Effect on adverse events:* There were no studies.

956 *Bowel lavage/prep used*

957 *Effect on success rates:* There was very weak evidence which suggested that this increases the
958 effectiveness of FMT [21,22,39].

959 *Effect on adverse events:* There were no studies.

960 *The Working Party discussed the above evidence and concluded that most routes of administration are*
961 *effective and where differences in effectiveness exist, they are subtle and not significant clinically. Thus,*
962 *any of these methods can be considered for FMT delivery. Based on the current evidence presented*
963 *here and in section 4.1, there is some concern that enema may be the least effective route and, as*
964 *such, it is preferred that whenever possible this should be avoided. Enema could still be considered as*
965 *a method of delivery when other options are not feasible. The Working Party observed that there was*
966 *no additional review regarding flexible sigmoidoscopy specifically; it was felt that given the nature of*
967 *this procedure, the efficacy of FMT via this route (and therefore recommendations pertaining to it)*
968 *would broadly be similar to colonoscopy, whilst recognising that colonoscopy allows more proximal*
969 *access to the colon and therefore a higher chance of material retention (and therefore potentially*
970 *success). For all routes of delivery, FMT appears to be equally safe, although there may be some*
971 *general risks associated with some delivery methods (e.g. endoscopy). Therefore, the Working Party*
972 *recommends that other factors, such as cost, patient preference, patient safety and environmental*
973 *concerns should be considered when choosing the route of FMT delivery. As an example, when*
974 *available, oral capsules could be offered to avoid unnecessary endoscopy to reduce potential*
975 *unnecessary harm, cost, and environmental impact [112]. However, the Working Party also noted that*
976 *the methods of encapsulation and the administration of encapsulated FMT to patients differ*
977 *considerably between the centres and more research is currently needed to determine the most*
978 *optimal regimen for this route of FMT delivery.*

979 *There is currently very little evidence that the site of delivery (within the GI tract) is important for FMT*
980 *effectiveness, and the Working Party agreed that the only important factor to consider is that FMT*
981 *must be delivered to a part of the colon where it can be retained. The members agreed that bowel*
982 *lavage/preparation, which is currently recommended for lower and upper GI delivery, should continue*
983 *in the light of the evidence suggesting a potential benefit. While the quality of the evidence is low, the*
984 *Working Party concluded that there is no benefit associated with the administration of PPI or other*
985 *anti-secretory medications nor antimotility medication. Therefore, PPI and other anti-secretory*
986 *medications are not necessary, and the Working Party advises against the use of antimotility agents*
987 *in line with general consensus that these may promote C. difficile toxin retention. Additionally, there*
988 *seems to be no effect associated with the volume of FMT used, although the Working Party*
989 *acknowledged that it is not the volume of the infusion but the amount and concentration of the stool*
990 *microbiota which is a determining factor and that the volume of faeces that needs to be infused will*
991 *also depend on other factors such as water and undigested food content, and the overall mass of the*

FMT guidelines: main document.

992 *stool. Future studies need to address the issue of a minimum effective dose that needs to be*
993 *administered for a successful FMT.*

994 *The Working Party also discussed the effect of anti-CDI antibiotics administered before FMT. Overall,*
995 *the Working Party noted that this was not supported by evidence, but, intuitively, recognised that there*
996 *is a need for a balance between sufficient anti-CDI antibiotics to minimise the burden of C. difficile prior*
997 *to administration of FMT and enough of a gap from the time antibiotics were given so that the risk of*
998 *damaging the new microbiome is minimised. The opinion of the Working Party was that 24 hours met*
999 *an appropriate balance.*

Recommendations

5.1: Choose any route of FMT delivery but, if possible, avoid enema.

5.2: When choosing the route of delivery, consider patient preference and acceptability, cost, and the impact on environment.

5.3: Consider enema for patients in whom other FMT delivery methods are not feasible.

5.4: There is no need to administer proton pump inhibitors or other antisecretory agents as a preparation for FMT.

5.5: Do not use antimotility agents as a preparation for FMT.

5.6: Use bowel preparation/lavage as a preparation for FMT.

5.7: After upper gastrointestinal tract administration is used, remove the tube following the flushing with water.

5.8: For patients at risk of regurgitation or those with swallowing disorders, avoid administration via upper gastrointestinal tract and deliver FMT via lower gastrointestinal tract instead.

5.9: If colonoscopic administration is used, ensure that the FMT is delivered to a site that will permit its retention.

Good practice points

GPP 5.1: Use polyethylene glycol preparation as a preferred solution for bowel lavage.

GPP 5.2: Consider using prokinetics (such as metoclopramide) prior to FMT via the upper gastrointestinal tract route

GPP 5.3: Follow best practice for prevention of further transmission of *C. difficile* when administering FMT to patients.

GPP 5.4: Consider a washout period of at least 24 hours between the last dose of antibiotic and treatment with FMT.

GPP 5.5: If upper gastrointestinal tract administration is used, nasogastric, nasoduodenal or nasojejunal tube, upper GI endoscopy or a permanent feeding tube may be used for delivery.

GPP 5.6: If upper gastrointestinal tract administration is used, administer no more than 100 mL of FMT to the gastrointestinal tract.

1000

1001 **4.6 Post-FMT factors influencing the outcome of FMT for patients with CDI**

1002 The risk factors for failure after administration of FMT, especially associated with the use of antibiotic
1003 therapy, started to emerge at the time the first BSG/HIS guidelines [3] were about to be published.
1004 The guidelines identified two studies which mentioned a potential link between the administration of
1005 non-CDI antibiotics in a short time after the FMT was given, and subsequently suggested that antibiotic
1006 therapy should ideally not be administered within the first eight weeks, and that an infectious disease
1007 specialist or a medical microbiologist should be consulted before the therapy is given. Other potential
1008 factors (e.g. diet or the use of probiotics) have also been discussed but their influence on FMT outcome
1009 remains unclear.

1010 *Use of non-CDI antibiotics*

1011 *Effect on success rates:* There was weak evidence which suggested a potential negative effect on the
1012 effectiveness of FMT [19,22,23].

1013 *Effect on adverse events:* There were no studies.

1014 *Other post-FMT factors*

1015 *Effect on success rates:* There was very weak evidence which suggested these do not influence the
1016 effectiveness of FMT [15,22,23].

1017 *Effect on adverse events:* There were no studies.

1018 *The Working Party agreed that there is a concern, although evidence is weak, that post-FMT, non-CDI*
1019 *antibiotics are a potential risk factor for FMT failure. As such, the Working Party recommended that*
1020 *for patients who require antibiotics, either long-term or within eight weeks of FMT, decision needs a*
1021 *formal assessment and a discussion with infection specialists or other appropriate specialist healthcare*
1022 *professionals. Currently, there is no reason to suspect that factors other than post-FMT antibiotics are*
1023 *risk factors for FMT failure.*

Recommendations

6.1: Wherever possible, avoid using non- *C. difficile* infection antibiotics for at least eight weeks after FMT.

6.2: Consult infection specialists, or other appropriate healthcare professional (e.g. gastroenterologists with experience of FMT) for advice whenever FMT recipients have an indication for long term antibiotics or have an indication for non- *C. difficile* infection antibiotics within eight weeks of FMT.

1024

1025 **4.7 Prophylactic FMT treatment to prevent *C. difficile* infection**

1026 Prophylaxis has become one area of interest in CDI more broadly and FMT is proposed as a potential
1027 therapy among other more traditional agents such as vancomycin, probiotics and bezlotoxumab [113].
1028 Although no studies were identified, the recognition has grown that CDI pathogenesis relates to gut
1029 microbiome disruption [114], therefore, there is a biological rationale that restoration of gut
1030 microbiome in vulnerable patients (e.g. patients with extensive exposure to antibiotics) via FMT could
1031 be a reasonable strategy to prevent CDI. Current debate also focuses on the definition of prophylaxis,
1032 specifically whether it should describe the prevention of recurrence or the prevention of new CDI in
1033 patients at risk. Previous BSG/HIS guidelines did not address this topic and thus, no recommendations
1034 were made.

1035 No studies were found in the existing literature which assessed the effect of prophylactic treatment
1036 on any of the included outcomes.

1037 **Additional data from excluded studies**

1038 The working party are aware of one ongoing trial which aims to evaluate the effectiveness of FMT
1039 (oral capsules) for the prevention of CDI in patients with history of CDI currently taking antibiotics
1040 [115].

1041 *Due to the lack of existing evidence the Working Party agreed that no recommendation can be made*
1042 *in favour or against prophylactic FMT. Instead, the Working party suggests that studies addressing this*
1043 *issue should be undertaken in the future to establish its feasibility and cost effectiveness.*

Recommendations
7.1: No recommendation
Good practice points
GPP 7.1: none

1044

1045 **4.8 FMT for non-CDI indications**

1046 In current clinical practice, FMT is only recommended for the treatment of recurrent CDI. Due to its
1047 success with CDI, FMT has been investigated for other diseases in which the gut microbiota has been
1048 implicated as a pathogenic agent. Previous BSG/HIS guidelines [3] reported that the majority of the
1049 studies investigating the effectiveness of FMT for non-CDI indications were of poor design and quality,
1050 and that only a small number of RCTs existed. The conditions which were reported in the previous
1051 guidelines included ulcerative colitis, irritable bowel syndrome, hepatic encephalopathy and
1052 metabolic syndrome, all of which showed a potential benefit. However, the lack of evidence regarding
1053 the choice of suitable patients and the most appropriate methods for FMT preparation and
1054 administration, led the Working Party to a decision not to recommend FMT in the context other than
1055 research. At the time the guidelines were published, it was also noted that there were ongoing trials
1056 for other conditions. Since then more diseases have now been linked with gut microbiome and a large
1057 number of systematic reviews and meta-analyses investigating the effectiveness of FMT for these
1058 conditions have become available.

FMT guidelines: main document.

1059 **Ulcerative colitis**

1060 *Effect on inducing remission:* There was moderate evidence which suggested FMT is effective in
1061 inducing remission in patients with UC [116-126].

1062 *Effect on adverse events:* There was strong evidence which suggested that FMT does not have an effect
1063 on the adverse events in this group of patients [116-118].

1064 *Additional data from excluded studies:* One study [127] reported that patients who received FMT and
1065 also followed an anti-inflammatory diet were more likely to achieve remission at eight weeks when
1066 compared to patients who received standard care.

1067 **Crohn's Disease**

1068 *Effect on success rates:* There was weak evidence which suggested FMT is effective in maintaining
1069 remission in patients with CD [129].

1070 *Effect on adverse events:* There were no studies.

1071 **Pouchitis**

1072 *Effect on success rates:* There was weak evidence which suggested that FMT has no effect on
1073 treatment of pouchitis [130-131].

1074 *Effect on adverse events:* There was weak evidence which suggested that FMT does not have an effect
1075 on the adverse events in this group of patients [130,131].

