International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

# Salbutamol and corticosteroid therapy in preschool children with acute wheezing: A systematic review

INPLASY2025100040
doi: 10.37766/inplasy2025.10.0040
Received: 12 October 2025
Published: 13 October 2025

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**ADMINISTRATIVE INFORMATION**

**Support -** Universiti Teknologi MARA.

**Review Stage at time of this submission -** Completed but not published.

**Conflicts of interest -** None declared.

**INPLASY registration number:** INPLASY2025100040

**Amendments -** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 October 2025 and was last updated on 13 October 2025.

## INTRODUCTION

**Review question / Objective** In preschool children (1–5 years) with acute wheeze and no asthma diagnosis (P), does adding corticosteroids (systemic or inhaled) to salbutamol (I) compared with salbutamol alone (C) improve clinical outcomes such as hospital admission, severity score, and length of stay (O)?

**Rationale** Wheezing in preschool children represents a diagnostic and therapeutic dilemma due to overlapping features with asthma and inconsistent treatment responses. Short-acting beta-agonists (SABA), particularly salbutamol, are standard first-line agents, but their efficacy varies with age and airway maturity. Corticosteroids, although central to asthma management, have shown inconsistent results in preschool wheeze—some studies report improved outcomes when added to salbutamol, while others show no benefit or even adverse effects such as cortisol suppression or prolonged hospitalization.

International guidelines (e.g., GINA, BTS/SIGN) differ in their recommendations, leading to variable clinical practices worldwide. Therefore, a systematic review is needed to synthesize current evidence comparing salbutamol alone versus salbutamol combined with corticosteroids in preschool children with acute wheezing. This synthesis will clarify treatment effectiveness, safety, and context-specific factors (phenotype, timing, delivery method, biomarkers), guiding evidence-based and standardized care.Wheezing is one of the most common respiratory symptoms in preschool children, affecting an estimated 30–40% before the age of six. It represents a heterogeneous condition encompassing multiple phenotypes such as episodic (viral) wheeze and multiple-trigger wheeze. The condition is typically precipitated by viral infections and may overlap with early features of asthma, but most preschoolers do not meet the full diagnostic criteria for asthma. This diagnostic ambiguity

creates uncertainty in management and variable clinical practices across healthcare settings.

Short-acting beta-agonists (SABA), primarily salbutamol, are considered first-line therapy for acute wheezing due to their bronchodilatory effects via smooth muscle relaxation. They are commonly administered through metered-dose inhalers (MDIs) with spacers or nebulizers. Although effective for many children, the response to salbutamol can vary depending on age and the maturity of beta-receptors, particularly in children under two years of age, where bronchodilator effects may be minimal.

Corticosteroids, either systemic (oral or intravenous) or inhaled, are widely used anti-inflammatory agents in asthma management. However, their role in preschool wheezing remains a matter of controversy. Some studies have shown clinical improvement and reduced hospital admissions when corticosteroids are added to salbutamol, while others report no additional benefit or adverse effects such as cortisol suppression and prolonged hospitalization. International guidelines, including GINA and BTS/SIGN, provide differing recommendations on corticosteroid use in preschool wheeze, reflecting the absence of standardized evidence-based consensus.

Given these inconsistencies, a systematic review is essential to synthesize existing evidence comparing salbutamol alone versus salbutamol combined with corticosteroids for acute preschool wheezing. This review aims to evaluate the effectiveness, safety, and optimal use of corticosteroids as adjunct therapy and to explore factors contributing to heterogeneous outcomes such as treatment timing, delivery method, phenotype variation, and biomarker responsiveness. The findings will help inform standardized clinical decision-making and guide future research directions in pediatric respiratory care.

**Condition being studied** Preschool wheezing (including episodic viral wheeze and multiple-trigger wheeze) , a common respiratory condition in children aged 1–5 years characterized by expiratory breathing difficulty and airway obstruction, often triggered by viral infections. Although some presentations resemble asthma, most preschool wheezers do not fulfill asthma diagnostic criteria. The condition's heterogeneity, variable natural history, and lack of definitive biomarkers make diagnosis and management challenging, especially in acute settings.

## METHODS

**Search strategy** A comprehensive search is conducted in PubMed, Web of Science, and Scopus for studies published from January 2009 to July 2025. The strategy combine MeSH and free-text terms related to preschool wheeze, salbutamol, corticosteroids, and clinical outcomes. The core string used is:

("viral-induced wheeze" OR "preschool wheeze") AND (salbutamol OR (salbutamol AND steroids)) AND (management OR treatment OR outcomes) AND (pediatric OR children OR preschool).
Searches will be limited to English-language, human studies in children aged 1–5 years. Duplicates will be removed and two reviewers will independently screen all titles, abstracts, and full texts. Reference lists of included studies will be manually checked to identify additional relevant articles.

