Antimicrobial prophylaxis in colorectal surgery: a systematic review of randomised controlled trials

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Authors' objectives
The review aimed to evaluate the relative efficacy of antimicrobial prophylaxis against post-operative wound infection in patients undergoing colorectal surgery.

Searching
MEDLINE (from 1984), EMBASE or EMBASE Alert (from 1983), and the Cochrane Controlled Trials Register were searched. The MEDLINE search strategy was reported in full. The references of retrieved articles were checked for other relevant trials. The journals Acta Chirurgica Scandinavica, British Journal of Surgery, Journal of Antimicrobial Chemotherapy, Archives of Surgery and Annals of Surgery were handsearched. Studies in all languages were eligible for the assessment of efficacy, whereas only those published in English were used to assess the adverse events.

Study selection

Study designs of evaluations included in the review
Randomised controlled trials (RCTs) were eligible for inclusion.

Specific interventions included in the review
Studies of antibiotic prophylaxis were eligible for inclusion. Most of the included studies compared different antibiotic regimens; only a few compared antibiotic prophylaxis with no antibiotic. In excess of 70 different antibiotic regimens were included, with differing routes of administration and differing dosages and/or combinations. Full details were given in the report.

Participants included in the review
Studies that included patients undergoing colorectal surgery were eligible for inclusion. Both elective and emergency surgery patients were included. Studies of abdominal surgery were included if the results for colorectal surgery could be separated from those for other procedures.

Outcomes assessed in the review
Studies that reported surgical wound outcomes were eligible for inclusion. The main outcome assessed in the review was the rate of surgical wound infection (SWI). Where possible, only abdominal wound infections were included. If it was unclear whether perineal wound infections or other infections related to surgical procedures were included in a trials' results, those results were included in the review. Other outcomes included systemic infections, duration of hospital stay, mortality and adverse events.

How were decisions on the relevance of primary studies made?
The relevance of each identified study was assessed by one reviewer and checked by another.

Assessment of study quality
Indicators of study quality included the method of randomisation (including allocation concealment), blind outcome assessment, withdrawals, a priori calculation of sample size, and whether the definition of SWI was provided. The validity of each study was assessed by one reviewer and checked by another.

Data extraction
Data were extracted by one reviewer using a predefined form and checked by another. If studies reported on more than one type of surgery, data were extracted for colorectal surgery only. The authors were contacted if their article reported
insufficient data on SWI.

**Methods of synthesis**

*How were the studies combined?*

The studies were grouped according to the main antibiotic used in the experimental treatment group. Studies that assessed the same treatment regimen were combined using meta-analyses to estimate a pooled Mantel-Haenszel odds ratio (OR) with 95% confidence intervals (CIs). A narrative synthesis was undertaken where statistical pooling was inappropriate.

*How were differences between studies investigated?*

Differences between the antibiotic regimens in the treatment and comparison groups were tabulated and described in the text. A chi-squared test was used to test for statistical heterogeneity in the meta-analyses.

**Results of the review**

A total of 147 RCTs (n=23,049) were included in the review.

The methodological quality of the included trials improved over time, but problems concerning randomisation, blinding and insufficient sample size remained.

Antibiotic prophylaxis significantly reduced the rate of SWI in comparison with no antibiotic (4 trials, n=293). The OR was 0.24 (95% CI: 0.13, 0.43).

The overall rate of SWI with various regimens of prophylactic antimicrobial agents in colorectal surgery across all the included studies was 11.1% (2,540 out of 22,927). It was 10.6% for the 120 trials in elective surgery only, and 13.4% for the 27 trials in both elective and emergency surgery patients.

In general, the efficacy of many different regimens appeared to be similar. However, many trials were too small to demonstrate a difference between treatments if one had existed. Some regimens appeared to be less effective, such as metronidazole, doxycycline, and piperacillin monotherapies. There was insufficient evidence to determine the relative efficacy of different routes of administration.

A meta-analysis of 17 studies that compared a single dose with multiple doses of the same antibiotic, or combination of antibiotics, showed no significant difference in SWI (OR 1.17, 95% CI: 0.89, 1.54). There was insufficient evidence to draw conclusions about single- versus multiple-dose prophylaxis in relation to the duration of the surgical operation.

A meta-analysis of 6 trials that compared a first-generation cephalosporin with a second- or third-generation cephalosporin showed no significant difference in SWI (OR 0.93, 95% CI: 0.46, 1.86).

Other efficacy outcomes were reported inconsistently in the trials and may, therefore, be influenced by detection and reporting bias. Results of these outcomes were provided in the report.

Seventy-four of 134 trials published in English reported adverse events. Patients with a history of allergy to drugs were not included in these trials. Commonly reported adverse events included skin rash, nausea and diarrhoea. Only one trial reported serious adverse events, namely post-operative bleeding in patients treated with latamoxef.

**Cost information**

The cost information reported in 18 of the included RCTs was summarised. For studies that were not conducted in the UK, the equivalent cost in pounds sterling was calculated using the exchange rate in the year of publication. The cost of antibiotic prophylaxis needs to be considered against the potentially greater costs of SWI, including treatment and prolonged hospital stay. Three trials reported that monotherapy was as effective but less expensive than combination therapy. The authors stated that guidelines for cost-effective use of antimicrobial prophylaxis in colorectal surgery should be developed locally.
Authors' conclusions
Antibiotic prophylaxis was effective in preventing SWI in colorectal surgery. There was no significant difference between many regimens, although some were inadequate. Multiple-dose regimens may be unnecessary. The evidence did not support the idea that new cephalosporins are more effective than first-generation cephalosporins.

CRD commentary
The objective of the review was clear, although extremely broad in terms of the intervention of interest. Trials were sought from several relevant sources and some attempt was made to minimise bias when selecting the studies for inclusion. The criteria used to assess study quality were appropriate. The quality of the trials in general was discussed at length, but the potential impact of individual study quality was not considered in the summary of results. Adverse events were not reviewed as extensively as efficacy. The authors' conclusion that antibiotic prophylaxis is effective in preventing SWI in colorectal surgery was supported by the four included trials of antibiotic prophylaxis versus no antibiotic (published in 1984 to 1985). The reviewers described the randomisation in these small trials as unclear, hence the reliability of their findings is uncertain. There also appears to have been too few robust trials or direct comparisons to support firm conclusions about the relative efficacy of alternative antibiotic regimens.

Implications of the review for practice and research
Practice: In terms of implications for policy, the authors stated two principles to follow when selecting an antimicrobial prophylactic regimen for colorectal surgery. First, the antibiotics should be active against both aerobic and anaerobic bacteria. Second, the administration should be timed to ensure that the tissue concentration of antibiotics around the wound is sufficient when bacterial contamination occurs. In addition, the authors stated that the universal use of a particular regimen should be avoided to minimise the development of antibiotic-resistant bacteria. These implications were not clearly derived from the evidence presented in this review.

Research: The authors stated that future research should focus on the understanding of the practical use of antimicrobial prophylaxis in colorectal surgery in the UK, and the cost-effectiveness of different regimens.

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Other publications of related interest

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MeSH
Abdomen /surgery; Administration, Oral; Administration, Topical; Antibiotic Prophylaxis /adverse effects /economics /methods; Cephalosporins /administration & dosage /therapeutic use; Colon /surgery; Cost-Benefit Analysis; Diarrhea /chemically induced; Drug Administration Schedule; Drug Costs; Drug Therapy, Combination /administration & dosage
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Record Status
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.