1076 **Irritable Bowel Syndrome**

1077 *Effect on success rates:* There was inconsistent evidence, and it was not possible to determine the
1078 effectiveness of FMT on achieving IBS remission [121,126,132-144].

1079 *Effect on adverse events:* There was strong evidence which suggested that FMT does not have an effect
1080 on the adverse events in this group of patients [132-134].

1081 *Effect on quality of life:* There was moderate evidence which suggested that IBS may improve quality
1082 of life for patients with IBS [132-134].

1083 *Additional data from excluded studies:* One review [140] suggested that while FMT may not show an
1084 overall advantage, the delivery via upper GI (via duodenoscopy or nasojejunal tube) may be more
1085 effective than the delivery via other methods.

1086 **Constipation**

1087 *Effect on success rates:* There was weak evidence which suggested FMT is effective in improving
1088 symptoms in patients with functional constipation [145].

1089 *Effect on adverse events:* There were no studies.

1090 *Effect on quality of life:* There was weak evidence which suggested FMT may improve the quality of
1091 life in patients with constipation[145].

1092 **Preventing hepatic encephalopathy in patients with decompensated cirrhosis**

1093 *Effect on success rates:* There was weak evidence which suggested FMT is effective in preventing
1094 hepatic encephalopathy [146,147].

1095 *Effect on adverse events:* There was weak evidence which suggested a possible negative effect of FMT
1096 on adverse events in this patient group [146].

FMT guidelines: main document.

1097 **Metabolic syndrome**

1098 *Effect on success rates:* There was weak evidence which suggested that FMT had no effect on
1099 improving biomarkers of metabolic syndrome [148,149].

1100 *Effect on adverse events:* There were no studies.

1101 *Additional data from excluded studies:* Four RCTs [150-153] reported no improvements in most of the
1102 markers associated with metabolic syndrome.

1103 **Obesity**

1104 *Effect on success rates:* There was moderate evidence which suggested no effect on reducing BMI in
1105 obese patients [154].

1106 *Effect on adverse events:* There were no studies.

1107 **Other conditions**

1108 Literature searches were conducted for other conditions for which it was known that FMT was
1109 investigated as a potential treatment options. No studies which fit the inclusion criteria were identified
1110 for the following conditions: autism spectrum disorder, multidrug resistance, immune checkpoint
1111 inhibitor colitis and graft vs host disease.

1112 The searches identified other conditions which were not searched for systematically but for which
1113 RCTs now exist. These included one study which reported that FMT may halt a progression of new-
1114 onset type 1 diabetes mellitus [155], one study which reported an increase in gut motility and some
1115 self-reported improvement in symptoms of Parkinson's disease [156], one study which reported no
1116 effect on controlling peripheral psoriatic arthritis [157], and one study which reported a reduced
1117 intestinal inflammation and an improvement in symptoms of progressive supranuclear palsy-
1118 Richardson's syndrome [158].

1119 **Data from excluded studies**

1120 *Infection/colonisation of gastrointestinal tract with multidrug resistant organisms*

1121 One RCT [159] reported no difference in decolonisation success when comparing patients who
1122 received FMT with antibiotics compared to patients who did not receive any treatment. A follow-up
1123 to this RCT [160] reported that the treatment with oral antibiotics temporary decreased the richness
1124 and diversity of gut microbiota but that after the administration of FMT, the proportion of
1125 *Enterobacteriaceae* decreased. One review [161] reported that decolonisation rates after FMT ranged
1126 from 20% to 90% for different types of microorganisms, but it reported that the spontaneous
1127 clearance was not considered in the studies.

1128 *Alcoholic hepatitis*

1129 One RCT [162] reported that, at 28 days and 90 days follow-up, patients who received FMT and
1130 antibiotics had higher rates of survival and that hepatic encephalopathy and ascites resolved in more
1131 patients in this group. Another RCT [163] reported that there was a lower rate of 90-day survival in
1132 patients who received prednisolone (34/60, 57%) when compared to those who received FMT (45/60,
1133 75%, $p = 0.044$).

1134 *The Working Party reviewed the above evidence and concluded that FMT cannot currently be*
1135 *recommended as a treatment of conditions other than CDI. The evidence indicates that patients with*
1136 *ulcerative colitis may benefit from FMT, however, at the moment, there is little information about the*
1137 *most effective protocols for the use of FMT in this condition and how its effectiveness and cost compare*
1138 *to other well-established treatment options. Most of the studies focused on the induction of remission*

FMT guidelines: main document.

1139 *in these patients but there is also a need for future studies to determine the role of FMT in maintaining*
1140 *remission. Some studies already identified that further FMT may be needed for achieving long-lasting*
1141 *effect [117,124,164-166]. The Working Party agrees with the recent consensus [167] of the experts*
1142 *who concluded that, at the moment, the studies are too small and methodologically heterogenous to*
1143 *determine the effectiveness of FMT for IBD, including ulcerative colitis, and that the risk of serious side*
1144 *effects, including exacerbation of IBD, cannot be ignored. As such, the Working Party agreed that FMT*
1145 *may be offered to patients with ulcerative colitis who are not suitable for the licenced treatment*
1146 *options or in whom these options have failed. There is also weak evidence which suggests that patients*
1147 *with other conditions, namely Crohn’s disease, IBS and constipation may benefit from FMT, but more*
1148 *research is required before any clinical decisions are made. For other conditions, including metabolic*
1149 *syndrome, autism spectrum, pouchitis, preventing hepatic encephalopathy, obesity and the treatment*
1150 *of multi-drug resistant microorganisms, further research is required to establish whether or not FMT*
1151 *is safe and effective. In the meantime, the Working Party agreed that FMT may be considered when*
1152 *the conventional treatment fails, and when the patients meet the eligibility criteria for compassionate*
1153 *use of FMT (described in the next section).*

Recommendations
8.1: Do not offer FMT routinely to patients with indications other than <i>C. difficile</i> infection.
8.2: Consider FMT on case by case basis for patients with ulcerative colitis in whom licenced treatment options have failed or for those who are not suitable for currently available treatments.
Good practice points
GPP 8.1: none

1154

1155 **4.9 Compassionate use of FMT**

1156 While clinical trials are a preferred option for accessing unlicenced medicinal products, this is not
1157 always possible. This may be because a patient may be too ill to enter a clinical trial, fails to meet some
1158 aspects of inclusion criteria, or that no trial is ongoing at the time the treatment is needed. For this
1159 reason, compassionate use programmes (also known as early access, or special access) were
1160 developed to provide access to unlicenced treatments [168]. These treatments may include products
1161 which are still in clinical development, or those that are already licenced in other countries. Example
1162 of compassionate use programmes include Expanded Access Program in the USA, Compassionate Use
1163 Program (for a group of patients with a specified condition) and Named Patient Program (NPP, for
1164 named patients) in the European Union (EU) and Early Access to Medicines (EAMS) in the UK [169].
1165 The EAMS scheme is available for manufacturers to apply for the early access to their products,
1166 however, another scheme The Supply of Unlicenced Medicinal Products (“specials”) allows the
1167 clinicians to request the unlicenced products in a manner similar to the EU’s NNP [170]. This scheme
1168 allows a supply of the medicinal products to the individual patients with “*special needs which a*
1169 *licenced product cannot meet*” [170] and also includes the off-label use of these products. In the
1170 section below, the term Compassionate Use Program was used to refer to the “specials” scheme as
1171 well as other similar programmes in other countries.

1172 Since publication of the last iteration of the guidelines, the range of medical conditions with a potential
1173 pathogenic link to a perturbed gut microbiome has continued to expand. Many of these conditions
1174 have no or limited treatment options. In many cases, the Working Party recognised that these
1175 remained associations, often without clear supporting mechanistic links that might deconvolute
1176 whether gut microbiome perturbation was a cause of the condition, consequence, or an
1177 epiphenomenon. A body of research has also explored whether FMT, alongside a conventional drug
1178 treatment, might augment the efficacy of that therapy, help to recover efficacy where this has been
1179 lost, or mitigate side effects of that medication. One prominent example of this scenario is cancer
1180 immunotherapy with immune checkpoint inhibitors (ICI), where early phase trial evidence suggests
1181 healthy donor FMT prior to anti-PD1 treatment for melanoma may boost efficacy in a subset of
1182 patients [171]. Further clinical trials demonstrated that FMT derived from anti-PD1 responders may
1183 be used to regain treatment response in certain melanoma patients who had become refractory to
1184 treatment [172,173], and also shows promise as an approach to potentially mitigate ICI-induced colitis
1185 in patients refractory to conventional immunomodulatory therapy [174].

1186 The Working Party discussed their clinical experience of considering potential suitability of FMT for
1187 patients with non-CDI medical conditions associated with perturbation of the gut microbiome. They
1188 felt that if all below three criteria were fulfilled, there were potential grounds for consideration of
1189 administration of FMT on a compassionate use basis.

- 1190 • There was a reasonable case from published literature to support a contribution of the gut
1191 microbiome to pathogenesis of the condition, and at least some published data relating to
1192 safety and efficacy of FMT in either a pre-clinical or clinical setting for this condition.
- 1193 • The patient had been unresponsive to/was not suitable for a range of conventional treatment
1194 options for their condition and had very limited treatment alternatives, which had already
1195 been utilised. The scenario in which this is envisaged is one in which the limited ability to
1196 provide further effective treatment of the condition may cause significant ongoing symptoms,
1197 significantly impair the patient's quality of life, and/or may risk progressive morbidity or even
1198 mortality for the patient.
- 1199 • The patient understood the treatment options that were available, including the potential
1200 risks and benefits of FMT (especially the potential for no benefit and/or complications related
1201 to the FMT), but was still willing to provide informed consent for FMT.

1202 However, the Working Party emphasised that a few additional criteria merited consideration. Firstly,
1203 it must be determined that a patient cannot be entered into ongoing relevant clinical trials, and
1204 potentially receive FMT instead via this pathway. Secondly, such cases should be considered in a
1205 multidisciplinary team (MDT) setting (including senior clinical representation from the specialist team
1206 referring the patient, and clinicians with experience in FMT, likely with a background in
1207 gastroenterology or microbiology/infectious diseases). The role of this MDT is to better clarify any
1208 prior experience of FMT within this setting, and/or the balance of risks and benefits from FMT versus
1209 alternative treatment options. Thirdly, there should be agreement as to what should be defined as
1210 success or failure of FMT in this particular scenario. There must also be a plan prior to treatment
1211 initiation, for a strategy regarding potential further FMT based upon the response to the initial
1212 therapy. Lastly, there should be comprehensive documentation/reporting of clinical data (and/or
1213 potentially stool and other biofluids collected from the patient for research, where such a resource

1214 exists) related to the outcome of this patient from FMT, to build knowledge and experience of the
1215 potential role for FMT within novel settings.

