

Averting the Unthinkable: Immunization to Prevent Childhood Deaths From Influenza

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In this issue of *Pediatrics*, Leonard et al¹ analyze the effectiveness of vaccination in reducing the risk of pediatric influenza-associated death over 8 seasons. Influenza causes severe illness and death in children yearly, yet influenza vaccination rates remain low. Representing the first report of its kind in nearly a decade,² this vaccine effectiveness (VE) analysis is timely and critical for conversations with families about the importance of annual influenza vaccination for all eligible children.

Influenza causes a wide range of pediatric illnesses, including upper and lower respiratory tract pathology and the potential for serious viral-induced complications (including myocarditis, hepatitis, and encephalitis) and bacterial co-infections.^{3,4} These complications occur more frequently in young children and those with certain health conditions, such as chronic lung disease (including asthma), neurologic disorders, immunocompromising conditions, and obesity.⁵ Vaccination protects children, including those with or without underlying medical conditions, against serious complications from influenza.⁶

Influenza vaccines are developed annually to target predicted circulating strains for the upcoming season.⁵ Influenza vaccination is recommended by the American Academy of Pediatrics (AAP) for all children 6 months and older who do not have a medical contraindication to vaccination.⁷ While there is generally high uptake of routine childhood vaccines, pediatric influenza vaccination rates remain comparatively and strikingly low, and have been decreasing since 2021.⁸ In the 2024 to 2025 respiratory season, only approximately half of children between the ages of 6 months and 17 years received at least 1 influenza vaccine.⁹ Medical contraindications to influenza vaccination are uncommon, and influenza vaccines are widely available and covered by both public and private insurers, including the Vaccines For Children program. An incomplete update of pediatric influenza vaccines likely represents parental hesitancy, lack of strong physician recommendation, or a combination of these factors. A recent study examining parental vaccine perspectives found that while 6% of US parents exhibited hesitancy regarding routine childhood vaccines, over 25% were hesitant about influenza vaccination for their children. Further, only 25% believed seasonal influenza vaccines are effective.¹⁰

Why might parents lack confidence in the influenza vaccine? Media reports frequently focus on VE in preventing outpatient laboratory-confirmed influenza. Recently estimated to be 46% in a test-negative design study using data pooled over 9 seasons, this number may fall short of parental expectations.¹¹ VE estimates are similar for preventing influenza-associated emergency department visits and hospitalizations (53%), with lower VE in high-risk groups (43%).⁶ While many pediatricians consider reducing the risk of medically attended influenza by approximately half as reason enough alone to vaccinate, this success may be overshadowed in the minds of parents who encounter misinformation about vaccine safety and may underestimate the potential severity of influenza in children.

Leonard et al have provided us with an updated VE mortality analysis from 2016 to 2025, excluding the 2020 to 2021 season (with only one documented

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Drs Hahn and Sardi drafted the initial manuscript and critically reviewed and revised the final manuscript. Dr Ratner co-wrote, critically reviewed, and revised the manuscript for important intellectual content. All authors approved the final manuscript as submitted and agreed to be accountable for all aspects of the work.

CONFLICT OF INTEREST DISCLOSURES: The authors have no conflicts to disclose.

FUNDING: No funding was secured for this study.

Accepted for Publication Date: April 30, 2026

<https://doi.org/10.1542/peds.2026-076867>

COMPANION PAPER: A companion to this article can be found online at www.pediatrics.org/cgi/doi/10.1542/peds.2026-076453.

