# Corticosteroids for preventing relapse following acute exacerbations of asthma (Review)

**Rowe BH, Spooner C, Ducharme F, Bretzlaff J, Bota G**

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[Intervention Review]

# Corticosteroids for preventing relapse following acute exacerbations of asthma

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## ABSTRACT

### Background

Acute asthma is responsible for many emergency department (ED) visits annually. Between 12 to 16% will relapse to require additional interventions within two weeks of ED discharge. Treatment of acute asthma is based on rapid reversal of bronchospasm and reducing airway inflammation.

### Objectives

To determine the benefit of corticosteroids (oral, intramuscular, or intravenous) for the treatment of asthmatic patients discharged from an acute care setting (i.e. usually the emergency department) after assessment and treatment of an acute asthmatic exacerbation.

### Search methods

We searched the Cochrane Airways Group Specialised Register and reference lists of articles. In addition, authors of all included studies were contacted to locate unpublished studies. The most recent search was run in October 2006.

### Selection criteria

Randomized controlled trials comparing two types of corticosteroids (oral, intra-muscular, or inhaled) with placebo for outpatient treatment of asthmatic exacerbations in adults or children.

### Data collection and analysis

Two review authors independently assessed trial quality and extracted data. Study authors were contacted for additional information.

### Main results

Six trials involving 374 people were included. One study used intramuscular corticosteroids, five studies used oral corticosteroids. The review was split into two reviews and although the latest search yielded no additional placebo controlled trials an additional IM study was included.

Significantly fewer patients in the corticosteroid group relapsed to receive additional care in the first week (Relative risk (RR) 0.38; 95% confidence interval (CI) 0.2 to 0.74). This favourable effect was maintained over the first 21 days (RR 0.47; 95% CI 0.25 to 0.89) and there were fewer subsequent hospitalizations (RR 0.35; 95% CI 0.13 to 0.95). Patients receiving corticosteroids had less need for beta$_2$-agonists (mean difference (MD) -3.3 activations/day; 95% CI -5.6 to -1.0). Changes in pulmonary function tests (SMD 0.045; 95% CI -0.47 to 0.56) and side effects (SMD 0.03; 95% CI -0.38 to 0.44) in the first 7 to 10 days, while rarely reported, showed no significant differences between the treatment groups. Statistically significant heterogeneity was identified for the side effect results; all other outcomes were homogeneous. From these results, as few as ten patients need to be treated to prevent relapse to additional care after an exacerbation of asthma.

**Authors' conclusions**

A short course of corticosteroids following assessment for an asthma exacerbation significantly reduces the number of relapses to additional care, hospitalizations and use of short-acting beta$_2$-agonist without an apparent increase in side effects. Intramuscular and oral corticosteroids are both effective.

## PLAIN LANGUAGE SUMMARY

**Corticosteroids for preventing relapse following acute exacerbations of asthma**

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. However, many people who are discharged from the emergency department following treatment for an asthma attacks have a relapse within 10 days. The review of six trials involving 374 people found that a short course of corticosteroids after discharge reduces the chances of a relapse, and lessens the need for using reliever inhalers without major adverse effects. The benefit lasts for about three weeks.

## BACKGROUND

Asthma is a common emergency department (ED) presentation in many parts of the world. In both the pediatric and adult populations, asthma is responsible for approximately 10 to 15/1000 ED visits (Bates 1990). Approximately 10 to 20% of patients presenting to the ED will require admission to the hospital (Weber 2002). Moreover, of patients discharged from North American EDs after initial treatment, between 12 to 16% will relapse to require additional interventions within two weeks (Rowe 1998; Emerman 1999). Finally, acute care for exacerbations may be received in an ED, clinic, or office setting. The distinguishing feature of the acute presentation is that patients require assessment and additional therapeutic interventions due to an exacerbation of their airways disease.

The outcomes of these assessments depend on the treatments which are prescribed in the acute care setting and upon discharge. Research indicates that many asthmatics maintain a poor quality of life (QoL) for weeks following exacerbations and are particularly prone to repeat exacerbations (Fitzgerald 1990; Rowe 1998). Clearly, the acute exacerbation of asthma is an important clinical and patient problem.

The approach to asthmatic exacerbations is based on pathophysiologic considerations including treatment of acute bronchospasm and airway oedema. Treatment guidelines exist in many countries (NAEPP 1997; CAEP/CTS 1999; BTS 2003); however, treatment approaches vary widely. This may be due in part to the rapidly changing management of the disease and the inability of guidelines to influence front-line health care workers (Cabana 1999). Most importantly, there remains significant debate about the use, dosage, route and length of corticosteroid (or glucocorticoid) treatment of the asthmatic in the in- and out-patient setting. This study is a systematic overview of all randomized controlled trials of corticosteroid treatment following diagnosis, treatment and discharge from the acute care setting. Our aim was to determine if there is clear evidence that treatment of asthmatic exacerbations with corticosteroids is beneficial.

Prior to the original review, only two previous overviews have been published dealing with corticosteroid treatment in asthmatic exacerbations (Engel 1991; Rowe 1992); however, both these studies contained methodological weaknesses that mandate a re-examination of the literature and a more focused systematic review of this intervention. Since that time, a variety of other narrative and

systematic reviews on this topic have been published.

## OBJECTIVES

The objective of this review was to determine the effect of any form of corticosteroids (intramuscular (IM), oral, inhaled) on relapse rate, pulmonary function tests (PFTs), quality of life (QoL), etc., for the treatment of asthmatic patients discharged from an acute care setting (that is, usually the ED) following the assessment and treatment of an acute asthmatic exacerbation.

## METHODS

### Criteria for considering studies for this review

#### Types of studies

Studies had to be randomized controlled trials.

#### Types of participants

Studies including patients presenting to an ED or other acute care setting were considered for inclusion in the overview. Studies recruiting pediatric or adult participants or both were reviewed, and this designation formed one of the proposed subgroup analyses.

#### Types of interventions

Patients randomized to receive either corticosteroids (oral, IM, or inhaled) or placebo following discharge from the acute care setting. Studies comparing two types of corticosteroids were also included. Finally, those patients who were randomized to receive an intramuscular corticosteroid injection prior to discharge or IM plus oral steroids were included. Obviously, asthmatic patients received additional regimens, such as beta$_2$-agonists, anti-cholinergics, theophylline compounds, anti-histamines, etc. Data for these co-interventions were recorded from studies or requested from authors.

#### Types of outcome measures

##### Primary outcomes

All patient outcomes were considered, however the primary dichotomous outcome was relapse to additional care. "Relapse" definitions varied but in general described a patient's perceived need for further assessment and treatment within the follow-up period. Two follow-up periods for relapse were considered for subgroups: 7 to 10 days and 21 days. However, all follow-up intervals were accepted.

##### Secondary outcomes

1. Relapse requiring hospitalization;
2. Presence of adverse outcomes (including side effects, death, etc);
3. Continuous data from pulmonary function testing (peak expiratory flow rates (PEFR), forced expiratory volume in one second (FEV-1), forced vital capacity (FVC), % predicted PEFR , FEV-1, FVC);
4. Symptom scores;
5. Beta$_2$-agonist use.

We attempted to contact the primary investigators of included studies to obtain individual patient data. We performed Intention to treat analyses.

### Search methods for identification of studies

#### Electronic searches

We identified trials using the Cochrane Airways Group Specialised Register of trials, which is derived from systematic searches of bibliographic databases including the Cochrane Central Register of Controlled Trials (CENTRAL), MEDLINE, EMBASE and CINAHL, and handsearching of respiratory journals and meeting abstracts. We searched all records in the Specialised Register coded as 'asthma' using the following terms:
(glucocorticoid* or steroid* or corticosteroid* or cortico-steroid* or prednis* or solumedrol or medrol or dexamethasone or methylpred* or solucortef or decadron) and (acute* or emerg* or relaps* or exacerb* or discharg*)
The most recent search was completed in October 2006; no new studies were identified.

#### Searching other resources

We contacted authors of all included studies to determine if they could identify additional unpublished and "in-progress" studies which met the inclusion criteria. In addition, we searched bibliographies from included studies, known reviews (Engel 1991; Rowe 1992) and texts for additional citations.

### Data collection and analysis

#### Selection of studies

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

### Data extraction and management

One of the review authors (BR) extracted data for the trials and entered this into the Cochrane Collaboration software program (Review Manager). We contacted primary study authors to verify the data and provide additional clarification and information for the review. Unfortunately, most authors could not access their original data source to perform supplemental analyses without some additional resource allocation. In these cases, expansions of graphic reproductions and estimations were used. Data were checked for reliability with the primary author, or by a second extractor (JB).

### Assessment of risk of bias in included studies

Two review authors (BR, CS) independently assessed the quality of included trials using two methods. First, using the Cochrane approach to assessment of allocation concealment, trials were scored and entered using the following principles:
Grade A: Adequate concealment
Grade B: Unclear concealment
Grade C: Obviously not adequate concealment .
Inter-rater reliability was measured by using simple agreement, kappa, and weighted kappa statistics. Disagreement was resolved by a third party adjudication (JB).
Second, each study was assessed for validity using a 0 to 5 scale described by Jadad 1996 and summarized as follows:
1) Was the study described as randomized (1 = yes;0 = no)?;
2) Was the study described as double-blind (1 = yes;0 = no)?;
3) Was there a description of withdrawals and dropouts (1 = yes; 0 = no)?;
4) Was the method of randomization well described and appropriate (1 = yes;0 = no);?;
5) Was the method of double blinding well described and appropriate (1 = yes;0 = no)?;
6) Deduct 1 point if methods for randomization or blinding were inappropriate. Inter-rater reliability was measured by using simple agreement, kappa, and weighted kappa statistics.

