

## Living Friendly Summaries of the Body of Evidence using Epistemonikos (FRISBEE)

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# What is the effectiveness of systemic corticosteroids in children with croup?

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## Abstract

Systemic corticosteroids constitute standard treatment in children with acute obstructive laryngitis (croup). However, there is some uncertainty in relation with the magnitude of the benefits and risks associated with their use. To answer this question, we used Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others. We identified six systematic reviews including 25 randomized trials relevant for the question of interest. We extracted data from the systematic reviews, reanalysed data of primary studies, conducted a meta-analysis and generated a summary of findings table using the GRADE approach. We concluded the use of systemic corticosteroids increases the number of patients with clinical improvement at 12 hours and reduces the risk of readmission.

## Problem

Acute obstructive laryngitis is one of the most frequent respiratory diseases in childhood, predominantly in children between 6 months and 6 years, with a higher incidence in late autumn and early winter [1],[2]. They are usually mild and self-limiting, although occasionally they can cause severe respiratory obstruction. Systemic corticosteroids reduce laryngeal edema by reducing the local inflammatory reaction, contracting lymphoid inflammation and impairing capillary permeability [1],[3]. Due to their potent anti-inflammatory effect, they have been one of the pillars of treatment in patients with croup. However, there is some degree of uncertainty regarding the magnitude of the benefits.

On the other hand, although the use of corticosteroids in high doses, or for long time, is associated to multiple adverse effects, the use of a single dose in acute obstructive laryngitis would constitute a safe therapy [4].

## Methods

To answer the question, we used Epistemonikos, the largest database of systematic reviews in health, which is maintained by screening multiple information sources, including MEDLINE, EMBASE, Cochrane, among others, to identify systematic reviews and their included primary studies. We extracted data from the identified reviews and reanalyzed data from primary studies included in those reviews. With this information we generated a structured summary using a pre-established format, which includes key messages, a summary of the body of evidence (presented as an evidence matrix in Epistemonikos), meta-analysis of the total of studies, a summary of findings table following the GRADE approach and a table of other considerations for decision-making.

### Key messages

- The use of systemic corticosteroids in children with acute obstructive laryngitis increases the number of patients with clinical improvement at 12 hours and reduces the risk of readmission.
- Adverse effects associated with a single dose in the treatment of acute obstructive laryngitis would not be associated to adverse effects.

### About the body of evidence for this question

<p>What is the evidence. See evidence matrix in Epistemonikos later</p>	<p>We found six systematic reviews [4],[5],[6],[7],[8],[9] including twenty-five randomized controlled trials [10],[11],[12],[13],[14],[15],[16],[17],[18],[19],[20],[21],[22],[23],[24],[25],[26],[27],[28],[29],[30],[31],[32],[33],[34] evaluating the use of corticosteroids compared to placebo.</p>
<p>What types of patients were included*</p>	<p>Eight trials included patients who consulted in an emergency department [12],[15],[16],[19],[21],[22],[25],[31] and sixteen included patients in the hospital setting [10],[11],[13],[14],[17],[18],[20],[23],[24],[26],[28],[29],[30],[33],[34]. One trial considered a group evaluated in emergency services that was then admitted to the hospital [32]. The age range ranged from 3 months to 12 years. Three trials included patients with mild laryngitis [12],[16],[31], three with moderate laryngitis [21],[22],[25] and one mild to moderate [15]. Eighteen trials did not classify the severity of laryngitis [10],[11],[13],[14],[17],[18],[19],[20],[23],[24],[26],[27],[28],[29],[30],[32],[33],[34].</p>
<p>What types of interventions were included*</p>	<p>Seventeen trials considered only the use of systemic corticosteroids (oral, nasogastric, intravenous, subcutaneous and intramuscular) [12],[13],[14],[17],[18],[19],[20],[23],[24],[25],[26],[28],[29],[30],[31],[33],[34] five evaluated inhaled corticosteroids [10],[11],[15],[21],[27] and three considered both systemic corticosteroids and inhaled [16],[22],[32]. The corticosteroids used were prednisone, dexamethasone, methylprednisolone, prednisolone and budesonide. The dosages used had great variation between the different trials. From the eighteen trials that considered the use of systemic corticosteroids, fourteen used dexamethasone in different single doses (0.6 mg/kg [12],[16],[17],[22],[25],[32],[33], 0.15 mg/kg [31], 0.3 mg/kg [19], 0.4 mg/kg [29], 0.5 mg/kg [24], between 4 and 12 mg total [20],[23],[28]). Two trials used 4 mg/kg methylprednisolone once or twice [14],[26] (equivalent to 0.8 mg/kg dexamethasone dose). Two trials used prednisolone, one at a dose of 2 mg/kg up to 24 hours post-extubation [13] (equivalent to 0.3 mg/kg dexamethasone), and another 2.5 mg at 6 hours without specifying time of treatment [18]. One trial used prednisone 2.5 to 5 mg three doses in one day (equivalent to 0.4 to 0.8 mg dexamethasone dose) [34] and one trial used dexamethasone used 0.04 mg/kg/day in 4 doses [30]. The rest of the trials used the inhalation route with budesonide from 1 to 4 mg per dose up to 4 doses, and nebulized dexamethasone from 10 to 20 mg.</p>
<p>What types of outcomes were measured</p>	<p>The trials measured multiple outcomes, however, the different systematic reviews grouped them as follows:</p> <ul style="list-style-type: none"> <li>• Croup score (change from 0 to 6, 12, 24 hours) according to score (Westley score and non-Westley score)</li> <li>• Westley score (change from 0 to 6, 12 and 24 hours) according to inpatient or outpatient</li> <li>• Westley score (change from 0 to 6, 12 and 24 hours) according to corticosteroid (budesonide, dexamethasone, fluticasone)</li> <li>• Readmissions/reconsultations according to inpatient or outpatient</li> <li>• Readmissions/reconsultations according to corticosteroid (budesonide, dexamethasone)</li> <li>• Readmissions/reconsultations according to croup severity</li> <li>• Length of stay according to inpatient or outpatient</li> <li>• Clinical improvement at 6, 12 and 24 hours according to inpatient or outpatient</li> <li>• Additional treatments (intubation/tracheostomy, use of antibiotics, supplemental corticosteroids, epinephrine and mist tent)</li> </ul>

