TABLE OF CONTENTS

HEADER ................................................................. 1
ABSTRACT ............................................................. 1
PLAIN LANGUAGE SUMMARY ........................................ 2
BACKGROUND .......................................................... 2
OBJECTIVES ........................................................... 2
METHODS ............................................................... 3
RESULTS ................................................................. 4
  Figure 1 .............................................................. 6
DISCUSSION ............................................................. 7
AUTHORS’ CONCLUSIONS .............................................. 8
ACKNOWLEDGEMENTS .................................................. 8
REFERENCES ............................................................. 9
CHARACTERISTICS OF STUDIES .................................... 11
DATA AND ANALYSES ................................................ 26
  Analysis 1.1. Comparison 1 Any steroid (po, IM, IV, inhaled) vs placebo, Outcome 1 Admitted to hospital (all times). 28
  Analysis 1.2. Comparison 1 Any steroid (po, IM, IV, inhaled) vs placebo, Outcome 2 Admitted to hospital (1-2 hours). 29
  Analysis 1.3. Comparison 1 Any steroid (po, IM, IV, inhaled) vs placebo, Outcome 3 Admitted to hospital (3-4 hours). 29
  Analysis 1.4. Comparison 1 Any steroid (po, IM, IV, inhaled) vs placebo, Outcome 4 Admitted to hospital (5-6 hours). 30
  Analysis 2.1. Comparison 2 Route of administration (Admission), Outcome 1 Intravenous vs placebo. .................. 31
  Analysis 2.2. Comparison 2 Route of administration (Admission), Outcome 2 Oral vs Placebo. ......................... 32
  Analysis 3.1. Comparison 3 Chronic corticosteroid use prior to ED, Outcome 1 Excluded. ............................... 32
  Analysis 3.2. Comparison 3 Chronic corticosteroid use prior to ED, Outcome 2 Mixed population. ..................... 33
  Analysis 4.1. Comparison 4 Severity at Admission, Outcome 1 High Admit Rate (Placebo Admission Rate > 40%). 34
  Analysis 4.2. Comparison 4 Severity at Admission, Outcome 2 Low Admit Rate (Placebo Admission Rate < 40%). 35
  Analysis 5.1. Comparison 5 Quality Assessment (Admission), Outcome 1 High quality (Cochrane). .................... 35
  Analysis 5.2. Comparison 5 Quality Assessment (Admission), Outcome 2 Low quality (Cochrane). ..................... 36
  Analysis 6.1. Comparison 6 Population, Outcome 1 Asthmatic Adults Only. .............................................. 37
  Analysis 6.2. Comparison 6 Population, Outcome 2 Asthmatic Children Only. ............................................ 38
  Analysis 6.2. Comparison 7 PEFR, Outcome 2 PEFR @ 60 minutes. ............................................................... 38
  Analysis 7.4. Comparison 7 PEFR, Outcome 4 PEFR @ 120 minutes. ............................................................. 39
  Analysis 7.5. Comparison 7 PEFR, Outcome 5 Final PEFR. ............................................................................. 39
  Analysis 8.1. Comparison 8 Adverse effects, Outcome 1 Nausea. ................................................................. 40
  Analysis 8.2. Comparison 8 Adverse effects, Outcome 2 Tremor. ................................................................. 41
  Analysis 8.3. Comparison 8 Adverse effects, Outcome 3 Headache. .............................................................. 41
  Analysis 9.1. Comparison 9 Symptoms scores, Outcome 1 Initial Score. ...................................................... 42
  Analysis 9.2. Comparison 9 Symptoms scores, Outcome 2 Final Score. ...................................................... 42
WHAT’S NEW ............................................................. 42
HISTORY ..................................................................... 43
CONTRIBUTIONS OF AUTHORS .................................. 43
DECLARATIONS OF INTEREST ..................................... 43
SOURCES OF SUPPORT ................................................. 43
INDEX TERMS ............................................................ 44
Early emergency department treatment of acute asthma with systemic corticosteroids

Brian H Rowe1, Carol Spooner2, Francine Ducharme3, Jennifer Bretzlaff4, Gary Bota4

1Department of Emergency Medicine, University of Alberta, Edmonton, Canada. 2Division of Emergency Medicine, 1G1.52 Walter Mackenzie Health Centre, Edmonton, Canada. 3Department of Pediatrics, McGill University Health Centre, Montreal, Canada. 4St Joseph’s Site, Sudbury Regional Hospital, Sudbury, Canada

Contact address: Brian H Rowe, Department of Emergency Medicine, University of Alberta, Room 1G1.43 Walter C. Mackenzie Health Sciences Centre, 8440 112th Street, Edmonton, Alberta, T6G 2B7, Canada. brian.rowe@ualberta.ca. (Editorial group: Cochrane Airways Group.)

Cochrane Database of Systematic Reviews, Issue 4, 2009 (Status in this issue: Unchanged)
Copyright © 2009 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
DOI: 10.1002/14651858.CD002178
This version first published online: 22 January 2001 in Issue 1, 2001.
Last assessed as up-to-date: 23 September 2002. (Help document - Dates and Statuses explained)


ABSTRACT

Background

The airway edema and secretions associated with acute asthma are most effectively treated with anti-inflammatories such as corticosteroids delivered by inhaled, oral, intravenous or intra-muscular routes. There is an unresolved debate about the use of systemic corticosteroids in the early treatment of acute asthma for emergency department patients.

Objectives

To determine the benefit of treating patients with acute asthma with systemic corticosteroids within an hour of presenting to the emergency department (ED).

Search strategy

Randomised controlled trials were identified from the Cochrane Airways Group Asthma Register. Primary authors and content experts were contacted to identify eligible studies. Bibliographies from included studies and known reviews were searched.

Selection criteria

Only randomised controlled trials (RCTs) or quasi-randomised trials were eligible for inclusion. Studies were included if patients presenting to the ED with acute asthma were treated with IV/IM or oral corticosteroids (CS) versus placebo within 1 hour of arrival and either admission rate or pulmonary function results were reported.

Data collection and analysis

Trial selection, data extraction and quality assessment were carried out independently by two reviewers, and confirmed with corresponding authors.

Main results

Twelve studies involving 863 patients (435 corticosteroids; 428 placebo) were included. Early use of CS for acute asthma in the ED significantly reduced admission rates (N = 11; pooled OR: 0.40, 95% CI: 0.21 to 0.78). This would correspond with a number needed
to treat of 8 (95% CI: 5 to 21). This benefit was more pronounced for those not receiving systemic CS prior to ED presentation (N = 7; OR: 0.37, 95% CI: 0.19 to 0.70) and those with more severe asthma (N = 7; OR: 0.35, 95% CI: 0.21 to 0.59). Oral CS therapy in children was particularly effective (N = 3; OR: 0.24, 95% CI: 0.11 to 0.53); no trials in adults used the oral route. Side effects were not significantly different between corticosteroid treatments and placebo.

An update search conducted in September 2002 did not yield any further trials.

Authors' conclusions

Use of corticosteroids within 1 hour of presentation to an ED significantly reduces the need for hospital admission in patients with acute asthma. Benefits appear greatest in patients with more severe asthma, and those not currently receiving steroids. Children appear to respond well to oral steroids.

**Plain Language Summary**

Early emergency department treatment of acute asthma with systemic corticosteroids

In an asthma attack, the airways (passages to the lungs) narrow from muscle spasms and swelling (inflammation). Bronchodilators (reliever inhalers to open up the lungs and airways) can be used for the spasms, and corticosteroids for the swelling. Corticosteroids can be inhaled, or taken by mouth (orally) or through a drip into the veins (intravenously). The review of trials found that systemic (oral or intravenous) corticosteroids reduce the need for people with asthma attacks to stay in hospital, with few adverse effects.

**Background**

Acute asthma is a common presenting complaint to emergency departments (ED). In the United States alone, acute asthma accounts for almost 2 million ED visits per year (Mannino 1998). Approximately 10-20% of these patients will require admission to the hospital, and, of those discharged from the ED after apparently successful treatment, approximately 10-20% will relapse within the subsequent two weeks (Camargo 1998a; Camargo 1998b). These results depend closely on the treatments prescribed in the ED and at discharge (Rowe 1997; Rowe 1999). Many asthmatics experience a poor quality of life for weeks following acute asthma during which they are particularly prone to repeat exacerbations (Fitzgerald 1990; Camargo 1998b).

Emergency treatment is based on the pathophysiology of acute asthma. Bronchospasm can generally be relieved with bronchodilators. The first treatment agents include beta 2-agonists which specifically target b-adrenergic receptors (Cates 2006). In some studies, quaternium agents administered in conjunction with beta 2-agonists have been shown to potentially increase the magnitude and duration of bronchodilation over that achieved with beta 2-agonists alone. A Cochrane review examined this therapy in children (Plotnik 1998). The airway edema and secretions associated with acute asthma are best treated with anti-inflammatories such as corticosteroids (CS) delivered by inhaled, oral, intravenous or intra-muscular routes. However, the timing, route, dose, and target population for CS treatment may vary markedly. The potential role of other agents in the initial management of acute asthma is still unclear.

Despite this general consensus, treatment approaches vary between and within emergency departments, perhaps because of the lack of evidence-based summaries of the research pertinent to this field. For example, there is an unresolved debate about the use of corticosteroids in the early treatment of acute asthma for ED patients (Engel 1991; Rowe 1992). Although previous overviews (Engel 1991; Rowe 1992; Rowe 1997) have attempted to clarify the evidence, several new trials have been completed since their publication; an update of the available evidence is needed.

**Objectives**

The objective of this review was to determine the effect (on admission rate, pulmonary functions [PFTs], physiologic measures, etc.) of any form of systemic corticosteroids (intravenous [IV], intramuscular [IM], oral [OCS]) administered early in the course of treatment for patients presenting to the ED with acute asthma.

Specific Aims: To quantify the effect of the combination of corticosteroids with other agents compared to the effect of these other agents alone.

The specific outcomes include:
• the effect of CS therapy on admission (e.g., time to decision, % admission);
• the effect of CS therapy on pulmonary functions; and
• the effect of CS therapy on side effects and vital signs (e.g., heart rate, respiratory rate, and blood pressure).

METHODS

Criteria for considering studies for this review

Types of studies
To be considered, studies had to be randomised controlled trials (RCT) or quasi RCTs (allocation on days of the week, or some other method).

Types of participants
Studies including patients of any age (adults, children > 2 years or combined) presenting to an ED were considered for inclusion. If a trial also recruited patients from other settings who could be removed easily from the study (for example if stratified randomisation was employed) the data would be included.

Types of interventions
The target intervention was the administration of IV, IM, or oral corticosteroids early (< 1 hour) in the ED treatment. Studies in which patients were admitted to the hospital and later given corticosteroids were excluded. The control intervention was the administration of placebo. Comparison of doses, delivery systems, or agents were included only if a placebo arm was incorporated. Details of co-interventions were recorded.

Types of outcome measures
(Yes/No). Attempts were made to contact the primary investigators of included studies to obtain individual patient data, however this was unsuccessful.

Primary outcomes
The primary outcome was admission to hospital.

Secondary outcomes
Lung function
Symptoms
Adverse events

Search methods for identification of studies

Electronic searches
The Cochrane Airways Review Group (ARG) has developed an “Asthma and Wheez* RCT” register through a comprehensive search of EMBASE, MEDLINE, and CINAHL. Hand searching of 20 common respiratory care journals has been completed and relevant RCTs have been added to this register. It is updated regularly with searches of CENTRAL, the Cochrane Collaboration’s RCT register. Search of the ARG register was completed using the following terms:

• Corticosteroid* OR steroid* OR glucocorticoid* OR prednis* OR solumedrol OR medrol OR dexamethasone OR methylpred* OR solucortef OR decadron AND Emerg* AND Discharge OR adm* OR hospit*.

We did not exclude trials on the basis of language. The current overview includes ARG register updates to January 1999.

Searching other resources
Randomised controlled trials were identified in the register using the following search strategy: placebo* OR trial* OR random* OR double-blind OR double blind OR single-blind OR single blind OR controlled study OR comparative study. Additional efforts to locate potential trials were as follows:

• Reference lists of all available primary studies were reviewed to identify potentially relevant citations.
• Inquiries were made regarding other published or unpublished trials known or supported by the authors of the primary studies so that these results could be included in this review.
• Structured searches of CENTRAL using Corticosteroids AND Asthma.
• Personal contact with colleagues, collaborators and other trialists working in the field of asthma was made to identify potentially relevant studies.
• Screening the reference lists of both review articles (Engel 1991; Rowe 1992).

Data collection and analysis

Selection of studies
From the title, abstract, or descriptors, two reviewers (BR, JB) independently reviewed literature searches to identify potentially relevant trials for full review. From the full text, using specific criteria, two reviewers (CS, FD) independently selected trials for inclusion in this review. Agreement was measured using kappa statistics. Disagreement was resolved by consensus or third party adjudication (BR).

Data extraction and management
Data for the trials were extracted by two reviewers (BR, JB) and entered into the Cochrane Collaboration software program (Review Manager). Primary study authors were requested to confirm data extraction and provide additional clarification and information for the review. In some cases, point estimates were obtained from expansions of graphic reproductions and calculations from other data presented in the paper.

