The Open Public Health Journal
DOI: 10.2174/0118749445199126052005432 8, 2026, 19, e187494451991

ISSN: 1874-9445
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SUPPLEMENTARY MATERIAL **OPEN ACCESS**

Salbutamol and Corticosteroid Therapy in Preschool Wheeze: A Systematic Review

Nasibah Azme[1,2], Husna Musa[3] and Nurdiyana Nasrudin[4,*]

[1]*Department of Physiology, Faculty of Medicine, Universiti Teknologi MARA, Sg. Buloh, Selangor, Malaysia*
[2]*Department of Medical Education, Faculty of Medicine, Universiti Teknologi MARA, Sg. Buloh, Selangor, Malaysia*
[3]*Department of Paediatrics, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia, Serdang, Selangor, Malaysia*
[4]*Department of Paediatrics, Faculty of Medicine, Universiti Teknologi MARA, Sg. Buloh, Selangor, Malaysia*

*Address correspondence to this author at the Department of Paediatrics, Faculty of Medicine, Universiti Teknologi MARA, Sg. Buloh, Selangor, Malaysia; E-mail: nurdiyana1530@uitm.edu.my

Cite as: Azme N, Musa H, Nasrudin N. Salbutamol and Corticosteroid Therapy in Preschool Wheeze: A Systematic Review. Open Public Health J, 2026; 19: e187494451991. http://dx.doi.org/10.2174/0118749445199126052005432

Published: June 02, 2026

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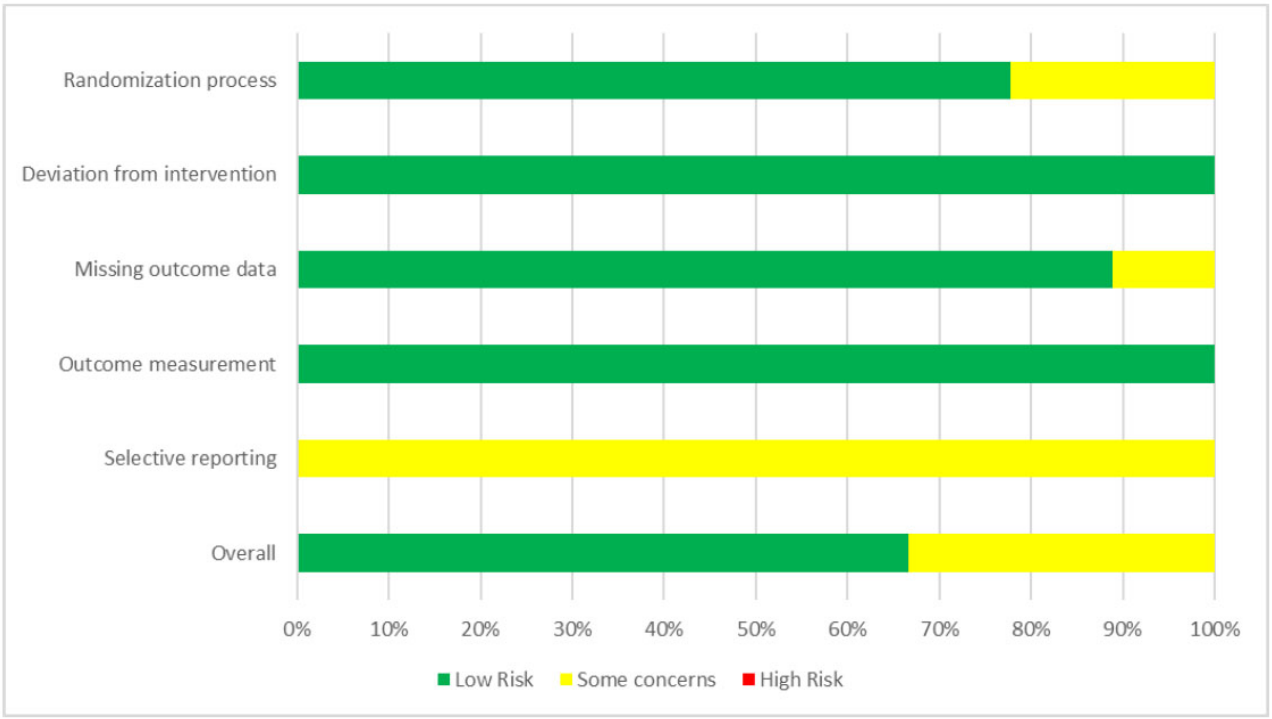

Fig. (S1). Risk of bias summary of included studies using the ROB2 tool.