\* The information about primary studies is extracted from the systematic reviews identified, unless otherwise specified.

### Summary of findings

The information on the effects of systemic corticosteroids in children with acute obstructive laryngitis is based on 13 randomized trials. The rest of the trials were not analyzed because they did not consider systemic steroids, or did not report the outcomes of interest. Six trials measured the outcome readmissions/reconsultations [12],[16],[22],[25],[28],[31], six endotracheal intubation/tracheostomy [19], [20],[22],[23],[28],[29] and five clinical improvement at 12 hours [14],[23],[26],[29],[33]. The summary of findings is as follows:

- The use of systemic corticosteroids in children with acute obstructive laryngitis reduces the risk of readmission. The certainty of the evidence is high.
- The use of systemic corticosteroids in children with acute obstructive laryngitis probably reduces the probability of requiring intubation or tracheostomy. The certainty of the evidence is moderate.
- The use of systemic corticosteroids in children with acute obstructive laryngitis increases the number of patients with clinical improvement at 12 hours. The certainty of the evidence is high.

Systemic corticosteroids for acute obstructive laryngitis in children				
<b>Patients</b>	Children with acute obstructive laryngitis. Hospital or non-hospital setting			
<b>Intervention</b>	Systemic corticosteroids			
<b>Comparison</b>	Placebo			
Outcome	Absolute effect *		Relative effect (95% CI)	Certainty of the evidence (GRADE)
	WITHOUT corticosteroids	WITH corticosteroids		
	Difference: patients per 1000			
Readmission / reconsultation	162 per 1000	60 per 1000	RR 0.33 (0.22 a 0.48)	⊕⊕⊕⊕ High
	Difference: 102 patients less per 1000 (Margin of error: 77 to 122 less)			
Intubation / tracheostomy	7 per 1000	3 per 1000	RR 0.48 (0.09 a 2.55)	⊕⊕⊕○ <sup>1</sup> Moderate
	Difference: 4 patients less per 1000 (Margin of error: 7 less to 12 more)			
Clinical improvement at 12 hrs.	607 per 1000	834 per 1000	RR 3.24 (1.8 a 5.81)	⊕⊕⊕⊕ High
	Difference: 227 patients more per 1000 (Margin of error: 129 to 293 more per 1000)			

Margin of error = 95% confidence interval (CI).  
 RR: Risk ratio.  
 GRADE: evidence grades of the GRADE Working Group (see later in this article).

\*The risk **WITHOUT corticosteroids** is based on the risk in the control group of the trials. The risk **WITH corticosteroids** (and its margin of error) is calculated from relative effect (and its margin of error).

<sup>1</sup> Although the confidence interval is wide, and includes the possibility of benefit and risk, since it is a rare event it is unlikely that clinical decisions may be modified if the real value moves away from the point estimate. On the other hand, the benefit on outcomes that are causally related suggests that it is highly unlikely that the real value is an increase in risk. For these reasons, the certainty of the evidence was reduced in only one level.

### About the certainty of the evidence (GRADE)\*

⊕⊕⊕⊕

**High:** This research provides a very good indication of the likely effect. The likelihood that the effect will be substantially different† is low.

⊕⊕⊕○

**Moderate:** This research provides a good indication of the likely effect. The likelihood that the effect will be substantially different† is moderate

⊕⊕○○

**Low:** This research provides some indication of the likely effect. However, the likelihood that it will be substantially different† is high.

⊕○○○

**Very low:** This research does not provide a reliable indication of the likely effect. The likelihood that the effect will be substantially different† is very high.

\*This concept is also called 'quality of the evidence' or 'confidence in effect estimates'.

† Substantially different = a large enough difference that it might affect a decision.