**Assessment of risk of bias in included studies**

Methodological quality assessment was performed independently by two reviewers using two methods. The first method used the Cochrane approach to assessment of allocation concealment (Grade A: adequate concealment; Grade B: uncertain concealment; Grade C: clearly inadequate concealment). In the second method, each study was assessed independently by two reviewers for validity using an ordinal scale (0-5) described by Jadad (Jadad 1996). One point is allocated for randomisation, blinding and description of withdrawals and drop-outs; an extra point can be added for methods of randomisation and blinding that are well described and adequate. Studies which use a clearly inadequate method of randomisation or blinding (such as alternating patients) lose the point allocated. The maximum score is five points and studies scoring below three points are usually regarded as being of low methodological quality. For both methods, inter-rater reliability was measured by kappa and weighted kappa statistics, and disagreement was resolved by third party adjudication.

**Assessment of heterogeneity**

For pooled effects, heterogeneity was tested using the Breslow-Day test; \( p < 0.05 \) was be considered statistically significant. Results are reported using a random effects model. In most cases, the results for fixed and random effects model were similar, except where there was significant heterogeneity.

**Data synthesis**

Trial data were combined using Review Manager. For continuous variables, a random effects weighted mean difference (WMD) or standardised mean difference (SMD) and 95% confidence interval (CI) was calculated for each study; All similar studies were pooled using random effects WMD or SMD and 95% CIs. For dichotomous variables, a random effects odds ratio (OR) with 95% confidence intervals (95% CI) was calculated for each study. All similar studies were pooled using random effects OR and 95% CIs.

**Subgroup analysis and investigation of heterogeneity**

Since significant heterogeneity existed, a series of subgroup analyses were performed (Oxman 1992). A priori, these studies were divided on the following basis:

- Steroid use: previous steroid use vs. no previous steroid use;
- Severity: severity was based on admission rates in placebo group (severe if admission = or > 40% in the placebo arm or non-severe if admission rate < 40% in the placebo arm);
- Outcome: assessment scores and time of outcome assessment (2, 4, 6 hours);
- Intervention: route of administration (IV vs. PO).

**Sensitivity analysis**

In addition, sensitivity analyses were conducted on fixed effect versus random effects modelling, and methodological quality (high versus low).

**RESULTS**

**Description of studies**

See: Characteristics of included studies; Characteristics of excluded studies.

**Results of the search**

Eighteen articles were identified by one or both of the reviewers as being potentially relevant. All of these articles were recovered and provided to two different reviewers for independent decision on inclusion. A total of 9 articles were included (kappa: 0.78). Following communication with authors, one additional article was identified (Connett 1994a), and one article was excluded because it dealt with in-hospital treatment (Deshpande 1986). This search was updated in 1999 and three additional trials were identified (Lin 1997; Lin 1999; McFadden 1976). An update search conducted in September 2002 did not yield any further trials.

**Included studies**

For descriptions of the design of each included study see Characteristics of included studies. The evidence that corticosteroids prevent admissions when used in early ED asthma care has been the result of research produced within the past 15 years. Since the previous overviews (Rowe 1992; Engel 1991), 6 additional studies have been published (Scarfone 1993; Connett 1994a; Wolfson 1994; Rodrigo 1994; Lin 1997; Lin 1999) and 1 additional study was identified (Deshpande 1986).

**Populations:** Six (55%) publications specifically examined the use of corticosteroids in adult patients and 5 (45%) involved pediatric patients. Most studies included patients if they exhibited clinical criteria for acute asthma and did not have known chronic medical
conditions. Patients receiving systemic corticosteroids prior to the exacerbation were excluded from five studies (Littenberg 1986; Storr 1987; Tal 1990; Scarfone 1993; Connnett 1994a; Wolfson 1994) and sub-grouped in another (Schneider 1988). Exclusions for current inhaled corticosteroid use were less frequently reported, and sub-group analyses could not be performed based on this population separation.

The severity of asthma at presentation was poorly documented, but by inference would be considered “severe”. For example, most studies (N = 7; 64%) had placebo arm admissions rates of > 40%. In addition, most studies excluded patients presenting for prescription refills, or with mild asthma. The range of admission rates in the placebo groups was 10 to 97%.

Interventions: The drug type, route of administration and dose varied across studies. Studies examined the use of oral (N = 3), intravenous (N = 7), or intramuscular (N = 1) steroids as a single therapy early in the ED. No studies specifically compared inhaled steroids to a placebo agent; however, two studies which added inhaled steroids to the systemic CS without a placebo arm were excluded (Scarfone 1995; Gutman 1997).

While the dose of steroids varied, all protocols required the corticosteroids to be administered “early” (between 30-45 minutes post arrival). In adults, solucortef (N = 1) or solumedrol (N = 5) was used in doses of 500 mg and 125 mg intravenously, respectively. Oral therapy only occurred in children, and consisted of doses of 1-2 mg/kg of prednisone or prednisolone. All doses would be considered “high” (Manser 1998).

Co-interventions: Different co-interventions were provided. Variable approaches to beta2-agonist delivery were reported; most patients received nebulised therapy, but one study did use MDI + spacer (Rodrigo 1994). Studies permitted flexible (N = 2: Littenberg 1986; Wolfson 1994) or insisted on rigorous (N = 9) dosing schedules for the in-ED beta2-agonists and other co-interventions. Theophylline use was routine in two studies (Littenberg 1986 - IV; Stein 1990 - oral) and administered to “failures” in one study (Schneider 1988). The use of anticholinergic agents in addition to beta2-agonists was rarely reported (Lin 1999).

Outcomes: A variety of outcome measures were reported. Hospital discharge or admission were the most common (11/12 studies); however, the criteria for admission/discharge and timing of decision varied considerably. In addition, several pulmonary function test outcomes (PEFR, FEV-1, FVC, % predicted PEFR, % predicted FEV-1, etc) were used to measure treatment effect but there was no consistent format for reporting. A pooled estimate was obtained using the final study measurement for % PEFR and PEFR using an SMD. Infrequently, symptom scores were reported as outcomes. Due to the variation in scales and scores used, no pooled analysis was possible for symptoms. Finally, side-effects (e.g., nausea, headache, tremor) were occasionally reported also.

Confirmation of data: We attempted to contact all authors to request confirmation of methods and data extraction and provide additional clarification and information for the review. While many authors responded, unfortunately, most could not access their original data source to perform supplemental analyses. Wherever possible, expansions of graphic reproductions and estimations were used.

Excluded studies
See Characteristics of excluded studies.

Risk of bias in included studies
Many of the studies were double-blind, all were placebo controlled, demonstrated an appreciation of the need for concealment of allocation, and reported a sufficient number of outcomes. The methodological quality of all studies, using the Jadad method, was rated as “high” (scores => 3). Using the Cochrane method, 5 studies (Littenberg 1986; Schneider 1988; Tal 1990; Connett 1994a; Wolfson 1994) were rated as having blinded allocation and 7 studies (McFadden 1976; Storr 1987; Stein 1990; Scarfone 1993; Rodrigo 1994; Lin 1997; Lin 1999) were rated as having unclear allocation concealment.

Effects of interventions
Pooling of data was carried out because the populations, interventions and outcomes were similar. Despite this, significant heterogeneity was identified in the pooled analyses so results are presented with the pooled data followed by subgroup analyses.

Main Comparison: Corticosteroids versus Placebo
Eleven of the 12 included studies provided sufficient information for pooling hospital admission rates. Most studies (9/11) provided a point estimate in favor of treatment with CS. Four studies demonstrated a statistically significant difference in favor of CS treatment, while no studies demonstrated a benefit with placebo treatment. Using a random effects model, the overall result suggests a significant reduction in admission following the early use of corticosteroids in ED asthma treatment (n = 11; pooled OR: 0.50, 95% CI: 0.31, 0.81, Figure 1). This would correspond with a number needed to treat (NNT) of 8 (95% CI: 5 to 21). However, heterogeneity was demonstrated in this pooled estimate (chi square = 21.3; df = 11; p < 0.05). As planned, the following subgroup analyses were performed to identify the source of the heterogeneity.
### Figure 1. Forest plot of comparison: 1 Any steroid (po, IM, IV, inhaled) vs placebo, outcome: 1.1 Admitted to hospital (all times).

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>CS Events</th>
<th>Total</th>
<th>Placebo Events</th>
<th>Total</th>
<th>Weight</th>
<th>M-H, Random, 95% CI</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connoll 1994a</td>
<td>13</td>
<td>16</td>
<td>18</td>
<td>18</td>
<td>6.0%</td>
<td>0.43 0.09, 2.09</td>
<td></td>
</tr>
<tr>
<td>Connoll 1994b</td>
<td>7</td>
<td>18</td>
<td>15</td>
<td>15</td>
<td>6.0%</td>
<td>0.16 0.03, 0.77</td>
<td></td>
</tr>
<tr>
<td>Lin 1997</td>
<td>7</td>
<td>23</td>
<td>5</td>
<td>22</td>
<td>7.4%</td>
<td>1.49 0.39, 5.65</td>
<td></td>
</tr>
<tr>
<td>Lin 1999</td>
<td>8</td>
<td>30</td>
<td>11</td>
<td>26</td>
<td>5.0%</td>
<td>0.52 0.15, 1.52</td>
<td></td>
</tr>
<tr>
<td>Littenberg 1986</td>
<td>9</td>
<td>46</td>
<td>23</td>
<td>46</td>
<td>10.6%</td>
<td>0.26 0.10, 0.69</td>
<td></td>
</tr>
<tr>
<td>Rodrigo 1984</td>
<td>4</td>
<td>49</td>
<td>5</td>
<td>48</td>
<td>7.1%</td>
<td>0.72 0.20, 3.11</td>
<td></td>
</tr>
<tr>
<td>Scandone 1993</td>
<td>11</td>
<td>56</td>
<td>19</td>
<td>39</td>
<td>10.5%</td>
<td>0.46 0.18, 1.19</td>
<td></td>
</tr>
<tr>
<td>Schneider 1988</td>
<td>5</td>
<td>27</td>
<td>12</td>
<td>27</td>
<td>8.1%</td>
<td>0.28 0.08, 0.97</td>
<td></td>
</tr>
<tr>
<td>Steiner 1990</td>
<td>21</td>
<td>44</td>
<td>23</td>
<td>47</td>
<td>11.7%</td>
<td>0.95 0.42, 2.17</td>
<td></td>
</tr>
<tr>
<td>Sten 1987</td>
<td>59</td>
<td>73</td>
<td>56</td>
<td>67</td>
<td>5.4%</td>
<td>0.80 0.02, 0.36</td>
<td></td>
</tr>
<tr>
<td>Tal 1990</td>
<td>4</td>
<td>17</td>
<td>1</td>
<td>13</td>
<td>5.8%</td>
<td>0.80 0.14, 3.52</td>
<td></td>
</tr>
<tr>
<td>Watson 1994</td>
<td>17</td>
<td>42</td>
<td>15</td>
<td>46</td>
<td>11.2%</td>
<td>1.41 0.59, 3.36</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>426</strong></td>
<td><strong>410</strong></td>
<td><strong>100.0%</strong></td>
<td></td>
<td><strong>0.50 0.31, 0.81</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 159

Heterogeneity: Tau² = 0.32; Chi² = 21.27, df = 11 (P = 0.03); I² = 48%

Test for overall effect: Z = 2.88 (P = 0.004)
Subgroup Analyses

Use of Systemic Steroids: Because the regular use of systemic corticosteroids in the days and weeks preceding the index visit could be a potential confounder, a subgroup analysis based on previous CS therapy was completed. When only studies involving patients not receiving systemic CS prior to ED presentation were considered, early ED CS therapy appeared effective (N = 7; OR: 0.37, 95% CI: 0.19 to 0.70). This would correspond with a number needed to treat of 6 (95% CI: 4 to 11). However, heterogeneity existed in this pooled analysis (chi square = 15.21; df = 7; p < 0.05). In studies with mixed populations the early use of CS in the ED appeared to be less effective (N = 5; OR: 0.82; 95% CI: 0.48 to 1.4), without significant heterogeneity (chi square = 3.53; df = 4; p > 0.1).

Severity of Disease: In the absence of any consistent application of PFT results to determine disease severity, the rate of admission in the placebo group was used as a proxy severity measure. Most studies (N = 7; 64%) had admission rates > 40%. When trials were stratified using this cut-off, trials with a high baseline admission rates experienced a significant reduction in admissions following early CS use (N = 7; OR: 0.35, 95% CI: 0.21 to 0.59) compared to those studies with lower severity (N = 4; OR: 1.21, 95% CI: 0.66 to 2.22). The pooled results were homogeneous for both the severe (chi square = 11.2; df = 7; p > 0.1) and non-severe (chi square = 1.4; df = 3; p > 0.1) groups. These results would correspond with a number needed to treat of 5 (95% CI: 4 to 7) in the severe group.

Age Subgroup: There did not appear to be any difference in the magnitude of the reduction in admission rate due to early CS use between studies of children (n = 5; OR: 0.40, 95% CI: 0.17 to 0.94) or adults (n = 6; OR: 0.58, 95% CI: 0.32 to 1.07). The pooled results were homogeneous for adults but not for children (chi square = 13.65; df = 5; p < 0.025).

