Authors' objectives
To review the efficacy of different treatments of symptomatic Clostridium difficile (C. difficile) intestinal disease using the methodology recommended by the Cochrane Collaboration for the conduct of systematic reviews.

Searching
The medical literature was searched from January 1978 to June 1996. The search strategy identified relevant papers using the following methods.

1. MEDLINE and EMBASE were searched using a strategy designed to search for controlled clinical trials. The search terms were: 'Clostridium difficile', 'Clostridium difficile diarrhoea', 'pseudomembranous colitis', 'Clostridium difficile enterocolitis', 'Clostridium difficile colitis', 'antibiotic-associated diarrhoea', 'antibiotic-associated pseudomembranous colitis', 'antibiotic-associated colitis', 'therapy' and 'treatment'.

2. The index of abstracts from meetings of the American Gastroenterology Association, as published in Gastroenterology, were handsearched for the years 1990 to 1996.

3. The references cited in published reviews and editorials relating to C. difficile, and in the papers identified by the other search strategies, were reviewed.

4. The authors of the trials were contacted for further information.

Study selection
Study designs of evaluations included in the review
Randomised controlled trials (RCTs) where the primary end point was the rate of clinical resolution, and the secondary end points were the following: rate of clinical relapse; the rate of clearance of C. difficile from stool cultures by the end of the course of treatment with the study interventions; and clearance of C. difficile toxin(s) from stool cultures by the end of the course of treatment with the study interventions.

Specific interventions included in the review
Vancomycin, metronidazole, bacitracin, colestipol, teicoplanin, fusidic acid, and placebo.

Participants included in the review
Patients with symptomatic C. difficile intestinal disease.

Outcomes assessed in the review
The outcome measures were: clinical resolution of the disease; clinical relapse after treatment; clearance of the organism C. difficile; and clearance of the toxin(s).

How were decisions on the relevance of primary studies made?
The authors do not state how the papers were selected for the review, or how many of the authors performed the selection.

Assessment of study quality
The authors do not report the method used to assessing validity, or how the validity assessment was performed. However, they stated that the most common limitations of trial design included a lack of blinding of the study participants, and the absence of tests for adequacy of blinding and allocation concealment.
Data extraction
The data were extracted independently by two of the authors. Any differences were resolved by consensus, and through arbitration with the third reviewer.

Methods of synthesis
How were the studies combined?
For each end point, each outcome measure was summarised as a dichotomous variable. For each trial, the outcomes were expressed as odds ratios (ORs) with 95% confidence intervals (95% CIs). ORs and CIs were calculated using biostatistical software (RevMan).

How were differences between studies investigated?
The authors do not state how differences between the studies were investigated.

Results of the review
Nine prospective RCTs with 469 patients were included, although there was some overlap between participants in two of the studies.

Two trials were placebo-controlled, 6 trials compared vancomycin with other antibiotics, and one trial compared teicoplanin with fusidic acid. The response rates for clinical resolution ranged from 21 (placebo) to 100% (vancomycin). On pooling the trials, no antibiotic showed a clear therapeutic superiority. The rates of clinical relapse ranged from 5 to 42%. Only one trial showed a significant advantage of one antibiotic over another for the prevention of relapse (teicoplanin versus fusidic acid).

Authors’ conclusions
The published data were limited, and further studies are therefore required.

CRD commentary
The authors made an extensive search of electronic databases and the references of papers found in the other searches. Since they limited themselves to English language studies and did not review unpublished data, it is unclear how many relevant studies may have been excluded.

The inclusion criteria and the primary and secondary end points were very well-described, and each included study was discussed. The authors calculated the ORs and CIs for the individual studies, but they did not report the way in which the studies were combined or how differences between the studies were investigated.

The authors stated that the response rates for the different antibiotics did not show statistically-significant differences, and it is possible that the low number of patients may obscure small differences in clinical efficacy because of type II error. The authors also stated that there was selection bias in the patients studied in the published trials, because none of the patients were stratified for severity of infection or for severity of co-morbidities. The authors also found considerable variation between the trials in terms of the clearance rates for the organism and toxin, suggesting that these markers are not clinically meaningful measures of outcome in the context of clinical trials of therapy of C. difficile intestinal infection.

Bibliographic details
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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.