Statins for sepsis: a critical and updated review
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CRD summary
This review investigated effectiveness of statins for treatment of sepsis. The authors concluded that statins had a beneficial effect on the outcome of infection, but could not make firm conclusions due to the poor quality of available data. This was an appropriate conclusion and is likely to be reliable.

Authors' objectives
To assess the effectiveness of statins for treatment of sepsis.

Searching
PUBMED, EMBASE, Scopus and The Cochrane Library were searched up to 15 December 2008 without language restrictions (search terms were provided). Reference lists from identified articles, ClinicalTrials.gov and www.clinical-trials.com were searched.

Study selection
Studies that compared infection-related outcomes among patients who received and did not receive statins were eligible for inclusion provided they were full-text peer-reviewed articles. Only patients with bacterial infections were eligible.

Patients in the included studies had community acquired pneumonia, bacteraemia, postoperative infection or had sepsis or were at risk of developing sepsis. Participants were treated in out-patient and in-patient settings. Type of statin and dose used in included studies was not reported. Definition of current statin use ranged from a prescription in the past 30 days to one year before the sepsis episode.

The authors stated neither how the papers were selected for the review nor how many reviewers performed the selection.

Assessment of study quality
The authors recorded whether or not studies used propensity scoring to attempt to control for confounding bias, but did not state how this assessment was performed.

Data extraction
Odds ratios (OR), relative risks (RR), hazard ratios (HR) and p-values were extracted where available.

The authors stated neither how data were extracted for the review nor how many reviewers performed data extraction.

Methods of synthesis
Results were discussed in a narrative synthesis grouped by type of infection. Study details were reported in tables and differences between studies were discussed in the text.

Results of the review
Twenty-two studies (n=177,260) were included: one randomised controlled trial (RCT); seven prospective cohort studies; 12 retrospective cohort studies; and two retrospective case-control studies. The sample size ranged from 53 to 69,168 patients. Approximately two thirds of the studies reported a statistically significant benefit with statin use.

Patients with sepsis or at risk of sepsis (nine studies): In one RCT there was no statistically significant difference between pravastatin and placebo in incidence of sepsis in patients with subarachnoid haemorrhage, although there was a reduction in sepsis-related mortality in the statin group (6.25% in the statin group versus 71.43% in the placebo group, p<0.001). Three cohort studies that used propensity-matched sub-cohorts reported a statistically significant association between use of statins and reduced sepsis-related hospitalisations and infection-related mortality. Two of five non-
matched cohort studies reported decreased sepsis/infection rates with statin use, one reported no difference and two did not report this outcome. Satin use was associated with decreased overall 30-day or hospital mortality in one study, increased mortality in one study and no difference in two studies.

Patients with community acquired pneumonia (seven studies): In five studies (including four with propensity-matched cohorts and one case-control study), statin use was associated with decreased 30-day mortality; one study reported no difference. Two case-control studies reported decreased risk of pneumonia or fatal pneumonia with current statin use.

Patients with bacteraemia (three studies): In two cohort studies statin use was associated with decreased hospital mortality and bacteraemia-attributable mortality; in one study mortality was not lower with statins.

Prevention of infection in postoperative setting (three studies): In one cohort study of cardiac surgery patients, statin use was not associated with reduced incidence of serious infection and in one study was associated with reduced incidence of infection. In the single study that used propensity score analysis there was no benefit with statin use.

Seven potentially relevant RCTs were identified that were ongoing or not published at the time of the review.

Authors’ conclusions
The findings suggested that statins had a beneficial effect on the outcome of infection, but no firm conclusions could be drawn as available data was mainly observational.

CRD commentary
The review addressed a clear question and was supported by appropriately broad inclusion criteria. A number of relevant databases were searched without language restrictions. Limited attempts were made to locate unpublished data, so relevant studies may have been missed. The authors identified two RCTs that they were unable to include as data were not published at the time of the review. Although it was not reported whether appropriate methods were used to reduce error and bias in study selection, data extraction and quality assessment, an earlier review that the authors were updating used such methods (see Publications of Related Interest); therefore, it is likely that such methods were used in this update. Relevant study details were reported, although there was a lack of information on type of statin, dose and comparator (potentially important sources of clinical variability between studies). A narrative synthesis seemed a reasonable approach. The authors’ conclusions were suitably cautious in reflecting the limited evidence available and are likely to be reliable.

Implications of the review for practice and research
Practice: The authors stated that there was no strong clinical evidence to support the use of statins in patients with sepsis.

Research: The authors did not state any implications for research, but highlighted that there were several relevant ongoing RCTs at the time of the review.

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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.