Sensitivity analyse

Timing of Outcome Assessment: Since steroids are believed to exert their effect over hours rather than minutes, one would expect a greater reduction in admission rate with longer ED treatment times. The sensitivity analysis confirmed this theory. However, few trialsists could provide additional time data, and these results should be interpreted cautiously. The early outcomes (< 2 hours) were not significant (N = 2; OR: 1.38, 95% CI: 0.41 to 4.67), whereas a benefit with CS therapy was demonstrated at 4 hours (N = 5; OR: 0.48, 95% CI: 0.24 to 0.97) and 6 hours (N = 7; OR: 0.28, 95% CI: 0.09 to 0.84) after administration. Significant heterogeneity (chi square = 17.7; df = 6; p < 0.01) was demonstrated for the 6 hour pooled results.

Route of Administration: Although no direct comparison of routes of administration could be made, the magnitude of the reduction in admission rates appeared greater with the oral routes (N = 3; OR: 0.24, 95% CI: 0.11 to 0.53) than IV (N = 7; OR: 0.68, 95% CI: 0.39 to 1.21) routes. The oral corticosteroid analysis did not demonstrate heterogeneity (p > 0.1) while the IV analysis did (chi square = 11.9; df = 6; p < 0.1). Whilst these results suggest at first sight that oral therapy may be more effective, it should be recalled that this route was only used in the treatment of children, whereas IV therapy was used in children and adults.

Other Outcomes

Pulmonary Functions: The most commonly and consistently reported pulmonary function data were PEFR and % predicted PEFR. The PEFR data were pooled using a SMD for the trials reporting end-of-treatment results. The analysis indicated a moderate effect of corticosteroids on PEFR (N = 7; SMD: 0.54; 95% CI: 0.01 to 1.1) with persistent heterogeneity (chi square = 49.25; df = 7; p < 0.001).

Adverse Reactions: Side effect monitoring was uncommon in these studies, and few adverse events were reported. Nausea (N = 2; OR = 0.48; 95% CI: 0.1 to 2.4), tremor (N = 4; OR = 0.82; 95% CI: 0.45 to 1.48), and headache (N = 2; OR = 1.04; 95% CI: 0.26 to 4.2) were similar in frequency; all pooled side effect results demonstrated homogeneity. An insufficient number of studies were available to provide meaningful sensitivity comparisons.

DISCUSSION

This systematic review summarises the latest evidence derived from randomised controlled trials for the early use of corticosteroids in the treatment of acute asthma in the ED setting. Overall, the results of this review indicate that patients who were treated with systemic corticosteroids within one hour of presentation to the emergency department were significantly less likely to be admitted to hospital. This benefit was not apparent for the first two hours of therapy and maximal at 6 hours. Thus, there appears to be benefit in delaying a decision to admit until 4-6 hours after CS therapy. Subgroup analysis suggests that patients with a greater likelihood of admission (i.e. the more severe) and those not recently treated with oral CS appeared to benefit most.

Oral therapy appears to be effective in children and in a comparison in children, oral and IV therapy were found to be equally effective (Barnett 1997). It is not possible to comment on the efficacy of oral steroids used in adults, since all trials in this age group used the IV route. Similarly, no conclusions can be drawn about dose-response effects, since all steroid doses were high.

Secondary analyses from pulmonary function data suggest that the benefit of corticosteroids is demonstrable by the measurement of the final PEFR or % predicted PEFR. The benefit represents a range of possible improvements in PFT, which also appears to be a clinically important improvement (Tiffany 1993).

Within the time course of this study, these doses of steroids did not appear to cause more tremor, headache or nausea than placebo.

The number needed to treat (NNT) with corticosteroids compared to placebo to prevent one admission is 5 (95% CI: 4 to 7)
for an admission rate of > 40% in the placebo arm. Alternatively, the NNT is higher and not statistically significant if the admission rate is low (< 20%) in the placebo arm. Since corticosteroids are inexpensive, readily available, and their safety in single-dose or short term therapy is accepted, early treatment using these drugs for most asthmatics would be prudent. This recommendation is in keeping with that provided by the Canadian Association of Emergency Physicians (CAEP; Beveridge 1996), national asthma plan in the US (NAEPP 1997), and British Thoracic Society (BTS; BTS 1997); all of whom recommend systemic corticosteroids for patients with acute asthma.

Methodological Limitations

Due to the heterogeneity of the pooled results in this meta-analysis and the overall small number of patients upon which the subgroup results are based, subgroup analyses need to be interpreted with caution (Oxman 1992). However, the overall findings would seem to apply to all patients with acute asthma presenting to the ED setting.

There is a possibility of publication bias or study selection bias in this meta-analysis. For example, by not identifying unpublished negative trials we may be over-estimating the effect of corticosteroid treatment. A comprehensive search of the published literature for potentially relevant studies was conducted, using a systematic strategy and objective inclusion criteria to avoid such biases. This was followed by attempts to contact corresponding and first authors. No unpublished or negative trials were uncovered, however we recognise that they may exist. In addition, examination of the funnel plots (OR vs. Sample size/weight) indicates symmetry, thus suggesting publication bias was unlikely.

Several other methodological issues limit the applicability of the results of this review. The admission rate for the placebo arm of these trials varied from 10% to 97%; 7 trials had admission rates above 40%. These rates are higher than expected and certainly higher than the 10 to 20% quoted in large multicenter studies in US and Canada (Camargo 1998a; Camargo 1998b). Since the subgroup analyses suggested a possible effect of severity on response to CS, this is an important area for future research. While the criteria for admission were variable or poorly documented, this does appear to be a clinically valuable measure of asthma outcome. Rigorous standardisation of this outcome would improve study comparability. For now, the results of this review apply to patients with severe asthma.

Evaluation of pulmonary function data was complicated by a lack of standardised reporting and changing analyses within the reports. For example, PFT analyses often changed from comparisons of treatment vs. control at the start of the study, to comparisons between admitted and non-admitted groups at the end. This precluded more formal evaluation of the effects of the interventions based on PFTs and also the effects of the intervention on PFTs at follow-up.

Authors’ Conclusions

Implications for practice

This overview reconfirms evidence from earlier systematic reviews (Rowe 1992; Engel 1991) and supports the use of steroids for treatment of emergency department patients assessed with acute asthma. Therapy with high dose systemic steroids should be commenced within one hour of presentation to the emergency department. Unless the patients failed to respond to early therapy, deteriorated or gave other reasons for concern, a decision whether to admit may be usefully delayed until 6 hours after treatment. In children, oral therapy appears to be very effective, although there are no data to provide guidance as to the efficacy of oral therapy for adults in this setting.

Implications for research

Further studies in this area will need to consider the results of the subgroup analyses. Studies which stratify patients into those recently receiving oral steroids vs those receiving maintenance inhaled steroids would seem appropriate. Documentation of asthma severity at presentation needs to be standardised to permit generalisability of trial results. Standardised assessment times would also be useful. A better description of admission criteria is required.

Acknowledgements

The authors wish to acknowledge the assistance of Stephen Milan, Jane Dennis, and Anna Bara of the Cochrane Airways Review Group. We would also like to acknowledge the assistance of the following corresponding authors: Dr. Randolphe Cole, Dr. Sandra Schneider, Dr. Gail Shapiro, Dr. Richard Scarfone, Dr. Warren Lenney, Dr. Asher Tal, and Dr. David Wolfson. Finally, the assistance of Prof. Paul Jones (ARG Editor) in reviewing the manuscript was greatly appreciated.
References to studies included in this review

McFadden 1976 (published data only)

Connett 1994b (published data only)

Lin 1997 (published data only)

Lin 1999 (published data only)

Littenberg 1986 (published data only)

McFadden 1976 (published data only)

McFadden 1994 (published data only)

Scarfone 1993 (published data only)

Schneider 1988 (published data only)

Stein 1990 (published data only)

Storr 1987 (published data only)

Tal 1990 (published data only)

Wolfsion 1994 (published data only)

References to studies excluded from this review

Aflalo 1999 (published data only)

Arnaud 1982 (published data only)

Barnett 1997 (published data only)

Deshpande 1986 (published data only)

Fanta 1983 (published data only)

Guttman 1997 (published data only)

Klig 1997 (published data only)

Murray 1995 (published data only)

Ogirala 1991 (published data only)

Pansegrow 1992 (published data only)
Additional references

Beveridge 1996

BTS 1997

Camargo 1998a

Camargo 1998b

Cates 2006

Chapman 1991

Edmonds 1999

Engel 1991

Fitzgerald 1990

Jadad 1996

Littenberg 1988

Mannino 1998

Manser 1998

NAEPP 1997

Oxman 1992

Plotnik 1998

Rowe 1992

Rowe 1997
Rowe 1999

Stein 1990

Tiffany 1993

* Indicates the major publication for the study
## Characteristics of included studies [ordered by study ID]

### Connett 1994a

| **Methods** | Randomisation: Treatments were numbered by a pharmacist in random order before the start of the study using a random numbers table.  
Blinding: double-blind.  
Number excluded: documented (26%).  
Withdrawals: 8 documented.  
Baseline characteristics: imbalances demonstrated; no adjusted analyses. |
| **Participants** | Location: Children’s Hospital in Brighton, UK.  
Participants: age > 18 mo. with acute asthma requiring admission (after 5 mg nebulised salbutamol and re-assessment in 30 minutes) if study investigator available.  
Asthma definition and severity: “severe”. severe asthma requiring admission  
Exclusion criteria: Mild asthma, croup, corticosteroids within the past 2 weeks. |
| **Interventions** | Intervention: 2 mg/kg oral prednisolone  
Control: identical placebo  
Co-interventions: 5 mg nebulized salbutamol q 1-4 hrs x 3 hrs. Supplemental oxygen was used for nebulisation. |
| **Outcomes** | Admission: based on history, physical findings, and response to therapy (at 4 hours).  
Pulmonary functions: PEFR and % predicted PEFR  
Adverse effects: tremor, hyperactivity, vomiting, headache.  
Vital signs: pulse rate, saturation,  
Symptoms: scale from 0-6.  
Lab: not reported.  
Timing of assessment: 0, q 30 minutes, 4 hours. |
| **Notes** | Jadad score:  
Author correspondence successful, but unable to provide data. |

### Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors’ judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Yes</td>
<td>Treatments were numbered by a pharmacist in random order before the start of the study using a random numbers table.</td>
</tr>
</tbody>
</table>
Connett 1994b

Methods
- Randomisation: Treatments were numbered by a pharmacist in random order before the start of the study using a random numbers table.
- Blinding: double-blind.
- Number excluded: documented (26%).
- Withdrawals: 8 documented.
- Baseline characteristics: imbalances demonstrated; no adjusted analyses.

Participants
- Location: Children’s Hospital in Brighton, UK.
- Participants: age > 18 mo., with acute asthma requiring admission (after 5 mg nebulised salbutamol and re-assessment in 30 minutes) if study investigator available.
- Asthma definition and severity: “severe”. Severe asthma requiring admission
- Exclusion criteria: Mild asthma, croup, corticosteroids within the past 2 weeks.

Interventions
- Intervention: 2 mg/kg soluble prednisolone (oral agent).
- Control: identical oral placebo.
- Co-interventions: After corticosteroid treatment children were treated with 0.15 mg/kg q 30 min x 3 hrs. Supplemental oxygen was used for nebulisation.

Outcomes
- Admission: based on history, physical findings, and response to therapy (at 4 hours).
- Pulmonary functions: PEFR and % predicted PEFR
- Adverse effects: tremor, hyperactivity, vomiting, headache.
- Vital signs: pulse rate, saturation.
- Symptoms: scale from 0-6.
- Lab: not reported.
- Timing of assessment: 0, q 30 minutes, 4 hours.

Notes
- Jadad score:

Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors’ judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment</td>
<td>Yes</td>
<td>Treatments were numbered by a pharmacist in random order before the start of the study using a random numbers table.</td>
</tr>
</tbody>
</table>
**Methods**

Randomisation: non-study nurse allocated treatment and provided a filled syringe with either saline or active drug.

Blinding: "double blinded" - similar appearing medication

Number excluded: convenience sample of 48 patients, exclusions not reported.

Withdrawals: 3 (repeat entry)

Baseline characteristics: no imbalances demonstrated; adjusted analyses performed.

**Participants**

Location: New York City hospital ED.

Participants: adults (> 17 yrs), acute asthma (clinical definition: prior diagnosis of asthma and history of improvement with B-agonists).

Asthma definition and severity: < 200 L/min PEFR

Exclusion criteria: age < 18, smoking history of > 20 pack years, pregnancy, received nebulised B-agonists from EM personnel prior to the study.

**Interventions**

Treatment: 125 mg methylprednisolone (MP) IV

Control: equivolume IV saline

Co-interventions in both groups: 2.5 mg albuterol with 0.5 mg ipratropium bromide, then q 20 min X 2 (2.5 mg albuterol), and 30 minutes later 2.5 mg albuterol. Supplemental oxygen was used for nebulisation and between treatments.

