

Effectiveness of Influenza Vaccination against Influenza-related Hospitalizations among Children: A Systematic Review

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ABSTRACT

Objectives: To assess the effectiveness of influenza vaccination in reducing the risk of influenza-related hospitalizations in the pediatric population.

Methods: A thorough search across four databases identified 412 relevant publications. After removing duplicates using Rayyan QCRI and screening for relevance, 196 full-text articles were reviewed, with 8 studies ultimately meeting the criteria for inclusion.

Results: We included eight studies with a total of 3,648,778 children. Most studies reported using live attenuated influenza vaccines (LAIV) and inactivated vaccines for the included children. The studies consistently show that influenza vaccination significantly reduces the risk of severe outcomes, including hospitalizations and emergency visits, especially among children and young populations. Even in seasons with strain mismatches or antigenic drift, the vaccine maintained approximately 40% effectiveness in preventing hospitalization. Vaccination provided notable protection for children under five, a group particularly vulnerable to severe complications. Both inactivated and LAIV demonstrated effectiveness in lowering hospitalization rates across different seasons, underscoring the importance of annual influenza immunization.

Conclusion: In conclusion, influenza vaccination is effective in reducing influenza-related hospitalizations, particularly among young children who are at heightened risk for severe disease. Even in seasons with antigenic variation, the vaccine demonstrated protective benefits, reinforcing its value in public health strategies aimed at reducing the burden of influenza. These findings advocate for increased vaccine coverage, particularly in vulnerable populations, to mitigate hospitalizations and support healthcare systems during influenza outbreaks.

Keywords: Influenza vaccination; Hospitalization prevention; Vaccination effectiveness; Children; Systematic review.

INTRODUCTION

Influenza infection continues to be a significant health concern for both adults and children. The World Health Organization estimates that there are 1 billion cases, 3 to 5 million of which are severe, and that each year, influenza causes between 290,000 and 650,000 respiratory fatalities [1]. Children are frequently at higher risk of contracting influenza than other age groups [2], and they are also responsible for the introduction and spread of influenza virus in homes and communities [3]. Notably, children under the age of five, and especially those under the age of two, are at a heightened risk of experiencing severe influenza-related complications, such as hospitalization and death [4]. According to CDC estimates, hospitalizations for flu-related illnesses

among children under five years old have ranged between 7000 to 26,000 during 2010 [5].

The best defense against seasonal and pandemic influenza at the moment is influenza vaccine. The World Health Organization (WHO) has advised vaccination for patients with chronic illnesses, older adults, pregnant women, children aged 6 to 59 months, and healthcare professionals since 2012 [6]. A universal vaccination guideline in the United States (US) covers the entire population starting at age six months, although other nations, like Finland, the United Kingdom (UK), and Canada, have included the pediatric population in their regular immunization programs [7, 8]. However, healthy children

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are not targeted by vaccination regimes in the majority of nations, including Spain [9].

Influenza remains a major public health concern globally, responsible for significant morbidity, mortality, and economic burden due to hospitalizations and healthcare expenses. Despite the seasonal availability of vaccines, influenza poses a persistent threat, particularly to vulnerable groups such as older adults, young children, and individuals with comorbidities. Vaccination has long been considered one of the most effective preventive measures against influenza infection, primarily reducing the severity and complications of the disease. However, the degree of protection influenza vaccines offer against severe outcomes, such as hospitalization, remains a topic of interest and debate.

This systematic review seeks to evaluate the effectiveness of influenza vaccination specifically in preventing influenza-related hospitalizations. By synthesizing existing studies, we aim to provide a comprehensive assessment of the vaccine's impact on hospitalization rates, contributing valuable insights to guide public health policies, vaccine recommendations, and targeted interventions. Understanding the vaccine's protective efficacy against severe outcomes is crucial for informed decision-making, especially in allocating resources to high-risk populations and improving vaccination uptake.

The primary objective of this systematic review is to assess the effectiveness of influenza vaccination in reducing the risk of influenza-related hospitalizations.

