Authors' objectives
To evaluate whether stress ulcer prophylaxis with histamine-2-receptor antagonists or antacids reduces mortality and morbidity in critically-ill patients.

Searching
MEDLINE and EMBASE were searched from 1966 onwards for articles available by October 1992; no search terms given. Additional literature was located through SciSearch, following identification of frequently cited references and examination of reference lists of all articles. Information on unpublished and ongoing studies was obtained by searching conference abstracts and databases of unpublished material, and by contacting authors of primary studies, the National Institutes of Health and Medical Research Council of Canada, and relevant pharmaceutical companies.

Study selection
Study designs of evaluations included in the review
Randomised or quasi-randomised (by identification number or date) clinical trials, plus overviews that had evaluated stress ulcer prophylaxis drugs. The included studies had to compare one or more prophylactic drugs with each other or with an untreated control group.

Specific interventions included in the review
Antacids, histamine-2-receptor antagonists, sucralfate, prostaglandins and pirenzepine.

Participants included in the review
Critically-ill patients.

Outcomes assessed in the review
Overt gastrointestinal bleeding, clinically-important bleeding, nosocomial pneumonia and mortality were assessed.

How were decisions on the relevance of primary studies made?
Two reviewers independently assessed titles and abstracts for each identified study.

Assessment of study quality
Methodological quality was based on study design, population, intervention and outcome; this was used to generate a validity score for each study ranging from 0 (poor) to 12 (excellent). Two reviewers independently assessed each study for methodological quality, and the completed validity forms were sent to the original authors for checking.

Data extraction
The data were abstracted independently by two reviewers, and the original authors were asked to check data extraction forms.

Methods of synthesis
How were the studies combined?
Common odds ratios (ORs) were calculated (several comparisons were made between different agents).

How were differences between studies investigated?
The studies were compared according to their methodological quality score.
**Results of the review**
Sixty-three clinical trials and 3 overviews were included.

The validity of the primary studies was variable; the mean overall score was 5.5.

Overt bleeding: compared with placebo or no therapy, histamine-2-receptor antagonists reduced overt bleeding (common OR 0.29, 95% confidence interval, CI: 0.17, 0.45), as did antacids (OR 0.40, 95% CI: 0.20, 0.79). Histamine-2-receptor antagonists were more effective in reducing overt bleeding than antacids (OR 0.56, 95% CI: 0.33, 0.97).

Clinically-important bleeding: compared with no therapy, histamine-2-receptor antagonists reduced the incidence of clinically-important bleeding (OR 0.35, 95% CI: 0.15, 0.76), as did antacids (OR 0.35, 95% CI: 0.08, 1.33).

Pneumonia: sucralfate reduced the incidence of pneumonia when compared with two gastric pH-altering agents (OR 0.50, 95% CI: 0.21, 0.79).

Mortality: sucralfate was associated with a lower mortality rate than antacid therapy (OR 0.70, 95% CI: 0.52, 0.94).

**Authors’ conclusions**
Stress ulcer prophylaxis is warranted in critically-ill patients who are mechanically ventilated or who have a coagulopathy. However, current evidence supports the use of sucralfate over other agents, both because of a reduction in pneumonia and a possible reduction in mortality. Further comparison of sucralfate with either histamine-receptor antagonists or antacids is warranted to improve the precision of the estimate of the effect on bleeding prevention.

**CRD commentary**
Some of the results presented in this review are taken from previously published meta-analyses.

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