### Assessment of heterogeneity

Heterogeneity was quantified using the I-squared ($I^2$)statistic ( Higgins 2002).

### Data synthesis

We combined all trials using Review Manager. Subgroup comparisons are identified in the Comparisons section. For dichotomous variables, we calculated individual and pooled statistics as relative risks (RR) with 95% confidence intervals (CI); a fixed-effect model was used. For continuous outcomes, we reported individual trials results as mean and pooled using mean differences (MD) or standardized mean differences (SMD) and 95% CIs using a random-effects model.

### Subgroup analysis and investigation of heterogeneity

Since significant statistical heterogeneity was not identified for the main outcomes, a priori subgroup analyses were not required (population: pediatric versus adult; outcomes: well-defined versus ill-defined). However, subgroup analyses were performed for oral versus intramuscular routes of administration; sensitivity analyses were possible for high versus low quality assessment scores.

## RESULTS

## Description of studies

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

### Results of the search

A search that yielded 229 references identified 169 (73%) original publications; 69 (41%) references were found in EMBASE, 41 (24%) in MEDLINE, 59 (35%) from both EMBASE and MEDLINE; one (1%) reference was cited in MEDLINE, EMBASE and CINAHL. An update search run in October 2006 did not yield any further trials.
Independent review of the abstracts and titles of these publications identified eight potentially relevant studies. The simple agreement for relevance was 98% with a kappa of 0.76 (very good agreement). Additional references were added from bibliographic searching of relevant articles and overviews (13), and from contact with authors (5); a total of 26 studies were reviewed for inclusion. Independent review of these potentially relevant articles resulted in seven studies being included in this meta-analysis; no relevant articles were selected from the bibliographic search or recommendations from authors.

### Included studies

Generally, the evidence for intervention with corticosteroids in asthma originates in older literature; however, for this review most

studies were produced in the past 15 years. Since the previous overviews (Engel 1991; Rowe 1992) two additional studies have been published (Lee 1993a; McNamara 1993), and one additional study has been identified (Deshpande 1986). Five of the seven studies were conducted in North America. Following a split in the review in 2007, the Hoffman paper (Hoffman 1988) was removed and we inserted in a new study comparing IM versus oral corticosteroid.

It is important to note that all participants included in these studies were released or "discharged" from the acute care setting, and were not admitted to hospital. The severity of the asthmatic exacerbation could not easily be determined from these studies. In general, significant reductions in the mean pulmonary functions at presentation were demonstrated. Participants generally required less than 80% predicted PEFR or FEV-1 to be eligible for inclusion in the trials. Mean pretreatment PEFRs were reported as: 158 to 169 L/min (Fiel 1983), 193 to 198 (McNamara 1993), and 200 to 210 L/min (Lee 1993a). Chapman reported a mean pretreatment FEV-1 of 46% predicted.

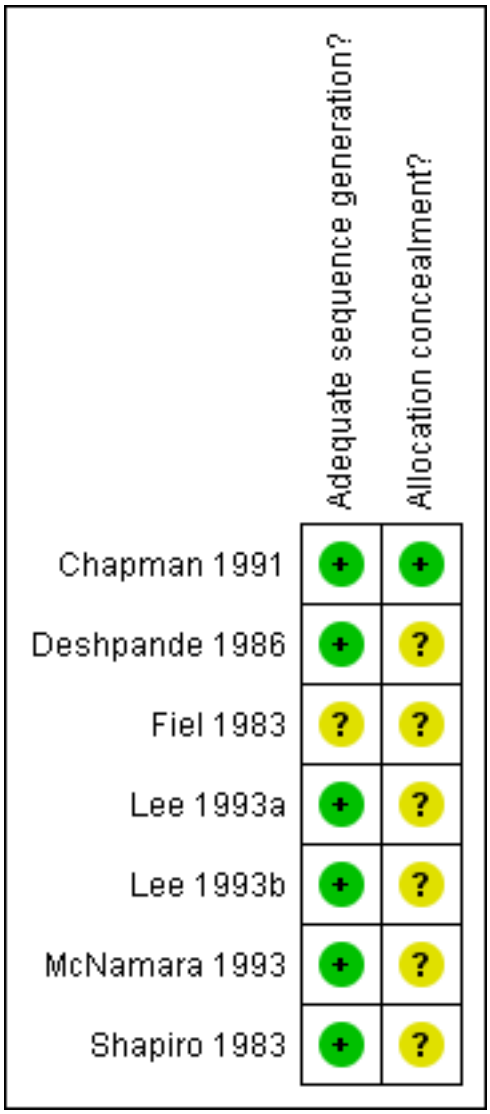
Different co-interventions were provided in each study, including theophylline, $beta_2$-agonists, and anticholinergics; however, none of the studies specifically provided inhaled steroid agents to their patients at discharge; use of inhaled steroids prior to the exacerbation was variable (range: 0 to 20%). The use of theophyllines has declined over the span of the studies, and these observations will be discussed in the Implications section. The duration of the oral steroid intervention also varied from 3 to 10 days.

A variety of outcome measures were reported with "relapse to additional care" being the most common. The definition of a relapse varied slightly, but generally included an unscheduled presentation to receive additional assessment and treatment. Scores from a variety of symptom scales were occasionally used to describe outcomes. Due to the different scores used, no consistent outcome analysis was possible. In addition, a number of pulmonary function results were employed (including PEFR, FEV-1, FVC, % predicted PEFR, % predicted FEV-1); however, consistent reporting was not found and this again limited the possible analyses. Finally, $beta_2$-agonist use and side-effects were occasionally reported.

## Risk of bias in included studies

Overall, the methodological quality was rated as high. Many of the studies were double-blind, placebo controlled, demonstrated an appreciation of the need for concealment of allocation, and reported a sufficient number of outcomes (see Figure 1).

**Figure 1. Methodological quality summary: review authors' judgements about each methodological quality item for each included study.**




Using the Jadad method, five studies were rated as "strong" (Chapman 1991; Deshpande 1986; Fiel 1983; Lee 1993a; Shapiro 1983), and one was rated as "weak" (McNamara 1993). Using the Cochrane methodology, three were rated as having blinded allocation, three were rated as having unclear allocation blinding, and one was rated as having non-blinded allocation.

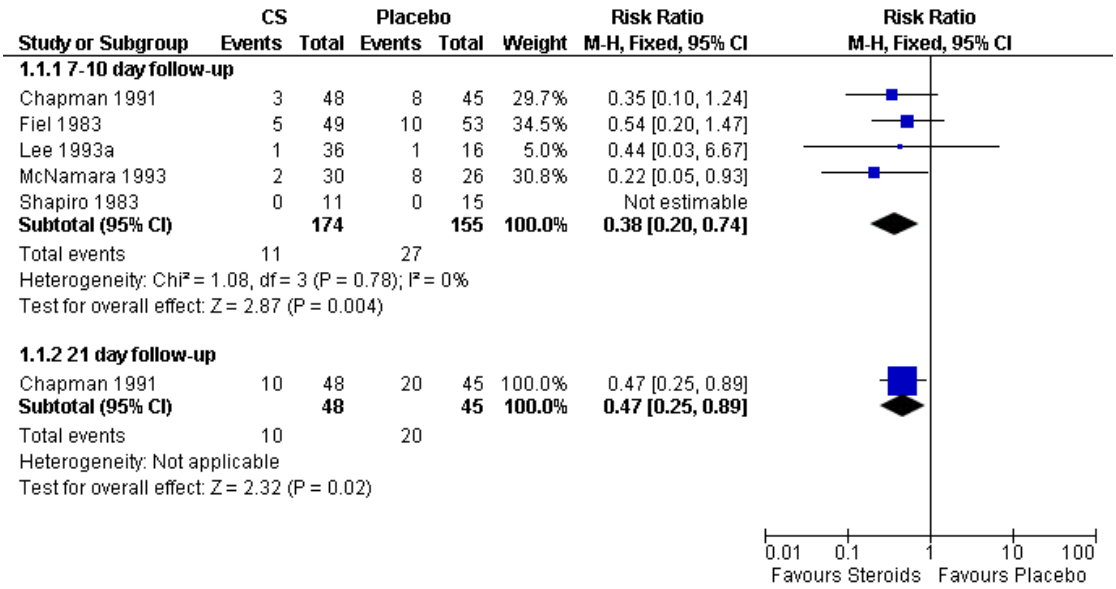
## Effects of interventions

Results from this meta-analysis are reported by outcome rather than time of follow-up assessment. The main results are reported as overall effects of oral and IM versus placebo; however, more demonstrated a persistent benefit (RR 0.47, 95% CI 0.25 to 0.89). studies used oral than IM steroids as an intervention.

### Relapse to Additional Care

Significantly fewer participants relapsed to require additional care at 7 to 10 days (RR 0.38; 95% CI 0.20 to 0.74; Figure 2) after an exacerbation when corticosteroids were used. In addition, fewer hospitalizations occurred in those participants receiving systemic corticosteroids (RR 0.35; 95% CI 0.13 to 0.95). No significant heterogeneity was found in these results (both $I^2$ = 0%). Relapse data were only reported in one study at 21 days, and steroids

**Figure 2. Forest plot of comparison: 1 Oral or Intramuscular corticosteroid (CS) versus placebo, outcome: 1.1 Relapse rates.**




### Oral versus IM Corticosteroids

The combined results for all corticosteroid treatment options (oral/IM) failed to identify heterogeneity. Oral corticosteroids provided a similar reduction in relapses when compared to placebo (RR 0.44; 95% CI 0.21 to 0.94). While IM corticosteroids appeared efficacious, due to small numbers the confidence intervals were wide (RR 0.30; 95% CI 0.08 to 1.09). Overall, no significant difference between IM corticosteroids and oral agents was found when assessment was made within the first 7 to 10 days.

