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**REVIEW** 

# Antibiotic prophylaxis for preventing recurrent cellulitis: A systematic review and meta-analysis



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## **KEYWORDS**

Cellulitis; Prophylaxis; Prevention; Recurrence **Summary** *Importance*: A significant proportion of patients who have had a first episode of erysipelas or uncomplicated cellulitis will subsequently develop a recurrence. There is disagreement about how effective antibiotic prophylaxis is for preventing recurrent cellulitis. *Objective*: To determine if antibiotic prophylaxis is effective in preventing recurrent cellulitis compared to no prophylaxis using a systematic review and meta-analysis.

Data sources: Studies in any language identified by searching Medline, EMBASE, Cochrane Library, CINAHL, TRIP database, clinical practice guidelines websites, and ongoing trials databases up to 31st August 2012. Search terms included cellulitis, erysipelas, controlled clinical trial, randomized, placebo, clinical trials, randomly, and trial.

Study selection: Only controlled trials comparing antibiotic prophylaxis to no antibiotic prophylaxis in patients age 16 years and above, and after 1 or more episodes of cellulitis, were included.

Data extraction and synthesis: Independent extraction of articles was done by 2 investigators using predefined data extraction templates, including study quality indicators. PROSPERO registration number: CRD42012002528. Meta-analyses were done using randomeffects models.

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Main outcomes and measures: The primary outcome was the number of patients with a recurrence of cellulitis. Secondary outcomes were (1) the time to next episode of recurrence, (2) quality of life measures, and (3) adverse events (e.g. allergic reactions, nausea).

Results: Five randomized controlled trials (n=535), with 260 patients in the intervention arm and 275 in the comparator group met our inclusion criteria. 44 patients (8%) in the antibiotic prophylaxis group and 97 patients (18%) in the comparator group had an episode of cellulitis. Antibiotic prophylaxis significantly reduced the number of patients having recurrent cellulitis, with a risk ratio (RR) of 0.46 (95% CI 0.26–0.79). None of the studies reported severe adverse effects to antibiotics. There was methodological heterogeneity amongst the studies in terms of types of antibiotic used, delivery modes, number of recurrences of cellulitis at study entry, and study quality.

Conclusion and relevance: Antibiotic prophylaxis can prevent recurrent cellulitis. Future research should aim to identify the ideal type, dosage, and duration of antibiotics for prophylaxis, as well as to identify the group of patients who will benefit most from antibiotic prophylaxis.

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# Introduction

Cellulitis of the lower extremities is an acute, painful and potentially serious infection of the skin and subcutaneous tissue associated with significant morbidity<sup>1,2</sup> and healthcare costs.<sup>3–5</sup> Erysipelas or uncomplicated cellulitis refers to non-suppurative, acute and spreading skin infection. Specifically, erysipelas tends to be more superficial and has prominent lymphatic involvement; while cellulitis extends deeper and involves subcutaneous tissues. We will use the terms erysipelas and cellulitis interchangeably in this paper. Risk factors for developing cellulitis of the leg include prior history of cellulitis, lymphoedema, toe web maceration, obesity and diabetes.<sup>6–9</sup>

Cellulitis is typically caused by b-haemolytic streptococci of group A, less often by group B, C, or G streptococci or *Staphylococcus aureus*. <sup>10,11</sup> Prior history of cellulitis is strongly associated with acute cellulitis. <sup>7,12</sup>

An attack of acute cellulitis may lead to a vicious circle of impaired lymphatic function leading to increased susceptibility to further recurrences of cellulitis. 13

However, the causal association is not clear. 14,15

In 2003, 428,274 patients were hospitalized in the US with a principle diagnosis of cellulitis, with cellulitis being responsible for 1.1% of all hospital discharges. <sup>16</sup> Sixteen to 30% of patients who have had a first episode of erysipelas or uncomplicated cellulitis will subsequently develop a recurrence. <sup>17–19</sup>

There is disagreement about how effective antibiotic prophylaxis is for preventing recurrent cellulitis. We undertook a systematic review and meta-analysis to evaluate the level and quality of available evidence regarding the efficacy and reported adverse effects of antibiotic prophylaxis against recurrent cellulitis.

# **Methods**

This systematic review protocol was registered with PROS-PERO on 11th September 2012 with registration number CRD42012002528.

#### Inclusion criteria

The defined cellulitis population included patients aged 16 years and above, and after one or more episodes of cellulitis. Participants with cellulitis secondary to filarial lymphoedema were excluded. We use cellulitis and erysipelas interchangeably in this paper.

The intervention was any antibiotic prophylaxis used for recurrent cellulitis. Any form of delivery, dose and duration of antibiotics was considered. The control group was patients without prophylactic antibiotics. Other forms of standard care (e.g. local skin care) were allowed in the control group.

The primary outcome was the number of patients with a recurrence of cellulitis. This outcome was recorded as (1) the number of patients with cellulitis, and (2) the number of episodes per patient. Also noted where possible was the total number of recurrences within a time period. Recurrence must have been diagnosed by a physician.

Secondary outcomes were (1) the time to next episode of recurrence, (2) quality of life measures, and (3) adverse events (e.g. allergic reactions, nausea). For these outcomes, there was no limit to the follow-up period after completion of antibiotics, but any events occurring during the taking of the antibiotic treatment was particularly noted.

### Search strategy

Two authors (OCC, HCHK) searched and scanned the electronic databases and other sources of studies. They developed and checked the search strategies used for each database with each other. The search strategies were 'translated' for each database where needed.

A search was done in the following databases: Cochrane Library (Cochrane Central Register of Controlled Trials (CENTRAL), CDSR, HTA, DARE, NHS EED), MEDLINE via OVID SP, EMBASE, CINAHL via EBSCOhost, guidelines websites (UK NICE, US National Guidelines Clearinghouse, Scotland SIGN), TRIP database, and ongoing trials databases (Clinicaltrials.gov; World Health Organization

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