

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

# Oral Antibiotics versus IV Antibiotics for Patients with Cellulitis or Soft Tissue Infections: Clinical Effectiveness and Guidelines

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## Research Questions

1. What is the comparative clinical effectiveness of oral antibiotics versus IV antibiotics for patients with cellulitis and/or other soft tissue infections?
2. What are the evidence-based guidelines regarding treatment of patients with cellulitis and/or other soft tissue infections with oral antibiotics or IV antibiotics?

## Key Findings

One systematic review and one randomized controlled trial were identified regarding the clinical effectiveness of oral versus IV antibiotics for patients with cellulitis or other soft tissue infections. In addition, one evidence-based guideline was identified regarding treatment of patients with cellulitis or other soft tissue infections with oral or IV antibiotics.

## Methods

A limited literature search was conducted by an information specialist on key resources including PubMed, 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 oral and IV antibiotics and cellulitis. For question #1 no search filters were applied to limit the retrieval by study type. For question #2, search filters were applied to limit retrieval to guidelines only. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2014 and November 26, 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>    | Q1-2: Patients of any age with cellulitis and/or other soft tissue infections in either the outpatient or hospital setting   |
| <b>Intervention</b>  | Q1-2: Oral antibiotics for cellulitis or soft tissue infection (e.g., oral cephalexin, clindamycin, probenecid, dioxycycline, primethoprine-sulphmephoxyzole)                                  |
| <b>Comparator</b>    | Q1-2: Intravenous antibiotics with or without oral antibiotics for cellulitis or soft tissue infection (e.g., cefazolin, cefazolin plus oral probenecid, ceftriaxone, clindamycin, penicillin) |
| <b>Outcomes</b>      | Q1: Clinical effectiveness: recovery; clinical cure; infection, Safety: adverse events (e.g., risk of <i>C. difficile</i> infection, diarrhea, headaches)<br>Q2: Evidence-based guidelines     |
| <b>Study Designs</b> | 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<sup>1</sup> and one randomized controlled trial<sup>2</sup> were identified regarding the clinical effectiveness of oral antibiotics versus IV antibiotics for patients with cellulitis or other soft tissue infections. In addition, one evidence-based guideline<sup>3</sup> was identified regarding treatment of patients with cellulitis or other soft tissue infections with oral or IV antibiotics. No relevant health technology assessments or non-randomized studies were identified.

Additional references of potential interest are provided in the appendix.

## Overall Summary of Findings

One systematic review<sup>1</sup> and one randomized controlled trial<sup>2</sup> were identified regarding the clinical effectiveness of oral antibiotics versus intravenous (IV) antibiotics for patients with cellulitis and/or other soft tissue infections. The authors of the systematic review found no evidence to support the use of IV antibiotics over oral antibiotics, however further higher quality evidence is needed.<sup>1</sup> The authors of the randomized controlled trial aimed to determine if oral cephalexin taken four times daily at 500mg was non-inferior to 2 grams of IV cefazolin plus probenecid.<sup>2</sup> The authors found no significant difference in treatment failure at 72 hours or clinical cure at 7 days, and concluded that oral cephalexin was a safe and effective alternative to outpatient IV cefazolin in the treatment of mild skin and soft tissue infections.<sup>2</sup>

Guidelines from the National Institute of Health Care Excellence (NICE) recommend oral antibiotics be used as a first line therapy if the patient can take oral medicines, and if the severity of their condition does not require intravenous antibiotics. In the case that intravenous antibiotics are given, NICE recommends reviewing treatment after 48 hours and considering a switch to oral antibiotics if possible. When MRSA infection is suspected or confirmed, NICE recommends using either vancomycin (IV), teicoplanin (IV) or linezolid (oral or IV) in combination with other IV or oral antibiotics.

## References Summarized

### Health Technology Assessments

No literature identified.

### Systematic Reviews and Meta-analyses

1. Brindle R, Williams OM, Barton E, Featherstone P. Assessment of antibiotic treatment of cellulitis and erysipelas: a systematic review and meta-analysis. *JAMA Dermatol.* 2019 Jun 12.  
[PubMed: PM31188407](https://pubmed.ncbi.nlm.nih.gov/31188407/)

## Randomized Controlled Trials

2. Dalen D, Fry A, Campbell SG, Eppler J, Zed PJ. Intravenous cefazolin plus oral probenecid versus oral cephalexin for the treatment of skin and soft tissue infections: a double-blind, non-inferiority, randomised controlled trial. *Emerg Med J.* 2018 Aug;35(8):492-498.  
[PubMed: PM29914924](https://pubmed.ncbi.nlm.nih.gov/29914924/)

## Non-Randomized Studies

No literature identified.