### Beta$_2$-agonist Use

Patients receiving any form of corticosteroids reported less need for beta$_2$-agonists at 7 to 10 days of follow-up (MD -3.3 activations/day; 95% CI -5.6 to -1.0). This finding was provided in only two studies and no significant heterogeneity was identified in this result.

### Side Effects

Total side effects were reported as being "rare" in most studies, but only two trials gave sufficient information to be included in this analysis. The pooled estimate revealed similar rates of side effects in both groups (RR 0.96; 95% CI 0.53 to 1.74); however, significant heterogeneity was identified ($I^2$ = 75.5%). An insufficient number of studies were available to provide meaningful sensitivity or subgroup comparisons, or firm conclusions.

### Pulmonary Function Testing

Pulmonary functions were rarely reported; two studies reported results at seven days (Shapiro 1983; Lee 1993a; Lee 1993b). No significant differences between the treatment groups were demonstrated at two to three days (SMD 0.48; 95% CI -1.2 to 2.2) or 7 to 10 days (SMD 0.09; 95% CI -0.46 to 0.63) of follow up. Insufficient studies reported pulmonary functions and provided meaningful sub-group comparisons.

### Symptoms

A variety of symptom scores were reported. It appeared that symptoms improved in those studies that reported this information. For example, no study reported worsening symptoms in the steroid group. Cough, shortness of breath, and wheezing were all significantly reduced in the corticosteroid treatment group; however due to poor reporting and lack of standardization, no meaningful comparisons could be made.

### Numbers Needed to Treat (NNT)

Given these results, applying the RR to a placebo group baseline relapse risk of 17%, and using Visual Rx (www.nntonline.net) only ten patients (95% CI 8 to 23) would require treatment with corticosteroids to prevent one relapse to additional care in the first 7 to 10 days after outpatient care for an exacerbation, *see* Figure 3. Using similar methods only 11 patients (95% CI 9 to 143) would

require treatment with corticosteroids to prevent one relapse to hospitalization after outpatient care for an exacerbation *see* Figure 4.

**Figure 3. Ten patients need to be treated with corticosteroids to prevent one relapse.**

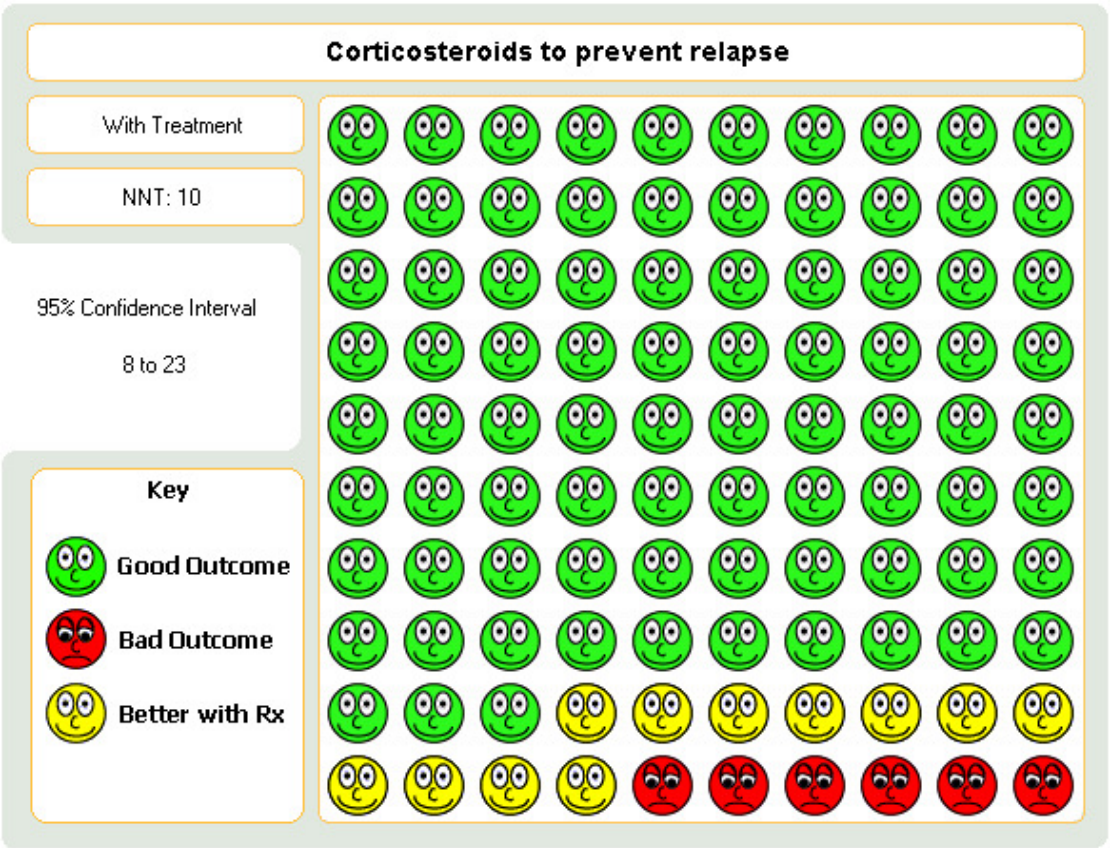
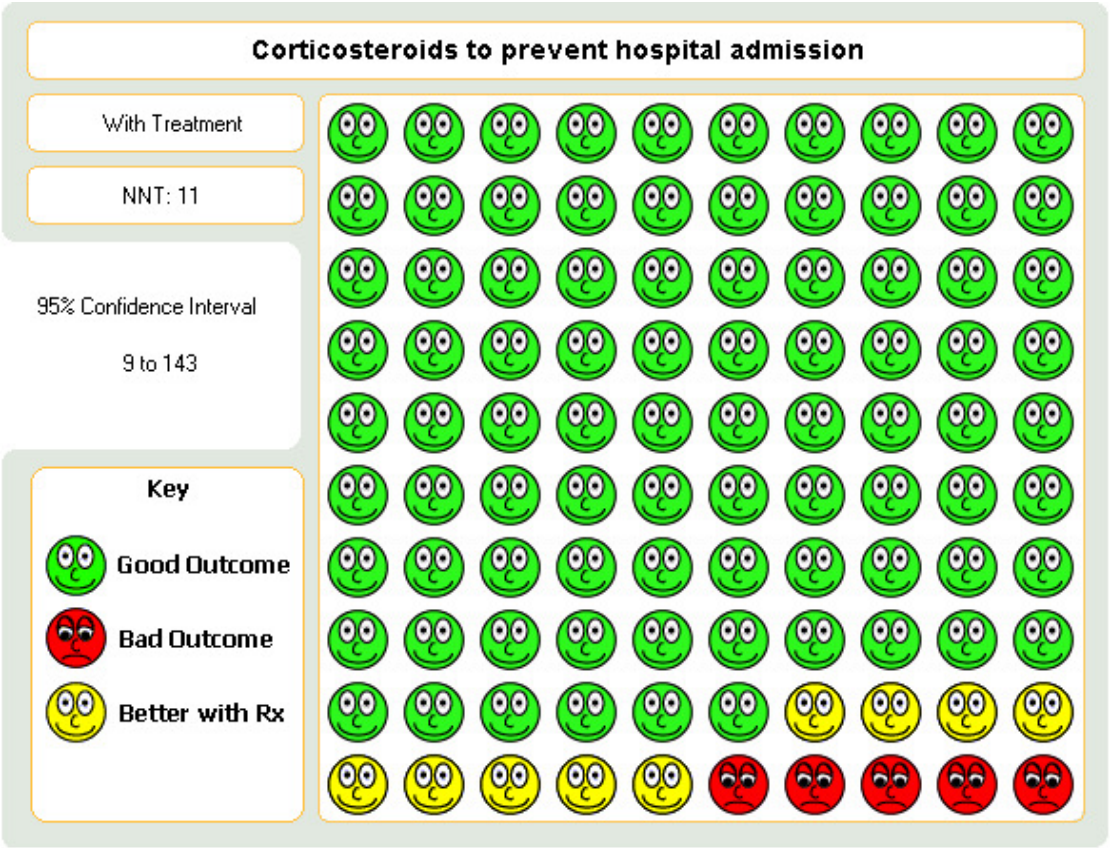


**Figure 4. Eleven patients need to be treated with corticosteroids to prevent on subsequent hospital admission.**




### Sensitivity/Subgroup Analyses

Sensitivity analyses on the results based on quality scores eliminated one paper (McNamara 1993); following this, the 7 to 10 day relapse results were unchanged (RR 0.45; 95% CI 0.21 to 0.96). Further subgroup analyses (*see* 'Methods') could not be performed due to small study numbers or missing data.