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## Other considerations for decision-making

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### To whom this evidence does and does not apply

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- The evidence presented in this summary is applicable to patients with mild, moderate or severe laryngitis.
  - Does not apply to a different age group than children under 13 years of age.
  - None of the trials included patients in the outpatient setting, however, in the absence of direct evidence, it is reasonable to extrapolate the information presented in this summary to this context.
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### About the outcomes included in this summary

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- It was decided to evaluate the outcomes of readmission/reconsultation and clinical improvement, because they are the most relevant outcomes for decision-making about the use of corticosteroids in laryngitis.
  - In addition, the outcome intubation/tracheostomy rate was considered due to its clinical relevance in laryngitis.
  - This selection is based on the opinion of the authors of the summary, but in general it agrees with the outcomes mentioned by systematic reviews.
  - Data on adverse effects of single dose corticosteroids were not presented in the summary of findings table, given the existing evidence on their safety [4].
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### Balance between benefits and risks, and certainty of the evidence

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- The benefits are of great magnitude, there is certainty about them, and the adverse effects are minimal. Therefore, the benefit/risk balance is very favorable to the intervention.
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### Resource considerations

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- It is a low cost intervention, and the benefits are important, so the balance between cost and benefits is very favorable.
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### What would patients and their doctors think about this intervention

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- Practically all patients and clinicians should be inclined to use this intervention with the evidence presented in this summary.
  - Due to the wide knowledge about the adverse effects of chronic use of corticosteroids, there may be resistance to the use of this treatment by parents or caregivers, which makes it necessary to explain the evidence on the safety of their use in this context.
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### Differences between this summary and other sources

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- The conclusions of this summary are consistent with the identified reviews, which report that both systemic and inhaled corticosteroids would be effective in the treatment of laryngitis. The magnitude of the effect on all outcomes was greater in this summary than in the main systematic review [4], which could be explained by the inclusion of only the trials that evaluated systemic corticosteroids.
  - This summary is consistent with the recommendations presented in the main guidelines on laryngitis in pediatrics [2],[3].
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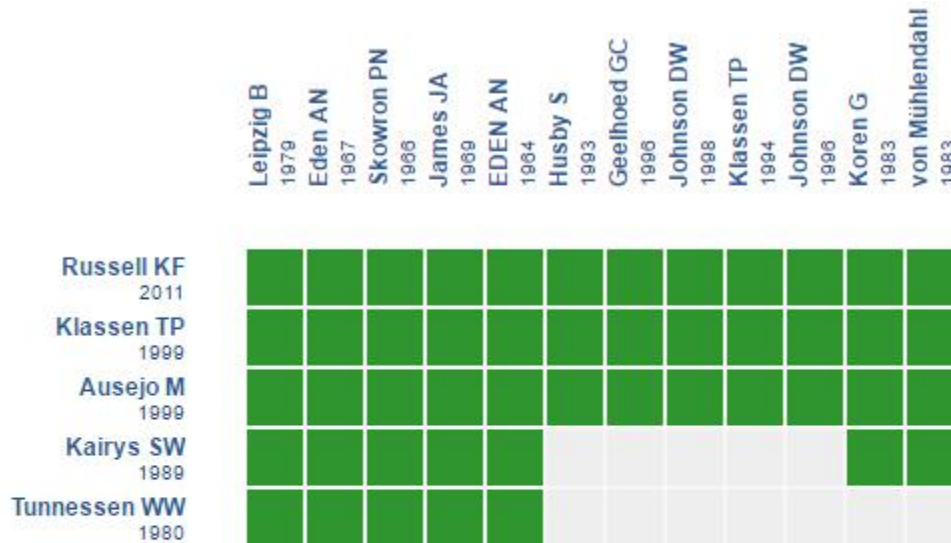
### Could this evidence change in the future?

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- The probability that future studies change the conclusions of this summary is low, due to the certainty of the existing evidence.
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How we conducted this summary

Using automated and collaborative means, we compiled all the relevant evidence for the question of interest and we present it as a matrix of evidence.



Starting from any systematic review, Epistemonikos builds a matrix based on existing connections in the database.  
 The author of the matrix can select relevant information for a specific health question (typically in PICO format) in order to display the information set for the question.  
 The rows represent systematic reviews that share at least one primary study, and columns display the studies.  
 The boxes in green correspond to studies included in the respective reviews.

Follow the link to access the **interactive version**: [Systemic corticosteroids versus placebo for croup](#)

## Notes

The upper portion of the matrix of evidence will display a warning of "new evidence" if new systematic reviews are published after the publication of this summary. Even though the project considers the periodical update of these summaries, users are invited to comment in *Medwave* or to contact the authors through email if they find new evidence and the summary should be updated earlier. After creating an account in Epistemonikos, users will be able to save the matrices and to receive automated notifications any time new evidence potentially relevant for the question appears.

The details about the methods used to produce these summaries are described here <http://dx.doi.org/10.5867/medwave.2014.06.5997>.

Epistemonikos foundation is a non-for-profit organization aiming to bring information closer to health decision-makers with technology. Its main development is Epistemonikos database ([www.epistemonikos.org](http://www.epistemonikos.org)).

These summaries follow a rigorous process of internal peer review.

**Conflicts of interest**  
 The authors do not have relevant interests to declare.

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