METHODS

In order to conduct a systematic review examining the efficacy of influenza vaccine in lowering the risk of hospitalizations associated to influenza, this study complied with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) [10]. To find pertinent English-language studies that investigate the efficacy of influenza vaccine in lowering the risk of influenza-related hospitalizations, a comprehensive electronic search was conducted across a number of databases, including PubMed, Web of Science, SCOPUS, and Science Direct. The search results were examined by two separate reviewers, who then chose studies that met the eligibility requirements, retrieved pertinent data, and used recognized evaluation instruments to rate the included research' quality.

Eligibility Criteria

Eligible studies must be published in English, focus on children who received influenza vaccination, and provide data regarding the effectiveness of influenza vaccination in reducing the risk of influenza-related hospitalizations. Both observational and interventional studies were considered, including cohort studies, case-control studies, and randomized controlled trials. Studies published within the last five years (2019-2024) were included. Excluded studies were encompassed those not involving human subjects, articles that lack relevant data. Additionally, reviews, commentaries, and conference abstracts were omitted to ensure the inclusion of high-quality, empirical research that contributes valuable insights to the topic.

Data Extraction

To ensure the reliability of the findings, the search results were verified using Rayyan (QCRI) [11]. The titles and abstracts obtained from the search were evaluated for relevance according to the predetermined inclusion and exclusion criteria. Studies that fulfilled the inclusion

criteria underwent a comprehensive review by the research team. Any discrepancies among reviewers were resolved through a consensus approach. Key information from each study, including titles, authors, publication year, study location, participant demographics, gender distribution, vaccination type, and main outcomes, were systematically documented using a structured data extraction form. Additionally, an independent evaluation tool was developed to assess the risk of bias in the selected studies.

Data Synthesis Strategy

Utilising information taken from pertinent studies, summary tables were created to offer a qualitative assessment of the research findings and elements. The best strategy for making use of the data from the included studies were decided upon after the data collection for the systematic review is finished.

Quality review

The Newcastle-Ottawa scale was employed to evaluate each qualifying study's risk of bias. Two reviewers individually evaluated each study. Evaluation disagreements were handled through consensus or consulting with a third reviewer. No research studies have been rejected due to the risk of bias [12].

RESULTS

The specified search strategy yielded 412 publications (**Figure 1**). After removing duplicates (n =216), 196 trials were evaluated based on title and abstract. Of these, 131 failed to satisfy eligibility criteria, leaving just 65 full-text articles for comprehensive review. A total of 8 satisfied the requirements for eligibility with evidence synthesis for analysis, all of them were case-controls [13-20].

Sociodemographic and clinical outcomes

We included eight studies with a total of 3,648,778 children. Most studies reported using LAIV and inactivated vaccines for the included children. In high-severity seasons, the vaccine was found to reduce the risk of hospitalization and emergency visits, even when there was concern about mismatches between vaccine strains and circulating viruses [13]. Additionally, even during seasons with antigenically drifted strains like clade 3C, influenza vaccines showed approximately 40% effectiveness against hospitalization and emergency visits, highlighting their role in mitigating severe outcomes despite antigenic variability [14].

Influenza vaccination significantly reduced the risk of hospitalization among young children, particularly those under five years, who are considered highly susceptible to severe influenza-related complications [15]. The vaccine's effectiveness was especially notable during peak influenza seasons, where a considerable number of hospitalizations and emergency visits could be prevented through immunization [16, 17].

Furthermore, LAIV provided substantial protection against laboratory-confirmed influenza hospitalizations in young children, further supporting their role in protecting vulnerable populations [18]. Other studies demonstrated the vaccine's efficacy in preventing laboratory-confirmed influenza-related hospitalizations and emergency visits due to both major influenza virus subtypes circulating in specific seasons [19]. Yearly vaccination with LAIV in eligible children offered strong protection against hospitalization, reinforcing the importance of annual vaccination campaigns to safeguard against severe influenza outcomes [20].

