

CADTH RAPID RESPONSE REPORT: REFERENCE LIST

# Interventions for the Treatment and Management of Clostridioides Difficile: Clinical Effectiveness and Guidelines

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## Research Questions

1. What is the clinical effectiveness of interventions used to treat or manage individuals with *Clostridioides difficile*?
2. What are the evidence-based guidelines regarding the treatment or management of individuals with *Clostridioides difficile*?

## Key Findings

One health technology assessment, five systematic reviews (four with meta-analysis) and seven evidence-based guidelines were identified regarding the treatment or management of individuals with *Clostridioides difficile*.

## Methods

A limited literature search was conducted by an information specialist on key resources including Medline via OVID, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused Internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were *Clostridioides difficile* and treatment. Search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, or network meta-analyses, and guidelines. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2014 and August 7, 2019. Internet links were provided, where available.

## Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

**Table 1: Selection Criteria**

<b>Population</b>	Any individual diagnosed with <i>C. difficile</i>
<b>Intervention</b>	Any intervention used to treat or manage individuals with <i>C. difficile</i>
<b>Comparator</b>	Q1: Any other intervention used to treat or manage individuals with <i>C. difficile</i> Q2: No comparator

<b>Outcomes</b>	Q1: Clinical effectiveness, safety Q2: Evidence-based guidelines
<b>Study Designs</b>	Health technology assessments, systematic reviews, meta-analyses, evidence-based guidelines

## Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by evidence-based guidelines. Due to the number of relevant systematic reviews, inclusion was limited to those published in 2019. Health technology assessments and evidence-based guidelines published between 2014 and 2019 were considered for inclusion.

One health technology assessment, five systematic reviews (four with meta-analysis) and seven evidence-based guidelines were identified regarding the treatment or management of individuals with *Clostridioides difficile*.

Additional references of potential interest are provided in the appendix.

### Health Technology Assessments

1. Health Quality Ontario. Fecal microbiota therapy for *Clostridium difficile* infection: a health technology assessment. *Ont Health Technol Assess Ser.* 2016;16(17):1-69. [PubMed: PM27516814](#)

### Systematic Reviews and Meta-analyses

2. Aziz M, Desai M, Fatima R, et al. Surotomycin (a novel cyclic lipopeptide) vs vancomycin for treatment of *Clostridioides difficile* infection: a systematic review and meta-analysis. *Curr Clin Pharmacol.* 2019;28:28. [epub ahead of print] [PubMed: PM30924421](#)
3. Aziz M, Simcha W, Fatima R, Rajani S, Eid A, Nawras A. Cadazolid vs vancomycin for treatment of *Clostridioides difficile* infection: systematic review with meta-analysis. *Curr Clin Pharmacol.* 2019;02:02. [epub ahead of print] [PubMed: PM31376824](#)
4. Hui W, Li T, Liu W, Zhou C, Gao F. Fecal microbiota transplantation for treatment of recurrent *C. difficile* infection: an updated randomized controlled trial meta-analysis. *PLoS ONE.* 2019;14(1):e0210016. [PubMed: PM30673716](#)
5. Ng QX, Loke W, Foo NX, Mo Y, Yeo WS, Soh AYS. A systematic review of the use of rifaximin for *Clostridium difficile* infections. *Anaerobe.* 2019;55:35-39. [PubMed: PM30391527](#)
6. Sridharan K, Sivaramakrishnan G. Which antimicrobial agent is likely to be the best for treating *Clostridium difficile* infections? A Bayesian network meta-analysis of randomized clinical trials. *Drug Res (Stuttg).* 2019;69(4):194-200. [PubMed: PM30193396](#)