## DISCUSSION

This meta-analysis summarises all of the current evidence regarding the treatment of patients with asthma exacerbations using systemic corticosteroids compared to placebo. Using comprehensive search strategies and methods to avoid selection bias, this review highlights the importance of providing corticosteroid treatment to patients treated as outpatients following an asthma exacerbation. The results indicate that all patients requiring assessment for an exacerbation appear to warrant consideration for this form of therapy. Most studies restricted enrolment to patients with pulmonary functions of less than 80% predicted, suggesting at least a moderate exacerbation. Corticosteroid therapy not only reduced relapses to additional care, it also reduced subsequent admissions to hospital and use of $beta_2$-agonists. Conversely, there appeared to be no significant difference with respect to pulmonary functions and side effects between treating with corticosteroids and placebo. Both of these conclusions, however, are based on data from a limited number of studies, thus these conclusions should be interpreted cautiously.

The difference between treating with corticosteroids compared to placebo is pronounced by 7 to 10 days follow up; as few as nine patients require treatment to prevent one relapse to additional care. In addition, the choice of therapy does not appear to affect these conclusions. Providing either oral or intramuscular agents appears to be equally beneficial; patient preference, compliance considerations and costs should all be weighed in the treatment

decision. Caution is advised when interpreting the results of the different routes due to the indirect comparisons included in this review and the limited data available. Another Cochrane review will formally summarize the IM versus oral corticosteroid data in more detail.

These recommendations are in keeping with those provided by the Canadian Association of Emergency Physicians (CAEP; CAEP/CTS 1999), National Asthma Education Prevention Plan (NAEPP 1997) and the British Thoracic Society (BTS 2003). All recommend systemic corticosteroids for patients with an exacerbation of asthma.

### Methodological limitations

Due to the small number of trials included in this meta-analysis and the overall small number of patients upon which these results are based, no firm conclusions regarding subgroups by severity or age can be made. The overall findings seem to apply to all patients. In addition, the small samples preclude an accurate assessment of side effects associated with the corticosteroid treatment.

There is a possibility of publication bias or study selection bias in this meta-analysis. For example, by missing unpublished negative trials we may be over estimating the effect of corticosteroid treatment. However, a comprehensive search of the published literature for potentially relevant studies was conducted, using a systematic strategy to avoid bias. This was followed by attempts to contact corresponding and first authors. No unpublished or negative trials were uncovered; however, we recognize they may exist. The review has been updated with additional searches and no new data pertaining to this research question have emerged.

Several other methodological issues limit the applicability of the results of this review. First, most studies were conducted in an emergency setting, and patient presentations may be less severe in ambulatory care, office or clinic settings than those studied. Consequently, these results need confirmation in the community setting. Second, baseline severity was variable and poorly documented. Thus, subgroup comparisons were not possible on the severity of the exacerbation presentation. We agree with others (Chapman 1991), however, who suggest patients included in these studies often had less severe exacerbations than patients with exacerbations who were not enrolled.

The definition of relapse, while variable, appears an effective measure of asthma outcome. Better standardization of this outcome would however improve study comparability. 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 relapse and non-relapse groups in the publication. 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 systematic review of randomized controlled trials confirms evidence from earlier meta-analyses (Engel 1991; Rowe 1992) and strongly supports the use of oral or intramuscular corticosteroids for treatment of outpatients released from the acute care setting with an exacerbation of asthma. Several recommendations can be made.

- Patients who present for assessment and treatment with an exacerbation of asthma are likely to benefit from either oral or intramuscular corticosteroid treatment at release to prevent relapse to additional care and reduce $beta_2$-agonist use.

- In this review, oral steroids were provided for a 7 to 10 day period, usually as a tapering dose. Small sample sizes prevented an examination of the relative effectiveness of various regimens and no definitive recommendation concerning dose or dosing protocol emerged from this review.

- Insufficient data are available to determine the relative advantage of the route of corticosteroid delivery (IM or PO) on outcomes. The place of IM treatment in asthma therapy may be best reserved for those patients with questionable compliance, inability to afford the price of oral prescription medications, or those who are otherwise unreliable (cognitive impairment, intoxication, etc);

### Implications for research

Despite the strength of the findings from this review, several questions regarding treatment of asthmatic exacerbations with corticosteroids remain unanswered.

- A systematic review of studies examining the benefit of adding inhaled corticosteroids to the out-patient management of patients with an asthma exacerbation has been completed, which suggests that inhaled corticosteroids may be beneficial when added to systemic corticosteroids (Edmonds 2003). Inhaled corticosteroids and combined agents including long-acting $beta_2$-agonists are increasingly employed; the role of systemic corticosteroids in addition to these agents would be an important area for future research.

- Patients with mild exacerbations may not require oral corticosteroids, and potentially may be released from the acute care setting on inhaled steroids and $beta_2$-agonist therapy; however, the definition of what constitutes a "mild" exacerbation is unclear at this time.

- Further detailed evaluation of predictors of relapse under the current recommendations is required. For example, many studies are unclear as to the predictors of relapse, since they did

not include corticosteroid use as criteria for release following assessment (Weber 2002). The severity of asthma at presentation, and other potential confounders (such as co-interventions), may impact calculations of the number needed to treat (i.e., less severe: may increase number needed to treat to benefit (NNTB); more severe: may decrease NNTB).

- Future research on asthmatic exacerbations must concentrate on well defined outcomes which may lead to more informative overviews in the future. More specifically, complete reporting of PFT data in a systematic fashion would assist in further work. Finally, better description of the methodology would be also be beneficial.

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## REFERENCES

### References to studies included in this review

**Chapman 1991** *{published data only}*
Chapman KR, Verbeek PR, White JG, Rebuck AS. Effect of a short course of prednisone in the prevention of early relapse after the emergency room treatment of acute asthma. *New England Journal of Medicine* 1991;**324**:788–94.

**Deshpande 1986** *{published data only}*
Deshpande A, McKenzie SA. Short course of steroids in home treatment of children with acute asthma. *British Medical Journal* 1986;**293**:169–71.

**Fiel 1983** *{published data only}*
Feil SB, Swartz MA, Glanz KG, Francis ME. Efficacy of short-term corticosteroid therapy in outpatient treatment of acute bronchial asthma. *American Journal of Medicine* 1983; **75**:259–62.

**Lee 1993a** *{published data only}*
Lee CH, Lee CJ, Lan RS, Tsai YH, Chiang YC, Wang WJ, et al.Repository dexamethasone in the treatment of acute bronchial asthma. *Changgeng Yi Xue Za Zhi* 1993;**16**:25–9.

**Lee 1993b** *{published data only}*
Lee CH, Lee CJ, Lan RS, Tsai YH, Chiang YC, Wang WJ, et al.Repository dexamethasone in the treatment of acute bronchial asthma. *Changgeng Yi Xue Za Zhi* 1993;**16**:25–9.

**McNamara 1993** *{published data only}*
McNamara RM, Rubin JM. Intramuscular methylprednisolone acetate for the prevention of relapse in acute asthma. *Annuals of Emergency Medicine* 1993;**22**: 1829–35.

**Shapiro 1983** *{published data only}*
Shapiro GG, Furukawa CT, Pierson WE, Gardinier R, Bierman CW. Double-blind evaluation of methylprednisolone versus placebo for acute asthma episodes. *Pediatrics* 1983;**71**:510–4.

### References to studies excluded from this review

**Connet 1994** *{published data only}*
Connet GT, et al.Prednisolone and salbutamol in the hospital treatment of acute asthma. *Archives of Disease in Childhood* 1994;**70**:170–3.

**Engel 1990** *{published data only}*
Engel T, et al.Methylprednisolone pulse therapy in acute severe asthma. *Allergy* 1990;**45**:224–30.

**Fanta 1983** *{published data only}*
Fanta CH, et al.Glucocorticoids in acute asthma. *American Journal of Medicine* 1983;**71**:845–51.

**Green 1995** *{published data only}*
Green SS, et al.Oral versus repository corticosteroid therapy after hospitalization for the treatment of asthma. *Journal of Allergy & Clinical Immunology* 1995;**95**:15–22.

**Harris 1986** *{published data only}*
Harris JB, Weinberger MM, Nassif E, Smith G, Milavetz G, Stillerman A. Early intervention with short courses of prednisone to prevent progression of asthma in ambulatory patients incompletely responsive to bronchodilators. *Journal of Pediatrics* 1986;**110**:627–33.

**Hoffman 1988** *{published data only}*
Hoffman IB, Feil SB. Oral versus repository corticosteroid therapy in acute asthma. *Chest* 1988;**93**(1):11–3.

**Littenberg 1986** *{published data only}*
Littenberg B, et al.A controlled trial methylprednisolone in the emergency treatment of acute asthma. *The New England Journal of Medicine* 1986;**314**:150–1.

**Loren 1980** *{published and unpublished data}*
Loren ML, Chai H, Leung P, Rohr C, Brenner AM. Corticosteroids in the treatment of acute exacerbations of asthma. *Annals of Allergy* 1980;**45**:67–71.

**McFadden 1976** *{published data only}*
McFadden ER, et al.A controlled study of the effects of single doses of hydrocortisone on the resolution of acute attacks of asthma. *The American Journal of Medicine* 1976; **60**:52–9.

**Morell 1992** *{published data only}*
Morell F, et al.Controlled trial of intravenous corticosteroids in severe acute asthma: effectiveness of low doses. *Thorax* 1992;**47**:584–7.

**Pedersen 1987** *{published data only}*
Pedersen BK, et al.Methylprednisolone pulse therapy in severe acute asthma. *Annals of Allergy* 1987;**42**:154–7.

**Schneider 1988** *{published data only}*
Schneider SM. High-dose methylprednisolone as initial therapy in acute severe asthma. *Journal of Asthma* 1988;**25**: 189–93.

**Storr 1987** *{published data only}*
Storr J. Effect of a single dose of prednisolone in acute childhood asthma. *The Lancet* 1987;**1**(8538):879–82.