Recommendations
9.1: Consider offering compassionate use of FMT in non- <i>C. difficile</i> infection settings only when a patient cannot be entered into a clinical trial and after discussion and approval in a multidisciplinary team setting.
9.2: When offering compassionate use of FMT, the following conditions must be met: <ul style="list-style-type: none">• There is a biological rationale to justify consideration.• Patient is at risk of significant clinical compromise due to a limited alternative range of therapeutic options.• Patient understands the risks and benefits of FMT compared to other treatment options.
9.3: Prior to treatment, define what will be considered as a success or failure of FMT.
9.4: Prior to treatment, agree potential strategy for further FMTs based upon initial clinical success.
Good practice points
GPP 9.1: none

1216

1217 **4.10 Self-banking of stool for potential future autologous FMT**

1218 The Working Party members reported that, in the past, they have been contacted by other clinicians
1219 and by patients enquiring about banking their own stool with a view to potential future autologous
1220 FMT. One such scenario might be a patient who has been informed about the imminent need for
1221 medical treatment which might be expected to significantly disrupt their gut microbiome, i.e., a
1222 prolonged course of antibiotics that might risk CDI, or a patient due to undergo intestinal surgery,
1223 immunosuppression, etc.). The Working Party discussed the published literature regarding this
1224 approach, including clinical evidence that stool collected from patients prior to their haematopoietic
1225 cell transplantation (HCT) could safely be given as FMT to them post-HCT, with associated restoration
1226 of pre-morbid microbiome diversity and composition [175]. A further enquiry that the Working Party
1227 had received related to whether a person in entirely good health could be considered for stool banking
1228 in case the scenario arose whereby autologous FMT might become an appropriate treatment option
1229 at some point in the future based upon changes of their health status. This conceptually might be
1230 considered to have a degree of comparability to cord blood banking, for which there is an HTA-
1231 regulated structure in the UK [176].

1232 The Working Party recognised some of the challenges related to this, which have already been
1233 discussed elsewhere [177]. Firstly, there are uncertainties related to how much stool might optimally
1234 be stored (with associated resource issues, such as freezer capacity), and for how long (raising
1235 concerns about the long-term stability of a gut microbiome community when potentially frozen for a
1236 prolonged period). Given that many conventional potential healthy stool donors fail screening due to
1237 the stringency of the process, there is a reasonable likelihood that a significant proportion of those

FMT guidelines: main document.

1238 considering self-stool banking would also fail conventional screening. While the fact that the patients
1239 would be receiving autologous FMT may reduce health risks compared to unrelated donor stool, there
1240 are clear issues related to laboratory processing and storage of material, particularly from a regulatory
1241 perspective, if this does not reach the same status on pathogen screening as healthy donor faecal
1242 material conventionally prepared into FMT. Other outstanding issues related to the regulatory
1243 framework which might govern this process, and/or potential funding arrangements and cost
1244 effectiveness of such an approach. As such, the Working Party concluded that while self-stool banking
1245 was of potential interest, it could not be currently advocated. However, this can be considered as a
1246 concept for further studies.

Recommendations
10.1: Do not routinely self-bank stool from faecal material donated by patients or healthy people for potential future autologous FMT.
Good practice points
GPP 10.1: none

1247

1248 **4.11 Regulation and oversight of FMT**

1249 There is no agreed definition as to what constitutes FMT, nor its active pharmaceutical ingredient(s),
1250 not its mechanism of action. This leads to variability in how and what is classified as FMT, and how it
1251 should be regulated. Briefly, FMT is either a biological product (e.g. USA), human tissue product (e.g.
1252 Italy), medicinal product (e.g. UK), or medical procedure (e.g. Denmark) [178]. In the UK, FMT is
1253 considered an unlicensed medicinal product that may be prepared, prescribed, and administered to
1254 patients on a named basis under section 10 of the Medicines Act, 1968 [179] (“pharmacy exemption”),
1255 provided that defined conditions are met. These include that the medicinal product is prepared or
1256 dispensed in a hospital or health centre by, or under the supervision of, a pharmacist, and in
1257 accordance with a doctor’s prescription. This process is overseen by regional Specialist Pharmacy
1258 Services (SPS) Quality Assurance (QA). If FMT is prepared as an unlicensed medicinal product and is to
1259 be shipped to another hospital or health centre for administration, this requires a license to supply
1260 unlicensed medicinal products (“specials”) [170]. Licensed facilities are regulated and audited by the
1261 Medicines and Healthcare Products Regulatory Agency (MHRA). If FMT is used as part of a clinical trial,
1262 it is considered an Investigational Medicinal Product (IMP) and must be manufactured in a
1263 Manufacturer’s/ Importation Authorisation - MIA (IMP) - licensed facility adhering to Good
1264 Manufacturing Practice (GMP) [180]. Each batch should be released by a qualified person (QP) against
1265 an approved, trial specific, Investigational Medicinal Product Dossier (IMPD) prior to participant
1266 administration. Licensed facilities are regulated and audited by the MHRA, and all trials must have
1267 received Clinical Trials Authorisation (CTA), amongst other approvals, prior to participant recruitment.

Recommendations
11.1: Centres that manufacture and dispense FMT must adhere to any regulations applicable to the area in which they are located.
Good practice points

GPP 11.1: none

1268

1269

5. Further research

1270

As highlighted above, there are gaps in the evidence for almost every topic presented in these guidelines. While the list is not exhaustive, the Working Party made some recommendations for research which they thought represented current research priorities.

1271

1272

Research recommendations

RR 1: Studies which investigate the effectiveness and cost effectiveness of FMT for a first episode of *C. difficile* infection.

RR 2: Studies which investigate potentially modifiable patient risk factors which, if corrected, can optimise the outcome of FMT, e.g. genetics, gut microbiota composition or functionality (e.g. via metabolomics), immunological status.

RR 3: Studies which investigate donor characteristics that determine the success or failure of FMT.

RR 4: Studies which investigate preparation and storage times beyond those currently recommended.

RR 5: Studies which investigate the highest temperature at which FMT preparations can be stored and for how long.

RR 6: Studies which investigate the optimal methods for capsule preparation.

RR 7: Studies which investigate the best regimen for administration of oral capsules (i.e. how many, over how many days etc.).

RR 8: Studies which investigate the clinical utility, feasibility and cost effectiveness of prophylactic FMT.

RR 9: RCTs which establish the effectiveness and cost-effectiveness of FMT for induction of remission as well as the maintenance of remission of ulcerative colitis compared to licenced treatment options.

RR 10: Studies which compare different types of FMT protocols for the management of ulcerative colitis.

RR 11: RCTs which investigate the effectiveness and cost-effectiveness of FMT for treatment of constipation using well-established, objective outcome measures.

RR 12: Larger RCTs which establish the effectiveness and cost-effectiveness of FMT for the management of patients with Crohn's disease.

RR 13: Studies which establish which subgroups of irritable bowel syndrome patients may benefit from FMT.

RR 14: RCTs which establish the effectiveness and cost-effectiveness of FMT for treatment, management or prevention of other conditions, including metabolic syndrome, autism spectrum, pouchitis, hepatic encephalopathy and colonisation with multi-drug resistant microorganisms.

RR 15: Studies which evaluate the effectiveness, feasibility and cost-effectiveness of utilising self-bank stools for potential future autologous FMT.

RR 16: Studies which investigate whether microbiological screening of donors for pathogens with low prevalence in healthy individuals is needed/justified.

RR17: Studies which investigate whether FMT has a role in reducing antibiotic use and thus reducing the development of resistance to existing antibiotics.

RR18: Avoid producing duplicate reviews, i.e. where the evidence has recently been reviewed in a peer-reviewed journal and there is no new evidence to change the conclusions.

1273

1274

1275 6. Further considerations: next-generation FMT and novel 1276 microbiome therapeutics

1277 The Working Party discussed several microbiome therapeutics, which have evolved from FMT, and are
1278 at various stages of development and clinical trials. There are several different approaches being used,
1279 including full spectrum microbiome products (which have the most direct comparability with
1280 conventional FMT), as well as products involving particular microbiome components (e.g., spore-
1281 based therapies, or defined microbial consortia). At the time of writing, two microbiome therapeutics
1282 have been approved by the US FDA for prevention of CDI relapses, namely RBX2660/Rebyota (Ferring;
1283 a rectally-administered FMT-type product [8]), and SER-109/Vowst (Seres/Nestle; a purified spore-
1284 based product [9]); no such products have been licensed for the use in any non-CDI indication.

1285 The Working Party discussed their expectation that several early and late phase clinical trials involving
1286 such products were ongoing globally, and there was a reasonable expectation of applications for
1287 licensing for use within the UK within the lifespan of this guideline. If such licensing was granted, there
1288 would be clear implications for use of 'conventional' FMT within the UK. For instance, licensing of a
1289 microbiome therapeutic for use in recurrent CDI would potentially negate the ability to supply FMT
1290 under a UK specials license, given that FMT is an unlicensed medicinal product. This may potentially
1291 also impact upon the ability to use FMT within a UK research setting, where there is currently highly-
1292 active clinical and translational research activity.

1293 The Working Party concluded that there was a clear need for ongoing dialogue between entities
1294 developing novel microbiome therapeutics, academic and hospital centres providing FMT, and
1295 regulators to ensure no interruption at any point in provision of therapy to eligible CDI patients, and
1296 that clinical and translational FMT/microbiome therapeutics research in this field in the UK remains
1297 globally competitive.

FMT guidelines: main document.

1298 The Working Party concluded that the following topics are now resolved and should not be included
1299 for an update in the future editions of the guidelines:

- 1300 1. *Effectiveness of FMT for recurrent CDI vs anti-CDI antibiotics/placebo in general population.*
1301 This topic can be revisited if new therapies, more effective than current antibiotic treatment,
1302 become available. Topics in relation to patients with different conditions and factors related
1303 to CDI infections (e.g. severity, first occurrence) should still be investigated.
- 1304 2. *Non-modifiable recipient factors e.g. age.* Current evidence suggests that these factors do not
1305 reduce the effectiveness of FMT to the point where recommendations would change. Future
1306 studies need to focus on identifying modifiable recipient and donor factors, optimising FMT
1307 administration and preventing CDI recurrence after FMT.

1308

1309 **References**

1310 1. Craven L.J., McIlroy J.R., Mullish B.H. et al. Letter: intestinal microbiota transfer-updating the
1311 nomenclature to increase acceptability. *Aliment Pharmacol Ther.* 2020 Nov;52(10):1622-
1312 1623.

1313 2. van Nood E., Vrieze A., Nieuwdorp M., et al. Duodenal infusion of donor feces for recurrent
1314 *Clostridium difficile*. *New England Journal of Medicine.* 2013 Jan 31;368(5):407-15.

1315 3. Mullish B.H., Quraishi M.N., Segal J.P. et al. The use of faecal microbiota transplant as
1316 treatment for recurrent or refractory *Clostridium difficile* infection and other potential
1317 indications: joint British Society of Gastroenterology (BSG) and Healthcare Infection Society
1318 (HIS) guidelines. *Gut.* 2018 Nov 1;67(11):1920-41.