Cross-over: treating physicians were permitted to administer 125 mg of MP if response was deemed inadequate.

**Outcomes**

Admission: accessory muscle use, RR > 24/min, ABG PCO2 > 44 mm Hg or PO2 < 70 mm Hg, pneumonia or T > 38.8 C, or failure to improve after 5-6 hours AND associated fatigue and shortness of breath.

Pulmonary functions: PEFR and % predicted PEFR

Adverse effects: agitation, tremor.

Vital signs: pulse rate.

Symptoms: none reported.

Lab: not reported.

Timing of assessment: 0, 20, 40, 60 minutes

**Notes**

Jadad score:

Author correspondence pending.

**Risk of bias**

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors’ judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Yes</td>
<td>Non-study nurse allocated treatment and provided a filled syringe with either saline or active drug.</td>
</tr>
</tbody>
</table>
Lin 1999

| Methods | Randomisation: sealed opaque envelopes, non-study physician read allocation, and filled syringe with either saline or active drug.  
| Blinding: “double blinded”  
| Number excluded: convenience sample of 60 patients, exclusions not reported.  
| Withdrawals: 4 (repeat entry)  
| Baseline characteristics: imbalance demonstrated. No adjusted analyses. |

| Participants | Location: New York City hospital ED.  
| Participants: adults (> 18 yrs), acute asthma (clinical definition: history, response to B-agonists, past prescription for B-agonists).  
| Asthma definition and severity: < 50% predicted PEFR after single nebulised 2.5 mg salbutamol.  
| Exclusion criteria: age < 18, smoking history of > 20 pack years, pregnancy, inability to perform PEFR. |

| Interventions | Treatment: 125 mg methylprednisolone (MP) IV.  
| Control: equivolume IV saline.  
| Co-interventions in both groups: 2.5 mg albuterol with 0.5 mg ipratropium bromide, then q 20 min X 3 - 2.5 mg albuterol, and 30 minutes later 2.5 mg albuterol. Supplemental oxygen was used for nebulisation and between treatments.  
| Cross-over: treating physicians were permitted to administer 125 mg of MP if response was deemed inadequate. |

| Outcomes | Admission: accessory muscle use, RR > 24/min, ABG PCO2 > 44 mm Hg or PO2 < 70 mm Hg, pneumonia or T > 38.8 degrees C, or failure to improve after 5-6 hours AND associated fatigue and shortness of breath.  
| Pulmonary functions: PEFR and % predicted PEFR  
| Adverse effects: tremor.  
| Vital signs: pulse rate.  
| Symptoms: “symptomatic complaints”  
| Lab: not reported  
| Timing of assessment: 0, 20, 40, 60, 90 minutes |

| Notes | Jadad score:  
| Author correspondence pending. |

### Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors’ judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Yes</td>
<td>Sealed opaque envelopes, non-study physician read allocation, and filled syringe with either saline or active drug.</td>
</tr>
</tbody>
</table>
### Littenberg 1986

| Methods | Randomisation: The vials were filled by a pharmacist at a remote site according to random sequence.  
Blinding: "double blinded" - similar appearance of treatment and placebo.  
Number excluded: not reported.  
Withdrawals: not reported.  
Baseline characteristics: no imbalances demonstrated. |
|-----------------|------------------------------------------------------------------------------------------------|
| Participants | Location: Adult ED in Hartford, USA.  
Participants: Patients >18 ys, acute exacerbation of asthma, no underlying medical conditions  
Asthma definition and severity: heterogeneous population.  
Exclusion criteria: Patients using steroid medication within 2 weeks of presentation, ED MD diagnosis of chronic bronchitis or emphysema. |
| Interventions | Intervention: within 30 minutes of arrival, 125 mg of IV methylprednisolone (MP) diluted to 3 ml with saline.  
Control: Identical 3 ml of saline IV.  
Co-interventions: Each patient was treated as indicated, with subcutaneous epinephrine or terbutaline, oxygen, metaproterenol sulfate (administered as an aerosol), and intravenous aminophylline.  
Cross-over: not permitted. |
| Outcomes | Admission: no criteria; physician determined.  
Symptom scores: mild, moderate, severe.  
PFRs: FVC, FEV-1.  
Adverse effects: "toxicity" but not defined.  
Timing: assessment made at 4 hours.  
Follow-up: relapse at 1 week. |
| Notes | Jadad score:  
No response from the author. |

### Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors’ judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Yes</td>
<td>The vials were filled by a pharmacist at a remote site according to random sequence.</td>
</tr>
</tbody>
</table>

### McFadden 1976

| Methods | Randomisation: Not reported.  
Blinding: "double blinded" - no report of method.  
Number excluded: not reported.  
Withdrawals: not reported.  
Baseline characteristics: description of patients limited; no adjusted analyses. |
|-----------------|------------------------------------------------------------------------------------------------|

---

Copyright © 2009 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
### McFadden 1976

**Participants**
- Location: EDs in Boston and Galveston, USA.
- Participants: adults (16-44 yr), acute allergic or intrinsic asthma.
- Asthma definition and severity: severe (% predicted FEV-1 < 30.1%).
- Exclusion criteria: use of corticosteroids within a month of ED presentation; no others reported.

**Interventions**
- Intervention: 0.25, 0.5, or 1.0 gm of hydrocortisone upon completion of interview (? time).
- Control: similar appearing saline solution.
- Co-interventions: 30 minutes after corticosteroid treatment, nebulised isoproterenol (0.5 ml) by positive pressure breathing. This was “repeated” variable times over the course of the care in the ED.

**Outcomes**
- Admission: not reported.
- Pulmonary functions: FEV-1 and % predicted FEV-1; airway resistance and conductance.
- Adverse effects: not reported.
- Vital signs: not reported.
- Symptoms: subjective dyspnea rating.
- Lab: not reported.
- Timing of assessment: 0, 30, 60 minutes; minimum of 6 hours.

**Notes**
- Jadad score: No data could be extracted for use in this review.

### Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors’ judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Unclear</td>
<td>Information not available</td>
</tr>
</tbody>
</table>

### Rodrigo 1994

**Methods**
- Randomisation: Random number allocation was used to randomise the patients.
- Blinding: “double blinded” - similar appearing agents.
- Number excluded: not reported.
- Withdrawals: not reported.
- Baseline characteristics: no imbalances demonstrated.

**Participants**
- Location: Military hospital in Montevideo, Uruguay.
- Participants: 98 adults (18 - 50 yrs), with bronchial asthma.
- Asthma definition and severity: PEFR and FEV-1 <50% of predicted value.
- Exclusion criteria: Hx of chronic cough, chronic sputum production; cardiac, hepatic, renal, or other medical disease.

**Interventions**
- Intervention: 500 mg of IV hydrocortisone as 3 ml solution immediately after arrival to the ED.
- Control: placebo of 3 ml of normal saline.
Rodrigo 1994  (Continued)

Co-interventions: salbutamol by MDI + spacer, 4 puffs actuated in rapid succession (100 micrograms per actuation), q 10 min. Hospitalization was mandatory if treatment time was greater than 6 hours. Prednisone 40 mg x 5 days tapered dose was prescribed to those patients discharged from the ED. Cross-over: not permitted.

Outcomes

Admission: discharged after 6 hours if met the following criteria: free of dyspnea, no accessory muscles use at rest, and no wheezing. 
Pulmonary functions: PEF, FEV-1, FVC (absolute and % predicted).
Adverse effects: tremor, headache, anxiety, palpitations, and nausea.
Vital signs: heart rate, respiratory rate, blood pressure.
Symptoms: 0-3 scale (mild, moderate, severe); accessory muscle use, dyspnea and wheezing were assessed throughout the patient's stay in the ER.
Lab: theophylline levels.
Timing of assessment: q 30 minutes.
Follow-up: phone call to discharged patients to determine relapse rates. A retrospective chart review was also done in order to identify any patients returning to the ED.

Notes

Jadad score: 
Authors corresponded.

Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors' judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Unclear</td>
<td>Information not available</td>
</tr>
</tbody>
</table>

Scarfone 1993

Methods

Randomisation: Randomisation of drug or placebo preparation was done by ED physicians who were not involved with the study. Randomisation was accomplished using a random numbers table.
Blinding: “double blindered”
Number excluded: not stated.
Withdrawals: 6 (5 steroids; 1 placebo).
Baseline characteristics: no imbalances demonstrated. No adjusted analyses.

Participants

Location: Children's Hospital in Philadelphia, USA.
Participants: 75 children (1-17 yrs), exacerbation of asthma with at least one prior episode of wheezing, and initial PIS > 8.
Asthma definition and severity: “moderate” as described by author. Subgroup: PIS > 10 vs PIS < 10
Exclusion criteria: use of inhaled or systemic steroids within the previous 72 hours, other serious medical condition, pneumonia, vomited study drug within 15 minutes of administration

Interventions

Intervention: 2 mg/kg of oral prednisone after first albuterol treatment.
Placebo: similar appearing placebo capsule.
If unable to swallow, capsule was mixed with 5 ml of juice; patients who vomited within 15 minutes, were given a repeat dose.
Scarfone 1993  (Continued)

| Co-intervention | Patients in each group were then treated with an identical regimen of frequent aerosolized albuterol, for a maximum of 4 hours.  
| Cross-over: not permitted. |

| Outcomes | Admission: Determined at 4 hours by blinded physician. Based on oxygen saturation of < 92%, poor aeration by auscultation, or continued significant retractions.  
| Pulmonary functions: PEFR and % predicted PEFR. Since 2/3 of patients < 6 yrs, PFT collection abandoned early in the study. Admission to hospital at 2 hours was provided by the author.  
| Adverse effects: not reported.  
| Vital signs: respiratory rate, oxygen saturation, respiratory rate.  
| Symptoms: pulmonary index score.  
| Lab: not reported  
| Timing of assessment: 2 and 4 hours.  
| Follow-up: relapse rates for those discharged from ED |

| Notes | Jadad score:  
| Dr. Scarfone responded to correspondence and provided additional information. |

<table>
<thead>
<tr>
<th>Risk of bias</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Item</strong></td>
</tr>
<tr>
<td>Allocation concealment?</td>
</tr>
</tbody>
</table>

Schneider 1988

| Methods | Randomisation: Patients were randomised using computer-generated random numbers and randomised separately according to chronic steroid dependency.  
| Blinding: double blinded - similar appearing  
| Number excluded:  
| Withdrawals: 2 (1 pneumonia: MP; 1 tachycardia: placebo)  
| Baseline characteristics: limited reporting; no adjusted analyses. |

| Participants | Location: Montefiore Hospital in Pittsburgh, USA.  
| Participants: 56 adults, Dx of asthma, acute bronchospasm and dyspnea,  
| Asthma definition and severity: FEV-1 < 70% predicted. No severity subgroups.  
| Exclusion criteria: TB, pregnancy, diabetes mellitus, pneumonia or congestive heart failure  
| Subgroups: Patients were considered non-steroid dependent if they had used no steroid treatment within the past 14 days. |

| Interventions | Intervention: methylprednisolone (MP: 30 mg/kg) infused over 30 min.  
| Control: saline placebo |
Co-interventions: Treatment begun with epinephrine, 0.3 ml sub-Q in patients < 35 yrs or isetharine 0.5 ml (updraft nebulization, followed by the inhalation of albuterol). If subsequent FEV-1 showed improvement > 20%, the patient received beta-agonist q 30 min until improvement ceased, or discharge criteria met. Patients failing to improve received IV aminophylline in addition to the beta-agonists.

Outcomes

Admission: hospitalized if failed to improve during initial or any subsequent 60 minute period of combined aminophylline maintenance infusion and beta-agonist therapy. Discharged if clinical signs and symptoms of bronchospasm had cleared and the FEV-1 =>70% of predicted or previous best.

Pulmonary functions: FEV-1 and % predicted FEV-1.

Adverse effects: none.

Vital signs: none.

Symptoms: none.

Lab: not reported.

Timing of assessment: entry, q 30 minutes

Follow-up: Patients were considered treatment failures if they required hospitalization within 7 days after being successfully treated. Relapses were determined by chart audits as all patients were likely to return to the same hospital.

Notes

Jadad score:
Dr. Schneider responded to correspondence, and was able to provide additional information including the data.

Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors' judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Yes</td>
<td>Patients were randomised using computer-generated random numbers and randomised separately according to chronic steroid dependency.</td>
</tr>
</tbody>
</table>

Stein 1990

Methods

Randomisation: Random numbers table. Drug prepared by ED physician not involved in recruitment.

Blinding: double blinded - similar appearing

Number excluded: not reported.

Withdrawals: 13 (%) of 104 visits. Described, but not reported in groups allocated.

Baseline characteristics: no imbalances demonstrated. No adjusted analyses.

Participants

Location: ED, Presbyterian Hospital, NY, USA.

Participants: 81 adults (91 visits) (18-45 yrs), acute bronchial asthma. Corticosteroid use permitted.

Asthma definition and severity: not reported.