## Guidelines and Recommendations

3. NICE. Cellulitis and erysipelas: antimicrobial prescribing [*NICE Clinical guideline no. 141*]. London (UK): National Institute for Health and Care Excellence (NICE); 2019 Sep. <https://www.nice.org.uk/guidance/ng141/resources/cellulitis-and-erysipelas-antimicrobial-prescribing-pdf-66141774778309>  
*See: Recommendations 1.1.5 & 1.1.6 – Managing cellulitis and erysipelas, , page 6 and Choice of Antibiotic, page 8*

## Appendix — Further Information

### Systematic Reviews – Protocol Paper

4. Bartoszko JJ, Mertz D, Thabane L, Loeb M. Antibiotic therapy for skin and soft tissue infections: a protocol for a systematic review and network meta-analysis. *Syst Rev*. 2018 Sep 11;7(1):138.  
[PubMed: PM30205844](#)

### Randomized Controlled Trial – Alternative Intervention

#### *IV Administration Not Specifically Mentioned*

5. Aboltins CA, Hutchinson AF, Sinnappu RN, et al. Oral versus parenteral antimicrobials for the treatment of cellulitis: a randomized non-inferiority trial. *J Antimicrob Chemother*. 2015 Feb;70(2):581-586.  
[PubMed: PM25336165](#)

### Non-Randomized Studies

#### *No Comparator*

6. Chan M, Ooi CK, Wong J, Zhong L, Lye D. Role of outpatient parenteral antibiotic therapy in the treatment of community acquired skin and soft tissue infections in Singapore. *BMC Infect Dis*. 2017 Jul 6;17(1):474.  
[PubMed: PM28683717](#)

#### *Alternative Intervention*

7. Furtado GH, Rocha J, Hayden R, et al. Early switch/early discharge opportunities for hospitalized patients with methicillin-resistant *Staphylococcus aureus* complicated skin and soft tissue infections in Brazil. *Braz J Infect Dis*. 2019 Mar - Apr;23(2):86-94.  
[PubMed: PM31078574](#)
8. Rentala M, Andrews S, Tiberio A, et al. Intravenous home infusion therapy instituted from a 24-hour clinical decision unit for patients with cellulitis. *Am J Emerg Med*. 2016 Jul;34(7):1273-1275.  
[PubMed: PM27182030](#)
9. Nathwani D, Eckmann C, Lawson W, et al. Influence of real-world characteristics on outcomes for patients with methicillin-resistant *Staphylococcal* skin and soft tissue infections: a multi-country medical chart review in Europe. *BMC Infect Dis*. 2014 Sep 2;14:476.  
[PubMed: PM25182029](#)

#### *Alternative Outcome*

10. Yadav K, Suh KN, Eagles D, et al. Predictors of oral antibiotic treatment failure for nonpurulent skin and soft tissue infections in the emergency department. *Acad Emerg Med*. 2019 Jan;26(1):51-59.  
[PubMed: PM29869364](#)

## Clinical Practice Guidelines – Methods Not Specified

11. Botros M, Kuhnke J, Embil J, et al. Best practice recommendations for the prevention and management of diabetic foot ulcers. North York (ON): Wounds Canada; 2019 Jan; <https://www.wrha.mb.ca/extranet/eipt/files/WCBPR-PreventionandManagementofDiabeticFootUlcers1573r5Efinal.pdf>  
Accessed 2019 Dec 09.  
*See: Antibiotic Selection, page 48 to 49*
12. Seattle Children's Hospital. Cellulitis and abscesses v2.0: initial ED phase [*clinical pathway*]. Seattle (WA): Seattle Children's Hospital; 2019 Sep; <https://www.seattlechildrens.org/pdf/cellulitis-and-abscess-pathway.pdf>  
Accessed 2019 Dec 09.
13. Stenstrom R. Cellulitis: treatment. Vancouver (BC): BC Emergency Medicine Network.; 2018 Oct; [https://www.bcemergencynetwork.ca/clinical\\_resource/cellulitis-treatment/](https://www.bcemergencynetwork.ca/clinical_resource/cellulitis-treatment/)  
Accessed 2019 Dec 09.
14. Sullivan T, de Barra E. Diagnosis and management of cellulitis. *Clin Med (Lond)*. 2018 Apr;18(2):160-163.  
<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6303460/>  
Accessed 2019 Dec 09.  
*See: Treatment*

## Review Articles

15. Donovan AK, Burger A, Moriates C, Sharpe BA, Herzke C. Hospital Medicine update: high-impact literature from March 2018 to April 2019. *J Hosp Med*. 2019 Oct 23;14:E1-e5.  
[PubMed: PM31634096](#)
16. Bassetti M, Eckmann C, Peghin M, Carnelutti A, Righi E. When to switch to an oral treatment and/or to discharge a patient with skin and soft tissue infections. *Curr Opin Infect Dis*. 2018 Apr;31(2):163-169.  
[PubMed: PM29324505](#)
17. Leong HN, Kurup A, Tan MY, Kwa ALH, Liau KH, Wilcox MH. Management of complicated skin and soft tissue infections with a special focus on the role of newer antibiotics. *Infect Drug Resist*. 2018;11:1959-1974.  
[PubMed: PM30464538](#)

## Additional References

18. Hamill LM, Thi YE, Keijzers G. Picking the low-hanging fruit: Why not choose oral antibiotics for skin and soft-tissue infections in the emergency department. *Emerg Med Australas*. 2019 Aug 27.  
[PubMed: PM31456350](#)

19. Cunha CB. Antibiotic stewardship program perspective: oral antibiotic therapy for common infectious diseases. *Med Clin North Am.* 2018 Sep;102(5):947-954.  
[PubMed: PM30126583](#)