1319 4. Johnson S., Lavergne V., Skinner A.M. et al. Clinical practice guideline by the Infectious
1320 Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America
1321 (SHEA): 2021 focused update guidelines on management of *Clostridioides difficile* infection in
1322 adults. *Clin Infect Dis.* 2021 Sep 1;73(5):e1029-44.

1323 5. Cammarota G., Ianiro G., Kelly C.R. et al. International consensus conference on stool
1324 banking for faecal microbiota transplantation in clinical practice. *Gut.* 2019 Dec
1325 1;68(12):2111-21.

1326 6. Lamb C.A., Kennedy N.A., Raine T. et al. British Society of Gastroenterology consensus
1327 guidelines on the management of inflammatory bowel disease in adults. *Gut.* 2019 Dec
1328 1;68(Suppl 3):s1-06.

1329 7. National Institute of Health and Care Excellence. Faecal microbiota transplant for recurrent
1330 *Clostridioides difficile* infection. London: Medical technologies guidance [MTG71]; 2022.
1331 Available at: <https://www.nice.org.uk/guidance/mtg71>. [last accessed August 2023].

1332 8. Walter J, Shanahan F. Fecal microbiota-based treatment for recurrent *Clostridioides difficile*
1333 infection. *Cell.* 2023 Mar 16;186(6):1087.

1334 9. Jain N., Umar T.P., Fahner A.F. et al. Advancing therapeutics for recurrent *clostridioides*
1335 *difficile* infections: an overview of vovst's FDA approval and implications. *Gut Microbes.*
1336 2023 Jan-Dec;15(1):2232137.

1337 10. Baunwall S.M.D., Terveer E.M., Dahlerup J.F. et al. The use of Faecal Microbiota
1338 Transplantation (FMT) in Europe: A Europe-wide survey. *Lancet Reg Health Eur.* 2021 Jul
1339 19;9:100181.

1340 11. Martinez-Gili L., McDonald J.A.K., Liu Z. et al. Understanding the mechanisms of efficacy of
1341 fecal microbiota transplant in treating recurrent *Clostridioides difficile* infection and beyond:
1342 the contribution of gut microbial-derived metabolites. *Gut Microbes.* 2020 Nov
1343 9;12(1):1810531.

1344 12. Hvas C.L., Dahl Jørgensen S.M., Jørgensen S.P. et al. Fecal Microbiota Transplantation Is
1345 Superior to Fidaxomicin for Treatment of Recurrent *Clostridium difficile* Infection.
1346 *Gastroenterology.* 2019 Apr;156(5):1324-1332.e3.

1347 13. Baunwall S.M.D., Andreasen S.E., Hansen M.M. et al. Faecal microbiota transplantation for
1348 first or second *Clostridioides difficile* infection (EarlyFMT): a randomised, double-blind,
1349 placebo-controlled trial. *Lancet Gastroenterol Hepatol.* 2022 Dec;7(12):1083-1091.

1350 14. Cammarota G., Masucci L., Ianiro G. et al. Randomised clinical trial: faecal microbiota
1351 transplantation by colonoscopy vs. vancomycin for the treatment of recurrent *Clostridium*
1352 *difficile* infection. *Aliment Pharmacol Ther.* 2015 May;41(9):835-43.

1353 15. Hota S.S., Sales V., Tomlinson G. et al. Oral Vancomycin Followed by Fecal Transplantation
1354 Versus Tapering Oral Vancomycin Treatment for Recurrent *Clostridium difficile* Infection: An
1355 Open-Label, Randomized Controlled Trial. *Clin Infect Dis.* 2017 Feb 1;64(3):265-271.

- 1356 16. Kelly C.R., Khoruts A., Staley C. et al. Effect of Fecal Microbiota Transplantation on Recurrence
1357 in Multiply Recurrent *Clostridium difficile* Infection: A Randomized Trial. *Ann Intern Med.*
1358 2016 Nov 1;165(9):609-616.
- 1359 17. Rupawala A.H., Gachette D., Bakhit M. et al. Management of Severe and Severe/Complicated
1360 *Clostridioides difficile* Infection Using Sequential Fecal Microbiota Transplant by Retention
1361 Enema. *Clin Infect Dis.* 2021 Aug 16;73(4):716-719.
- 1362 18. Popa D., Neamtu B., Mihalache M. et al. Fecal Microbiota Transplant in Severe and Non-
1363 Severe *Clostridioides difficile* Infection. Is There a Role of FMT in Primary Severe CDI? *J Clin*
1364 *Med.* 2021 Dec 13;10(24):5822.
- 1365 19. Alghamdi A.A., Tabb D. Fecal microbiota transplantation after oral vancomycin for recurrent
1366 *Clostridium difficile* infection. *Infectious Diseases in Clinical Practice.* 2019 Nov 1;27(6):356-9.
- 1367 20. Kachlíková M., Sabaka P., Koščálová A. et al. Comorbid status and the faecal microbial
1368 transplantation failure in treatment of recurrent *Clostridioides difficile* infection—pilot
1369 prospective observational cohort study. *BMC infectious diseases.* 2020 Dec;20:1-9.
- 1370 21. Peri R., Aguilar R.C., Tüffers K. et al. The impact of technical and clinical factors on fecal
1371 microbiota transfer outcomes for the treatment of recurrent *Clostridioides difficile* infections
1372 in Germany. *United European Gastroenterol J.* 2019 Jun;7(5):716-722.
- 1373 22. Tariq R., Saha S., Solanky D. et al. Predictors and Management of Failed Fecal Microbiota
1374 Transplantation for Recurrent *Clostridioides difficile* Infection. *J Clin Gastroenterol.* 2021 Jul
1375 1;55(6):542-547.
- 1376 23. Terveer E.M., Vendrik K.E., Ooijevaar R.E. et al. Faecal microbiota transplantation for
1377 *Clostridioides difficile* infection: Four years' experience of the Netherlands Donor Feces Bank.
1378 *United European Gastroenterol J.* 2020 Dec;8(10):1236-1247.
- 1379 24. Watts A., Sninsky J.A., Richey R.R. et al. Family Stool Donation Predicts Failure of Fecal
1380 Microbiota Transplant for *Clostridioides difficile* Infection. *Gastro Hep Advances,* 2022;
1381 1(2):141-146.
- 1382 25. Ponte A., Pinho R., Mota M. et al. Fecal microbiota transplantation in refractory or recurrent
1383 *Clostridium difficile* infection: a real-life experience in a non-academic center. *Rev Esp Enferm*
1384 *Dig.* 2018 May;110(5):311-315.
- 1385 26. Dogra S., Oneto C., Sherman A. et al. Long-Term Efficacy and Safety of Fecal Microbiota
1386 Transplantation for *C. difficile* Infections Across Academic and Private Clinical Settings.
1387 *Journal of Clinical Gastroenterology.* 2022 Oct 14:10-97.
- 1388 27. Yoon H., Shim H.I., Seol M. et al. Factors Related to Outcomes of Fecal Microbiota
1389 Transplantation in Patients with *Clostridioides difficile* Infection. *Gut Liver.* 2021 Jan
1390 15;15(1):61-69.
- 1391 28. Hirten R.P., Grinspan A., Fu S.C. et al. Microbial Engraftment and Efficacy of Fecal Microbiota
1392 Transplant for *Clostridium Difficile* in Patients With and Without Inflammatory Bowel
1393 Disease. *Inflamm Bowel Dis.* 2019 May 4;25(6):969-979.
- 1394 29. McCune V.L., Quraishi M.N., Manzoor S. et al. Results from the first English stool bank using
1395 faecal microbiota transplant as a medicinal product for the treatment of *Clostridioides*
1396 *difficile* infection. *EClinicalMedicine.* 2020 Mar 16;20:100301.
- 1397 30. Roshan N., Clancy A.K., Borody T.J. Faecal microbiota transplantation is effective for the initial
1398 treatment of *Clostridium difficile* infection: a retrospective clinical review. *Infectious Diseases*
1399 *and Therapy.* 2020 Dec;9:935-42.
- 1400 31. Tariq R., Disbrow M.B., Dibaise J.K. et al. Efficacy of Fecal Microbiota Transplantation for
1401 Recurrent *C. Difficile* Infection in Inflammatory Bowel Disease. *Inflamm Bowel Dis.* 2020 Aug
1402 20;26(9):1415-1420.

- 1403 32. Allegretti J.R., Kelly C.R., Grinspan A. et al. Outcomes of Fecal Microbiota Transplantation in
1404 Patients With Inflammatory Bowel Diseases and Recurrent *Clostridioides difficile* Infection.
1405 *Gastroenterology*. 2020 Nov;159(5):1982-1984.
- 1406 33. Ianiro G., Bibbò S., Porcari S. et al. Fecal microbiota transplantation for recurrent *C. difficile*
1407 infection in patients with inflammatory bowel disease: experience of a large-volume
1408 European FMT center. *Gut Microbes*. 2021 Jan-Dec;13(1):1994834.
- 1409 34. Porcari S., Severino A., Rondinella D. et al. Fecal microbiota transplantation for recurrent
1410 *Clostridioides difficile* infection in patients with concurrent ulcerative colitis. *Journal of*
1411 *Autoimmunity*. 2023 Apr 19:103033.
- 1412 35. van Lingen E., Baunwall S., Lieberknecht S. et al. Short-and long-term follow-up after fecal
1413 microbiota transplantation as treatment for recurrent *Clostridioides difficile* infection in
1414 patients with inflammatory bowel disease. *Therapeutic Advances in Gastroenterology*. 2023
1415 Mar;16:17562848231156285.
- 1416 36. Tabbaa O., Rastogi P., Alukal J. et al. Long-term Safety and Efficacy of Fecal Microbiota
1417 Transplantation in the Treatment of *Clostridium difficile* Infection in Patients With and
1418 Without Inflammatory Bowel Disease: A Tertiary Care Center's Experience: 106. *Official*
1419 *journal of the American College of Gastroenterology | ACG*. 2017 Oct 1;112:S51-2.
- 1420 37. Raghu Subramanian C., Talluri S., Khan S.U. et al. Fecal Microbiota Transplantation for
1421 Recurrent *Clostridium difficile* Infection in Patients With Multiple Comorbidities: Long-Term
1422 Safety and Efficacy Results From a Tertiary Care Community Hospital. *Gastroenterology Res*.
1423 2020 Aug;13(4):138-145.
- 1424 38. Vaughn B.P., Fischer M., Kelly C.R. et al. Effectiveness and Safety of Colonic and Capsule Fecal
1425 Microbiota Transplantation for Recurrent *Clostridioides difficile* Infection. *Clin Gastroenterol*
1426 *Hepatol*. 2022 Sep 17:S1542-3565(22)00880-1.
- 1427 39. Weingarden A.R., Treiger O., Ulsh L. et al. Delivery of Fecal Material to Terminal Ileum Is
1428 Associated with Long-Term Success of Fecal Microbiota Transplantation. *Digestive Diseases*
1429 *and Sciences*. 2023 May;68(5):2006-14.
- 1430 40. Pringle P.L., Soto M.T., Chung R.T. et al. Patients With Cirrhosis Require More Fecal Microbiota
1431 Capsules to Cure Refractory and Recurrent *Clostridium difficile* Infections. *Clin Gastroenterol*
1432 *Hepatol*. 2019 Mar;17(4):791-793.
- 1433 41. Kim P., Gadani A., Abdul-Baki H. et al. Fecal microbiota transplantation in recurrent
1434 *Clostridium difficile* infection: A retrospective single-center chart review. *JGH Open*. 2018 Oct
1435 15;3(1):4-9.
- 1436 42. Navalkale B.D., Polistico J., Sandhu A. et al. Clinical outcomes after faecal microbiota
1437 transplant by retention enema in both immunocompetent and immunocompromised
1438 patients with recurrent *Clostridioides difficile* infections at an academic medical centre. *J*
1439 *Hosp Infect*. 2020 Dec;106(4):643-648.
- 1440 43. Cheminet G., Kapel N., Bleibtreu A. et al. French Group for Fecal Microbiota Transplantation
1441 (GFTF). Faecal microbiota transplantation with frozen capsules for relapsing *Clostridium*
1442 *difficile* infections: the first experience from 15 consecutive patients in France. *J Hosp Infect*.
1443 2018 Oct;100(2):148-151.
- 1444 44. Urbonas T., Ianiro G., Gedgaudas R. et al. Fecal Microbiome Transplantation for Recurrent
1445 *Clostridioides difficile* Infection: Treatment Efficacy, Short and Long-term Follow-up Results
1446 from Consecutive Case Series. *J Gastrointestin Liver Dis*. 2021 Dec 21;30(4):470-476.
- 1447 45. Mendelsohn R.B., Kaltsas A., King S. et al. Fecal Microbiota Transplantation Is Safe for
1448 *Clostridioides difficile* Infection in Patients with Solid Tumors Undergoing Chemotherapy. *Dig*
1449 *Dis Sci*. 2022 Jun;67(6):2503-2509.

