Authors' objectives
To review the effect of enteral nutrition (EN) on nosocomial pneumonia in critically ill patients, as summarised in randomised clinical trials.

Searching
Two databases, MEDLINE and EMBASE, were searched from 1980 onwards. The textwords and keywords used to search MEDLINE were: 'critical care', 'intensive care units', 'pneumonia', 'respiratory tract infection', 'mechanical ventilation', 'gastropulmonary', 'enteral nutrition', 'randomized controlled trials' and 'prospective studies'. The terms used to search EMBASE were 'pneumonia', 'prevention' and 'control'. Frequently cited articles were identified and SciSearch was used to locate any additional randomised controlled trials. The Cochrane Controlled Trials Register, the Cochrane Database of Systematic Reviews and DARE were also searched via the Cochrane Library. Studies reported in any language were considered. The reference lists of all primary and review articles were reviewed.

Study selection
Study designs of evaluations included in the review
Published randomised controlled trials assessing the effect of nutritional support in humans were eligible for inclusion in the review.

Specific interventions included in the review
Studies assessing the effect of nutritional support were eligible for inclusion in the review. In particular, the studies included compared the following: total parenteral nutrition (TPN) and EN; early and late nasoduodenal feeding; gastric and jejunal feeding; intermittent and continuous feeding; modular tube feeds (MTF) and standard feeds (Osmolite and Traumacal); and early immune-enhancing feeding and standard feeding.

Participants included in the review
Critically ill patients, including those who had suffered trauma or burns. Studies assessing the effect of nutritional support in critically ill adults were eligible for inclusion in the review. Relevant nutritional interventions in seriously but not necessarily critically ill patients were excluded a priori. Only studies enrolling non-neutropenic adults without the human immunodeficiency virus were considered.

Outcomes assessed in the review
Studies assessing the effect of nutritional support on the incidence of nosocomial pneumonia were eligible for inclusion in the review. The a priori exclusions were studies examining surrogate end points for pneumonia, studies that did not report how pneumonia was diagnosed, and studies evaluating or reporting composite infectious outcomes.

How were decisions on the relevance of primary studies made?
Two reviewers independently applied the selection criteria to the full manuscripts.

Assessment of study quality
The authors do not report a formal method for assessing validity. However, a number of factors which pertain to study quality were commented upon: the method of treatment allocation; the proportion of patients who were excluded post-randomisation; whether co-interventions were described; whether the end points were assessed by investigators blinded to the intervention; and the outcome definitions used. Any disagreements between the reviewers in terms of the design characteristics were resolved by discussion and consensus. Two reviewers independently abstracted data pertaining to study quality from the studies.
Data extraction
Two reviewers abstracted the data from the studies. Any disagreements between the reviewers in terms of the raw data abstraction were resolved by discussion and consensus.

The data extracted included: study author; intervention(s) and comparator(s); study population; the method by which the patients were assigned to groups; any co-interventions given; the number of exclusions from the analysis after randomisation, and the reasons for these exclusions; whether the outcome assessor was blinded to the randomisation group; the definition of nosocomial pneumonia (ventilator-associated pneumonia); the pneumonia rate in each arm of the trial and the relative risk, which was expressed as the risk ratio (RR) with associated 95% confidence intervals (CIs).

Methods of synthesis
How were the studies combined?
The studies were grouped according to the interventions being tested. A narrative overview of the studies in each particular group was given. No statistical or graphical assessment of publication bias was reported.

How were differences between studies investigated?
Heterogeneity was not statistically assessed where the studies were grouped together. However, the narrative overview also discussed factors that may lead to differences between the studies. These factors included differences in the concealment of randomisation; the effect of blinding of the patient, caregiver and assessor to the randomisation group; and the effect of co-interventions, diagnostic criteria and outcome measures.

Results of the review
Ten studies with a total of 583 patients were included. There were 4 studies (total n=265) of EN compared with TPN, one trial (n=38) of early versus delayed nasoduodenal feeding, one trial (n=38) of gastric versus jejunal tube feeding, one trial (n=60) of intermittent versus continuous enteral feeding, and 3 trials (total n=181) evaluating different enteral feeding formulae.

The four trials comparing TPN with EN yielded inconsistent results. In one trial, there was a trend towards a lower rate of pneumonia associated with EN (0% compared with 20% in the TPN group; RR undefined), while in another, the pneumonia rate was significantly lower in the EN group (RR 0.38, 95% CI: 0.16, 0.90). In the remaining two studies, the pneumonia rate was slightly higher in patients receiving EN (RR 1.23, 95% CI: 0.51, 2.95; RR 1.06, 95% CI: 0.56, 2.02), but this was not statistically significant.

One study compared early nasoduodenal feeding begun within 24 hours with nasoduodenal feeding delayed for 72 hours. In patients receiving early feeds, there was a non significant trend towards increased rates of pneumonia; the rates of pneumonia were 42 and 21% for early and late feeds, respectively (RR 2.0, 95% CI: 0.72, 5.54).

Considering the potential for EN to cause aspiration pneumonia, one study tested the effect of the delivery site. Two cases of pneumonia were identified among the 19 patients receiving pre-pyloric gastric feeds, while no cases were observed in the 19 patients receiving post-pyloric feeds through a jejunal tube (RR undefined).

In the single trial comparing intermittent and continuous EN, 5 of the 30 patients in each group developed nosocomial pneumonia (RR 1, 95% CI: 0.32, 3.10).

One study evaluated a MTF, i.e. a high-protein, low-fat, linoleic acid-restricted formulation enhanced with arginine, cysteine, vitamin A, zinc, omega-3-polyunsaturated fatty acids, and ascorbic acid. When compared against standard preparations (Traumacal and Osmolite), lower pneumonia rates were observed in the MTF patients. This difference was statistically significant when comparing Traumacal with MTF (RR 0.25, 95% CI: 0.06, 0.99), but statistically non significant when comparing Osmolite with MTF (RR 0.27, 95% CI: 0.07, 1.15).

There was no difference in the rates of pneumonia when Immun-Aid was compared with Vivonex (RR 0.92, 95% CI: 0.24, 3.48). However, when Immun-Aid was compared with Promote, it was found to be associated with a non significant trend towards a lower pneumonia rate (0% compared with 18% in the Promote group; RR undefined).
Authors’ conclusions
Nutritional interventions in critically ill patients appear to have a modest and inconsistent effect on nosocomial pneumonia. This body of evidence neither supports nor refutes the gastropulmonary route of infection.

CRD commentary
The authors provided a clear and concise description of the research question being studied in this review, and formulated inclusion and exclusion criteria appropriate to the question. They also gave full details of how the criteria were applied. The search strategy appears to have been appropriate, but it is possible that the choice of databases may have reduced the possibility of locating all studies. MEDLINE is potentially biased towards studies conducted by medical practitioners. The inclusion of a database with a more comprehensive coverage of the allied health, psychological and nursing literature may have strengthened the study. The authors did not report any attempt to locate unpublished literature (e.g. the SIGLE database). They also did not state whether they contacted experts in the field.

The validity assessment seems to have been appropriate. Suitable details of the individual studies appear to have been presented. The conclusions drawn, and the research recommendation made on the basis of these conclusions, follow from the evidence presented.

Implications of the review for practice and research
Practice: The authors did not state any implications for practice.

Research: The authors state that the interventions studied in this review require further investigation in large-scale studies.

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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.