## Guidelines and Recommendations

7. Mullane KM, Dubberke ER, AST ID Community of Practice. Management of Clostridioides (formerly Clostridium) difficile infection (CDI) in solid organ transplant recipients: guidelines from the American Society of Transplantation Community of Practice. *Clin Transplant*. 2019:e13564.  
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8. Sartelli M, Di Bella S, McFarland LV, et al. 2019 update of the WSES guidelines for management of Clostridioides (Clostridium) difficile infection in surgical patients. *World J Emerg Surg*. 2019;14:8.  
[PubMed: PM30858872](#)
9. Diorio C, Robinson PD, Ammann RA, et al. Guideline for the management of Clostridium difficile infection in children and adolescents with cancer and pediatric hematopoietic stem-cell transplantation recipients. *J Clin Oncol*. 2018;JCO1800407.  
[PubMed: PM30216124](#)
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[PubMed: PM29462280](#)
11. Mullish BH, Quraishi MN, Segal JP, et al. The use of faecal microbiota transplant as treatment for recurrent or refractory Clostridium difficile infection and other potential indications: joint British Society of Gastroenterology (BSG) and Healthcare Infection Society (HIS) guidelines. *J Hosp Infect*. 2018;100 Suppl 1:S1-S31.  
[PubMed: PM30173851](#)
12. Loo WG, Davis I, Embil J, et al. Association of Medical Microbiology and Infectious Disease Canada treatment practice guidelines for Clostridium difficile infection. *JAMMI*. 2018;3.2;  
<https://www.ammi.ca/Content/AMMI%20Canada%20treatment%20practice%20guidelines%20for%20Clostridium%20difficile%20infection.pdf>. Accessed 2019 Aug 12.
13. National Institute for Health and Care Excellence. Faecal microbiota transplant for recurrent Clostridium difficile infection (*Interventional procedures guideline 485*) 2014;  
<https://www.nice.org.uk/guidance/ipg485>. Accessed 2019 Aug 12.  
See: Recommendations

## Appendix — Further Information

### Previous CADTH Reports

14. Lyophilized- versus frozen fecal microbiota transplant for recurrent *Clostridium difficile* infection, irritable bowel disease, and irritable bowel syndrome: a review of clinical effectiveness, cost-effectiveness, and guidelines. (*CADTH Rapid response report: summary with critical appraisal*). Ottawa (ON): CADTH; 2019: <https://www.cadth.ca/lyophilized-versus-frozen-fecal-microbiota-transplant-recurrent-clostridium-difficile-infection>. Accessed 2019 Aug 14.
15. Fidaxomicin pulse therapy for *Clostridium difficile* infection: clinical effectiveness. (*CADTH Rapid response report: reference list*). Ottawa (ON): CADTH; 2019: <https://www.cadth.ca/fidaxomicin-pulse-therapy-clostridium-difficile-infection-clinical-effectiveness-0>. Accessed 2019 Aug 12.
16. Probiotics for antibiotic-associated diarrhea and *Clostridium difficile* infection: a review of guidelines. (*CADTH Rapid response report: summary with critical appraisal*). Ottawa (ON): CADTH; 2018: <https://www.cadth.ca/probiotics-antibiotic-associated-diarrhea-and-clostridium-difficile-infection-review-guidelines>. Accessed 2019 Aug 12.
17. Fecal bacteriotherapy for adult patients with recurrent *Clostridium difficile* infection: update of clinical and cost-effectiveness, and guidelines. (*CADTH Rapid response report: reference list*). Ottawa (ON): CADTH; 2014: <https://www.cadth.ca/fecal-bacteriotherapy-adult-patients-recurrent-clostridium-difficile-infection-update-clinical-and>. Accessed 2019 Aug 12.