**Wilson 1990** *{published data only}*
Wilson NM. Treatment of acute episodic asthma in preschool children using intermittent high dose inhaled steroids at home. *Archives of Disease in Childhood* 1990; **675**:407–10.

## Additional references

**Bates 1990**
Bates DV, Baker-Anderson M, Sizto R. Asthma attack periodicity: a study of hospital emergency visits in Vancouver. *Environmental Research* 1990;**51**:51–70.

**BTS 2003**
British Thoracic Society, Scottish Intercollegiate Guidelines N. British guideline on the management of asthma. *Thorax* 2003;**58**(Suppl 1):1–94.

**Cabana 1999**
Cabana MD, Rand CS, Powe NR, et al.Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA* 1999;**282**(15):1458–65.

**CAEP/CTS 1999**
Boulet L-P, Becker A, Bérubé D, Beveridge R, Ernst P, on behalf of the Canadian Asthma Consensus Group. [Canadian asthma consensus report, 1999]. *CMAJ* 1999; **161**(11 Suppl):S1–62.

**Edmonds 2003**
Edmonds ML, Camargo CA Jr, Brenner B, Rowe BH. Inhaled steroids in acute asthma following emergency department discharge. *Cochrane Database of Systematic Reviews* 2003, Issue 4.

**Emerman 1999**
Emerman CL, Woodruff PG, Cydulka RK, et al.Prospective multicenter study of relapse following treatment for acute asthma among adults presenting to the emergency department. *Chest* 1999;**115**:919–27.

**Engel 1991**
Engel T, Heinig JH. Glucocorticoid therapy in acute severe asthma: a critical review. *European Respiratory Journal* 1991; **4**:1–9.

**Fitzgerald 1990**
Fitzgerald JM, Hargreaves FE. Acute asthma: Emergency department management and prospective evaluation of outcome. *Canadian Medical Association Journal* 1990;**142**: 591–5.

**Higgins 2002**
Higgins JP, Thompson SG. Quantifying heterogeneity in a meta-analysis. *Statistics in Medicine* 2002;**21**(11):1539–58.

**Jadad 1996**
Jadad AR, Moore RA, Carroll D, Jenkinson C, Reynolds DJ, Gavaghan DJ, et al.Assessing the quality of reports of randomized clinical trials: Is blinding necessary?. *Controlled Clinical Trials* 1996;**17**:1–12.

**NAEPP 1997**
National Asthma Education Prevention Program (NAEPP). *NAEPP Expert Panel Report II: Guidelines for the Diagnosis and Management of Asthma*. Bethesda, MD: National Institutes of Health, 1997.

**Rowe 1992**
Rowe BH, Keller J, Oxman AD. Steroid use in the emergency department treatment of asthma exacerbations: a meta-analysis. *American Journal of Emergency Medicine* 1992;**10**:301–10.

**Rowe 1998**
Rowe BH, Bota GW, Pollack CV, Emond SD, Camargo CA. Management of acute asthma among adults presenting to Canadian versus US Emergency Departments. *Annals of Emergency Medicine* 1998;**32**(3 (Pt2)):S2–S3.

**Stein 1990**
Stein LM, Cole RP. Early administration of corticosteroids in emergency room treatment of acute asthma. *Archives of Internal Medicine* 1990;**112**:822–7.

**Weber 2002**
Weber EJ, Silverman RA, Callaham ML, Pollack CV Jr, Woodruff PG, Clark S, et al.A prospective multicenter study of factors associated with hospital admission among adults with acute asthma. *The American Journal of Medicine* 2002;**113**:371–8.

* *Indicates the major publication for the study*

## CHARACTERISTICS OF STUDIES

### Characteristics of included studies *[ordered by study ID]*

**Chapman 1991**

| | |
|---|---|
| Methods | A randomized double-blind placebo controlled clinical trial comparing oral steroids to placebo. Method of randomization was not described; primary author stated randomization was by computer generated central pharmacy. Allocation was concealed using sealed envelopes |
| Participants | Patients presenting to the emergency department with acute exacerbations of asthma who were likely to be sent home upon completion of therapy. Patients had to fulfill American Thoracic Society criteria for diagnosis of asthma.<br>Ages: 16 years of age and older.<br>Severity: Not indicated.<br>PFTs: Mean pretreatment FVC was 2.74 L (62 % of predicted) and mean FEV-1 was 1.73 L (46% of predicted) |
| Interventions | 40 mg of prednisone decreased by 5 mg per day until supply was exhausted. Control group received placebo inert tablets identical in appearance and taste. Co-interventions were permitted (theophylline compounds and bronchodilators) |
| Outcomes | The main outcome was relapse to additional care defined as "an unscheduled medical visit occasioned by the patient's perceived need for further medical treatment". In addition, the patients had diary cards and made spirometric measurements. The outcome measurements were performed at days 1, 7, and 14 as well as a telephone contact at 21 days |
| Notes | Correspondence with author provided clarification and additional information. The researchers were unable to re-analyze the data for subgroup comparisons |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Adequate sequence generation? | Yes | Computer generated randomisation scheme |
| Allocation concealment? | Yes | Centralised randomisation by pharmacy |

**Deshpande 1986**

| | |
|---|---|
| Methods | A randomized, double-blind placebo controlled clinical trial comparing oral steroid to placebo. A random numbers table was used for randomization |
| Participants | Children presenting to a pediatric chest clinic with an acute exacerbation asthma were included in the study, provided that they were able to use a peak flow meter.<br>Ages: Children ages 5 through 15 (mean 10.5).<br>Severity: Not indicated.<br>PFTs: Patients were included if their PEFR was between 15 and 80% of the expected value for their height and age |

**Deshpande 1986** (*Continued*)

| | |
|---|---|
| Interventions | Each child received one dose of nebulized salbutamol (2 mg in 5 ml physiological saline). Patients were then randomized to receive either prednisolone or identical placebo. The dosage schedule for the medication was as follows:<br>Day 1: 2 mg/kg<br>Day 2: 1 mg/kg<br>Day 3: 0.5 mg/kg |
| Outcomes | The main outcome was relapse; however, it was not specifically defined. Participants (with assistance from their parents if necessary) were asked to record the PEFR in the morning and evening before treatment with bronchodilators, until the follow-up on day 4. Participants were allowed to continue any other previously prescribed treatment, and were asked to document the frequency. Symptom scores were calculated at presentation as well as day 4 |
| Notes | Author wrote that after the study was completed, participants were advised to seek follow up after 24 hours; therefore, 4 participants were admitted on day 4 in the placebo group and none in the treatment group. Study data were not available; PEFRs were estimated from graphs at day 3 |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Adequate sequence generation? | Yes | Random numbers table was used for randomization |
| Allocation concealment? | Unclear | Information not available |

**Fiel 1983**

| | |
|---|---|
| Methods | A randomized double-blind placebo controlled clinical trial comparing oral steroids to placebo. Method of randomization was not described |
| Participants | Patients who presented to the Temple University Hospital Emergency Department with acute asthma and fitting the diagnostic criteria set by the American Thoracic Society.<br>Ages: Patients between the ages of 15 and 45.<br>Severity: Not indicated.<br>PFTs: Mean pretreatment PEFR was 168.8 L/min (SD 85.9) in the treatment group and 157.9 L/min (SD 84.9) in the control group |
| Interventions | Intravenous methylprednisolone 4 mg per kilogram and tapering schedule of oral methylprednisolone starting at the dosage of 32 mg BID and decreasing to 0 mg over 8 days. Placebo group received identical placebo injection and oral tablets. Co-interventions were monitored |
| Outcomes | The main outcome was relapse defined as "the need for further emergency care within 10 days of enrollment". Contact by phone or by person between 7 and 10 days. Participants were assessed with respect to symptoms, drug compliance, adverse affects, and relapse |

**Fiel 1983** (*Continued*)

| | |
|---|---|
| Notes | Authors did not respond: Additional information obtained from review of supplemental publication (Glanz K, Feil SB, Swartz MA, Francis ME. Compliance with an experimental drug regimen for the treatment of asthma: Its magnitude, importance and correlates. J Chron Dis 1984;37:815-24.) |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Adequate sequence generation? | Unclear | Described as randomised; other information not available |
| Allocation concealment? | Unclear | Information not available |

**Lee 1993a**

| | |
|---|---|
| Methods | A randomized, double blind, placebo-controlled clinical trial comparing oral and IM steroids to placebo. Randomization was achieved by means of a set of computer-generated set of random-numbers in blocks of nine |
| Participants | Patients requiring immediate therapy but not hospitalization for an acute exacerbation of asthma were included in the study. Fifty patients who had not ever received corticosteroids prior to admission were included and any patient receiving herb/drug treatments or any medication of an uncertain origin were excluded from the study.<br>Ages: Mean ages were 42 (SD 4) for Group A (PO), 37 (SD 4) for Group B (IM), and 40 (SD 4) for Group C (Control).<br>Severity: Fischl index was used to determine severity at presentation. All groups were similar : Group A: 2.8 (SD 0.7), Group B: 2.9 (SD 0.3), and Group C: 2.8 (SD 0.7).<br>PFTs: PEFRs (L/min) at presentation: Group A: 200 (SD 25), Group B: 210 (SD 30), and Group C: 208 (SD 26) |
| Interventions | Patients were randomized to receive two treatments in three groups:<br>A. Oral tablets: dexamethasone 1.5 mg twice a day and tapered to zero at day 8 (3.0 mg day 1 and 2, 2.0 mg day 3, 1.5 mg day 4, 1.0 mg day 5 0.75 mg day 6 and 0.5 mg day 7); active or placebo.<br>AND;<br>B. Intramuscular injection: 10 mg dexamethasone by intramuscular injection OR placebo intramuscular injection.<br>Participants in Group "A" received placebo IM and placebo oral tablets, Group "B" received IM dexamethasone and oral placebo, and Group "C" received placebo injection and oral dexamethasone.<br>All participants received oral anhydrous long-acting theophylline at a dose of 250 mg twice daily |
| Outcomes | The main outcome was relapse defined as the need for another emergency room visit within 7 days of enrolment into the study. Follow up at 7 days after ED presentation was completed to collect symptom scores, adverse effects, relapse and frequency of beta-agonist usage |
| Notes | Lee 1993a reports the information from po dexamethasone vs placebo; Lee 1993b reports information for IM dexamethasone injection vs placebo. The authors did not respond |