Exclusion criteria: serious underlying medical illness (sickle cell, HIV, cancer, heart disease), pneumonia, pregnancy, or temperature >38.3 C. Patients could be entered >1.
**Stein 1990**  
*(Continued)*

| Interventions | Intervention: 125 mg IV methylprednisolone (MP; 3 ml) 30 minutes after initial treatment.  
Control: IV normal saline  
Co-interventions: 3 aerosolized metaproterenol (q 30 min X 2 hrs) and oral theophylline therapy. |
|---|---|
| Outcomes | Admission: At discretion of treating physician, no specific criteria: relief of wheezing, clear chest examinations, or minimal wheezing. Six hours after study entry, remaining patients were treated with 40mg IV MP. Hospitalization was mandatory if total treatment time was greater than 12 hours.  
Pulmonary functions: PEFR.  
Adverse effects: not reported.  
Vital signs: temperature, pulse rate, respiratory rate, and blood pressure.  
Symptoms: 0-3 (none, mild, moderate, severe).  
Lab: theophylline levels, complete lymphocyte level, electrolytes.  
Timing of assessment: entry, 30 minutes, and 2, 4, 6 hours.  
Duration in the ED: measured.  
Relapse: 2 and 7 day follow-up of discharged patients. |
| Notes | Jadad score: Author provided 6 hour admission data for this analyses. |

**Risk of bias**

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors’ judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Unclear</td>
<td>Information not available</td>
</tr>
</tbody>
</table>

**Storr 1987**

| Methods | Randomisation: Hospital pharmacy using random numbers table  
Blinding: double blinded - similar appearing and tasting (grapefruit-flavoured mixture)  
Number excluded: well described.  
Withdrawals: described, and based on allocation (prednisone = 2; placebo = 2).  
Baseline characteristics: no imbalances demonstrated. No adjusted analyses. |
|---|---|
| Participants | Location: Children's Hospital, Brighton, UK.  
Participants: 140 children, moderate-severe acute asthma. Information on the subgroup of patients receiving inhaled steroids at the study enrolment was available.  
Asthma definition and severity: moderate-severe  
Exclusion criteria: croup, pneumonia, pertussis, congenital heart disease, mental retardation. Any child receiving a steroid within the previous 48 hours was excluded, as well as any child vomiting the study medication within 1 hour of ingestion. |
| Interventions | Intervention: Children < 5 given 30 mg of oral prednisone, =>5 received 60 mg .  
Control: identical placebo.  
Co-interventions: nebulised salbutamol 5 mg in 2 ml saline on admission and three or more times daily when needed. |
### Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission</td>
<td>At six hours, by treating MD, no specific criteria.</td>
</tr>
<tr>
<td>Pulmonary functions</td>
<td>PEFR and % predicted.</td>
</tr>
<tr>
<td>Adverse effects</td>
<td>none</td>
</tr>
<tr>
<td>Vital signs</td>
<td>none</td>
</tr>
<tr>
<td>Symptoms</td>
<td>0 - 10 scale (0 = good, 10 = poor)</td>
</tr>
<tr>
<td>Lab</td>
<td>not reported</td>
</tr>
<tr>
<td>Timing of assessment</td>
<td>entry, 30 minutes, and 4 hours.</td>
</tr>
<tr>
<td>Administrative data</td>
<td>times of admission, length of hospital stay.</td>
</tr>
</tbody>
</table>

### Notes

Jadad score:
Dr. Storr responded to correspondence and provided additional information.

### Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors' judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Unclear</td>
<td>Hospital pharmacy using random numbers table</td>
</tr>
</tbody>
</table>

### Tal 1990

#### Methods

Randomisation: Central pharmacy prepared solution using a random numbers table.
Blinding: double blinded - similar appearance - all delivered by IM injection.
Number excluded: not reported.
Withdrawals: 2 (described).
Baseline characteristics: minimal imbalance demonstrated. No adjusted analyses.

#### Participants

Location: ED at Children's Hospital in Beer Sheva, Isreal.
Participants: 75 children (6-60 mo), acute asthma, at least 3 prior episodes of wheezing. Only the subgroup of patients between 25-54 months were used in this analysis
Asthma definition and severity: moderate (PIS: 6-8) and severe (PIS: 9-11).
Exclusion criteria: pneumonia, cystic fibrosis, foreign body aspiration, broncho-pulmonary dysplasia, or other respiratory illness. Corticosteroids within 1 month prior to presentation. PIS < 5 and > 11.

#### Interventions

Intervention: single dose of IM methylprednisolone (MP: 4mg/kg).
Control: single dose of IM saline placebo.
Co-interventions: salbutamol nebulisation at presentation and q 30 min following intervention. Oxygen was used to drive delivery.

#### Outcomes

Admission: decision made at 3 hours based on clinical criteria at the discretion of the senior resident.
Pulmonary functions: PFTs were not recorded due to the young age of the sample.
Adverse effects: not recorded.
Vital signs: no.
Symptoms: 0 - 12. Pulmonary index score (PIS).
### Tal 1990 (Continued)

<table>
<thead>
<tr>
<th>Lab</th>
<th>not routine (at discretion of MD).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timing of assessment: entry, 30 minutes and 3 hours. All made by same physician.</td>
<td></td>
</tr>
<tr>
<td>Relapse</td>
<td>Telephone contact at 5 days to determine relapse.</td>
</tr>
</tbody>
</table>

### Notes

<table>
<thead>
<tr>
<th>Jadad score:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dr. Tal responded and provided supplemental information in addition to data extraction verification. A matched pairs design (matched on the basis of age group and disease severity) was employed and the analyses in the paper are more robust than the ones employed for this meta-analysis.</td>
</tr>
</tbody>
</table>

### Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors’ judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Yes</td>
<td>A - Adequate</td>
</tr>
</tbody>
</table>

### Wolfson 1994

#### Methods

Randomisation: A predetermined random sequence established by the pharmacist to allocated treatment; vials were prepared daily by a pharmacist.

Blinding: double blinded - similar appearance

Number excluded: not reported.

Withdrawals: none reported.

Baseline characteristics: no imbalances demonstrated. No adjusted analyses.

#### Participants

Location: ED Children's Hospital, Chicago, USA.

Participants: 88 children, (4 - 18 yrs), Dx of asthma, acute asthma, without other serious medical problems

Exclusion criteria: First-time episodes of wheezing, fever > 38.5 C, patients who had taken systemic corticosteroids within 2 weeks of presentation.

Asthma definition and severity: none.

No child enrolled > once.

#### Interventions

Intervention: Maximum 125 mg IV methylprednisolone (MP: 2 mg/kg) within 45 minutes of arrival.

Control: equivalent volume (2 ml) saline placebo

Co-interventions: usual ED management of their acute exacerbation including subcutaneous epinephrine, IV access, oxygen, and B-agonists (at the discretion of the treating MD).

#### Outcomes

Admission: at 3 hours, clinical decision (lack of resolution of wheezing) made by non-treating MD.

Pulmonary functions: PEFR (discontinued at some time during the study due to technical difficulties).

Adverse effects: none.

Vital signs: "recorded".

Symptoms: 0 - 10 (Woods-Downes Asthma Score).

Lab: not reported

Timing of assessment: entry and discharge or admission (mean of 2.8 hours - CS group; 3.0 hours - placebo group).
Wolfson 1994  (Continued)

<table>
<thead>
<tr>
<th>Administrative: time to disposition, length of stay. Follow-up: 24 hours for discharged patients.</th>
</tr>
</thead>
</table>

Notes

Jadad score:
Dr. Wolfson responded to correspondence, but was unable to provide additional information.

### Risk of bias

<table>
<thead>
<tr>
<th>Item</th>
<th>Authors’ judgement</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allocation concealment?</td>
<td>Yes</td>
<td>A predetermined random sequence established by the pharmacist to allocated treatment; vials were prepared daily by a pharmacist.</td>
</tr>
</tbody>
</table>
### Characteristics of excluded studies  
*ordered by study ID*

<table>
<thead>
<tr>
<th>Study</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Afilalo 1999</td>
<td>RCT of inhaled corticosteroids vs standard care in ED.</td>
</tr>
<tr>
<td>Arnaud 1982</td>
<td>RCT of in-patients receiving corticosteroids.</td>
</tr>
<tr>
<td>Deshpande 1986</td>
<td>Home-based, out-patient treatment with corticosteroids (correspondence with authors).</td>
</tr>
<tr>
<td>Fanta 1983</td>
<td>In-patient treatment protocol.</td>
</tr>
<tr>
<td>Guttman 1997</td>
<td>RCT of inhaled corticosteroids vs standard care in ED. No placebo arm</td>
</tr>
<tr>
<td>Klig 1997</td>
<td>IV vs oral corticosteroids for out-patient care. No placebo arm</td>
</tr>
<tr>
<td>Morray 1995</td>
<td>Not an RCT.</td>
</tr>
<tr>
<td>Ogirala 1991</td>
<td>Patients were experiencing chronic asthma, as opposed to an acute exacerbation.</td>
</tr>
<tr>
<td>Pansegrouw 1992</td>
<td>RCT of inhaled corticosteroids vs standard care in ED. No placebo arm</td>
</tr>
<tr>
<td>Rodrigo 1998</td>
<td>RCT of inhaled corticosteroids vs standard care in ED. No placebo arm</td>
</tr>
<tr>
<td>Scarfone 1995</td>
<td>RCT comparing two different delivery systems (oral vs nebulization), doses, and therapeutic agents (prednisone vs dexamethasone) for the treatment of acute asthma. Admission rates were reported, but no placebo arm was documented.</td>
</tr>
<tr>
<td>Schuckerman 1998</td>
<td>IV vs oral RCT in out-patient setting. No placebo arm</td>
</tr>
<tr>
<td>Shapiro 1983</td>
<td>RCT of oral steroids as out-patients after discharge from the acute care setting.</td>
</tr>
<tr>
<td>Sung 1997</td>
<td>RCT of inhaled corticosteroids vs standard care in ED.</td>
</tr>
<tr>
<td>Volovitz 1998</td>
<td>RCT of inhaled corticosteroids vs standard care in ED.</td>
</tr>
</tbody>
</table>
## DATA AND ANALYSES

### Comparison 1. Any steroid (po, IM, IV, inhaled) vs placebo

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Admitted to hospital (all times)</td>
<td>12</td>
<td>844</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.50 [0.31, 0.81]</td>
</tr>
<tr>
<td>2 Admitted to hospital (1-2 hours)</td>
<td>2</td>
<td>126</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>1.38 [0.41, 4.67]</td>
</tr>
<tr>
<td>3 Admitted to hospital (3-4 hours)</td>
<td>6</td>
<td>366</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.47 [0.24, 0.91]</td>
</tr>
<tr>
<td>4 Admitted to hospital (5-6 hours)</td>
<td>7</td>
<td>606</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.31 [0.15, 0.64]</td>
</tr>
</tbody>
</table>

### Comparison 2. Route of administration (Admission)

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 IV vs placebo</td>
<td>7</td>
<td>529</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.68 [0.39, 1.21]</td>
</tr>
<tr>
<td>2 Oral vs Placebo</td>
<td>4</td>
<td>291</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.24 [0.11, 0.53]</td>
</tr>
</tbody>
</table>

### Comparison 3. Chronic corticosteroid use prior to ED

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Excluded</td>
<td>8</td>
<td>545</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.37 [0.19, 0.70]</td>
</tr>
<tr>
<td>2 Mixed population</td>
<td>5</td>
<td>305</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.82 [0.48, 1.40]</td>
</tr>
</tbody>
</table>

### Comparison 4. Severity at Admission

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 High Admit Rate (Placebo Admission Rate &gt; 40%)</td>
<td>8</td>
<td>589</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.35 [0.21, 0.59]</td>
</tr>
<tr>
<td>2 Low Admit Rate (Placebo Admission Rate &lt; 40%)</td>
<td>4</td>
<td>261</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>1.21 [0.66, 2.22]</td>
</tr>
</tbody>
</table>
### Comparison 5. Quality Assessment (Admission)

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 High quality (Cochrane)</td>
<td>6</td>
<td>339</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.44 [0.21, 0.90]</td>
</tr>
<tr>
<td>2 Low quality (Cochrane)</td>
<td>6</td>
<td>505</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.58 [0.28, 1.18]</td>
</tr>
</tbody>
</table>

### Comparison 6. Population

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Asthmatic Adults Only</td>
<td>6</td>
<td>441</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.58 [0.32, 1.07]</td>
</tr>
<tr>
<td>2 Asthmatic Children Only</td>
<td>6</td>
<td>409</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.40 [0.17, 0.94]</td>
</tr>
</tbody>
</table>

### Comparison 7. PEFR

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 PEFR @ 60 minutes</td>
<td>4</td>
<td>132</td>
<td>Std. Mean Difference (IV, Random, 95% CI)</td>
<td>0.22 [-0.41, 0.86]</td>
</tr>
<tr>
<td>4 PEFR @ 120 minutes</td>
<td>1</td>
<td>56</td>
<td>Std. Mean Difference (IV, Random, 95% CI)</td>
<td>-0.36 [-0.89, 0.16]</td>
</tr>
<tr>
<td>5 Final PEFR</td>
<td>8</td>
<td>479</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>-7.91 [-15.98, 0.17]</td>
</tr>
</tbody>
</table>