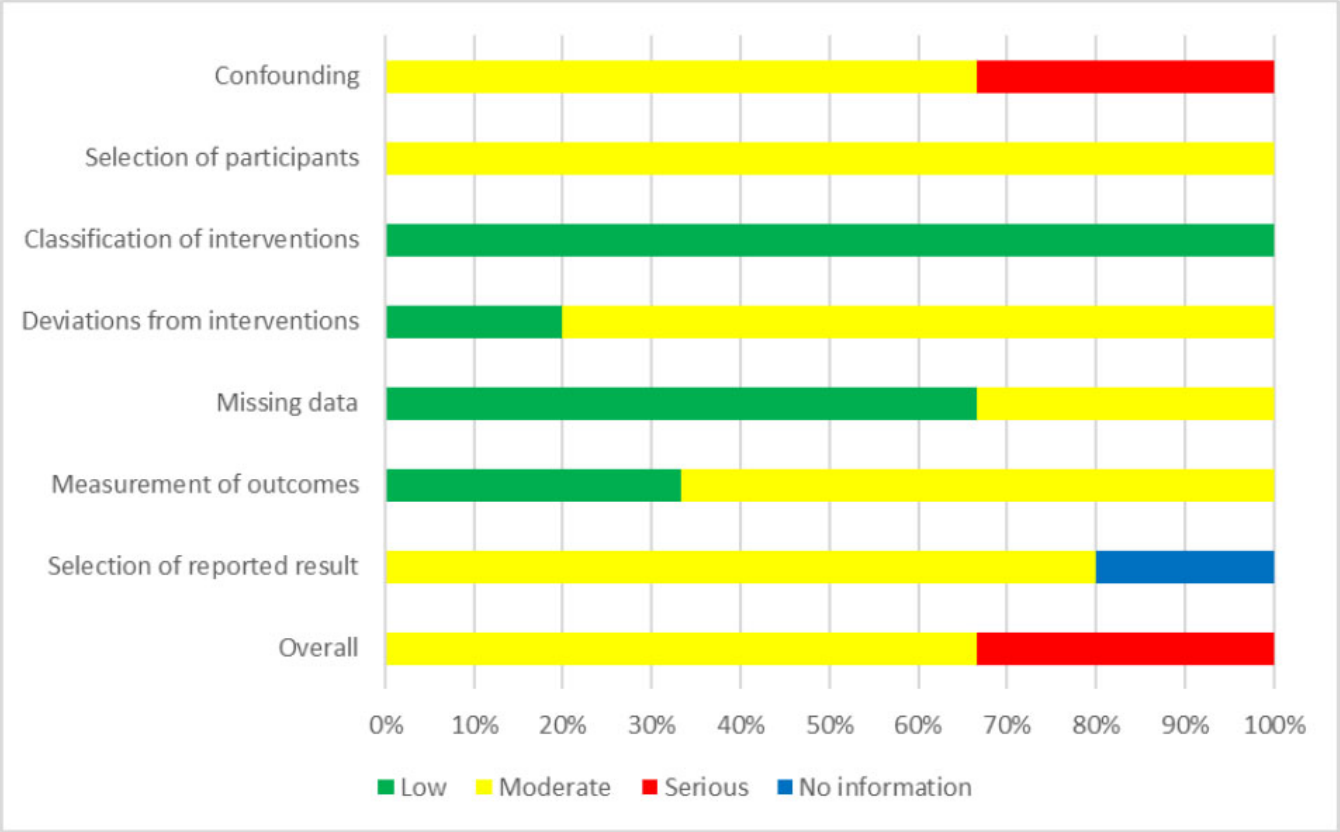

Fig. (S2). Risk of bias summary of included studies using the ROBINS-I tool.