**Lee 1993a** (*Continued*)

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Adequate sequence generation? | Yes | Randomization was achieved by means of a set of computer-generated set of random-numbers in blocks of nine |
| Allocation concealment? | Unclear | Information not available |

**Lee 1993b**

| | |
|---|---|
| Methods | See Lee 1993a |
| Participants | See Lee 1993a |
| Interventions | See Lee 1993a |
| Outcomes | See Lee 1993a |
| Notes | Lee 1993b reports the information from IM steroids vs placebo |

| *Risk of bias* | | |
|---|---|---|
| **Item** | **Authors' judgement** | **Description** |
| Adequate sequence generation? | Yes | As for Lee 1993a |
| Allocation concealment? | Unclear | As for Lee 1993a |

**McNamara 1993**

| | |
|---|---|
| Methods | A randomized, single-blind, placebo-controlled clinical trial comparing IM steroids to placebo. An open random numbers table was used to randomize patients. Concealment of allocation was not discussed |
| Participants | Patients with an acute exacerbation of asthma presenting to the emergency department, judged by the emergency physician eligible to be sent home. Allocation determined at time of discharge by a nurse assistant.<br>Ages: Patients between the ages of 18 and 45.<br>Severity: Patients were asked to self-describe their asthma as either mild, moderate or severe. In the steroid group; 9 mild, 14 moderate, 7 severe. In the control group; 10 mild, 13 moderate, 3 severe.<br>PFTs: Pretreatment PEFRs were 193 L/min (SD 68) for the steroid group and 198 (SD 68) L/min for the control group |
| Interventions | The treatment group received intramuscular injection of 240 mg methylprednisolone vs saline placebo. "The syringe was not covered; however, the treating physician did not view the syringe." |

**McNamara 1993** (*Continued*)

| | |
|---|---|
| Outcomes | The main outcome was relapse defined as a need to seek non-routine medical care for symptoms of asthma within 7 days of study entry. Peak expiratory flow rates were also collected. Admissions to hospital and deaths were recorded |
| Notes | 3 patients in the placebo group died. Correspondence with author provided clarification and additional information |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Adequate sequence generation? | Yes | An open random numbers table was used to randomize patients. |
| Allocation concealment? | Unclear | Information not available |

**Shapiro 1983**

| | |
|---|---|
| Methods | A randomized, double-blind, placebo-controlled, clinical trial comparing oral steroids to placebo. A random numbers table was used for randomization |
| Participants | Patients were children of an Allergy Clinic of a Children's Orthopaedic Hospital and Medical Centre, or of a private practice of one of the investigators. All patients experienced an acute exacerbation of asthma requiring 3 consecutive treatments of beta-adrenergic therapy. Patients were excluded if they had taken inhaled or oral corticosteroids in the previous 2 weeks. If the child was unable to perform PFTs, or had a previous history of marked deterioration and hospitalization for status asthmaticus, the child was excluded.<br>Severity: Not indicated.<br>PFTs: Patients were included if they had persistent depression in FEV-1 of < 80% of predicted |
| Interventions | Treatment group received methylprednisolone 32 mg by mouth for 8 days while control group received placebo tablets. All participants continued to take theophylline at a dosage that was considered adequate to maintain a serum concentration of 10 to 20 ug/ml. All participants took metaproterenol, 10 to 20 mg TID routinely and up to every 4 hours as needed |
| Outcomes | The main outcome was relapse defined as the need to seek additional care. Relapse at 24 hours, 7 days, and 14 days was assessed as well as admission rates and PFTs |
| Notes | |

***Risk of bias***

| Item | Authors' judgement | Description |
|---|---|---|
| Adequate sequence generation? | Yes | A random numbers table was used for randomization |

**Shapiro 1983** (*Continued*)

| | | |
|---|---|---|
| Allocation concealment? | Unclear | Information not available |

FEV-1: forced expiratory volume in one second
FVC: forced vital capacity
PEFR: peak expiratory flow rates
PFT: pulmonary function test
vs: versus

## Characteristics of excluded studies *[ordered by study ID]*

| Study | Reason for exclusion |
|---|---|
| Connet 1994 | Patients were admitted and relapse was not reported. |
| Engel 1990 | Patients were admitted and relapse was not reported. |
| Fanta 1983 | Patients were admitted and relapse was not reported. |
| Green 1995 | Patients were admitted and relapse was not reported. |
| Harris 1986 | Patients were monitored before emergency department presentation and were treated at home in attempts to prevent emergency visits |
| Hoffman 1988 | RCT comparing IM vs oral corticosteroids only; no placebo arm |
| Littenberg 1986 | A multi-treatment approach was used. Relapse data was not collected |
| Loren 1980 | Patients were hospitalized. |
| McFadden 1976 | Not the required outcome measures. (Patients were not followed for relapse.) |
| Morell 1992 | Patients were admitted and relapse was not reported. |
| Pedersen 1987 | Patients were admitted and relapse was not reported. |
| Schneider 1988 | Patients were hospitalized. |
| Storr 1987 | Patients were admitted and relapse was not reported. |
| Wilson 1990 | Not a randomized controlled trial. |

IM: intra-muscular
vs: versus

## DATA AND ANALYSES

### Comparison 1. Oral or Intramuscular corticosteroid (CS) versus placebo

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Relapse rates | 5 | | Risk Ratio (M-H, Fixed, 95% CI) | Subtotals only |
| 1.1 7-10 day follow-up | 5 | 329 | Risk Ratio (M-H, Fixed, 95% CI) | 0.38 [0.20, 0.74] |
| 1.2 21 day follow-up | 1 | 93 | Risk Ratio (M-H, Fixed, 95% CI) | 0.47 [0.25, 0.89] |
| 2 PFTs 2-3 days | 2 | 71 | Std. Mean Difference (IV, Random, 95% CI) | 0.48 [-1.19, 2.15] |
| 3 PFTs 7-10 days | 3 | 78 | Std. Mean Difference (IV, Random, 95% CI) | 0.09 [-0.46, 0.63] |
| 4 Admissions to hospital | 4 | 210 | Risk Ratio (M-H, Fixed, 95% CI) | 0.35 [0.13, 0.95] |
| 5 Beta-agonist use | 2 | | Mean Difference (IV, Random, 95% CI) | Subtotals only |
| 5.1 7-10 days | 2 | 133 | Mean Difference (IV, Random, 95% CI) | -3.31 [-5.59, -1.03] |
| 5.2 14 days | 1 | 70 | Mean Difference (IV, Random, 95% CI) | -2.3 [-5.36, 0.76] |
| 6 Side effects | 2 | 132 | Risk Ratio (M-H, Fixed, 95% CI) | 0.96 [0.53, 1.74] |
| 7 High Quality Studies (Relapse Rates) | 4 | 273 | Risk Ratio (M-H, Fixed, 95% CI) | 0.45 [0.21, 0.96] |

### Comparison 2. Oral corticosteroids versus placebo

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Relapse rates | 4 | | Risk Ratio (M-H, Fixed, 95% CI) | Subtotals only |
| 1.1 7-10 day follow-up | 4 | 256 | Risk Ratio (M-H, Fixed, 95% CI) | 0.44 [0.21, 0.94] |
| 1.2 21 day follow-up | 1 | 93 | Risk Ratio (M-H, Fixed, 95% CI) | 0.47 [0.25, 0.89] |
| 2 PFTs | 2 | 61 | Mean Difference (IV, Random, 95% CI) | 6.66 [-3.50, 16.83] |

### Comparison 3. Intramuscular corticosteroids versus placebo

| Outcome or subgroup title | No. of studies | No. of participants | Statistical method | Effect size |
|---|---|---|---|---|
| 1 Relapse rates | 2 | 89 | Risk Ratio (M-H, Random, 95% CI) | 0.30 [0.08, 1.09] |
| 1.1 7-10 day follow-up | 2 | 89 | Risk Ratio (M-H, Random, 95% CI) | 0.30 [0.08, 1.09] |
| 2 PFTs | 1 | 33 | Mean Difference (IV, Random, 95% CI) | -10.0 [-28.90, 8.90] |

## Analysis 1.1. Comparison 1 Oral or Intramuscular corticosteroid (CS) versus placebo, Outcome 1 Relapse rates.

Review: Corticosteroids for preventing relapse following acute exacerbations of asthma