- 1450 46. Ali H., Khurana S., Ma W. et al. Safety and efficacy of fecal microbiota transplantation to treat
1451 and prevent recurrent *Clostridioides difficile* in cancer patients. *J Cancer*. 2021 Sep
1452 7;12(21):6498-6506.
- 1453 47. Cheng Y.W., Phelps E., Ganapini V. et al. Fecal microbiota transplantation for the treatment of
1454 recurrent and severe *Clostridium difficile* infection in solid organ transplant recipients: A
1455 multicenter experience. *Am J Transplant*. 2019 Feb;19(2):501-511.
- 1456 48. Cheng Y.W., Alhaffar D., Saha S. et al. Fecal Microbiota Transplantation Is Safe and Effective in
1457 Patients With *Clostridioides difficile* Infection and Cirrhosis. *Clin Gastroenterol Hepatol*. 2021
1458 Aug;19(8):1627-1634.
- 1459 49. Meighani A., Alimirah M., Ramesh M. et al. Fecal Microbiota Transplantation for
1460 *Clostridioides Difficile* Infection in Patients with Chronic Liver Disease. *Int J Hepatol*. 2020 Jan
1461 27;2020:1874570.
- 1462 50. Boicean A., Neamtu B., Birsan S. et al. Fecal microbiota transplantation in patients co-
1463 infected with SARS-CoV2 and *Clostridioides difficile*. *Biomedicines*. 2022 Dec 21;11(1):7.
- 1464 51. Niccum B.A., Stein D.J., Behm B.W. et al. Zinc Deficiency and the Recurrence of *Clostridium*
1465 *difficile* Infection after Fecal Microbiota Transplant: A Retrospective Cohort Study. *J Nutr*
1466 *Metab*. 2018 Oct 10;2018:9682975.
- 1467 52. Lynch S.M., Mu J., Grady J.J. et al. Fecal Microbiota Transplantation for *Clostridium difficile*
1468 Infection: A One-Center Experience. *Dig Dis*. 2019;37(6):467-472.
- 1469 53. Hammeken L.H., Baunwall S.M., Dahlerup J.F. et al. Health-related quality of life in patients
1470 with recurrent *Clostridioides difficile* infections. *Therapeutic Advances in Gastroenterology*.
1471 2022 Feb;15:17562848221078441.
- 1472 54. Cold F., Svensson C.K., Petersen A.M. et al. Long-term safety following faecal microbiota
1473 transplantation as a treatment for recurrent *Clostridioides difficile* infection compared with
1474 patients treated with a fixed bacterial mixture: results from a retrospective cohort study.
1475 *Cells*. 2022 Jan 27;11(3):435.
- 1476 55. Hocquart M., Lagier J.C., Cassir N. et al. Early Fecal Microbiota Transplantation Improves
1477 Survival in Severe *Clostridium difficile* Infections. *Clin Infect Dis*. 2018 Feb 10;66(5):645-650.
- 1478 56. Cheng Y.W., Phelps E., Nemes S. et al. Fecal Microbiota Transplant Decreases Mortality in
1479 Patients with Refractory Severe or Fulminant *Clostridioides difficile* Infection. *Clin*
1480 *Gastroenterol Hepatol*. 2020 Sep;18(10):2234-2243.e1.
- 1481 57. Tixier E.N., Verheyen E., Ungaro R.C. et al. Faecal microbiota transplant decreases mortality
1482 in severe and fulminant *Clostridioides difficile* infection in critically ill patients. *Aliment*
1483 *Pharmacol Ther*. 2019 Nov;50(10):1094-1099.
- 1484 58. Saha S., Mara K., Pardi D.S. et al. Durability of Response to Fecal Microbiota Transplantation
1485 After Exposure to Risk Factors for Recurrence in Patients With *Clostridioides difficile*
1486 Infection. *Clin Infect Dis*. 2021 Oct 5;73(7):e1706-e1712.
- 1487 59. Saha S., Mara K., Pardi D.S. et al. Long-term Safety of Fecal Microbiota Transplantation for
1488 Recurrent *Clostridioides difficile* Infection. *Gastroenterology*. 2021 May;160(6):1961-
1489 1969.e3.
- 1490 60. Perler B.K., Chen B., Phelps E. et al. Long-Term Efficacy and Safety of Fecal Microbiota
1491 Transplantation for Treatment of Recurrent *Clostridioides difficile* Infection. *J Clin*
1492 *Gastroenterol*. 2020 Sep;54(8):701-706.
- 1493 61. Shin J.H., Chaplin A.S., Hays R.A. et al. Outcomes of a Multidisciplinary Clinic in Evaluating
1494 Recurrent *Clostridioides difficile* Infection Patients for Fecal Microbiota Transplant: A
1495 Retrospective Cohort Analysis. *J Clin Med*. 2019 Jul 16;8(7):1036.

- 1496 62. Lee C.H., Chai J., Hammond K. et al. Long-term durability and safety of fecal microbiota
1497 transplantation for recurrent or refractory *Clostridioides difficile* infection with or without
1498 antibiotic exposure. *Eur J Clin Microbiol Infect Dis*. 2019 Sep;38(9):1731-1735.
- 1499 63. Allegretti J.R., Allegretti A.S., Phelps E. et al. Asymptomatic *Clostridium difficile* carriage rate
1500 post-fecal microbiota transplant is low: a prospective clinical and stool assessment. *Clin*
1501 *Microbiol Infect*. 2018 Jul;24(7):780.e1-780.e3.
- 1502 64. Dawwas G.K., Brensinger C.M., Vajravelu R.K. et al. Long-term Outcomes Following Multiply
1503 Recurrent *Clostridioides difficile* Infection and Fecal Microbiota Transplantation. *Clin*
1504 *Gastroenterol Hepatol*. 2022 Apr;20(4):806-816.e6.
- 1505 65. Ooijevaar R.E., van Nood E., Goorhuis A. et al. Ten-Year Follow-Up of Patients Treated with
1506 Fecal Microbiota Transplantation for Recurrent *Clostridioides difficile* Infection from a
1507 Randomized Controlled Trial and Review of the Literature. *Microorganisms*. 2021; 9(3):548.
- 1508 66. Rapoport E.A., Baig M., Puli S.R. Adverse events in fecal microbiota transplantation: a
1509 systematic review and meta-analysis. *Annals of Gastroenterology*. 2022 Mar;35(2):150.
- 1510 67. Beran A., Sharma S., Ghazaleh S. et al. Predictors of Fecal Microbiota Transplant Failure in
1511 *Clostridioides difficile* Infection: An Updated Meta-analysis. *J Clin Gastroenterol*. 2023 Apr
1512 1;57(4):389-399.
- 1513 68. Nivet C., Duhalde V., Beaurain M. et al. Fecal Microbiota Transplantation for Refractory
1514 *Clostridioides Difficile* Infection Is Effective and Well Tolerated Even in Very Old Subjects: A
1515 Real-Life Study. *J Nutr Health Aging*. 2022;26(3):290-296.
- 1516 69. Barberio B., Facchin S., Mele E. et al. Faecal microbiota transplantation in *Clostridioides*
1517 *difficile* infection: real-life experience from an academic Italian hospital. *Therapeutic*
1518 *Advances in Gastroenterology*. 2020 Jul;13:1756284820934315.
- 1519 70. Porcari S., Benech N., Valles-Colomer M. Key determinants of success in fecal microbiota
1520 transplantation: From microbiome to clinic. *Cell Host Microbe*. 2023 May 10;31(5):712-733.
- 1521 71. Dubois N.E., Read C.Y., O'Brien K. et al. Challenges of Screening Prospective Stool Donors for
1522 Fecal Microbiota Transplantation. *Biol Res Nurs*. 2021 Jan;23(1):21-30.
- 1523 72. McSweeney B., Allegretti J.R., Fischer M. et al. In search of stool donors: a multicenter study
1524 of prior knowledge, perceptions, motivators, and deterrents among potential donors for
1525 fecal microbiota transplantation. *Gut Microbes*. 2020;11(1):51-62.
- 1526 73. Ianiro G., Punčochář M., Karcher N. et al. Variability of strain engraftment and predictability
1527 of microbiome composition after fecal microbiota transplantation across different diseases.
1528 *Nat Med*. 2022 Sep;28(9):1913-1923.
- 1529 74. Schmidt, T.S.B., Li, S.S., Maistrenko, O.M. et al. Drivers and determinants of strain dynamics
1530 following fecal microbiota transplantation. *Nature Medicine*. 2022 Sep;28(9):1902-12.
- 1531 75. Shanahan F., Ghosh T.S., O'Toole P.W. The Healthy Microbiome-What Is the Definition of a
1532 Healthy Gut Microbiome? *Gastroenterology*. 2021 Jan;160(2):483-494.
- 1533 76. Azimirad M., Yadegar A., Asadzadeh Aghdaei H. et al. Enterotoxigenic *Clostridium perfringens*
1534 Infection as an Adverse Event After Faecal Microbiota Transplantation in Two Patients With
1535 Ulcerative Colitis and Recurrent *Clostridium difficile* Infection: A Neglected Agent in Donor
1536 Screening. *J Crohns Colitis*. 2019 Jul 25;13(7):960-961.
- 1537 77. Kralicek S.E., Jenkins C., Allegretti J.R. et al. Transmission of the Potential Pathogen Atypical
1538 Enteropathogenic *Escherichia coli* by Fecal Microbiota Transplant. *Gastroenterology*. 2023
1539 Jul;165(1):279-282.e1.
- 1540 78. Zellmer C., Sater M.R.A., Huntley M.H. et al. Shiga Toxin-Producing *Escherichia coli*
1541 Transmission via Fecal Microbiota Transplant. *Clin Infect Dis*. 2021 Jun 1;72(11):e876-e880.