Table S1. Modified McMaster critical review form for quantitative studies.

Author, Year, Country	Level of Evidence	Total Score	1	2	3	4	5	6	7	8	9	10	11
Ater *et al.*, 2012,Israel [19]	2b	9	1	1	1	0	1	1	1	1	1	0	1
Bannier *et al.*, 2022, Netherlands [6]	2b	8	1	1	1	0	0	1	1	1	1	0	1
Ciftci *et al.*, 2021, Turkey [20]	1b	11	1	1	1	1	1	1	1	1	1	1	1
Clavenna *et al.*, 2014, Italy [21]	1b	11	1	1	1	1	1	1	1	1	1	1	1
Csonka *et al.*, 2021, Finland [17]	3	8	1	1	1	0	0	0	1	1	1	1	1
Gileles-Hillel *et al.*, 2021, Israel [8]	2b	9	1	1	1	0	1	0	1	1	1	1	1
Levine *et al.*, 2019, Israel [22]	2b	8	1	1	1	0	0	0	1	1	1	1	1
Mallol *et al.*, 2009, Chile [23]	1b	10	1	1	1	0	1	1	1	1	1	1	1
Mecklin *et al.*, 2011, Finland [24]	3	9	1	1	1	0	1	1	1	0	1	1	1
Mecklin *et al.*, 2012, Finland [25]	3	10	1	1	1	0	1	1	1	1	1	1	1
Papi *et al.*, 2009, Italy [26]	1b	11	1	1	1	1	1	1	1	1	1	1	1
Papi *et al.*, 2011, Italy [27]	2b	9	1	1	1	0	1	1	1	1	1	0	1
Razi *et al.*, 2017, Turkey [7]	1b	10	1	1	1	0	1	1	1	1	1	1	1
Taha *et al.*, 2021, Egypt [28]	1b	9	1	1	1	0	1	1	1	1	1	1	0
van de Kant, 2011, Netherlands [4]	2b	9	1	1	1	0	0	1	1	1	1	1	1

Note: Level of evidence: 1b= Individual randomized controlled trial (with narrow confidence interval, low bias), 2b= Individual cohort study (low-quality RCT or good observational cohort), 3 = non-experimental, correlational, individual case-control or non-concurrent cohort study.
Critical appraisal scoring criteria: 1 = study purpose clearly stated; 2 = relevant literature reviewed; 3 = sample thoroughly described; 4 = sample size justified; 5 = reliable outcome measures; 6 = valid outcome measures; 7 = results presented with statistical significance; 8 = appropriate analysis methods; 9 = educational relevance discussed; 10 = dropouts reported; 11 = conclusions deemed appropriate.

Table S2. Inter-rater reliability between reviewers.

-	Reviewer 2: Relevant	Reviewer 2: Not Relevant	Total
Reviewer 1: Relevant	139	3	142
Reviewer 1: Not Relevant	7	16	23
Total	146	19	165

Note: • Observed Agreement (Po): 0.939 (93.9%).
• Expected Agreement (Pe): 0.778 (77.8%).
• Cohen's Kappa (κ): 0.728.

Table S3. ROB2 risk of bias assessment of included studies.

Study	Randomization	Deviation from Intervention	Missing Outcome Data	Outcome Measurement	Selective Reporting	Overall
Ater *et al.* 2012 [19]	Low Risk	Low Risk	Low Risk	Low Risk	Some concerns	Low Risk
Bannier *et al.* 2022 [6]	Low Risk	Low Risk	Some concerns	Low Risk	Some concerns	Some concerns
Ciftci *et al.* 2021 [20]	Some concerns	Low Risk	Low Risk	Low Risk	Some concerns	Some concerns
Clavenna *et al.* 2014 [21]	Low Risk	Low Risk	Low Risk	Low Risk	Some concerns	Low Risk
Mallol *et al.* 2009 [23]	Low Risk	Low Risk	Low Risk	Low Risk	Some concerns	Low Risk
Papi *et al.* 2009 [26]	Low Risk	Low Risk	Low Risk	Low Risk	Some concerns	Low Risk
Papi *et al.* 2021 [27]	Some concerns	Low Risk	Low Risk	Low Risk	Some concerns	Some concerns
Razi *et al.* 2017 [7]	Low Risk	Low Risk	Low Risk	Low Risk	Some concerns	Low Risk
Taha *et al.* 2021 [28]	Low Risk	Low Risk	Low Risk	Low Risk	Some concerns	Low Risk