Comparison: 1 Oral or Intramuscular corticosteroid (CS) versus placebo

Outcome: 1 Relapse rates

| Study or subgroup | CS n/N | Placebo n/N | Risk Ratio M-H,Fixed,95% CI | Risk Ratio M-H,Fixed,95% CI |
|---|---|---|---|---|
| 1 7-10 day follow-up | | | | |
| Chapman 1991 | 3/48 | 8/45 | | 0.35 [ 0.10, 1.24 ] |
| Fiel 1983 | 5/49 | 10/53 | | 0.54 [ 0.20, 1.47 ] |
| Lee 1993a | 1/36 | 1/16 | | 0.44 [ 0.03, 6.67 ] |
| McNamara 1993 | 2/30 | 8/26 | | 0.22 [ 0.05, 0.93 ] |
| Shapiro 1983 | 0/11 | 0/15 | | 0.0 [ 0.0, 0.0 ] |
| **Subtotal (95% CI)** | **174** | **155** | | **0.38 [ 0.20, 0.74 ]** |
| Total events: 11 (CS), 27 (Placebo) | | | | |
| Heterogeneity: $Chi^2$ = 1.08, df = 3 (P = 0.78); $I^2$ =0.0% | | | | |
| Test for overall effect: Z = 2.87 (P = 0.0041) | | | | |
| 2 21 day follow-up | | | | |
| Chapman 1991 | 10/48 | 20/45 | | 0.47 [ 0.25, 0.89 ] |
| **Subtotal (95% CI)** | **48** | **45** | | **0.47 [ 0.25, 0.89 ]** |
| Total events: 10 (CS), 20 (Placebo) | | | | |
| Heterogeneity: not applicable | | | | |
| Test for overall effect: Z = 2.32 (P = 0.021) | | | | |

### Analysis 1.2. Comparison 1 Oral or Intramuscular corticosteroid (CS) versus placebo, Outcome 2 PFTs 2-3 days.

Review: Corticosteroids for preventing relapse following acute exacerbations of asthma

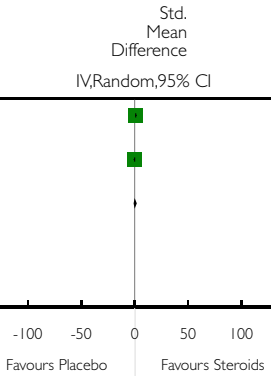
Comparison: 1 Oral or Intramuscular corticosteroid (CS) versus placebo

Outcome: 2 PFTs 2-3 days

| Study or subgroup | CS N | Mean(SD) | Placebo N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Deshpande 1986 | 22 | 84 (14.9) | 21 | 60.2 (20.1) | | 50.5 % | 1.33 [ 0.66, 1.99 ] |
| Shapiro 1983 | 13 | 70 (20) | 15 | 79 (25) | | 49.5 % | -0.38 [ -1.13, 0.37 ] |
| **Total (95% CI)** | **35** | | **36** | | | **100.0 %** | **0.48 [ -1.19, 2.15 ]** |

Heterogeneity: $Tau^2 = 1.33$; $Chi^2 = 11.13$, df = 1 (P = 0.00085); $I^2 = 91\%$

Test for overall effect: Z = 0.56 (P = 0.57)




### Analysis 1.3. Comparison 1 Oral or Intramuscular corticosteroid (CS) versus placebo, Outcome 3 PFTs 7-10 days.

Review: Corticosteroids for preventing relapse following acute exacerbations of asthma

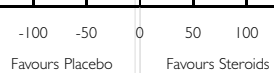
Comparison: 1 Oral or Intramuscular corticosteroid (CS) versus placebo

Outcome: 3 PFTs 7-10 days

| Study or subgroup | PO CS N | Mean(SD) | Placebo N | Mean(SD) | Std. Mean Difference IV,Random,95% CI | Weight | Std. Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| Lee 1993a | 19 | 370 (30) | 8 | 370 (30) | | 33.1 % | 0.0 [ -0.83, 0.83 ] |
| Lee 1993b | 17 | 360 (25) | 8 | 370 (30) | | 31.9 % | -0.36 [ -1.21, 0.48 ] |
| Shapiro 1983 | 11 | 99 (16) | 15 | 90 (14) | | 35.0 % | 0.59 [ -0.21, 1.38 ] |
| **Total (95% CI)** | **47** | | **31** | | | **100.0 %** | **0.09 [ -0.46, 0.63 ]** |

Heterogeneity: $Tau^2 = 0.06$; $Chi^2 = 2.63$, df = 2 (P = 0.27); $I^2 = 24\%$

Test for overall effect: Z = 0.32 (P = 0.75)



### Analysis 1.4. Comparison 1 Oral or Intramuscular corticosteroid (CS) versus placebo, Outcome 4 Admissions to hospital.

Review: Corticosteroids for preventing relapse following acute exacerbations of asthma

Comparison: 1 Oral or Intramuscular corticosteroid (CS) versus placebo

Outcome: 4 Admissions to hospital

| Study or subgroup | CS n/N | Placebo n/N | Risk Ratio M-H,Fixed,95% CI | Risk Ratio M-H,Fixed,95% CI |
|---|---|---|---|---|
| Fiel 1983 | 3/34 | 9/42 | | 0.41 [ 0.12, 1.40 ] |
| Lee 1993a | 1/36 | 1/16 | | 0.44 [ 0.03, 6.67 ] |
| McNamara 1993 | 1/30 | 4/26 | | 0.22 [ 0.03, 1.82 ] |
| Shapiro 1983 | 0/11 | 0/15 | | 0.0 [ 0.0, 0.0 ] |
| **Total (95% CI)** | **111** | **99** | | **0.35 [ 0.13, 0.95 ]** |

Total events: 5 (CS), 14 (Placebo)

Heterogeneity: $Chi^2 = 0.29$, df = 2 (P = 0.87); $I^2 = 0.0\%$

Test for overall effect: Z = 2.07 (P = 0.038)

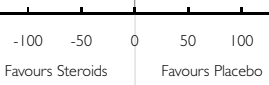
### Analysis 1.5. Comparison 1 Oral or Intramuscular corticosteroid (CS) versus placebo, Outcome 5 Beta-agonist use.

Review: Corticosteroids for preventing relapse following acute exacerbations of asthma

Comparison: 1 Oral or Intramuscular corticosteroid (CS) versus placebo

Outcome: 5 Beta-agonist use

| Study or subgroup | CS N | Mean(SD) | Placebo N | Mean(SD) | Mean Difference IV,Random,95% CI | Weight | Mean Difference IV,Random,95% CI |
|---|---|---|---|---|---|---|---|
| 1 7-10 days | | | | | | | |
| Chapman 1991 | 44 | 4.8 (5.3) | 37 | 7.5 (7.2) | | 66.3 % | -2.70 [ -5.50, 0.10 ] |
| Lee 1993a | 36 | 1.5 (5.3) | 16 | 6 (7.2) | | 33.7 % | -4.50 [ -8.43, -0.57 ] |
| **Subtotal (95% CI)** | **80** | | **53** | | | **100.0 %** | **-3.31 [ -5.59, -1.03 ]** |
| Heterogeneity: $Tau^2$ = 0.0; $Chi^2$ = 0.53, df = 1 (P = 0.46); $I^2$ =0.0% | | | | | | | |
| Test for overall effect: Z = 2.84 (P = 0.0045) | | | | | | | |
| 2 14 days | | | | | | | |
| Chapman 1991 | 40 | 3.5 (5.3) | 30 | 5.8 (7.2) | | 100.0 % | -2.30 [ -5.36, 0.76 ] |
| **Subtotal (95% CI)** | **40** | | **30** | | | **100.0 %** | **-2.30 [ -5.36, 0.76 ]** |
| Heterogeneity: not applicable | | | | | | | |
| Test for overall effect: Z = 1.48 (P = 0.14) | | | | | | | |



### Analysis 1.6. Comparison 1 Oral or Intramuscular corticosteroid (CS) versus placebo, Outcome 6 Side effects.

Review: Corticosteroids for preventing relapse following acute exacerbations of asthma

Comparison: 1 Oral or Intramuscular corticosteroid (CS) versus placebo

Outcome: 6 Side effects

| Study or subgroup | CS n/N | Placebo n/N | Risk Ratio M-H,Fixed,95% CI | Weight | Risk Ratio M-H,Fixed,95% CI |
|---|---|---|---|---|---|
| Fiel 1983 | 9/42 | 3/34 | | 20.5 % | 2.43 [ 0.71, 8.27 ] |
| McNamara 1993 | 8/30 | 12/26 | | 79.5 % | 0.58 [ 0.28, 1.19 ] |
| **Total (95% CI)** | **72** | **60** | | **100.0 %** | **0.96 [ 0.53, 1.74 ]** |

Total events: 17 (CS), 15 (Placebo)

Heterogeneity: $Chi^2$ = 4.08, df = 1 (P = 0.04); $I^2$ =76%

Test for overall effect: Z = 0.14 (P = 0.89)


### Analysis 1.7. Comparison 1 Oral or Intramuscular corticosteroid (CS) versus placebo, Outcome 7 High Quality Studies (Relapse Rates).