### Comparison 8. Adverse effects

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Nausea</td>
<td>3</td>
<td>168</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.48 [0.10, 2.38]</td>
</tr>
<tr>
<td>2 Tremor</td>
<td>5</td>
<td>269</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>0.82 [0.45, 1.48]</td>
</tr>
<tr>
<td>3 Headache</td>
<td>2</td>
<td>134</td>
<td>Odds Ratio (M-H, Random, 95% CI)</td>
<td>1.04 [0.26, 4.23]</td>
</tr>
</tbody>
</table>
### Comparison 9. Symptoms scores

<table>
<thead>
<tr>
<th>Outcome or subgroup title</th>
<th>No. of studies</th>
<th>No. of participants</th>
<th>Statistical method</th>
<th>Effect size</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Initial Score</td>
<td>3</td>
<td>257</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>-0.06 [-0.32, 0.20]</td>
</tr>
<tr>
<td>2 Final Score</td>
<td>2</td>
<td>179</td>
<td>Mean Difference (IV, Random, 95% CI)</td>
<td>-0.27 [-0.59, 0.06]</td>
</tr>
</tbody>
</table>

### Analysis 1.1. Comparison 1 Any steroid (po, IM, IV, inhaled) vs placebo, Outcome 1 Admitted to hospital (all times).

**Review:** Early emergency department treatment of acute asthma with systemic corticosteroids

**Comparison:** 1 Any steroid (po, IM, IV, inhaled) vs placebo

**Outcome:** 1 Admitted to hospital (all times)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS n/N</th>
<th>Placebo n/N</th>
<th>Odds Ratio M-H,Random,95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connett 1994a</td>
<td>13/19</td>
<td>15/18</td>
<td>0.43 [0.09, 2.09]</td>
<td>6.0 %</td>
<td></td>
</tr>
<tr>
<td>Connett 1994b</td>
<td>7/18</td>
<td>12/15</td>
<td>0.16 [0.03, 0.77]</td>
<td>6.0 %</td>
<td></td>
</tr>
<tr>
<td>Lin 1997</td>
<td>7/23</td>
<td>5/22</td>
<td>1.49 [0.39, 5.65]</td>
<td>7.4 %</td>
<td></td>
</tr>
<tr>
<td>Lin 1999</td>
<td>8/30</td>
<td>11/26</td>
<td>0.50 [0.16, 1.52]</td>
<td>9.0 %</td>
<td></td>
</tr>
<tr>
<td>Littenberg 1986</td>
<td>9/48</td>
<td>23/49</td>
<td>0.26 [0.10, 0.65]</td>
<td>10.8 %</td>
<td></td>
</tr>
<tr>
<td>Rodrigo 1994</td>
<td>4/49</td>
<td>5/49</td>
<td>0.78 [0.20, 3.11]</td>
<td>7.1 %</td>
<td></td>
</tr>
<tr>
<td>Scarfone 1993</td>
<td>11/36</td>
<td>19/39</td>
<td>0.46 [0.18, 1.19]</td>
<td>10.5 %</td>
<td></td>
</tr>
<tr>
<td>Schneider 1988</td>
<td>5/27</td>
<td>12/27</td>
<td>0.28 [0.08, 0.97]</td>
<td>8.1 %</td>
<td></td>
</tr>
<tr>
<td>Stein 1990</td>
<td>21/44</td>
<td>23/47</td>
<td>0.95 [0.42, 2.17]</td>
<td>11.7 %</td>
<td></td>
</tr>
<tr>
<td>Storr 1987</td>
<td>53/73</td>
<td>65/67</td>
<td>0.08 [0.02, 0.36]</td>
<td>6.4 %</td>
<td></td>
</tr>
<tr>
<td>Tal 1990</td>
<td>4/17</td>
<td>4/13</td>
<td>0.69 [0.14, 3.52]</td>
<td>5.8 %</td>
<td></td>
</tr>
<tr>
<td>Wolfson 1994</td>
<td>17/42</td>
<td>15/46</td>
<td>1.41 [0.59, 3.36]</td>
<td>11.2 %</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>426</strong></td>
<td><strong>418</strong></td>
<td></td>
<td><strong>100.0 %</strong></td>
<td><strong>0.50 [0.31, 0.81]</strong></td>
</tr>
</tbody>
</table>

Total events: 159 (CS), 209 (Placebo)

Heterogeneity: $\tau^2 = 0.32; \chi^2 = 21.27, df = 11 (P = 0.03); \hat{I}^2 = 48$

Test for overall effect: $Z = 2.86 (P = 0.0043)$
### Analysis 1.2. Comparison 1 Any steroid (po, IM, IV, inhaled) vs placebo, Outcome 2 Admitted to hospital (1-2 hours).

**Review:** Early emergency department treatment of acute asthma with systemic corticosteroids

**Comparison:** Any steroid (po, IM, IV, inhaled) vs placebo

**Outcome:** Admitted to hospital (1-2 hours)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS (n/N)</th>
<th>Placebo (n/N)</th>
<th>Odds Ratio M-H, Random 95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lin 1997</td>
<td>7/23</td>
<td>4/22</td>
<td></td>
<td>75.2%</td>
<td>1.97 [0.49, 7.99]</td>
</tr>
<tr>
<td>Scarfone 1993</td>
<td>1/41</td>
<td>2/40</td>
<td></td>
<td>24.8%</td>
<td>0.48 [0.04, 5.46]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>64</strong></td>
<td><strong>62</strong></td>
<td></td>
<td><strong>100.0%</strong></td>
<td><strong>1.38 [0.41, 4.67]</strong></td>
</tr>
</tbody>
</table>

Total events: 8 (CS), 6 (Placebo)

Heterogeneity: Tau² = 0.0; Chi² = 0.98, df = 1 (P = 0.32); I² = 0%

Test for overall effect: Z = 0.52 (P = 0.60)

### Analysis 1.3. Comparison 1 Any steroid (po, IM, IV, inhaled) vs placebo, Outcome 3 Admitted to hospital (3-4 hours).

**Review:** Early emergency department treatment of acute asthma with systemic corticosteroids

**Comparison:** Any steroid (po, IM, IV, inhaled) vs placebo

**Outcome:** Admitted to hospital (3-4 hours)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS (n/N)</th>
<th>Placebo (n/N)</th>
<th>Odds Ratio M-H, Random 95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H, Random 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connett 1994a</td>
<td>13/19</td>
<td>15/18</td>
<td></td>
<td>12.0%</td>
<td>0.43 [0.09, 2.09]</td>
</tr>
<tr>
<td>Connett 1994b</td>
<td>7/18</td>
<td>12/15</td>
<td></td>
<td>11.9%</td>
<td>0.16 [0.03, 0.77]</td>
</tr>
<tr>
<td>Littenberg 1986</td>
<td>9/48</td>
<td>23/49</td>
<td></td>
<td>21.4%</td>
<td>0.26 [0.10, 0.65]</td>
</tr>
<tr>
<td>Scarfone 1993</td>
<td>11/41</td>
<td>19/40</td>
<td></td>
<td>21.1%</td>
<td>0.41 [0.16, 1.03]</td>
</tr>
<tr>
<td>Tal 1990</td>
<td>4/17</td>
<td>4/13</td>
<td></td>
<td>11.4%</td>
<td>0.69 [0.14, 3.52]</td>
</tr>
<tr>
<td>Wolfson 1994</td>
<td>17/42</td>
<td>15/46</td>
<td></td>
<td>22.2%</td>
<td>1.41 [0.59, 3.36]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>185</strong></td>
<td><strong>181</strong></td>
<td></td>
<td><strong>100.0%</strong></td>
<td><strong>0.47 [0.24, 0.91]</strong></td>
</tr>
</tbody>
</table>

Total events: 61 (CS), 88 (Placebo)

Heterogeneity: Tau² = 0.32; Chi² = 9.73, df = 5 (P = 0.08); I² = 49%

Test for overall effect: Z = 2.24 (P = 0.025)
Analysis 1.4. Comparison 1 Any steroid (po, IM, IV, inhaled) vs placebo, Outcome 4 Admitted to hospital (5-6 hours).

Comparison: Any steroid (po, IM, IV, inhaled) vs placebo

Outcome: Admitted to hospital (5-6 hours)

Study or subgroup  CS  Placebo  Odds Ratio  Weight  Odds Ratio
               n/N  n/N  M-H,Random,95% CI  M-H,Random,95% CI

Connett 1994a  10/37  27/33  14.3 %  0.08 [ 0.03, 0.26 ]
Lin 1999  8/30  11/26  14.5 %  0.50 [ 0.16, 1.52 ]
Littenberg 1986  9/48  23/49  16.4 %  0.26 [ 0.10, 0.65 ]
Rodrigo 1994  4/49  5/49  12.4 %  0.78 [ 0.20, 3.11 ]
Schneider 1988  5/27  12/27  13.6 %  0.28 [ 0.08, 0.97 ]
Stein 1990  21/44  23/47  17.3 %  0.95 [ 0.42, 2.17 ]
Storr 1987  53/73  65/67  11.5 %  0.08 [ 0.02, 0.36 ]

Total (95% CI)  308  298  100.0 %  0.31 [ 0.15, 0.64 ]

Total events: 110 (CS), 166 (Placebo)
Heterogeneity: Tau² = 0.63; Ch² = 17.77, df = 6 (P = 0.01); I² = 66%
Test for overall effect: Z = 3.16 (P = 0.0016)
Analysis 2.1. Comparison 2 Route of administration (Admission), Outcome 1 IV vs placebo.

Review: Early emergency department treatment of acute asthma with systemic corticosteroids

Comparison: Route of administration (Admission)

Outcome: IV vs placebo

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS n/N</th>
<th>Placebo n/N</th>
<th>Odds Ratio M-H,Random,95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lin 1997</td>
<td>7/23</td>
<td>4/22</td>
<td>10.6 % 1.97 [0.49, 7.99]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lin 1999</td>
<td>8/30</td>
<td>11/26</td>
<td>13.8 % 0.50 [0.16, 1.52]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Littenberg 1986</td>
<td>9/48</td>
<td>23/49</td>
<td>16.7 % 0.26 [0.10, 0.65]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rodrigo 1994</td>
<td>4/49</td>
<td>5/49</td>
<td>10.8 % 0.78 [0.20, 3.11]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schneider 1988</td>
<td>5/27</td>
<td>12/27</td>
<td>12.4 % 0.28 [0.08, 0.97]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stein 1990</td>
<td>21/44</td>
<td>23/47</td>
<td>18.2 % 0.95 [0.42, 2.17]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wolfson 1994</td>
<td>17/42</td>
<td>15/46</td>
<td>17.4 % 1.41 [0.59, 3.36]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>263</td>
<td>266</td>
<td>100.0 % 0.68 [0.39, 1.21]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 71 (CS), 93 (Placebo)

Heterogeneity: $\tau^2 = 0.29$; $Chi^2 = 1.99$, df = 6 ($P = 0.06$); $I^2 = 50$

Test for overall effect: $Z = 1.31$ ($P = 0.19$)

IV steroids Placebo
Analysis 2.2. Comparison 2 Route of administration (Admission), Outcome 2 Oral vs Placebo.

Review: Early emergency department treatment of acute asthma with systemic corticosteroids

Comparison: 2 Route of administration (Admission)

Outcome: 2 Oral vs Placebo

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS n/N</th>
<th>Placebo n/N</th>
<th>Odds Ratio M-H,Random,95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connett 1994a</td>
<td>13/19</td>
<td>15/18</td>
<td>19.5 % 0.43 [0.09, 2.09]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connett 1994b</td>
<td>7/18</td>
<td>12/15</td>
<td>19.3 % 0.16 [0.03, 0.77]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scarfone 1993</td>
<td>11/41</td>
<td>19/40</td>
<td>40.1 % 0.41 [0.16, 1.03]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Storr 1987</td>
<td>53/73</td>
<td>65/67</td>
<td>21.0 % 0.08 [0.02, 0.36]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>151</td>
<td>140</td>
<td><strong>100.0 % 0.24 [0.11, 0.53]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 84 (CS), 111 (Placebo)
Heterogeneity: $\tau^2 = 0.17; \chi^2 = 4.07, df = 3 (P = 0.25); I^2 = 26$
Test for overall effect: $Z = 3.53 (P = 0.00041)$

Analysis 3.1. Comparison 3 Chronic corticosteroid use prior to ED, Outcome 1 Excluded.

Review: Early emergency department treatment of acute asthma with systemic corticosteroids

Comparison: 3 Chronic corticosteroid use prior to ED

Outcome: 1 Excluded

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS n/N</th>
<th>Placebo n/N</th>
<th>Odds Ratio M-H,Random,95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connett 1994a</td>
<td>13/19</td>
<td>15/18</td>
<td>10.0 % 0.43 [0.09, 2.09]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connett 1994b</td>
<td>7/18</td>
<td>12/15</td>
<td>9.9 % 0.16 [0.03, 0.77]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Littenberg 1986</td>
<td>9/48</td>
<td>23/49</td>
<td>16.4 % 0.26 [0.10, 0.65]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scarfone 1993</td>
<td>11/41</td>
<td>19/40</td>
<td>16.2 % 0.41 [0.16, 1.03]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schneider 1988</td>
<td>3/19</td>
<td>8/20</td>
<td>10.4 % 0.28 [0.06, 1.29]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Storr 1987</td>
<td>53/73</td>
<td>65/67</td>
<td>10.6 % 0.08 [0.02, 0.36]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tal 1990</td>
<td>4/17</td>
<td>4/13</td>
<td>9.6 % 0.69 [0.14, 3.52]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wolfson 1994</td>
<td>17/42</td>
<td>15/46</td>
<td>16.9 % 1.41 [0.59, 3.36]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

(Continued...)
### Analysis 3.2. Comparison 3 Chronic corticosteroid use prior to ED, Outcome 2 Mixed population.