No grey literature or clinical trial registry searches will be performed.

**Participant or population** Preschool children aged 1–5 years presenting with acute wheezing episodes in emergency or outpatient settings, without a formal diagnosis of asthma.
Children with recurrent viral-induced or multiple-trigger wheeze were eligible.
Those with confirmed asthma or other chronic cardiopulmonary diseases were excluded.

**Intervention** Salbutamol administered via nebulizer or metered-dose inhaler, in combination with corticosteroids, including:

Systemic steroids: prednisolone, methylprednisolone, dexamethasone, betamethasone
Inhaled steroids: budesonide, beclomethasone.

**Comparator** Salbutamol administered alone or with placebo, using the same or comparable delivery routes.

**Study designs to be included** This review will include randomized controlled trials (RCTs), crossover or quasi-experimental studies, prospective and retrospective cohort studies, case-control studies, and observational surveys or emergency department audits that evaluate the clinical outcomes of salbutamol alone or salbutamol combined with corticosteroids in preschool children with acute wheeze.

**Eligibility criteria** Inclusion Criteria:

Preschool children aged 1–5 years with acute wheezing not diagnosed as asthma.
Studies evaluating salbutamol alone or salbutamol combined with corticosteroids.
English-language publications from January 2009 to July 2025.
Original data published in peer-reviewed journals.
Exclusion Criteria:
Studies involving children with established asthma or other chronic respiratory diseases.
Review articles, editorials, conference abstracts, and non-English publications.

**Information sources** Electronic databases searched: PubMed, Web of Science, and Scopus.
Additional sources: Manual searches of reference lists from key papers.
Grey literature: Not included; no trial registry search performed.

Search strategy used Boolean operators:
("viral-induced wheeze" OR "preschool wheeze")
AND (salbutamol OR (salbutamol AND steroids))
AND (management OR treatment OR outcomes)
AND (pediatric OR children OR preschool).

**Main outcome(s)**
Primary outcomes:
Hospital admission rate
Clinical severity score improvement (e.g., PIS, CAS, ASS, WCSS)
Length of hospital stay (LOS)

Secondary outcomes:
Time to discharge from ED
Relapse or re-hospitalization within the same illness episode
Oxygen requirement and need for escalation of care
Adverse events (cortisol suppression, tachycardia, tremor, electrolyte imbalance)
Parental satisfaction and treatment adherence.

**Data management**
Duplicate records were removed prior to screening.
Screening proceeded in two phases: (1) title/abstract screening, then (2) full-text assessment against predefined eligibility criteria.
Two reviewers screened and extracted data; disagreements were resolved by discussion (and by a third reviewer if needed).
Extracted items included: study design, setting/country, sample/age, inclusion/exclusion, intervention details (salbutamol dosing/route/frequency; corticosteroid type/route/timing/duration), comparators, co-interventions (e.g., hypertonic saline), outcomes (admission, severity scores, LOS, relapse, AEs), and notes for synthesis.
The PRISMA flow documented counts at each stage (78 identified → 69 screened → 36 full texts → 13 included).

**Quality assessment / Risk of bias analysis** For the protocol, we will state: risk of bias will be appraised qualitatively, considering selection processes, exposure/intervention measurement, outcome ascertainment, confounding control, and completeness/clarity of reporting.
Assessment will be done independently by two reviewers with consensus resolution.

**Strategy of data synthesis** A narrative synthesis will summarize study characteristics and findings due to heterogeneity in designs, interventions (steroid types/routes/timing), delivery devices, and outcomes.
Results will be organized by primary outcomes (admission, severity scores, LOS).
No quantitative pooling/meta-analysis is planned based on the heterogeneity described.

**Subgroup analysis**
Exploratory, qualitative contrasts will consider:
Wheeze phenotype (episodic viral vs multiple-trigger),
Corticosteroid route/type (systemic vs inhaled; budesonide/beclomethasone; dexamethasone/betamethasone/prednisolone),
Timing of steroid initiation (early in ED vs later),
Delivery device for salbutamol (MDI + spacer vs nebulizer),
Biomarker signals (e.g., VOC, FeNO) where reported.

**Sensitivity analysis** Given the narrative approach and mixed designs, no formal quantitative sensitivity analyses are planned.
Robustness will be explored by highlighting studies with higher risk of bias or atypical methods and contrasting their findings with the broader set.

**Language restriction** English-language studies only.

**Country(ies) involved** Malaysia.

**Other relevant information**
Conducted in line with PRISMA 2020.
Time window: January 2009 – July 2025.
Databases: PubMed, Web of Science, Scopus.
PRISMA counts: 78 identified → 69 screened → 36 full texts → 13 included (with reasons for exclusion as you listed).

**Keywords** salbutamol, corticosteroids, preschool wheeze.

**Dissemination plans** Findings will be prepared for journal submission and conference presentation upon completion of the review.

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