- 1542 79. DeFilipp Z., Bloom P.P., Torres Soto M. et al. Drug-resistant *E. coli* bacteremia transmitted by
1543 fecal microbiota transplant. *New England Journal of Medicine*. 2019 Nov 21;381(21):2043-
1544 50.
- 1545 80. Chiu C.H., Chiu C.T. Drug-Resistant Bacteremia after Fecal Microbiota Transplant. *N Engl J*
1546 *Med*. 2020 May 14;382(20):1960-1961.
- 1547 81. Ianiro G., Mullish B.H., Kelly C.R. et al. Reorganisation of faecal microbiota transplant services
1548 during the COVID-19 pandemic. *Gut*. 2020 Sep;69(9):1555-1563.
- 1549 82. Galpérine T., Engelmann I., Hantz S. et al. Cytomegalovirus in donors for fecal microbiota
1550 transplantation, the phantom menace? *PLoS One*. 2023 Jun 29;18(6):e0287847.
- 1551 83. Grosen A.K., Mikkelsen S., Baunwall S.M.D. et al. Risk of *Helicobacter pylori* transmission by
1552 faecal microbiota transplantation via oral capsules. *Clin Microbiol Infect*. 2023
1553 Jun;29(6):799.e1-799.e4.
- 1554 84. Terveer E.M., van Gool T., Ooijevaar R.E. et al. Human Transmission of *Blastocystis* by Fecal
1555 Microbiota Transplantation Without Development of Gastrointestinal Symptoms in
1556 Recipients. *Clin Infect Dis*. 2020 Dec 17;71(10):2630-2636.
- 1557 85. Drewes J.L., Corona A., Sanchez U. et al. Transmission and clearance of potential
1558 procarcinogenic bacteria during fecal microbiota transplantation for recurrent *Clostridioides*
1559 *difficile*. *JCI Insight*. 2019 Oct 3;4(19):e130848.
- 1560 86. Dubinsky V., Dotan I., Gophna U. Carriage of Colibactin-producing Bacteria and Colorectal
1561 Cancer Risk. *Trends Microbiol*. 2020 Nov;28(11):874-876.
- 1562 87. Nooij S., Ducarmon Q.R., Laros J.F.J. et al. Fecal Microbiota Transplantation Influences
1563 Procarcinogenic *Escherichia coli* in Recipient Recurrent *Clostridioides difficile* Patients.
1564 *Gastroenterology*. 2021 Oct;161(4):1218-1228.e5.
- 1565 88. Ianiro G., Punčochář M., Karcher N. et al. Variability of strain engraftment and predictability
1566 of microbiome composition after fecal microbiota transplantation across different diseases.
1567 *Nat Med*. 2022 Sep;28(9):1913-1923.
- 1568 89. He J., He X., Ma Y. et al. A comprehensive approach to stool donor screening for faecal
1569 microbiota transplantation in China. *Microb Cell Fact*. 2021 Nov 27;20(1):216.
- 1570 90. Allegretti J.R., Kassam Z., Chan W.W. Small Intestinal Bacterial Overgrowth: Should Screening
1571 Be Included in the Pre-fecal Microbiota Transplantation Evaluation? *Dig Dis Sci*. 2018
1572 Jan;63(1):193-197.
- 1573 91. Ng R.W., Dharmaratne P., Wong S. et al. Revisiting the donor screening protocol of faecal
1574 microbiota transplantation (FMT): a systematic review. *Gut*. 2023 May 4;gutjnl-2023-329515.
- 1575 92. Klapsa D., Wilton T., Zealand A. et al. Sustained detection of type 2 poliovirus in London
1576 sewage between February and July, 2022, by enhanced environmental surveillance. *Lancet*.
1577 2022 Oct 29;400(10362):1531-1538.
- 1578 93. Speck P.G., Mitchell J.G. Faecal microbiota transplantation donor stools need screening for
1579 poliovirus. *Gut* 2018;67:1559-1560.
- 1580 94. Papanicolas L.E., Choo J.M., Wang Y. et al. Bacterial viability in faecal transplants: Which
1581 bacteria survive? *EBioMedicine*. 2019 Mar;41:509-516.
- 1582 95. Satokari R., Pietilä L., Mattila E. et al. Faecal banking at -20° C facilitates faecal microbiota
1583 transplantation for recurrent *Clostridioides difficile* infection in clinical practice. *Infectious*
1584 *Diseases*. 2020 Sep 1;52(9):662-5.
- 1585 96. Staley C., Halaweish H., Graiziger C. et al. Lower endoscopic delivery of freeze-dried intestinal
1586 microbiota results in more rapid and efficient engraftment than oral administration. *Scientific*
1587 *reports*. 2021 Feb 25;11(1):4519.

- 1588 97. Vignvári S., Sipos D., Solt J. et al. Faecal microbiota transplantation for *Clostridium difficile*
1589 infection using a lyophilized inoculum from non-related donors: A case series involving 19
1590 patients. *Acta Microbiol Immunol Hung.* 2019 Mar 1;66(1):69-78.
- 1591 98. Reigadas E., Bouza E., Olmedo M. et al. Faecal microbiota transplantation for recurrent
1592 *Clostridioides difficile* infection: experience with lyophilized oral capsules. *J Hosp Infect.* 2020
1593 Jun;105(2):319-324.
- 1594 99. Varga A., Kocsis B., Sipos D. et al. How to Apply FMT More Effectively, Conveniently and
1595 Flexible - A Comparison of FMT Methods. *Front Cell Infect Microbiol.* 2021 Jun 4;11:657320.
- 1596 100. Allegratti J.R., Elliott R.J., Ladha A. et al. Stool processing speed and storage duration
1597 do not impact the clinical effectiveness of fecal microbiota transplantation. *Gut Microbes.*
1598 2020 Nov 1;11(6):1806-1808.
- 1599 101. Shimizu H., Arai K., Asahara T. et al. Stool preparation under anaerobic conditions
1600 contributes to retention of obligate anaerobes: potential improvement for fecal microbiota
1601 transplantation. *BMC microbiology.* 2021 Dec;21(1):1-9.
- 1602 102. Burz S.D., Abraham A.L., Fonseca F. et al. A Guide for Ex Vivo Handling and Storage of
1603 Stool Samples Intended for Fecal Microbiota Transplantation. *Sci Rep.* 2019 Jun 20;9(1):8897.
- 1604 103. Dorsaz S., Charretier Y., Girard M. et al. Changes in Microbiota Profiles After
1605 Prolonged Frozen Storage of Stool Suspensions. *Front Cell Infect Microbiol.* 2020 Feb
1606 28;10:77.
- 1607 104. Quaranta G., Fancello G., Ianiro G. et al. Laboratory handling practice for faecal
1608 microbiota transplantation. *Journal of applied microbiology.* 2020 Mar 1;128(3):893-8.
- 1609 105. Gratton J., Phetcharaburanin J., Mullish B.H. et al. Optimized Sample Handling
1610 Strategy for Metabolic Profiling of Human Feces. *Anal Chem.* 2016 May 3;88(9):4661-8.
- 1611 106. Bestfater C., Vehreschild M.J.G.T., Stallmach A. et al. Clinical effectiveness of
1612 bidirectional fecal microbiota transfer in the treatment of recurrent *Clostridioides difficile*
1613 infections. *Dig Liver Dis.* 2021 Jun;53(6):706-711.
- 1614 107. Reigadas E., Olmedo M., Valerio M. et al. Fecal microbiota transplantation for
1615 recurrent *Clostridium difficile* infection: Experience, protocol, and results. *Rev Esp Quimioter.*
1616 2018 Oct;31(5):411-418.
- 1617 108. Jiang Z.D., Jenq R.R., Ajami N.J. et al. Safety and preliminary efficacy of orally
1618 administered lyophilized fecal microbiota product compared with frozen product given by
1619 enema for recurrent *Clostridium difficile* infection: A randomized clinical trial. *PLoS One.*
1620 2018 Nov 2;13(11):e0205064.
- 1621 109. Svensson C.K., Cold F., Ribberholt I. et al. The Efficacy of Faecal Microbiota Transplant
1622 and Rectal Bacteriotherapy in Patients with Recurrent *Clostridioides difficile* Infection: A
1623 Retrospective Cohort Study. *Cells.* 2022; 11(20):3272.
- 1624 110. Osman M., Budree S., Kelly C.R. et al. Effectiveness and Safety of Fecal Microbiota
1625 Transplantation for *Clostridioides Difficile* Infection: Results From a 5344-Patient Cohort
1626 Study. *Gastroenterology.* 2022 Jul;163(1):319-322.
- 1627 111. Vignvári S., Vincze Á., Solt J. et al. Experiences with fecal microbiota transplantation in
1628 *Clostridium difficile* infections via upper gastrointestinal tract. *Acta Microbiol Immunol Hung.*
1629 2019 Jun 1;66(2):179-188.
- 1630 112. Sebastian S., Dhar A., Baddeley R. et al. Green endoscopy: British Society of
1631 Gastroenterology (BSG), Joint Accreditation Group (JAG) and Centre for Sustainable Health
1632 (CSH) joint consensus on practical measures for environmental sustainability in endoscopy.
1633 *Gut.* 2023 Jan 1;72(1):12-26.