Review: Early emergency department treatment of acute asthma with systemic corticosteroids

Comparison: 3 Chronic corticosteroid use prior to ED

Outcome: 2 Mixed population

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS</th>
<th>Placebo</th>
<th>Odds Ratio</th>
<th>Weight</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H,Random,95% CI</td>
<td></td>
<td>M-H,Random,95% CI</td>
</tr>
<tr>
<td>Lin 1997</td>
<td>7/23</td>
<td>4/22</td>
<td>14.5 % 1.97 [ 0.49, 7.99 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lin 1999</td>
<td>8/30</td>
<td>11/26</td>
<td>22.6 % 0.50 [ 0.16, 1.52 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rodrigo 1994</td>
<td>4/49</td>
<td>5/49</td>
<td>15.0 % 0.78 [ 0.20, 3.11 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schneider 1988</td>
<td>2/8</td>
<td>4/7</td>
<td>5.9 % 0.25 [ 0.03, 2.24 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stein 1990</td>
<td>21/44</td>
<td>23/47</td>
<td>42.0 % 0.95 [ 0.42, 2.17 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>154</td>
<td>151</td>
<td>100.0 % 0.82 [ 0.48, 1.40 ]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 42 (CS), 47 (Placebo)

Heterogeneity: $\tau^2 = 0.0$, $\chi^2 = 3.53$, df = 4 ($P = 0.47$); $I^2 = 0.0$

Test for overall effect: $Z = 0.73$ ($P = 0.46$)
### Analysis 4.1. Comparison 4 Severity at Admission, Outcome 1 High Admit Rate (Placebo Admission Rate > 40%).

**Review**: Early emergency department treatment of acute asthma with systemic corticosteroids

**Comparison**: Severity at Admission

**Outcome**: 1 High Admit Rate (Placebo Admission Rate > 40%)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS n/N</th>
<th>Placebo n/N</th>
<th>Odds Ratio M-H,Random,95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connett 1994a</td>
<td>13/19</td>
<td>15/18</td>
<td>8.1 % 0.43 [0.09, 2.09]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connett 1994b</td>
<td>7/18</td>
<td>12/15</td>
<td>8.0 % 0.16 [0.03, 0.77]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lin 1999</td>
<td>8/30</td>
<td>11/26</td>
<td>13.0 % 0.50 [0.16, 1.52]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Littenberg 1986</td>
<td>9/48</td>
<td>23/49</td>
<td>16.3 % 0.26 [0.10, 0.65]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Scarfone 1993</td>
<td>11/41</td>
<td>19/40</td>
<td>16.1 % 0.41 [0.16, 1.03]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schneider 1988</td>
<td>5/27</td>
<td>12/27</td>
<td>11.5 % 0.28 [0.08, 0.97]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stein 1990</td>
<td>21/44</td>
<td>23/47</td>
<td>18.2 % 0.95 [0.42, 2.17]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Storr 1987</td>
<td>53/73</td>
<td>65/67</td>
<td>8.7 % 0.08 [0.02, 0.36]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>300</strong></td>
<td><strong>289</strong></td>
<td><strong>100.0 % 0.35 [0.21, 0.59]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 127 (CS), 180 (Placebo)

Heterogeneity: $\tau^2 = 0.20; \ Chi^2 = 11.25, df = 7 (P = 0.013); I^2 = 38\%$

Test for overall effect: $Z = 3.99 (P = 0.000066)$

---

Early emergency department treatment of acute asthma with systemic corticosteroids (Review)

Copyright © 2009 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
Analysis 4.2.  Comparison 4 Severity at Admission, Outcome 2 Low Admit Rate (Placebo Admission Rate < 40%).

Review: Early emergency department treatment of acute asthma with systemic corticosteroids

Comparison: 4 Severity at Admission

Outcome: 2 Low Admit Rate (Placebo Admission Rate < 40%)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS</th>
<th>Placebo</th>
<th>Odds Ratio M-H,Random,95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lin 1997</td>
<td>7/23</td>
<td>4/22</td>
<td>18.7 % 1.97 [0.49, 7.99]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rodrigo 1994</td>
<td>4/49</td>
<td>5/49</td>
<td>19.3 % 0.78 [0.20, 3.11]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tal 1990</td>
<td>4/17</td>
<td>4/13</td>
<td>13.9 % 0.69 [0.14, 3.52]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wolfson 1994</td>
<td>17/42</td>
<td>15/46</td>
<td>48.2 % 1.41 [0.59, 3.36]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>131</strong></td>
<td><strong>130</strong></td>
<td><strong>100.0 % 1.21 [0.66, 2.22]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 32 (CS), 28 (Placebo)
Heterogeneity: $\tau^2 = 0.0; \chi^2 = 1.41; df = 3 (P = 0.70); I^2 = 0.0%$
Test for overall effect: $Z = 0.62 (P = 0.53)$

Analysis 5.1.  Comparison 5 Quality Assessment (Admission), Outcome 1 High quality (Cochrane).

Review: Early emergency department treatment of acute asthma with systemic corticosteroids

Comparison: 5 Quality Assessment (Admission)

Outcome: 1 High quality (Cochrane)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS</th>
<th>Placebo</th>
<th>Odds Ratio M-H,Random,95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connett 1994a</td>
<td>13/19</td>
<td>15/18</td>
<td>13.0 % 0.43 [0.09, 2.09]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connett 1994b</td>
<td>7/18</td>
<td>12/15</td>
<td>12.9 % 0.16 [0.03, 0.77]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Littenberg 1986</td>
<td>9/48</td>
<td>23/49</td>
<td>21.9 % 0.26 [0.10, 0.65]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schneider 1988</td>
<td>5/27</td>
<td>12/27</td>
<td>17.0 % 0.28 [0.08, 0.97]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tal 1990</td>
<td>4/17</td>
<td>4/13</td>
<td>12.5 % 0.69 [0.14, 3.52]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Wolfson 1994</td>
<td>17/42</td>
<td>15/46</td>
<td>22.6 % 1.41 [0.59, 3.36]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>171</strong></td>
<td><strong>168</strong></td>
<td><strong>100.0 % 0.44 [0.21, 0.90]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 55 (CS), 81 (Placebo)
Heterogeneity: $\tau^2 = 0.41; \chi^2 = 10.32; df = 5 (P = 0.07); I^2 = 52%$
Test for overall effect: $Z = 2.23 (P = 0.026)$

---

Early emergency department treatment of acute asthma with systemic corticosteroids (Review)

Copyright © 2009 The Cochrane Collaboration. Published by John Wiley & Sons, Ltd.
**Analysis 5.2. Comparison 5 Quality Assessment (Admission), Outcome 2 Low quality (Cochrane).**

Review: Early emergency department treatment of acute asthma with systemic corticosteroids

Comparison: 5 Quality Assessment (Admission)

Outcome: 2 Low quality (Cochrane)

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS n/N</th>
<th>Placebo n/N</th>
<th>Odds Ratio M-H,Random 95% CI</th>
<th>Weight %</th>
<th>Odds Ratio M-H,Random 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lin 1997</td>
<td>7/23</td>
<td>4/22</td>
<td>14.0 % 1.97 [0.49, 7.99]</td>
<td>17.3 %</td>
<td>0.50 [0.16, 1.52]</td>
</tr>
<tr>
<td>Lin 1999</td>
<td>8/30</td>
<td>11/26</td>
<td>17.3 % 0.50 [0.16, 1.52]</td>
<td>14.3 %</td>
<td>0.78 [0.20, 3.11]</td>
</tr>
<tr>
<td>Rodrigo 1994</td>
<td>4/49</td>
<td>5/49</td>
<td>19.8 % 0.46 [0.18, 1.19]</td>
<td>14.3 %</td>
<td>0.78 [0.20, 3.11]</td>
</tr>
<tr>
<td>Scarpone 1993</td>
<td>11/36</td>
<td>19/39</td>
<td>21.6 % 0.95 [0.42, 2.17]</td>
<td>19.8 %</td>
<td>0.46 [0.18, 1.19]</td>
</tr>
<tr>
<td>Stein 1990</td>
<td>21/44</td>
<td>23/47</td>
<td>21.6 % 0.95 [0.42, 2.17]</td>
<td>21.6 %</td>
<td>0.95 [0.42, 2.17]</td>
</tr>
<tr>
<td>Storr 1987</td>
<td>53/73</td>
<td>65/67</td>
<td>13.0 % 0.08 [0.02, 0.36]</td>
<td>13.0 %</td>
<td>0.08 [0.02, 0.36]</td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>255</strong></td>
<td><strong>250</strong></td>
<td><strong>100.0 % 0.58 [0.28, 1.18]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 104 (CS), 127 (Placebo)

Heterogeneity: $\tau^2 = 0.44$, $\chi^2 = 11.61$, df = 5 ($P = 0.04$); $I^2 = 57\%$

Test for overall effect: $Z = 1.51$ ($P = 0.13$)
### Analysis 6.1. Comparison 6 Population, Outcome 1 Asthmatic Adults Only.

Review: Early emergency department treatment of acute asthma with systemic corticosteroids  
Comparison: 6 Population  
Outcome: 1 Asthmatic Adults Only

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS n/N</th>
<th>Placebo n/N</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
<th>Weight %</th>
<th>Odds Ratio M-H, Random, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lin 1997</td>
<td>7/23</td>
<td>4/22</td>
<td>12.5 % 1.97 [0.49, 7.99]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lin 1999</td>
<td>8/30</td>
<td>11/26</td>
<td>16.6 % 0.50 [0.16, 1.52]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Littenberg 1986</td>
<td>9/48</td>
<td>23/49</td>
<td>20.6 % 0.26 [0.10, 0.65]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rodrigo 1994</td>
<td>4/49</td>
<td>5/49</td>
<td>12.8 % 0.78 [0.20, 3.11]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Schneider 1988</td>
<td>5/27</td>
<td>12/27</td>
<td>14.8 % 0.28 [0.08, 0.97]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stein 1990</td>
<td>21/44</td>
<td>23/47</td>
<td>22.7 % 0.95 [0.42, 2.17]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>221</strong></td>
<td><strong>220</strong></td>
<td>100.0 % 0.58 [0.32, 1.07]</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 54 (CS), 78 (Placebo)  
Heterogeneity: Tau² = 0.24; Chi² = 8.78, df = 5 (P = 0.12); I² = 43%  
Test for overall effect: Z = 1.75 (P = 0.080)
## Analysis 6.2. Comparison 6 Population, Outcome 2 Asthmatic Children Only.

Review: Early emergency department treatment of acute asthma with systemic corticosteroids

Comparison: 6 Population

Outcome: 2 Asthmatic Children Only

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS n/N</th>
<th>Placebo n/N</th>
<th>Odds Ratio M-H,Random,95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connett 1994a</td>
<td>13/19</td>
<td>15/18</td>
<td></td>
<td>14.4 %</td>
<td>0.43 [0.09, 2.09]</td>
</tr>
<tr>
<td>Connett 1994b</td>
<td>7/18</td>
<td>12/15</td>
<td></td>
<td>14.3 %</td>
<td>0.16 [0.03, 0.77]</td>
</tr>
<tr>
<td>Scarfone 1993</td>
<td>11/41</td>
<td>19/40</td>
<td></td>
<td>20.9 %</td>
<td>0.41 [0.16, 1.03]</td>
</tr>
<tr>
<td>Storr 1987</td>
<td>53/73</td>
<td>65/67</td>
<td></td>
<td>15.0 %</td>
<td>0.08 [0.02, 0.36]</td>
</tr>
<tr>
<td>Tal 1990</td>
<td>4/17</td>
<td>4/13</td>
<td></td>
<td>13.9 %</td>
<td>0.69 [0.14, 3.52]</td>
</tr>
<tr>
<td>Wolfson 1994</td>
<td>17/42</td>
<td>15/46</td>
<td></td>
<td>21.5 %</td>
<td>1.41 [0.59, 3.36]</td>
</tr>
</tbody>
</table>

Total (95% CI) 210 199 100.0 % 0.40 [0.17, 0.94]

Total events: 105 (CS), 130 (Placebo)

Heterogeneity: Tau² = 0.71; Chi² = 13.65, df = 5 (P = 0.02); I² = 63%

Test for overall effect: Z = 2.10 (P = 0.035)

## Analysis 7.2. Comparison 7 PEFR, Outcome 2 PEFR @ 60 minutes.

Review: Early emergency department treatment of acute asthma with systemic corticosteroids

Comparison: 7 PEFR

Outcome: 2 PEFR @ 60 minutes

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Systemic CS N</th>
<th>Mean(SD)</th>
<th>Placebo N</th>
<th>Mean(SD)</th>
<th>Std. Mean Difference IV,Random,95% CI</th>
<th>Weight</th>
<th>Std. Mean Difference IV,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connett 1994a</td>
<td>7</td>
<td>-41 (4.8)</td>
<td>8</td>
<td>-42.7 (3.7)</td>
<td></td>
<td>19.5 %</td>
<td>0.38 [0.65, 1.40]</td>
</tr>
<tr>
<td>Connett 1994b</td>
<td>9</td>
<td>-44.2 (4.4)</td>
<td>7</td>
<td>-44.3 (3.5)</td>
<td></td>
<td>20.3 %</td>
<td>0.02 [-0.96, 1.01]</td>
</tr>
<tr>
<td>Lin 1997</td>
<td>23</td>
<td>-48 (9.6)</td>
<td>22</td>
<td>-56 (8.6)</td>
<td></td>
<td>29.0 %</td>
<td>0.86 [0.25, 1.47]</td>
</tr>
<tr>
<td>Lin 1999</td>
<td>30</td>
<td>-234 (100)</td>
<td>26</td>
<td>-200 (100)</td>
<td></td>
<td>31.2 %</td>
<td>-0.34 [-0.86, 0.19]</td>
</tr>
</tbody>
</table>

Total (95% CI) 69 63 100.0 % 0.22 [-0.41, 0.86]

Heterogeneity: Tau² = 0.26; Chi² = 8.62, df = 3 (P = 0.03); I² = 65%

Test for overall effect: Z = 0.69 (P = 0.49)
### Analysis 7.4. Comparison 7 PEFR, Outcome 4 PEFR @ 120 minutes.