Table S4. ROBINS-I risk of bias assessment of included studies.

Study	Bias due to Confounding	Bias due to Selection of Participants	Bias in Classification of Interventions	Bias due to Deviations from Intended Interventions	Bias due to Missing Data	Bias in Measurement of Outcomes	Bias in Selection of the Reported Result	Overall
Csonka *et al.* 2021 [17]	Moderate	Moderate	Low	Low	Low	Moderate	No information	Moderate
Gileles-Hillel *et al.* 2021 [8]	Moderate	Moderate	Low	Moderate	Low	Moderate	Moderate	Moderate
Levine *et al.* 2019 [22]	Moderate	Moderate	Low	Moderate	Low	Moderate	Moderate	Moderate
Mecklin *et al.* 2011 [24]	Serious	Moderate	Low	Moderate	Moderate	Low	Moderate	Serious
Mecklin *et al.* 2012 [25]	Serious	Moderate	Low	Moderate	Moderate	Low	Moderate	Serious
van de Kant 2011 [4]	Moderate	Moderate	Low	Moderate	Low	Moderate	Moderate	Moderate

PRISMA 2020 Checklist

Section and Topic	Item #	Checklist Item	Location where Item is Reported
TITLE			
Title	1	Identify the report as a systematic review.	Title
ABSTRACT			
Abstract	2	See the PRISMA 2020 for Abstracts checklist.	Abstract
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of existing knowledge.	Intro
Objectives	4	Provide an explicit statement of the objective(s) or question(s) the review addresses.	Intro
METHODS			
Eligibility criteria	5	Specify the inclusion and exclusion criteria for the review and how studies were grouped for the syntheses.	Page 4