- 1634 113. van Prehn J., Reigadas E., Vogelzang E.H. et al. European Society of Clinical
1635 Microbiology and Infectious Diseases: 2021 update on the treatment guidance document for
1636 *Clostridioides difficile* infection in adults. *Clin Microbiol Infect.* 2021 Dec;27 Suppl 2:S1-S21.
- 1637 114. Kachrimanidou M., Tsintarakis E. Insights into the Role of Human Gut Microbiota in
1638 *Clostridioides difficile* Infection. *Microorganisms.* 2020 Jan 31;8(2):200.
- 1639 115. Kates A.E., Gaulke I., De Wolfe T. et al. Fecal microbiota transplantation for patients
1640 on antibiotic treatment with *C. difficile* infection history (GRAFT): Study protocol for a phase
1641 II, randomized, double-blind, placebo-controlled trial to prevent recurrent *C. difficile*
1642 infections. *Contemp Clin Trials Commun.* 2020 May 19;18:100576.
- 1643 116. El Hage Chehade N., Ghoneim S., Shah S. et al. Efficacy of Fecal Microbiota
1644 Transplantation in the Treatment of Active Ulcerative Colitis: A Systematic Review and Meta-
1645 Analysis of Double-Blind Randomized Controlled Trials. *Inflamm Bowel Dis.* 2023 May
1646 2;29(5):808-817.
- 1647 117. Březina J., Bajer L., Wohl P. et al. Fecal Microbial Transplantation versus Mesalamine
1648 Enema for Treatment of Active Left-Sided Ulcerative Colitis-Results of a Randomized
1649 Controlled Trial. *J Clin Med.* 2021 Jun 22;10(13):2753.
- 1650 118. Tkach S., Dorofeyev A., Kuzenko I. et al. Efficacy and safety of fecal microbiota
1651 transplantation via colonoscopy as add-on therapy in patients with mild-to-moderate
1652 ulcerative colitis: A randomized clinical trial. *Frontiers in Medicine.* 2023 Jan 12;9:1049849.
- 1653 119. Liu X., Li Y., Wu K. et al. Fecal microbiota transplantation as therapy for treatment of
1654 active ulcerative colitis: a systematic review and meta-analysis. *Gastroenterology Research
1655 and Practice.* 2021 Apr 24;2021.
- 1656 120. Zhao H.L., Chen S.Z., Xu H.M. et al. Efficacy and safety of fecal microbiota
1657 transplantation for treating patients with ulcerative colitis: A systematic review and meta-
1658 analysis. *Journal of Digestive Diseases.* 2020 Oct;21(10):534-48.
- 1659 121. Mocanu V., Rajaruban S., Dang J. et al. Repeated fecal microbial transplantations and
1660 antibiotic pre-treatment are linked to improved clinical response and remission in
1661 inflammatory bowel disease: a systematic review and pooled proportion meta-analysis.
1662 *Journal of Clinical Medicine.* 2021 Mar 1;10(5):959.
- 1663 122. Tang L.L., Feng W.Z., Cheng J.J. et al. Clinical remission of ulcerative colitis after
1664 different modes of faecal microbiota transplantation: a meta-analysis. *International Journal
1665 of Colorectal Disease.* 2020 Jun;35:1025-34.
- 1666 123. Zhou H.Y., Guo B., Lufumpa E. et al. Comparative of the effectiveness and safety of
1667 biological agents, tofacitinib, and fecal microbiota transplantation in ulcerative colitis:
1668 systematic review and network meta-analysis. *Immunological investigations.* 2021 May
1669 19;50(4):323-37.
- 1670 124. Costello S.P., Hughes P.A., Waters O. et al. Effect of fecal microbiota transplantation
1671 on 8-week remission in patients with ulcerative colitis: a randomized clinical trial. *Jama.* 2019
1672 Jan 15;321(2):156-64.
- 1673 125. Vuyyuru S.K., Kedia S., Kalaivani M. et al. Efficacy and safety of fecal transplantation
1674 versus targeted therapies in ulcerative colitis: network meta-analysis. *Future Microbiology.*
1675 2021 Oct;16(15):1215-27.
- 1676 126. Li Y., Zhang T., Sun J. et al. Fecal microbiota transplantation and health outcomes: An
1677 umbrella review of meta-analyses of randomized controlled trials. *Frontiers in Cellular and
1678 Infection Microbiology.* 2022 Jun 27;12:899845.
- 1679 127. Kedia S., Virmani S., K Vuyyuru S. et al. Faecal microbiota transplantation with anti-
1680 inflammatory diet (FMT-AID) followed by anti-inflammatory diet alone is effective in inducing

- 1681 and maintaining remission over 1 year in mild to moderate ulcerative colitis: a randomised
1682 controlled trial. *Gut*. 2022 Dec;71(12):2401-2413.
- 1683 128. Lahtinen P., Jalanka J., Mattila E. et al. Fecal microbiota transplantation for the
1684 maintenance of remission in patients with ulcerative colitis: A randomized controlled trial.
1685 *World J Gastroenterol*. 2023 May 7;29(17):2666-2678.
- 1686 129. Sokol H., Landman C., Seksik P. et al. Fecal microbiota transplantation to maintain
1687 remission in Crohn's disease: a pilot randomized controlled study. *Microbiome*. 2020 Feb
1688 3;8(1):12.
- 1689 130. Herfarth H., Barnes E.L., Long M.D. et al. Combined Endoscopic and Oral Fecal
1690 Microbiota Transplantation in Patients with Antibiotic-Dependent Pouchitis: Low Clinical
1691 Efficacy due to Low Donor Microbial Engraftment. *Inflamm Intest Dis*. 2019 May;4(1):1-6.
- 1692 131. Karjalainen E.K., Renkonen-Sinisalo L., Satokari R. et al. Fecal Microbiota
1693 Transplantation in Chronic Pouchitis: A Randomized, Parallel, Double-Blinded Clinical Trial.
1694 *Inflamm Bowel Dis*. 2021 Oct 20;27(11):1766-1772.
- 1695 132. Wu J., Lv L., Wang C. Efficacy of Fecal Microbiota Transplantation in Irritable Bowel
1696 Syndrome: A Meta-Analysis of Randomized Controlled Trials. *Front Cell Infect Microbiol*. 2022
1697 Feb 28;12:827395.
- 1698 133. Singh P., Alm E.J., Kelley J.M. et al. Effect of antibiotic pretreatment on bacterial
1699 engraftment after Fecal Microbiota Transplant (FMT) in IBS-D. *Gut Microbes*. 2022 Jan-
1700 Dec;14(1):2020067.
- 1701 134. Tkach S., Dorofeyev A., Kuzenko I. et al. Fecal microbiota transplantation in patients
1702 with post-infectious irritable bowel syndrome: A randomized, clinical trial. *Front Med*
1703 (Lausanne). 2022 Oct 20;9:994911.
- 1704 135. Halkjær S.I., Lo B., Cold F. et al. Fecal microbiota transplantation for the treatment of
1705 irritable bowel syndrome: A systematic review and meta-analysis. *World Journal of*
1706 *Gastroenterology*. 2023 May 5;29(20):3185.
- 1707 136. Samuthpongton C., Kantagowit P., Pittayanon R. et al. Fecal microbiota
1708 transplantation in irritable bowel syndrome: A meta-analysis of randomized controlled trials.
1709 *Frontiers in Medicine*. 2022 Nov 3;9:1039284.
- 1710 137. Zhao H.J., Zhang X.J., Zhang N.N. et al. Fecal microbiota transplantation for patients
1711 with irritable bowel syndrome: a meta-analysis of randomized controlled trials. *Frontiers in*
1712 *Nutrition*. 2022 May 27;9:890357.
- 1713 138. Ianiro G., Eusebi L.H., Black C.J. et al. Systematic review with meta-analysis: efficacy
1714 of faecal microbiota transplantation for the treatment of irritable bowel syndrome.
1715 *Alimentary pharmacology & therapeutics*. 2019 Aug;50(3):240-8.
- 1716 139. Abdelghafar Y.A., AbdelQadir Y.H., Motawea K.R. et al. Efficacy and safety of fecal
1717 microbiota transplant in irritable bowel syndrome: An update based on meta-analysis of
1718 randomized control trials. *Health science reports*. 2022 Sep;5(5):e814.
- 1719 140. Rokkas T., Hold G.L. A systematic review, pairwise meta-analysis and network meta-
1720 analysis of randomized controlled trials exploring the role of fecal microbiota transplantation
1721 in irritable bowel syndrome. *European Journal of Gastroenterology & Hepatology*. 2023 Apr
1722 1;35(4):471-9.
- 1723 141. Elhusein A.M., Fadlalmola H.A. Efficacy of fecal microbiota transplantation in irritable
1724 bowel syndrome patients: an updated systematic review and meta-analysis.
1725 *Gastroenterology Nursing*. 2022 Jan 1;45(1):11-20.
- 1726 142. Xu D., Chen V.L., Steiner C.A. et al. Efficacy of fecal microbiota transplantation in
1727 irritable bowel syndrome: a systematic review and meta-analysis. *The American journal of*
1728 *gastroenterology*. 2019 Jul;114(7):1043.

- 1729 143. Rodrigues T., Rodrigues Fialho S., Araújo J.R. et al. Procedures in Fecal Microbiota
1730 Transplantation for Treating Irritable Bowel Syndrome: Systematic Review and Meta-Analysis.
1731 Journal of Clinical Medicine. 2023 Feb 21;12(5):1725.
- 1732 144. Mohan B.P., Loganathan P., Khan S.R. et al. Fecal microbiota transplant delivered via
1733 invasive routes in irritable bowel syndrome: A systematic review and meta-analysis of
1734 randomized controlled trials. Indian Journal of Gastroenterology. 2023 May 29:1-9.
- 1735 145. Fang S., Wu S., Ji L. et al. The combined therapy of fecal microbiota transplantation
1736 and laxatives for functional constipation in adults: A systematic review and meta-analysis of
1737 randomized controlled trials. Medicine (Baltimore). 2021 Apr 9;100(14):e25390.
- 1738 146. Hong A.S., Tun K.M., Hong J.M. et al. Fecal Microbiota Transplantation in
1739 Decompensated Cirrhosis: A Systematic Review on Safety and Efficacy. Antibiotics (Basel).
1740 2022 Jun 23;11(7):838.
- 1741 147. Tun K.M., Hong A.S., Batra K. et al. A Systematic Review of the Efficacy and Safety of
1742 Fecal Microbiota Transplantation in the Treatment of Hepatic Encephalopathy and
1743 Clostridioides difficile Infection in Patients With Cirrhosis. Cureus. 2022 May
1744 31;14(5):e25537.
- 1745 148. Mocanu V., Zhang Z., Deehan E.C. et al. Fecal microbial transplantation and fiber
1746 supplementation in patients with severe obesity and metabolic syndrome: a randomized
1747 double-blind, placebo-controlled phase 2 trial. Nat Med. 2021 Jul;27(7):1272-1279.
- 1748 149. Smits L.P., Kootte R.S., Levin E. et al. Effect of Vegan Fecal Microbiota Transplantation
1749 on Carnitine- and Choline-Derived Trimethylamine-N-Oxide Production and Vascular
1750 Inflammation in Patients With Metabolic Syndrome. J Am Heart Assoc. 2018 Mar
1751 26;7(7):e008342.
- 1752 150. Koopen A.M., Almeida E.L., Attaye I. et al. Effect of Fecal Microbiota Transplantation
1753 Combined With Mediterranean Diet on Insulin Sensitivity in Subjects With Metabolic
1754 Syndrome. Front Microbiol. 2021 Jun 10;12:662159.
- 1755 151. Craven L., Rahman A., Nair Parvathy S. et al. Allogenic Fecal Microbiota
1756 Transplantation in Patients With Nonalcoholic Fatty Liver Disease Improves Abnormal Small
1757 Intestinal Permeability: A Randomized Control Trial. Am J Gastroenterol. 2020
1758 Jul;115(7):1055-1065.
- 1759 152. Yu E.W., Gao L., Stastka P. et al. Fecal microbiota transplantation for the improvement
1760 of metabolism in obesity: The FMT-TRIM double-blind placebo-controlled pilot trial. PLoS
1761 Med. 2020 Mar 9;17(3):e1003051.
- 1762 153. de Groot P., Scheithauer T., Bakker G.J. et al. Donor metabolic characteristics drive
1763 effects of faecal microbiota transplantation on recipient insulin sensitivity, energy
1764 expenditure and intestinal transit time. Gut. 2020 Mar;69(3):502-512.
- 1765 154. Allegretti J.R., Kassam Z., Mullish B.H. et al. Effects of Fecal Microbiota
1766 Transplantation With Oral Capsules in Obese Patients. Clin Gastroenterol Hepatol. 2020
1767 Apr;18(4):855-863.
- 1768 155. De Groot P., Nikolic T., Pellegrini S. et al. Faecal microbiota transplantation halts
1769 progression of human new-onset type 1 diabetes in a randomised controlled trial. Gut. 2021
1770 Jan 1;70(1):92-105.
- 1771 156. DuPont H.L., Suescun J., Jiang Z.D. et al. Fecal microbiota transplantation in
1772 Parkinson's disease—A randomized repeat-dose, placebo-controlled clinical pilot study.
1773 Frontiers in Neurology. 2023 Mar 2;14:1104759.
- 1774 157. Kraggsnaes M.S., Kjeldsen J., Horn H.C. et al. Safety and efficacy of faecal microbiota
1775 transplantation for active peripheral psoriatic arthritis: an exploratory randomised placebo-
1776 controlled trial. Annals of the rheumatic diseases. 2021 Sep 1;80(9):1158-67.

