CRD summary
The authors concluded that perioperative steroids had a favourable impact on postoperative outcomes after liver resection. These conclusions seem to reflect the results of the review, but their reliability is uncertain due to small samples, poor-quality of evidence, and analyses with wide variations.

Authors' objectives
To evaluate the effects of intravenous perioperative steroids on ischaemia reperfusion injury and surgical stress response, in patients undergoing liver resection.

Searching
MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials (CENTRAL) were searched for studies, published in English, from 1966 onwards. Search terms were reported. Reference lists of retrieved articles were handsearched.

Study selection
Non-randomised or randomised controlled trials (RCTs) that compared perioperative administration of intravenous steroids, with either standard care or placebo, for patients over 18 years old, who were undergoing liver resection, were eligible for inclusion. Trials were included irrespective of vascular control procedures. Liver transplantation trials were excluded, as were trials that did not directly investigate ischaemia reperfusion injury.

Three trials were conducted in Japan, two in Italy, and one in Germany. Publication dates ranged from 1996 to 2011. The mean age of the patients was 66 years. The steroids were methylprednisolone or hydrocortisone (long- or short-acting glucocorticosteroids). Where reported, the drug protocol and vascular exclusion technique varied. The most common reasons for liver resection were hepatocellular carcinoma, liver metastases, cholangiocarcinoma, and living-donor hepatectomy.

The authors did not state how many reviewers were involved in trial selection.

Assessment of study quality
Trial quality was assessed, using the Jadad scale (range 0 to 5), for randomisation, blinding and attrition rate. The authors did not report how many reviewers were involved in quality assessment.

Data extraction
The relevant outcomes were extracted to calculate risk ratios and mean differences, with their 95% confidence intervals. The trial authors were contacted for additional data.

Two reviewers independently extracted trial data; any disagreements were resolved by consensus after discussion with the other three reviewers.

Methods of synthesis
Pooled risk ratios and weighted mean differences, with their 95% confidence intervals, were calculated using a fixed-effect model where there was no evidence of heterogeneity; otherwise a random-effects model was used. Statistical heterogeneity was assessed using Cochran’s Q and $I^2$. A funnel plot was used to assess publication bias.

Sensitivity analysis was performed to examine the association between the impact of the intervention and preoperative liver dysfunction, drug regimen, and method quality. Meta-regression was used to assess the influence of variables such as the duration of operation, the extent of liver resection, and the dose of steroid.
Results of the review
Six trials (five RCTs and one non-randomised controlled trial) were included in the review (396 patients; range 17 to 200). One trial scored 1, three scored 2, one scored 3, and one scored 4, on Jadad scale. Three trials reported allocation concealment; none reported an intention-to-treat analysis. There was a low risk of selection bias, and a low attrition rate.

Compared with control, patients in the steroid group had significantly lower postoperative morbidity (RR 0.76, 95% CI 0.57 to 0.99; I=0; six trials). There was no significant difference between steroid administration and control for infection complications, wound problems, bile leak, pleural effusion, and liver failure. No trial reported an increase in glucose intolerance for the steroid group.

The steroid group had a significantly greater rise in early postoperative interleukin 10 levels (WMD 19.56 picograms per mL, 95% CI 4.55 to 34.56) and reduced postoperative blood levels of bilirubin (WMD -11.35 micromoles per L, 95% CI -19.77 to -2.92), inflammatory markers, such as interleukin 6 (WMD -112.01 to -51.50), and C-reactive protein (WMD -55.81 mg per mL, 95% CI -72.86 to -38.75), compared with controls. All analyses had high levels of heterogeneity.

There was no significant difference in alanine transaminase, and aspartate aminotransferase levels, and the mean length of hospital stay, between the two groups.

The results of the sensitivity analyses and meta-regression were reported. The funnel plot suggested the presence of publication bias.

Authors' conclusions
Perioperative steroids had a favourable impact on postoperative outcomes after liver resection.

CRD commentary
The review question and inclusion criteria were clear. Relevant sources were searched, but unpublished trials, and those in languages other than English, were not sought, so relevant evidence may have been missed. Some evidence of publication bias was found, but the analysis was unreliable with so few trials. Appropriate methods to reduce reviewer error and bias were used for data extraction, but it was unclear whether similar methods were used for trial selection and quality assessment. A relevant tool was used to assess quality, and the reliability of most trials was low. Appropriate methods were used to pool the data and to assess heterogeneity.

The authors' conclusions seem to reflect the results of the review. The reliability of these conclusions was uncertain, due to the small samples, poor quality (Jadad score 1 or 2), and wide confidence intervals, with high heterogeneity, for most analyses. The authors tried to explore this heterogeneity in sensitivity analyses and multivariate meta-regression. Long-term follow-up was not available, so the potential long-term adverse effects of glucocorticosteroids are unknown.

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

Research: The authors stated that further studies should have long follow-up periods and systematically monitor for oncological outcomes, and adverse effects such as steroid-induced diabetes.

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Bibliographic details

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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.