**Review:** Early emergency department treatment of acute asthma with systemic corticosteroids

**Comparison:** PEFR

**Outcome:** 4 PEFR @ 120 minutes

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Systemic CS</th>
<th>Placebo</th>
<th>Std. Mean Difference</th>
<th>Weight</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lin 1999</td>
<td>30</td>
<td>26</td>
<td>-0.36 [ -0.89, 0.16 ]</td>
<td>100.0 %</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>30</strong></td>
<td><strong>26</strong></td>
<td><strong>-0.36 [ -0.89, 0.16 ]</strong></td>
<td><strong>100.0 %</strong></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: not applicable

Test for overall effect: Z = 1.35 (P = 0.18)

### Analysis 7.5. Comparison 7 PEFR, Outcome 5 Final PEFR.

**Review:** Early emergency department treatment of acute asthma with systemic corticosteroids

**Comparison:** PEFR

**Outcome:** 5 Final PEFR

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>Systemic CS</th>
<th>Placebo</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connett 1994a</td>
<td>7</td>
<td>8</td>
<td>-8.10 [ -12.86, -3.34 ]</td>
<td>16.2 %</td>
<td></td>
</tr>
<tr>
<td>Connett 1994b</td>
<td>9</td>
<td>7</td>
<td>-25.70 [ -31.05, -20.35 ]</td>
<td>16.0 %</td>
<td></td>
</tr>
<tr>
<td>Lin 1997</td>
<td>23</td>
<td>22</td>
<td>8.00 [ 2.68, 13.32 ]</td>
<td>16.0 %</td>
<td></td>
</tr>
<tr>
<td>Lin 1999</td>
<td>30</td>
<td>26</td>
<td>-37.00 [ -89.52, 15.52 ]</td>
<td>2.1 %</td>
<td></td>
</tr>
<tr>
<td>Littenberg 1986</td>
<td>48</td>
<td>49</td>
<td>-7.20 [ -10.19, -4.21 ]</td>
<td>16.8 %</td>
<td></td>
</tr>
<tr>
<td>Rodrigo 1994</td>
<td>49</td>
<td>49</td>
<td>-2.50 [ -9.12, 4.12 ]</td>
<td>15.4 %</td>
<td></td>
</tr>
<tr>
<td>Stein 1990</td>
<td>44</td>
<td>47</td>
<td>6.00 [ -35.53, 47.53 ]</td>
<td>3.1 %</td>
<td></td>
</tr>
<tr>
<td>Storr 1987</td>
<td>32</td>
<td>29</td>
<td>-11.00 [ -19.54, -2.46 ]</td>
<td>14.4 %</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>242</strong></td>
<td><strong>237</strong></td>
<td><strong>-7.91 [ -15.98, 0.17 ]</strong></td>
<td><strong>100.0 %</strong></td>
<td></td>
</tr>
</tbody>
</table>

Heterogeneity: Tau² = 98.62; Chi² = 81.63, df = 7 (P<0.00001); I² =91%

Test for overall effect: Z = 1.92 (P = 0.055)
### Analysis 8.1. Comparison 8 Adverse effects, Outcome 1 Nausea.

**Review:** Early emergency department treatment of acute asthma with systemic corticosteroids

**Comparison:** 8 Adverse effects

**Outcome:** 1 Nausea

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS</th>
<th>Placebo</th>
<th>Odds Ratio</th>
<th>Weight</th>
<th>Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/N</td>
<td>n/N</td>
<td>M-H, Random, 95% CI</td>
<td>M-H, Random, 95% CI</td>
<td></td>
</tr>
<tr>
<td>Connett 1994a</td>
<td>0/19</td>
<td>1/18</td>
<td>22.2 %</td>
<td>0.30 [ 0.01, 7.83 ]</td>
<td></td>
</tr>
<tr>
<td>Connett 1994b</td>
<td>1/18</td>
<td>4/15</td>
<td>40.5 %</td>
<td>0.16 [ 0.02, 1.64 ]</td>
<td></td>
</tr>
<tr>
<td>Rodrigo 1994</td>
<td>2/49</td>
<td>1/49</td>
<td>37.3 %</td>
<td>2.04 [ 0.18, 23.29 ]</td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td><strong>86</strong></td>
<td><strong>82</strong></td>
<td><strong>100.0 %</strong></td>
<td><strong>0.48 [ 0.10, 2.38 ]</strong></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 3 (CS), 6 (Placebo)
Heterogeneity: $\tau^2 = 0.26, \text{Ch}^2 = 2.29, \text{df} = 2 (P = 0.32); I^2 = 13\%$

Test for overall effect: Z = 0.90 (P = 0.37)
Analysis 8.2. Comparison 8 Adverse effects, Outcome 2 Tremor.

Review: Early emergency department treatment of acute asthma with systemic corticosteroids

Comparison: 8 Adverse effects

Outcome: 2 Tremor

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS n/N</th>
<th>Placebo n/N</th>
<th>Odds Ratio M-H,Random,95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connett 1994a</td>
<td>2/19</td>
<td>2/18</td>
<td>8.1 % 0.94 [ 0.12, 7.50 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Connett 1994b</td>
<td>7/18</td>
<td>5/15</td>
<td>17.1 % 1.27 [ 0.30, 5.33 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lin 1997</td>
<td>7/23</td>
<td>9/22</td>
<td>23.2 % 0.63 [ 0.18, 2.16 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lin 1999</td>
<td>6/30</td>
<td>7/26</td>
<td>22.6 % 0.68 [ 0.20, 2.36 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rodrigo 1994</td>
<td>7/49</td>
<td>8/49</td>
<td>28.9 % 0.85 [ 0.28, 2.57 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>139</td>
<td>130</td>
<td><strong>100.0 % 0.82 [ 0.45, 1.48 ]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 29 (CS), 31 (Placebo)

Heterogeneity: Tau² = 0.0; Chi² = 0.65, df = 4 (P = 0.96); I² =0.0%

Test for overall effect: Z = 0.67 (P = 0.50)

Analysis 8.3. Comparison 8 Adverse effects, Outcome 3 Headache.

Review: Early emergency department treatment of acute asthma with systemic corticosteroids

Comparison: 8 Adverse effects

Outcome: 3 Headache

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS n/N</th>
<th>Placebo n/N</th>
<th>Odds Ratio M-H,Random,95% CI</th>
<th>Weight</th>
<th>Odds Ratio M-H,Random,95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Connett 1994b</td>
<td>0/18</td>
<td>1/18</td>
<td>18.4 % 0.32 [ 0.01, 8.27 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rodrigo 1994</td>
<td>4/49</td>
<td>3/49</td>
<td>81.6 % 1.36 [ 0.29, 6.44 ]</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total (95% CI)</strong></td>
<td>67</td>
<td>67</td>
<td><strong>100.0 % 1.04 [ 0.26, 4.23 ]</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Total events: 4 (CS), 4 (Placebo)

Heterogeneity: Tau² = 0.0; Chi² = 0.63, df = 1 (P = 0.43); I² =0.0%

Test for overall effect: Z = 0.06 (P = 0.96)
Analysis 9.1. Comparison 9 Symptoms scores, Outcome 1 Initial Score.

Review: Early emergency department treatment of acute asthma with systemic corticosteroids

Comparison: 9 Symptoms scores

Outcome: 1 Initial Score

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS</th>
<th>Placebo</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stein 1990</td>
<td>44</td>
<td>-1.95 (0.75)</td>
<td>47</td>
<td>-2.11 (0.84)</td>
<td>29.6 %</td>
</tr>
<tr>
<td>Tal 1990</td>
<td>39</td>
<td>-9.2 (1.3)</td>
<td>39</td>
<td>-9.2 (1.2)</td>
<td>15.8 %</td>
</tr>
<tr>
<td>Wolfson 1994</td>
<td>42</td>
<td>-3.2 (0.1)</td>
<td>46</td>
<td>-3 (0.1)</td>
<td>54.6 %</td>
</tr>
</tbody>
</table>

Total (95% CI) 125 132

100.0 % -0.06 [-0.32, 0.20]

Heterogeneity: $\tau^2 = 0.03$; $\chi^2 = 5.05$, df = 2 ($P = 0.08$); $I^2 = 60$

Test for overall effect: $Z = 0.46$ ($P = 0.64$)

Analysis 9.2. Comparison 9 Symptoms scores, Outcome 2 Final Score.

Review: Early emergency department treatment of acute asthma with systemic corticosteroids

Comparison: 9 Symptoms scores

Outcome: 2 Final Score

<table>
<thead>
<tr>
<th>Study or subgroup</th>
<th>CS</th>
<th>Placebo</th>
<th>Mean Difference</th>
<th>Weight</th>
<th>Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stein 1990</td>
<td>44</td>
<td>-0.67 (0.81)</td>
<td>47</td>
<td>-0.61 (0.78)</td>
<td>38.7 %</td>
</tr>
<tr>
<td>Wolfson 1994</td>
<td>42</td>
<td>-1.4 (0.2)</td>
<td>46</td>
<td>-1 (0.2)</td>
<td>61.3 %</td>
</tr>
</tbody>
</table>

Total (95% CI) 86 93

100.0 % -0.27 [-0.59, 0.06]

Heterogeneity: $\tau^2 = 0.04$; $\chi^2 = 3.90$, df = 1 ($P = 0.05$); $I^2 = 74$

Test for overall effect: $Z = 1.62$ ($P = 0.11$)
WHAT'S NEW

Last assessed as up-to-date: 23 September 2002.

23 July 2008   Amended   Converted to new review format.

HISTORY

Protocol first published: Issue 1, 1998
Review first published: Issue 2, 2000

2 November 2000   New citation required and conclusions have changed   Substantive amendment

CONTRIBUTIONS OF AUTHORS

Rowe BH: initiated review, wrote protocol and funding application, completed searches and selection, completed data entry and analysis, principal author and assigned ARG editor.

Spooner C: contributed to protocol, study selection, completed quality assessment, performed editing and manuscript review, and converted final review to RevMan4.

Ducharme FM: contributed to protocol, contributed to study selection and quality assessment, and completed manuscript review.

Bretzlaff JA: contributed to protocol, completed searches and study selection, completed data extraction and entry, and manuscript review.

Bota GW: contributed to protocol, study selection and manuscript review.

DECLARATIONS OF INTEREST

The authors who have been involved in this review have done so without any known conflicts of interest. They are not involved with the primary studies. Dr. Rowe has received unrestricted educational grants for research from Astra, Janssen-Ortho, Boehringer-Ingelheim, Forest, Glaxo, Merck, and Sepracor. Dr. Ducharme has received support from Boehringer-Ingelheim. However, none of the authors are considered paid consultants by any pharmaceutical company that produces CS agents.

SOURCES OF SUPPORT

Early emergency department treatment of acute asthma with systemic corticosteroids (Review)
Internal sources

- Division of Emergency Medicine, University of Alberta, Faculty of Medicine and Dentistry, Edmonton, AB, Canada.
- NHS Research and Development, UK.

External sources

- Ministry of Health (Ontario); Emergency Health Services RAC #11469N, Canada.

INDEX TERMS

Medical Subject Headings (MeSH)
*Emergency Service, Hospital; Acute Disease; Administration, Oral; Asthma [*drug therapy]; Glucocorticoids [*therapeutic use]; Injections, Intramuscular; Injections, Intravenous; Placebo Effect; Randomized Controlled Trials as Topic

MeSH check words
Adult; Child; Humans