- 1777 158. Tian H., Wang J., Feng R. et al. Efficacy of faecal microbiota transplantation in
1778 patients with progressive supranuclear palsy-Richardson's syndrome: a phase 2, single
1779 centre, randomised clinical trial. *EClinicalMedicine*. 2023 Apr 1;58.
- 1780 159. Huttner B.D., de Lastours V., Wassenberg M. et al. A 5-day course of oral antibiotics
1781 followed by faecal transplantation to eradicate carriage of multidrug-resistant
1782 Enterobacteriaceae: a randomized clinical trial. *Clin Microbiol Infect*. 2019 Jul;25(7):830-838.
- 1783 160. Leo S., Lazarevic V., Girard M. et al. Metagenomic characterization of gut microbiota
1784 of carriers of extended-spectrum beta-lactamase or carbapenemase-producing
1785 Enterobacteriaceae following treatment with oral antibiotics and fecal microbiota
1786 transplantation: results from a multicenter randomized trial. *Microorganisms*. 2020; Jun
1787 8(6):941–915.
- 1788 161. Bilsen M.P., Lambregts M.M.C., van Prehn J. et al. Faecal microbiota replacement to
1789 eradicate antimicrobial resistant bacteria in the intestinal tract - a systematic review. *Curr*
1790 *Opin Gastroenterol*. 2022 Jan 1;38(1):15-25.
- 1791 162. Sharma A., Roy A., Premkumar M. et al. Fecal microbiota transplantation in alcohol-
1792 associated acute-on-chronic liver failure: an open-label clinical trial. *Hepatol Int*. 2022
1793 Apr;16(2):433-446.
- 1794 163. Pande A., Sharma S., Khillan V. et al. Fecal microbiota transplantation compared with
1795 prednisolone in severe alcoholic hepatitis patients: a randomized trial. *Hepatol Int*. 2023
1796 Feb;17(1):249-261.
- 1797 164. Moayyedi P., Surette M.G., Kim P.T. et al. Fecal microbiota transplantation induces
1798 remission in patients with active ulcerative colitis in a randomized controlled trial.
1799 *Gastroenterology*. 2015 Jul 1;149(1):102-9.
- 1800 165. Paramsothy S., Kamm M.A., Kaakoush N.O. et al. Multidonor intensive faecal
1801 microbiota transplantation for active ulcerative colitis: a randomised placebo-controlled trial.
1802 *The Lancet*. 2017 Mar 25;389(10075):1218-28.
- 1803 166. Rossen N.G., Fuentes S., van der Spek M.J. et al. Findings from a randomized
1804 controlled trial of fecal transplantation for patients with ulcerative colitis. *Gastroenterology*.
1805 2015 Jul 1;149(1):110-8.
- 1806 167. Lopetuso L.R., Deleu S., Godny L. et al. The first international Rome consensus
1807 conference on gut microbiota and faecal microbiota transplantation in inflammatory bowel
1808 disease. *Gut*. 2023 Jun 20.
- 1809 168. Aliu P., Sarp S., Reichenbach R. et al. International Country-Level Trends, Factors, and
1810 Disparities in Compassionate Use Access to Unlicensed Products for Patients With Serious
1811 Medical Conditions. *JAMA Health Forum*. 2022 Apr 15;3(4):e220475.
- 1812 169. Patil S. Early access programs: Benefits, challenges, and key considerations for
1813 successful implementation. *Perspect Clin Res*. 2016 Jan-Mar;7(1):4-8.
- 1814 170. Medicines and Healthcare Products Regulatory Agency, 2023. The supply of
1815 unlicensed medicinal products (“specials”) MHRA Guidance Note 14. Available at:
1816 [https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_d](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1156182/The_supply_of_unlicensed_medicinal_products_special_GN14.pdf)
1817 [ata/file/1156182/The supply of unlicensed medicinal products special GN14.pdf](https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1156182/The_supply_of_unlicensed_medicinal_products_special_GN14.pdf). Last
1818 accessed 08/09/2023.
- 1819 171. Routy B., Lenehan J.G., Miller Jr W.H. et al. Fecal microbiota transplantation plus anti-
1820 PD-1 immunotherapy in advanced melanoma: a phase I trial. *Nature medicine*. 2023 Jul 6:1-
1821 2.
- 1822 172. Baruch E.N., Youngster I., Ben-Betzalel G. et al. Fecal microbiota transplant promotes
1823 response in immunotherapy-refractory melanoma patients. *Science*. 2021 Feb
1824 5;371(6529):602-9.

- 1825 173. Davar D., Dzutsev A.K., McCulloch J.A. et al. Fecal microbiota transplant overcomes
1826 resistance to anti-PD-1 therapy in melanoma patients. *Science*. 2021 Feb 5;371(6529):595-
1827 602.
- 1828 174. Halsey T.M., Thomas A.S., Hayase T. et al. Microbiome alteration via fecal microbiota
1829 transplantation is effective for refractory immune checkpoint inhibitor-induced colitis. *Sci*
1830 *Transl Med*. 2023 Jun 14;15(700):eabq4006.
- 1831 175. Taur Y., Coyte K., Schluter J. et al. Reconstitution of the gut microbiota of antibiotic-
1832 treated patients by autologous fecal microbiota transplant. *Sci Transl Med*. 2018 Sep
1833 26;10(460):eaap9489.
- 1834 176. Human Tissue Authority, 2021. The HTA's role in cord blood banking. Available at:
1835 <https://www.hta.gov.uk/guidance-public/cord-blood-banking/htas-role-cord-blood-banking>.
1836 Last accessed 08/09/2023.
- 1837 177. Ke S., Weiss S.T., Liu Y.Y. Rejuvenating the human gut microbiome. *Trends in*
1838 *Molecular Medicine*. 2022 Aug 1;28(8):619-30.
- 1839 178. Merrick B., Allen L., Zain NM. et al. Regulation, risk and safety of Faecal Microbiota
1840 Transplant. *Infect Prev Pract*. 2020 Sep;2(3):100069.
- 1841 179. Medicines Act, 1968. Available at: <https://www.legislation.gov.uk/ukpga/1968/67>.
1842 Last accessed 08/09/2023.
- 1843 180. Medicines and Healthcare products Regulatory Agency and Department of Health
1844 and Social Care, 2014. Good manufacturing practice and good distribution practice. Available
1845 at: [https://www.gov.uk/guidance/good-manufacturing-practice-and-good-distribution-](https://www.gov.uk/guidance/good-manufacturing-practice-and-good-distribution-practice#full-publication-update-history)
1846 [practice#full-publication-update-history](https://www.gov.uk/guidance/good-manufacturing-practice-and-good-distribution-practice#full-publication-update-history). Last accessed 08/09/2023.

1847
1848
1849

1850 **Disclaimer from the British Society of Gastroenterology:** *These BSG guidelines represent a consensus*
1851 *of best practice based on the available evidence at the time of preparation. They may not apply in all*
1852 *situations and should be interpreted in the light of specific clinical situations and resource availability.*
1853 *Further controlled clinical studies may be needed to clarify aspects of these statements, and revision*
1854 *may be necessary as new data appear. Clinical consideration may justify a course of action at variance*
1855 *to these recommendations, but we suggest that reasons for this are documented in the medical record.*
1856 *BSG guidelines are intended to be an educational device to provide information that may assist in*
1857 *providing care to patients. They are not rules and should not be construed as establishing a legal*
1858 *standard of care or as encouraging, advocating, requiring, or discouraging any particular treatment.*

FMT guidelines: main document.

1859 [List of abbreviations](#)

- 1860 BSG – British Society of Gastroenterology
- 1861 CBA – controlled before/after
- 1862 CDI - *Clostridioides difficile* (*C. diff*) infection
- 1863 CI – confidence interval
- 1864 CMV - cytomegalovirus
- 1865 CPD – continuing professional development
- 1866 CVD – cardiovascular disease
- 1867 FMT – faecal microbiota transplant(ation)
- 1868 GRADE – Grading of Recommendations Assessment, Development and Evaluation
- 1869 HIS – Healthcare Infection Society
- 1870 HR – hazard ratio
- 1871 ITS – interrupted time series
- 1872 NICE – National Institute for Health and Care Excellence
- 1873 nRCT – non-randomised controlled trial
- 1874 OR – odds ratio
- 1875 PCR – polymerase chain reaction
- 1876 PICO – Population-Intervention-Comparison-Outcome
- 1877 PFO – Population-Predictive Factor-Outcome
- 1878 RCT – randomised controlled trial
- 1879 RR – risk ratio
- 1880 SSI – surgical site infection
- 1881 UBA – uncontrolled before/after
- 1882 UK – United Kingdom