International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Comprehensive evaluation of therapeutic effectiveness and safety profiles of baloxavir marboxil for managing influenza virus infection in pediatric populations: a systematic review with pooled meta-analytic data

INPLASY2025110063

doi: 10.37766/inplasy2025.11.0063

Received: 20 November 2025

Published: 20 November 2025

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ADMINISTRATIVE INFORMATION

Support - None.

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

Conflicts of interest - None declared.

INPLASY registration number: INPLASY2025110063

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 November 2025 and was last updated on 20 November 2025.

INTRODUCTION

Review question / Objective Influenza, clinically recognized as a highly contagious acute respiratory illness caused by orthomyxoviridae viruses, exhibits rapid transmission dynamics and pandemic potential, which poses a continuous threat to public health, with the pediatric population being particularly vulnerable. WHO virological surveillance indicates that annual global attack rates reach 5%-10% in adults and 20%-30% in pediatric populations, creating substantial strain on healthcare infrastructure. Influenza not only leads to significant direct medical burdens but also may trigger serious complications such as otitis media and pneumonia.

Currently,, neuraminidase inhibitors (NAIs) represent the standard treatment for pediatric influenza, including oseltamivir, peramivir, zanamivir, and laninamivir. Oseltamivir, the most commonly used oral NAI, is widely prescribed for the treatment and prevention of pediatric influenza but may cause gastrointestinal discomfort as an adverse effect. Peramivir and zanamivir, administered via intravenous injection and inhalation, respectively, are suitable for severe cases or patients unable to take oral medication. Laninamivir, which requires a single inhaled dose, is considered a convenient option for pediatric patients. However, while these conventional antiviral agents demonstrate certain efficacy, they also present several challenges. Oseltamivir requires a five-day, twice-daily dosing regimen, which imposes high adherence demands in children. The emergence of resistant viral strains has limited its clinical utility, while the drug is frequently associated with gastrointestinal adverse effects and demonstrates uncertain efficacy in severe cases. These limitations prompted the World Health Organization to downgrade oseltamivir from core to complementary medication in its 2017 guidelines, accelerating the exploration of safer and more effective influenza prevention and treatment strategies.

Against this backdrop, baloxavir marboxil warrants attention as an antiviral agent with an innovative

mechanism of action. It functions by inhibiting the polymerase acidic (PA) subunit of the influenza viral polymerase complex, thereby blocking viral replication. Distinguished from conventional antiviral drugs, it exhibits a distinct mechanism of action and demonstrates broad-spectrum activity against both influenza A and B viruses. Furthermore, its single oral dosing regimen presents potential advantages for pediatric treatment.
Although numerous studies have evaluated the efficacy and safety of baloxavir marboxil in adult influenza, research on its use in pediatric populations remains limited, with a lack of systematic comparisons to other antiviral agents. Therefore, this study employs a meta-analysis to systematically review published literature on the efficacy and safety of baloxavir marboxil in children with influenza. The study aims to objectively evaluate its clinical effectiveness and adverse reactions, thereby providing an evidence-based basis for optimizing pediatric antiviral treatment strategies.

Condition being studied Although numerous studies have evaluated the efficacy and safety of baloxavir marboxil in adult influenza, research on its use in pediatric populations remains limited, with a lack of systematic comparisons to other antiviral agents. Therefore, this study employs a meta-analysis to systematically review published literature on the efficacy and safety of baloxavir marboxil in children with influenza. The study aims to objectively evaluate its clinical effectiveness and adverse reactions, thereby providing an evidence-based basis for optimizing pediatric antiviral treatment strategies.By objectively assessing its clinical effectiveness and adverse effects, this study aims to provide scientific evidence to guide pediatric clinical practice.

METHODS

Participant or population Studies involving children under 18 years old with confirmed influenza.

Intervention RCTs or cohort studies investigating iIntervention with baloxavir marboxil, either alone or in combination with other antiviral agents. Control groups receiving neuraminidase inhibitors or placebo.

Comparator Studies reporting efficacy outcomes (e.g., fever resolution time, symptom improvement time) and safety outcomes (e.g., incidence of adverse events).

Study designs to be included RCTs or cohort studies investigating iIntervention with baloxavir marboxil, either alone or in combination with other antiviral agents.

Eligibility criteria nclusion criteria: (1) Studies involving children under 18 years old with confirmed influenza. (2) RCTs or cohort studies investigating iIntervention with baloxavir marboxil, either alone or in combination with other antiviral agents. (3) Control groups receiving neuraminidase inhibitors or placebo. (4) Studies reporting efficacy outcomes (e.g., fever resolution time, symptom improvement time) and safety outcomes (e.g., incidence of adverse events).
Exclusion criteria: (1) Non-original studies (e.g., reviews, case reports), qualitative studies, review articles, non-interventional studies, studies available only as abstracts, etc. (2) Studies that did not clearly distinguish pediatric populations. (3) Studies lacking complete data or data that could not be extracted for analysis.

Information sources Studies reporting efficacy outcomes (e.g., fever resolution time, symptom improvement time) and safety outcomes (e.g., incidence of adverse events).

Main outcome(s) Studies reporting efficacy outcomes (e.g., fever resolution time, symptom improvement time) and safety outcomes (e.g., incidence of adverse events).

Quality assessment / Risk of bias analysis The methodological rigor of included studies underwent systematic appraisal through dual evaluation mechanisms. Randomized controlled trials were scrutinized using the Cochrane Collaboration's Bias Evaluation Framework, with particular emphasis on allocation concealment protocols, blinding implementation status, and attrition rate analysis. For non-randomized observational investigations, the Newcastle-Ottawa Quality Appraisal Instrument was applied to quantify selection bias probability, inter-group comparability metrics, and outcome verification reliability.

Strategy of data synthesis A standardized data extraction form was developed using Office Excel 2019, and Ttwo investigators conducted parallel data retrieval and collation processes utilizing a standardized collection template. This protocol captured essential parameters such as authorship details, trial design specifications, cohort demographics, therapeutic interventions, comparator groups, and key endpoints related to clinical effectiveness and adverse events.

Discrepancies in interpretation were resolved through iterative cross-verification procedures involving a senior research coordinator, ensuring consensus through structured arbitration sessions.

Subgroup analysis Subgroup analyses stratified by viral subtypes revealed divergent outcomes. Subsequent stratified examination revealed distinct therapeutic patterns across viral subtypes.

Sensitivity analysis Interstudy variability was rigorously evaluated through dual statistical metrics: Cochran's Q-test for quantifying heterogeneity magnitude, supplemented by I^2 index measurement to assess inconsistency proportions. The analytical framework adopted a stratified approach based on heterogeneity thresholds - Mantel-Haenszel fixed-effect models were employed when homogeneity criteria were satisfied (Q-test P-value ≥0.1 concurrent with I^2 ≤50%), whereas DerSimonian-Laird random-effects models were preferentially utilized under significant heterogeneity conditions (P50%). This model selection protocol effectively balanced type I error control with between-study variance incorporation.

Country(ies) involved China - Department of Pediatrics and Pediatric Endocrinology, Xianju People's Hospital.

Keywords Baloxavir marboxil; Influenza; Safety; Efficacy; Meta-analysis.

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