Section and Topic	Item #	Checklist Item	Location where Item is Reported
Information sources	6	Specify all databases, registers, websites, organisations, reference lists and other sources searched or consulted to identify studies. Specify the date when each source was last searched or consulted.	Page 5
Search strategy	7	Present the full search strategies for all databases, registers and websites, including any filters and limits used.	Page 5
Selection process	8	Specify the methods used to decide whether a study met the inclusion criteria of the review, including how many reviewers screened each record and each report retrieved, whether they worked independently, and if applicable, details of automation tools used in the process.	Page 4-5
Data collection process	9	Specify the methods used to collect data from reports, including how many reviewers collected data from each report, whether they worked independently, any processes for obtaining or confirming data from study investigators, and if applicable, details of automation tools used in the process.	Page 4-5
Data items	10a	List and define all outcomes for which data were sought. Specify whether all results that were compatible with each outcome domain in each study were sought (e.g. for all measures, time points, analyses), and if not, the methods used to decide which results to collect.	Page 5
	10b	List and define all other variables for which data were sought (e.g. participant and intervention characteristics, funding sources). Describe any assumptions made about any missing or unclear information.	Page 4-5
Study risk of bias assessment	11	Specify the methods used to assess risk of bias in the included studies, including details of the tool(s) used, how many reviewers assessed each study and whether they worked independently, and if applicable, details of automation tools used in the process.	Page 5 Methodological quality was assessed using the Modified McMaster Critical Review Form for Quantitative Studies (Law et al., 1998); inter-rater agreement (Cohen's κ) indicated substantial reliability. Risk of bias was qualitatively evaluated based on McMaster domains, as the review included only human clinical studies.
Effect measures	12	Specify for each outcome the effect measure(s) (e.g. risk ratio, mean difference) used in the synthesis or presentation of results.	N/A
Synthesis methods	13a	Describe the processes used to decide which studies were eligible for each synthesis (e.g. tabulating the study intervention characteristics and comparing against the planned groups for each synthesis (item #5)).	Page 6-19
	13b	Describe any methods required to prepare the data for presentation or synthesis, such as handling of missing summary statistics, or data conversions.	Page 6-19
	13c	Describe any methods used to tabulate or visually display results of individual studies and syntheses.	Table **1**
	13d	Describe any methods used to synthesize results and provide a rationale for the choice(s). If meta-analysis was performed, describe the model(s), method(s) to identify the presence and extent of statistical heterogeneity, and software package(s) used.	N/A
	13e	Describe any methods used to explore possible causes of heterogeneity among study results (e.g. subgroup analysis, meta-regression).	N/A
	13f	Describe any sensitivity analyses conducted to assess robustness of the synthesized results.	N/A
Reporting bias assessment	14	Describe any methods used to assess risk of bias due to missing results in a synthesis (arising from reporting biases).	Methodological quality was assessed using the Modified McMaster Critical Review Form for Quantitative Studies (Law et al., 1998); inter-rater agreement (Cohen's κ) indicated substantial reliability. Risk of bias was qualitatively evaluated based on McMaster domains, as the review included only human clinical studies.
Certainty assessment	15	Describe any methods used to assess certainty (or confidence) in the body of evidence for an outcome.	Supplementary
RESULTS			
Study selection	16a	Describe the results of the search and selection process, from the number of records identified in the search to the number of studies included in the review, ideally using a flow diagram.	Page 8-9
	16b	Cite studies that might appear to meet the inclusion criteria, but which were excluded, and explain why they were excluded.	Page 8-9
Study characteristics	17	Cite each included study and present its characteristics.	Page 10-19, Table **1**

Section and Topic	Item #	Checklist Item	Location where Item is Reported
Risk of bias in studies	18	Present assessments of risk of bias for each included study.	
Results of individual studies	19	For all outcomes, present, for each study: (a) summary statistics for each group (where appropriate) and (b) an effect estimate and its precision (e.g. confidence/credible interval), ideally using structured tables or plots.	Table **1**
Results of syntheses	20a	For each synthesis, briefly summarise the characteristics and risk of bias among contributing studies.	Page 9
	20b	Present results of all statistical syntheses conducted. If meta-analysis was done, present for each the summary estimate and its precision (e.g. confidence/credible interval) and measures of statistical heterogeneity. If comparing groups, describe the direction of the effect.	N/A
	20c	Present results of all investigations of possible causes of heterogeneity among study results.	N/A
	20d	Present results of all sensitivity analyses conducted to assess the robustness of the synthesized results.	N/A
Reporting biases	21	Present assessments of risk of bias due to missing results (arising from reporting biases) for each synthesis assessed.	9
Certainty of evidence	22	Present assessments of certainty (or confidence) in the body of evidence for each outcome assessed.	Supplementary
DISCUSSION			
Discussion	23a	Provide a general interpretation of the results in the context of other evidence.	23-28
	23b	Discuss any limitations of the evidence included in the review.	Page 30
	23c	Discuss any limitations of the review processes used.	Page 30
	23d	Discuss implications of the results for practice, policy, and future research.	Page 29-31
OTHER INFORMATION			
Registration and protocol	24a	Provide registration information for the review, including register name and registration number, or state that the review was not registered.	Page 4
	24b	Indicate where the review protocol can be accessed, or state that a protocol was not prepared.	Page 4
	24c	Describe and explain any amendments to information provided at registration or in the protocol.	N/A
Support	25	Describe sources of financial or non-financial support for the review, and the role of the funders or sponsors in the review.	N/A
Competing interests	26	Declare any competing interests of review authors.	N/A
Availability of data, code and other materials	27	Report which of the following are publicly available and where they can be found: template data collection forms; data extracted from included studies; data used for all analyses; analytic code; any other materials used in the review.	Data Availability Statement: