Impact of selective decontamination of the digestive tract on carriage and infection due to Gram-negative and Gram-positive bacteria: a systematic review of randomised controlled trials
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CRD summary
The authors concluded that selective digestive decontamination improved Gram-negative bacteria outcomes, but did not significantly increase Gram-positive outcomes. The authors advised caution when considering Gram-positive results. This was a well-conducted review and the authors’ conclusions and advice are likely to be reliable.

Authors’ objectives
To evaluate the effect of selective digestive decontamination on Gram-negative and Gram-positive carriage and severe infections.

Searching
MEDLINE (from 1976), EMBASE (from 1980) and Cochrane Central Register of Controlled Trials (CENTRAL) were searched to June 2006. Search terms were reported. No language restrictions were applied. In addition, reference lists of systematic reviews, meta-analysis and identified studies were screened and unspecified conference abstracts and proceedings of scientific meetings were searched. Searches were conducted for published and unpublished studies.

Study selection
Randomised controlled trials (RCTs) that compared enteral antibiotics (with or without parental antibiotics) for selective digestive decontamination with no treatment or placebo in critically-ill patients (either selected or unselected) were eligible for inclusion. Trials had to assess infection outcomes. Trials of neutropenic, stem cell and bone marrow transplant patients were excluded. The primary review outcomes were overall carrier state, oropharyngeal and rectal carriage of Gram-negative and Gram-positive infections, and infections of the lower airways or bloodstream due to Gram-negative or Gram-positive bacteria.

The included studies evaluated different selective digestive decontamination regimens. Most regimens included parenteral antibiotics (predominantly a third generation cephalosporin); others included only enteral antibiotics administered via the oropharyngeal and/or intestinal route. Participants included trauma, paediatric, burns, cardiac, surgical, stroke, pancreatitis and acute liver failure and liver transplantation patients.

Three reviewers independently selected studies.

Assessment of study quality
Three reviewers independently assessed validity based on the seven criteria described by Heyland et al. Criteria included randomisation, blinding, patient selection, description of sample, reproducibility and definitions of carriage and infection. Possible scores ranged from 0 to 14. Scores from the three reviewers were summed to produce a total score for each criterion.

Data extraction
Where possible, data were extracted on an intention-to-treat basis. The numbers of patients with each specified Gram-positive and Gram-negative outcome were extracted from each study.

Three reviewers independently extracted data and resolved disagreements by discussion.

Methods of synthesis
Pooled odds ratios (OR) and 95% confidence intervals (CI) were calculated using a random-effects model; 0.5 was added to cells with zero events. Heterogeneity was assessed using the Cochrane Q statistic and the $I^2$ statistic ($p<0.10$ or $I^2>50\%$ were considered indicative of significant heterogeneity). Pre-specified sub-group analyses were used to examine the effect of mode of administration (parenteral plus enteral, or enteral only), quality of randomisation,
blinding of patients and caregivers, and study quality. In addition, infections due to Gram-negative micro-organisms were analysed separately. Publication bias was assessed using a funnel plot.

**Results of the review**
Fifty-four RCTs were included (9,473 patients). Twenty-one RCTs were blinded and 16 RCTs used adequate methods of randomisation. The median quality score was 9.3 (interquartile range 8 to 11).

**Gram-negative outcomes**: Selective digestive decontamination was associated with a statistically significant reduction in oropharyngeal carriage (OR 0.13, 95% CI 0.07 to 0.23; 20 RCTs), rectal carriage (OR 0.15, 95% CI 0.07 to 0.31; 15 RCTs), overall infection (OR 0.17, 95% CI 0.10 to 0.28; eight RCTs), lower respiratory tract infection (OR 0.11, 95% CI 0.06 to 0.20; 14 RCTs) and bloodstream infection (OR 0.35, 95% CI 0.21 to 0.67; 18 RCTs). The authors stated that parenteral plus enteral antibiotics were more effective at reducing carriage and severe infections due to Gram-negative bacteria, but this was not based on direct head-to-head trials.

**Gram-positive outcomes**: There were no statistically significant differences between selective digestive decontamination and control for oropharyngeal or rectal carriage, overall infections or bloodstream infections. Selective digestive decontamination was associated with a statistically significant reduction in lower respiratory tract infection (OR 0.52, 95% CI 0.34 to 0.78; 14 RCTs).

No significant heterogeneity was found for any of the analyses. The authors stated that the funnel plot showed no evidence of publication bias.

**Authors’ conclusions**
Selective digestive decontamination improved Gram-negative bacteria outcomes but did not significantly increase Gram-positive outcomes. The authors advised caution when considering Gram-positive results due to potential variations in prevalence or endemicity of Gram-positive organisms in different populations.

**CRD commentary**
The review question was clearly stated. Inclusion criteria were defined for intervention, participants, outcomes and study design. Several relevant sources were searched and no language restrictions were applied to the search. Attempts were made to locate unpublished studies; the funnel plot showed no evidence of publication bias. Appropriate methods were used to minimise reviewer error and bias during the review process.

Only RCTs were included in the review. Quality was assessed and reported, and the effect of study quality on results was examined. Appropriate methods were used for the meta-analyses. Heterogeneity was assessed. Various pre-defined subgroup analyses conducted. One result for Gram-negative outcomes was not based on direct evidence. Limitations of the review were discussed.

This was a well-conducted review and the authors’ conclusions and advice about cautious interpretation of Gram-positive findings are likely to be reliable.

**Implications of the review for practice and research**
The authors did not state any implications for practice or further research.

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