Review: Corticosteroids for preventing relapse following acute exacerbations of asthma

Comparison: 1 Oral or Intramuscular corticosteroid (CS) versus placebo

Outcome: 7 High Quality Studies (Relapse Rates)

| Study or subgroup | CS n/N | Placebo n/N | Risk Ratio M-H,Fixed,95% CI | Risk Ratio M-H,Fixed,95% CI |
|---|---|---|---|---|
| Chapman 1991 | 3/48 | 8/45 | | 0.35 [ 0.10, 1.24 ] |
| Fiel 1983 | 5/49 | 10/53 | | 0.54 [ 0.20, 1.47 ] |
| Lee 1993a | 1/36 | 1/16 | | 0.44 [ 0.03, 6.67 ] |
| Shapiro 1983 | 0/11 | 0/15 | | 0.0 [ 0.0, 0.0 ] |
| **Total (95% CI)** | **144** | **129** | | **0.45 [ 0.21, 0.96 ]** |

Total events: 9 (CS), 19 (Placebo)

Heterogeneity: $Chi^2$ = 0.28, df = 2 (P = 0.87); $I^2$ =0.0%

Test for overall effect: Z = 2.07 (P = 0.038)

### Analysis 2.1. Comparison 2 Oral corticosteroids versus placebo, Outcome 1 Relapse rates.

Review: Corticosteroids for preventing relapse following acute exacerbations of asthma

Comparison: 2 Oral corticosteroids versus placebo

Outcome: 1 Relapse rates

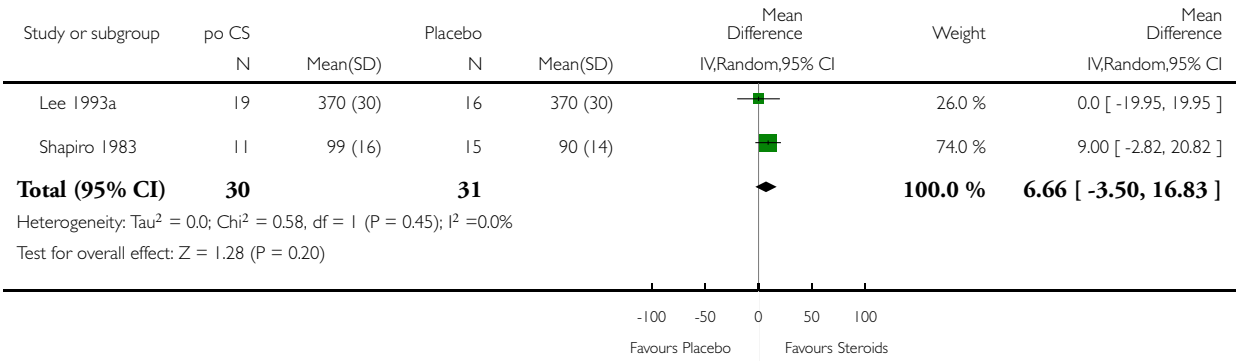
| Study or subgroup | po CS n/N | Placebo n/N | Risk Ratio M-H,Fixed,95% CI | Risk Ratio M-H,Fixed,95% CI |
|---|---|---|---|---|
| 1 7-10 day follow-up | | | | |
| Chapman 1991 | 3/48 | 8/45 | | 0.35 [ 0.10, 1.24 ] |
| Fiel 1983 | 5/49 | 10/53 | | 0.54 [ 0.20, 1.47 ] |
| Lee 1993a | 0/19 | 1/16 | | 0.28 [ 0.01, 6.51 ] |
| Shapiro 1983 | 0/11 | 0/15 | | 0.0 [ 0.0, 0.0 ] |
| **Subtotal (95% CI)** | **127** | **129** | | **0.44 [ 0.21, 0.94 ]** |
| Total events: 8 (po CS), 19 (Placebo) | | | | |
| Heterogeneity: $Chi^2$ = 0.36, df = 2 (P = 0.84); $I^2$ =0.0% | | | | |
| Test for overall effect: Z = 2.13 (P = 0.033) | | | | |
| 2 21 day follow-up | | | | |
| Chapman 1991 | 10/48 | 20/45 | | 0.47 [ 0.25, 0.89 ] |
| **Subtotal (95% CI)** | **48** | **45** | | **0.47 [ 0.25, 0.89 ]** |
| Total events: 10 (po CS), 20 (Placebo) | | | | |
| Heterogeneity: not applicable | | | | |
| Test for overall effect: Z = 2.32 (P = 0.021) | | | | |

### Analysis 2.2. Comparison 2 Oral corticosteroids versus placebo, Outcome 2 PFTs.

Review: Corticosteroids for preventing relapse following acute exacerbations of asthma

Comparison: 2 Oral corticosteroids versus placebo

Outcome: 2 PFTs

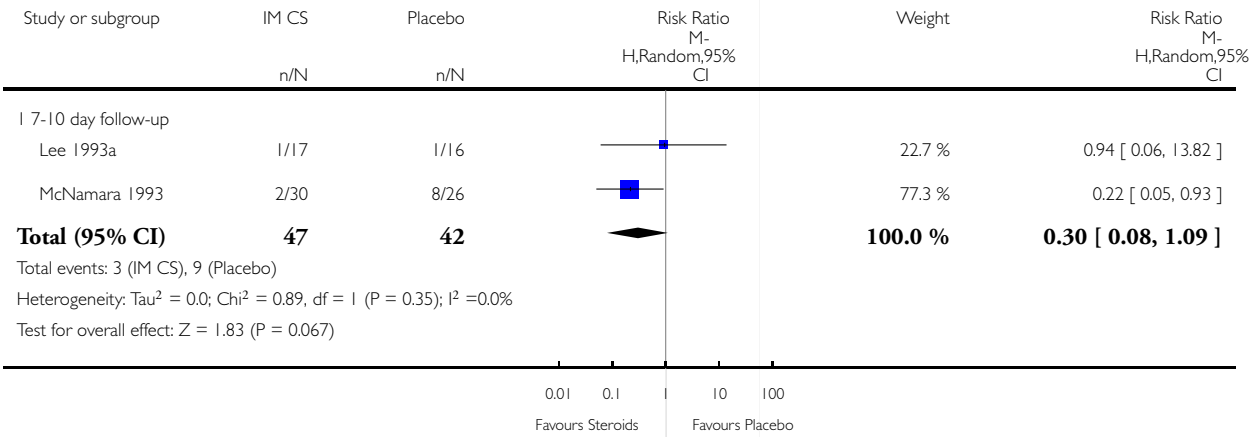



### Analysis 3.1. Comparison 3 Intramuscular corticosteroids versus placebo, Outcome 1 Relapse rates.

Review: Corticosteroids for preventing relapse following acute exacerbations of asthma

Comparison: 3 Intramuscular corticosteroids versus placebo

Outcome: 1 Relapse rates

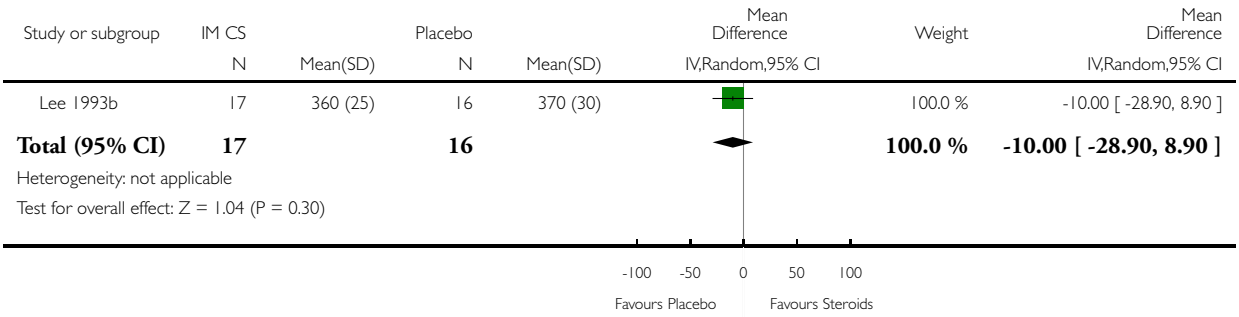


**Analysis 3.2. Comparison 3 Intramuscular corticosteroids versus placebo, Outcome 2 PFTs.**

Review: Corticosteroids for preventing relapse following acute exacerbations of asthma

Comparison: 3 Intramuscular corticosteroids versus placebo

Outcome: 2 PFTs




## WHAT'S NEW

Last assessed as up-to-date: 11 April 2007.

| Date | Event | Description |
|---|---|---|
| 23 July 2008 | Amended | Converted to new review format. |

## HISTORY

Protocol first published: Issue 1, 1999

Review first published: Issue 3, 2000

| Date | Event | Description |
|---|---|---|
| 12 April 2007 | New citation required and conclusions have changed | Substantive amendment |

## CONTRIBUTIONS OF AUTHORS

BHR initiated the review, wrote the protocol, performed the searches, contributed to selection for inclusion, extracted data, and is the principal author. CHS and FMD contributed to the protocol development, performed selection for inclusion and quality assessments, and contributed to editing. JAB managed the searches, selection for inclusion and quality assessments, data extraction and entry, and draft manuscript development. GWB contributed to protocol development and editing. CHS converted the review to RevMan 4.0.

## DECLARATIONS OF INTEREST

Drs. Rowe and Ducharme has received some research grant and consulting fees from GlaxoSmithKline and AstraZeneca, both of whom produce inhaled corticosteroid preparations. The authors of this review were not involved in the original studies included in this review and have no financial or other links to corporations who manufacture corticosteroids.

## SOURCES OF SUPPORT


### Internal sources

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

### External sources

- Ministry of Health - Emergency Health Services RAC (# 11469N), Toronto, Ontario, Canada.
- Canada Research Chairs Program, Government of Canada, Canada.


## INDEX TERMS

### Medical Subject Headings (MeSH)

Acute Disease; Adrenal Cortex Hormones [*administration & dosage]; Anti-Asthmatic Agents [*administration & dosage]; Asthma [*prevention & control]; Randomized Controlled Trials as Topic; Recurrence [prevention & control]

### MeSH check words

Humans