

# Safety and Efficacy of Corticosteroids for the Treatment of Septic Shock: A Systematic Review and Meta-Analysis

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**Background.** Septic shock is common and results in significant morbidity and mortality. Adjunctive treatment with corticosteroids is common, but definitive data are lacking. We aimed to determine the efficacy and safety of corticosteroid therapy among patients with septic shock.

**Methods.** Medline, Embase, Cochrane Library, Web of Science, and Google Scholar were searched for randomized trials and observational studies published from January 1993 through December 2008. Studies were selected if they included adults with septic shock, discussed treatment with intravenous corticosteroids, and reported at least 1 outcome of interest (e.g., mortality, shock reversal, or incidence of superinfection). Two reviewers independently agreed on eligibility, assessed methodologic quality, and abstracted data.

**Results.** Pooled relative risks (RRs) and 95% confidence intervals (CIs) were estimated for 28-day all-cause mortality, shock reversal at 7 days, and incidence of superinfection with use of random-effects models. Analyses, stratified by adrenal responsiveness, were prespecified. Eight studies (6 randomized trials) involving a total of 1876 patients were selected. Overall, corticosteroid therapy did not result in a statistically significant difference in mortality (42.2% [369 of 875 patients] vs. 38.4% [384 of 1001]; RR, 1.00; 95% CI, 0.84–1.18). A statistically significant difference in the incidence of shock reversal at 7 days was observed between patients who received corticosteroids and those who did not (64.9% [314 of 484 patients] vs. 47.5% [228 of 480]; RR, 1.41; 95% CI, 1.22–1.64), with similar point estimates for both corticotropin stimulation test responders and nonresponders. No statistically significant difference was found in the incidence of superinfection between patients treated with corticosteroids and patients not treated with corticosteroids (25.3% [114 of 450 patients] vs. 22.7% [100 of 441]; RR, 1.11; 95% CI, 0.86–1.42).

**Conclusions.** In patients with septic shock, corticosteroid therapy appears to be safe but does not reduce 28-day all-cause mortality rates. It does, however, significantly reduce the incidence of vasopressor-dependent shock, which may be a clinically worthwhile goal.

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## Take-aways:

- In this meta-analysis, corticosteroid therapy had no effect on 28-day all-cause mortality among patients with septic shock, regardless of adrenal responsiveness. However, the incidence of shock reversal at 7 days was significantly higher among patients who received corticosteroids than among control subjects and was similar among corticotropin stimulation test responders

and nonresponders.

- Steroids: Effective for helping reverse shock
- Steroids: Safe (lack of harm demonstrated)

## Meta-analysis of adult septic shock patients

### Background

- The physiologic response to septic shock includes hypothalamic-pituitary-adrenal axis stimulation, which is thought to be an important protective survival response. Circulating pro-inflammatory mediators caused by sepsis may result in a state of relative corticosteroid insufficiency with reduced cortisol production and increased cortisol tissue resistance
- ACTH stim test is imperfect, but best measure of CIRCI

### Results

- Most common corticosteroid used was hydrocortisone
- Overall mortality did not correlate to corticosteroid use
  - 42.2% mortality in steroid
  - 38.4% in control
  - Older studies tended to favor corticosteroids more than newer, larger studies
- Shock reversal was greater in steroid groups than controls
- Superinfection rates were not different
  - Super infection is defined as a second infection superimposed on causative infection

Previous meta-analysis by Annane showed survival benefit. All studies included in that meta-analysis were included in this, and more (such as CORTICUS trial)