Table 1. Outcome measures of the included studies

Study ID	Country	Study design	Sociodemographic	Population type	Vaccination type	Main outcomes	NOS
Kim et al., 2022 [13]	USA	Case-control	Participants: 7664 Age range: 6 months – 17 years Males: 4252 (55%)	Children	NS	Vaccination provided significant protection against severe influenza outcomes that required hospitalization or ED visits among children during high-severity seasons where vaccine mismatch was a concern.	7
Campbell et al., 2020 [14]	USA	Case-control	Participants: 1792 Age range: 6 months – 17 years Males: 998 (56%)	Children	Inactivated influenza vaccine & LAIV	Even during a season when antigenically drifted clade 3C was prevalent, the vaccine was around 40% effective against hospitalizations and emergency department visits associated to A(H3N2). The most common A(H3N2) influenza viruses in circulation were 3a influenza viruses.	7
Wang et al., 2019 [15]	Taiwan	Case-control	Participants: 1514 Age range: 6-12 months Males: 780 (51.5%)	Children <5 years	inactivated influenza vaccine	Taiwanese children under five years old who receive the seasonal influenza vaccination are less likely to be hospitalized due to influenza.	7
Pendrey et al., 2024 [16]	USA	Case-control	Participants: 3,631,840 Age range: 0.5-14	Children	NS	It is possible to determine how many hospitalizations and emergency department visits linked to influenza could be prevented by immunization. Hospital use and costs are significantly decreased by influenza vaccination, even during the height of the flu season.	6
Yildirim et al., 2021 [17]	USA	Case-control	Participants: 1024 Age range: 0-9 Males: 527 (51.5%)	Young children	Inactivated influenza vaccine & LAIV	Childhood hospitalization, including possible intensive care unit admission and pneumonia, is significantly reduced by influenza immunization. Children who had partial vaccinations also showed benefits.	7
Boddington et al., 2022 [18]	UK	Case-control	Participants: 227 Age range: 2-7 Males: 135 (59.5%)	Young children	LAIV	LAIV immunization offered good protection against hospitalization due to laboratory-confirmed influenza illness.	6
Campbell et al., 2021 [19]	USA	Case-control	Participants: 2029 Age range: 0-17 Males: 1149 (57%)	Children	NS	Substantial protection against laboratory-confirmed influenza- related hospitalizations and emergency department visits linked to the two main influenza viruses affecting children, including the newly developing B/Victoria virus subclade, was offered by influenza vaccine.	6
Pebody et al., 2020 [20]	UK	Case-control	Participants: 2685 Age range: 2-17 Males: 1106 (41.1%)	Children	LAIV	This study shows that yearly influenza vaccinations offer significant protection against hospitalization for children who qualify.	7

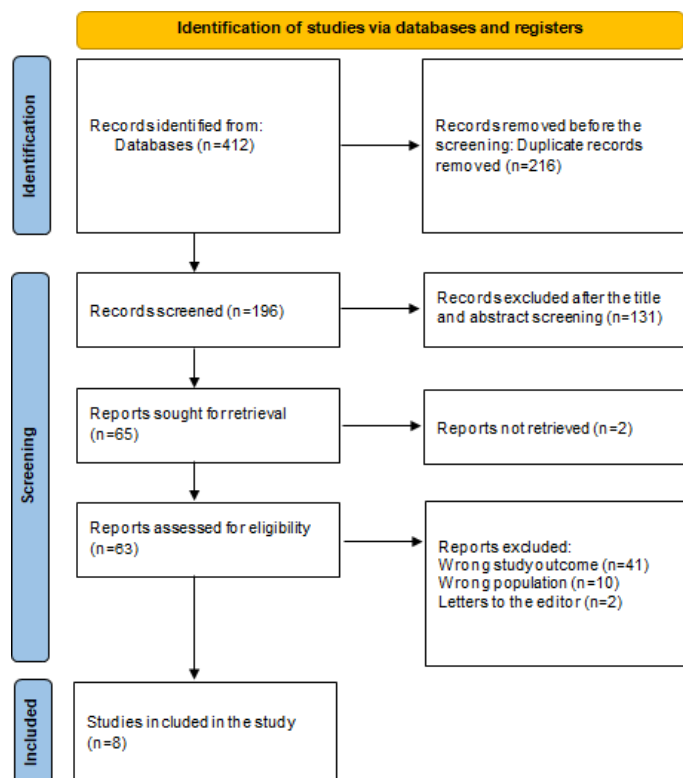


Figure 1. PRISMA flowchart.