### Systematic Reviews and Meta-analyses – Unknown Comparator

18. Lai CY, Sung J, Cheng F, et al. Systematic review with meta-analysis: review of donor features, procedures and outcomes in 168 clinical studies of faecal microbiota transplantation. *Aliment Pharmacol Ther*. 2019;49(4):354-363. [PubMed: PM30628108](#)
19. Tariq R, Pardi DS, Bartlett MG, Khanna S. Low cure rates in controlled trials of fecal microbiota transplantation for recurrent *Clostridium difficile* infection: a systematic review and meta-analysis. *Clin Infect Dis*. 2019;68(8):1351-1358. [PubMed: PM30957161](#)

### Guidelines and Recommendations – Rigour of Methodology Low or Unclear

20. Abreu YAAT, Velarde-Ruiz Velasco JA, Zavala-Solares MR, et al. Consensus on the prevention, diagnosis, and treatment of *Clostridium difficile* infection. *Rev Gastroenterol Mex*. 2019;84(2):204-219. [PubMed: PM30987771](#)
21. Institut national d'excellence en santé et en services sociaux. Treatment of *clostridium difficile*- associated diarrhea or colitis. Montreal (QC) INESSS; 2017: [https://www.inesss.qc.ca/fileadmin/doc/INESSS/Rapports/Traitement/Guide\\_Cdifficile-EN.pdf](https://www.inesss.qc.ca/fileadmin/doc/INESSS/Rapports/Traitement/Guide_Cdifficile-EN.pdf). Accessed 2019 Aug 12.  
See: Treatment Principles, page 3

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24. Sokol H, Galperine T, Kapel N, et al. Faecal microbiota transplantation in recurrent Clostridium difficile infection: recommendations from the French Group of Faecal microbiota Transplantation. *Dig Liver Dis*. 2016;48(3):242-247. [PubMed: PM26433619](#)
25. Trubiano JA, Cheng AC, Korman TM, et al. Australasian Society of Infectious Diseases updated guidelines for the management of Clostridium difficile infection in adults and children in Australia and New Zealand. *Intern Med J*. 2016;46(4):479-493. [PubMed: PM27062204](#)
26. Michigan Medicine. Clostridium difficile infection in adults and children. Ann Arbor (MI): University of Michigan; 2016: <http://www.med.umich.edu/1info/FHP/practiceguides/InptCDiff/C-Diff.pdf>. Accessed 2019 Aug 12.  
See: *Treatment*
27. Faust SN, Wilcox MH, Banaszkiwicz A, Bouza E, Raymond J, Gerding DN. Lack of evidence for an unmet need to treat Clostridium difficile infection in infants aged <2 years: expert recommendations on how to address this issue. *Clin Infect Dis*. 2015;60(6):912-918. [PubMed: PM25422389](#)
28. Piekarska A, Kinika Chorob Zakaznych i Hepatologii. Recommendations for the management of symptomatic Clostridium difficile infection (CDI). *Przegl Epidemiol*. 2015;69(2):289-290, 401-282. [PubMed: PM26233089](#)
29. Debast SB, Bauer MP, Kuijper EJ, European Society of Clinical Microbiology and Infectious Diseases. European Society of Clinical Microbiology and Infectious Diseases: update of the treatment guidance document for Clostridium difficile infection. *Clin Microbiol Infect*. 2014;20 Suppl 2:1-26. [PubMed: PM24118601](#)

## Review Articles

30. Brown CC, Manis MM, Bohm NM, Curry SR. Oral vancomycin for secondary prophylaxis of Clostridium difficile infection. *Ann Pharmacother*. 2019;53(4):396-401. [PubMed: PM30450942](#)
31. Sarna KV, Gross AE. Vancomycin versus metronidazole for nonsevere Clostridioides difficile infection: are the data adequate to change practice? *Ann Pharmacother*. 2019;53(8):845-852. [PubMed: PM30734567](#)

32. Grace E, Chahine EB. Updates on Clostridioides (Clostridium) difficile infection with emphasis on long-term care. *Sr Care Pharm*. 2019;34(1):29-42.  
[PubMed: PM30821676](#)
33. Tran MN, Kullar R, Goldstein EJC. Investigational drug therapies currently in early-stage clinical development for the treatment of Clostridioides (Clostridium) difficile infection. *Expert Opin Investig Drugs*. 2019;28(4):323-335.  
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