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CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Bacteriophage Therapy for Multi-Drug Resistant Bacterial Infections: Clinical Effectiveness and Guidelines

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

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Research Questions

1. What is the clinical effectiveness of phage therapy for multi-drug resistant bacterial infections in patients who have limited or failed antibiotic regimen?
2. What are the evidence-based guidelines regarding the use of phage therapy for multi-drug resistant bacterial infections?

Key Findings

One systematic review and two randomized controlled trials were identified regarding the clinical effectiveness of phage therapy for multi-drug resistant bacterial infections who have previously failed antibiotic treatment. No relevant evidence-based guidelines were identified.

Methods

A limited literature search was conducted on key resources including MEDLINE (via Ovid), the Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases, Canadian and major international health technology agencies, as well as a focused Internet search. Methodological filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, and guidelines. An additional focused search with main concepts appeared in title only was conducted. For this focused search, no study design filters were applied. The search was also limited to English language documents published between January 1, 2014 and April 5, 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	Patients with multi-drug resistant (MDR) bacterial infections who have limited or failed antibiotic regimen. (e.g., Pseudomonas aeruginosa peritonitis)
Intervention	Bacteriophage Therapy
Comparators	Q1: Any comparator; No comparator Q2: No comparator
Outcomes	Q1: Clinical effectiveness (e.g. mortality, disease progression), safety, harms Q2: Guidelines
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.

One systematic review and two randomized controlled trials were identified regarding the effectiveness of phage therapy for patients with multi-drug resistant bacterial infections who have failed a previous antibiotic regimen. No relevant health technology assessments, non-randomized studies, or evidence-based guidelines were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

One systematic review[1] and two randomized controlled trials (RCTs),[2,3] were identified regarding the effectiveness of phage therapy for patients with multi-drug resistant bacterial infections who have failed a previous antibiotic regimen.

The systematic review[1] assessed the effectiveness and safety of phage therapy against multi-drug resistant organisms in clinical practice. The authors identified 30 articles that met the inclusion criteria and determined that a majority of studies showed efficacy and safety in support of phage therapy.[1]

The first RCT[2] aimed to compare the effectiveness and tolerability of phage therapy with standard of care in adults patients who had a burn wound clinically infected with Pseudomonas aeruginosa. Over a seven day period, patients were randomized to receive topical phage therapy plus standard care or standard care only. Overall, researchers concluded that standard of care was more effective in reaching the median time to sustained reduction in bacterial burden compared to the oral phage therapy.[2]

The second RCT[3] examined whether oral phage therapy was effective and safe for treating 120 hospitalized children with acute diarrhea. Patients received one of the following oral treatments over a four day period: T4-like coliphages, a commercial Russia coliphage product, or a placebo. The researchers concluded there were no adverse events associated with oral phage therapy but it did not demonstrate clinical effectiveness by improving diarrhea outcomes due to insufficient phage coverage and the need for higher dosages.[3]

No evidence-based guidelines were identified; therefore, no summary can be provided.

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. El Haddad L, Harb CP, Gebara MA, Stibich MA, Chemaly RF. A systematic and critical review of bacteriophage therapy against multi-drug resistant ESKAPE Organisms in Humans. *Clin Infect Dis*. 2018 Nov 03. [Epub ahead of print].
PubMed: PM30395179

Randomized Controlled Trials

2. Jault P, Leclerc T, Jennes S, et al. Efficacy and tolerability of a cocktail of bacteriophages to treat burn wounds infected by Pseudomonas aeruginosa (PhagoBurn): a randomised, controlled, double-blind phase 1/2 trial. *Lancet Infect Dis*. 2019 Jan;19(1):35-45.
PubMed: PM30292481

3. Sarker SA, Sultana S, Reuteler G, et al. Oral phage therapy of acute bacterial diarrhea with two coliphage preparations: a randomized trial in children from Bangladesh. *EBioMedicine*. 2016 Feb;4:124-137.
PubMed: PM26981577

Non-Randomized Studies

No literature identified.

Guidelines and Recommendations

No literature identified.

Appendix — Further Information

Systematic Reviews and Meta-Analyses – Ongoing

4. Saperkin NV, Ruizendaal E, Kovalishena OV, Scholten RJPM. 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. Accessed 2019 Apr 17.

Case Studies

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PubMed: PM30869755

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PubMed: PM28807909

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PubMed: PM26862360

In Vitro/Vivo Studies

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PubMed: PM30650088

12. Cha K, Oh HK, Jang JY, et al. Characterization of two novel bacteriophages Infecting Multidrug-Resistant (MDR) Acinetobacter baumannii and evaluation of their therapeutic efficacy in vivo. *Front Microbiol*. 2018;9:696.
PubMed: PM29755420

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PubMed: PM29777835

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PubMed: PM30563133

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PubMed: PM28007922

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PubMed: PM28090384

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PubMed: PM25834712

Control or Storage Measures

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Dosage Forms

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Review Articles

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