DISCUSSION

The findings from this systematic review highlight the robust effectiveness of influenza vaccination in reducing influenza-related hospitalizations, particularly among children and young populations. These studies collectively emphasize that vaccination, including both inactivated and live attenuated formulations, plays a significant role in mitigating severe influenza outcomes, even in seasons where antigenic drift or strain mismatches occur. Despite moderate variations in effectiveness across studies, the consistent reduction in hospitalization rates points to the vaccine's protective impact. This is especially crucial for children under five, who are at increased risk of severe influenza complications. The observed effectiveness in this population suggests that broadening vaccine coverage in vulnerable groups can yield substantial public health benefits by decreasing the strain on healthcare systems during peak influenza seasons.

Orrico-Sánchez *et al.* reported that in accordance with the recommendations of international organizations, this research indicates that pediatric immunization is generally an effective approach for preventing influenza in healthy children [21]. **Kalligeros *et al.*** also found that complete yearly immunization should be promoted since it provided a considerable defense against hospitalization due to influenza in the pediatric population [22].

After examining the observational studies, the results are largely encouraging and seem to support the efficacy of the influenza vaccine in children in good health. They should be regarded cautiously, though, as there is a considerable chance of bias given the nature of the investigations. The results of this and other research may be impacted by the wide variations in observational study design and methods, the limited number of participants, and seasonal variations in the predominant influenza viruses. Furthermore, research has not taken into account the potential mismatch between vaccine and circulating

viruses, which could account for the large confidence intervals in vaccine effectiveness statistics. Therefore, when using observational research to make conclusions, caution must be used.

Immunization against childhood influenza should be a successful strategy to lower the disease's overall burden and, in particular, its grave implications (hospitalization and sequelae) in children. Furthermore, childhood influenza vaccination stops influenza from spreading to older individuals who are less susceptible to immunization and to those who are more susceptible [23]. Nearly half of influenza infections in children are asymptomatic or have very weak symptoms [24], making schoolchildren efficient and significant influenza spreaders [2]. Furthermore, children have larger viral loads and transmit the virus for longer periods of time, which makes it easier for infections to spread indiscriminately since they are more likely to come into close contact with other family members [2], who may then distribute the virus at work.

The clinical implications of these findings are substantial. Influenza vaccination should be prioritized as a core preventive measure in pediatric and high-risk populations to reduce hospitalization and associated healthcare costs. Healthcare providers should advocate for annual vaccination, emphasizing its role in preventing severe outcomes rather than solely aiming to avoid mild or moderate influenza symptoms. The findings also support targeted vaccination strategies during high-severity seasons or when viral strains are known to have antigenic drift. Additionally, partial immunization appears beneficial, suggesting that even children who have not completed the full vaccine series can gain some level of protection. This reinforces the importance of initiating immunization as early as possible in the flu season.

STRENGTHS AND LIMITATIONS

This systematic review draws from a range of studies across different seasons and geographical regions, providing a comprehensive evaluation of the vaccine's effectiveness against influenza-related hospitalizations. The inclusion of diverse age groups, particularly children, allows for insights into the vaccine's impact on vulnerable populations. Moreover, by examining real-world outcomes, this review contributes to an evidence base that supports influenza vaccination as a means to reduce the severity of illness and healthcare utilization.

Several limitations should be acknowledged. The variability in study designs, population demographics, and diagnostic criteria may introduce heterogeneity, potentially affecting the comparability of results across studies. Additionally, some studies were conducted in seasons with specific strains or in the context of antigenic drift, which may not fully reflect the vaccine's performance in seasons with different circulating strains. Furthermore, the reliance on case-control study designs may introduce biases, such as recall bias in vaccination reporting or potential confounders not accounted for in some analyses. Lastly, while partial immunization showed benefits, the degree of protection may vary, warranting caution when interpreting results for children with incomplete vaccination.

CONCLUSION

In conclusion, influenza vaccination is effective in reducing influenza-related hospitalizations, particularly among young children who are at heightened risk for severe disease. Even in seasons with antigenic variation, the vaccine demonstrated protective benefits, reinforcing its value in public health strategies aimed at reducing the burden of influenza. These findings advocate for increased vaccine coverage, particularly in vulnerable

populations, to mitigate hospitalizations and support healthcare systems during influenza outbreaks. The results underscore the critical role of annual vaccination in preventing severe influenza outcomes and highlight the need for ongoing surveillance to monitor vaccine effectiveness as viral strains evolve.

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