

CADTH RAPID RESPONSE REPORT: REFERENCE LIST

Bacteriophage Therapy for Treatment of *Clostridioides difficile*: Clinical Effectiveness and Guidelines

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Research Questions

1. What is the clinical effectiveness of bacteriophage therapy for the treatment of *Clostridioides difficile*?
2. What are the evidence-based guidelines regarding the use of bacteriophage therapy for the treatment of *Clostridioides difficile*?

Key Findings

No literature was identified regarding the clinical effectiveness of bacteriophage therapy for the treatment of *Clostridioides difficile*. In addition, no evidence-based guidelines were identified regarding the use of bacteriophage therapy for the treatment of *Clostridioides difficile*.

Methods

A limited literature search was conducted by an information specialist on key resources including Medline, Cumulative Index to Nursing and Allied Health Literature (CINAHL), 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 bacteriophages or phages and *c. difficile*. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 1999 and November 22, 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

Population	Any individual diagnosed with <i>Clostridioides difficile</i>
Intervention	Bacteriophage therapy
Comparators	Q1: Any other therapy used to treat or manage <i>Clostridioides difficile</i> (e.g., antibiotics) No treatment No comparator Q2: Not applicable
Outcomes	Q1: Clinical effectiveness and safety (e.g., resolution of the infection, health-related quality of life, gastrointestinal problems, adverse events) Q2: Evidence-based guidelines for the use of bacteriophage therapy
Study Designs	Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, 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 randomized controlled trials, non-randomized studies, and evidence-based guidelines.

No literature was identified regarding the clinical effectiveness of bacteriophage therapy for the treatment of *Clostridioides difficile*. In addition, no evidence-based guidelines were identified regarding the use of bacteriophage therapy for the treatment of *Clostridioides difficile*.

Additional references of potential interest are provided in the appendix.

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

No literature identified.

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

No literature identified.

Guidelines and Recommendations

No literature identified.

Appendix — Further Information

Previous CADTH Reports

1. Bacteriophage Therapy for Multi-Drug Resistant Bacterial Infections: Clinical Effectiveness and Guidelines. (CADTH Rapid Response Report: Summary of Abstracts). Ottawa (ON): CADTH; 2019: <https://www.cadth.ca/bacteriophage-therapy-multi-drug-resistant-bacterial-infections-clinical-effectiveness-and-0>

Systematic Reviews

Protocol

2. Saperkin N, Ruizendaal E, Kovalishena O, Scholten R. Bacteriophage therapy for the prevention or treatment of bacterial infections in humans (CRD42018100813). PROSPERO: International prospective register of systematic reviews. York (GB): University of York Centre for Reviews and Dissemination; 2018: http://www.crd.york.ac.uk/PROSPERO/display_record.php?ID=CRD42018100813

Review Articles

3. Sabino J, Hirten RP, Colombel JF. Review article: bacteriophages in gastroenterology—from biology to clinical applications. *Aliment Pharmacol Ther.* 2019 Nov 07. [PubMed: PM31696976](#)
4. Yang J, Yang H. Non-antibiotic therapy for *Clostridioides difficile* infection: a review. *Crit Rev Clin Lab Sci.* 2019 Nov;56(7):493-509. [PubMed: PM31411909](#)
5. Hargreaves KR, Clokie MR. *Clostridium difficile* phages: still difficult? *Front Microbiol.* 2014;5:184. [PubMed: PM24808893](#)
6. Sangster W, Hegarty JP, Stewart DB. Phage therapy for *Clostridium difficile* infection: An alternative to antibiotics? *Semin Colon Rectal Surg.* 2014;25(3):167-170. <https://www.sciencedirect.com/science/article/abs/pii/S1043148914000372>
7. Rea MC, Alemayehu D, Ross RP, Hill C. Gut solutions to a gut problem: bacteriocins, probiotics and bacteriophage for control of *Clostridium difficile* infection. *J Med Microbiol.* 2013 Sep;62(Pt 9):1369-1378. [PubMed: PM23699066](#)
8. Zucca M, Scutera S, Savoia D. Novel avenues for *Clostridium difficile* infection drug discovery. *Expert Opin Drug Discov.* 2013 Apr;8(4):459-477. [PubMed: PM23427910](#)
9. Carson CF, Riley TV. Non-antibiotic therapies for infectious diseases. *Commun Dis Intell Q Rep.* 2003;27 Suppl:S143-146. [PubMed: PM12807291](#)