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To cite: Hahn C, Sardi A, and Ratner AJ. Averting the Unthinkable: Immunization to Prevent Childhood Deaths From Influenza. *Pediatrics*. 2026; 158(2):e2026076867

influenza-associated pediatric death in the setting of unprecedented infection control measures during the COVID-19 pandemic). Using a case-cohort study design, the vaccine status of influenza-associated deaths was compared to that of children in national survey data, controlling for age, state of residence, time of year, and high-risk conditions. Their results are impressive—finding VE for prevention of influenza-associated death for their overall population and across seasons to be 80% (95% CI, 75%–84%). They also report VE separately for children with high-risk conditions (77% [95% CI, 71%–82%]) and those without (87% [95% CI, 84%–89%]). Unsurprisingly, they detected variability in VE across influenza seasons. The highest VE was in the season with the highest mortality (2024–2025), in which VE was a striking 95% (95% CI, 93%–96%) for non-high-risk children and 84% (95% CI, 81%–87%) for those with high-risk conditions. VE was also higher in younger children (6 months to 4 years) with high-risk conditions (83% [95% CI, 78%–88%]) and those without (89% [95% CI, 86%–91%]). The authors performed a sensitivity analysis to account for possible overestimation of vaccine coverage in survey responses, demonstrating persistent high vaccine protection even if coverage estimates were decreased by 10 or 20 percentage points, leading to VE estimates of 75% (95% CI, 70%–79%) and 68% (95% CI, 63%–73%), respectively.

The authors highlight that the number of children who died from influenza in the 2024 to 2025 respiratory season was 289, the highest since universal reporting was initiated in 2004. Of these, 89% of vaccine-eligible children were unvaccinated or incompletely vaccinated. Crucially, children *without* high-risk health conditions constituted over half of influenza-associated pediatric deaths. Thus, while children with underlying medical conditions are certainly at increased individual risk for influenza-related complications, including death, they are by no means the only children who are dying from influenza. The majority of pediatric influenza deaths occur in children with no high-risk conditions.

This study demonstrates the necessity of ongoing public health surveillance to understand influenza mortality in children. Mortality data were obtained through the US Influenza-Associated Pediatric Mortality Surveillance System—a national reporting system maintained by the Centers for Disease Control and Prevention (CDC). Within this system, influenza-associated pediatric death is defined as death in a child under 18 years from an influenza-compatible illness with laboratory-confirmed influenza and no well period between illness and death.¹² Case reports by state and local health departments include demographic information, vaccine status, clinical course, and location of death. Underreporting represents a significant potential limitation of this system, as only cases of laboratory-confirmed influenza are included. Still, ongoing funding and

support for these robust local and national surveillance efforts are essential to recognize dynamic patterns of severe disease and inform vaccine practices.

Regarding vaccine surveillance, vaccine coverage was estimated on a statewide level utilizing 2 additional CDC-supported programs—the National Immunization Survey-Flu and the National Health Interview Survey. While these surveys capture important geographical vaccine coverage data, they do not account for variations in local epidemiology at the county or city level. There can be striking differences in vaccine uptake and disease risk for locations in close proximity, as observed with other vaccine-preventable diseases such as measles.¹³ Such differences can be due to differences in vaccine hesitancy or discrepancies in health care access, leading to vulnerable pockets prone to outbreaks in areas that may have otherwise high vaccine coverage. Future studies may include more granular geographic cohorts to compare the vaccine status of case patients. The need for such data spotlights the importance of continued support of vaccine registries that provide coverage data at county, city, and zip code levels to make this type of analysis possible.

Regular seasonal vaccination remains safe and the most effective way to prevent serious illness and death from influenza in children. Increased vaccine uptake is necessary to decrease pediatric influenza mortality. Leonard et al provide crucial data to share with families when counseling on the significant reduction in risk of influenza-associated mortality offered by the influenza vaccine, especially in children without known risk factors for severe influenza who represent the majority of deaths. As pediatricians, we need to shift parental expectations of the influenza vaccine from preventing all cases of influenza infection to protecting against severe disease and the tragedy of influenza-associated child mortality. The maintenance of public health infrastructure, including active surveillance and vaccine registries, is essential for accurate analysis of VE and determining where vaccine advocacy efforts are needed.

ABBREVIATIONS

AAP: American Academy of Pediatrics
 CDC: Centers for Disease Control and Prevention
 VE: vaccine effectiveness

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