



Published in final edited form as:

Clin Infect Dis. 2025 October 06; 81(3): 667–678. doi:10.1093/cid/ciae597.

Influenza vaccine effectiveness against hospitalizations and emergency department or urgent care encounters for children, adolescents, and adults during the 2023–2024 season, United States

Mark W. Tenforde, MD, PhD¹, Emily L. Reeves, MPH¹, Zachary A. Weber, PhD², Sara Y. Tartof, PhD, MPH³, Nicola P. Klein, MD, PhD⁴, Kristin Dascomb, MD, PhD⁵, Malini B. DeSilva, MD, MPH⁶, Duck-Hye Yang, PhD², Shaun J. Grannis, MD, MS^{7,8}, Stephanie A. Irving, MHS⁹, Toan C. Ong, PhD¹⁰, Ruth Link-Gelles, PhD, MPH^{1,11}, S. Bianca Salas, MPH³, Lina S. Sy, MPH³, Bruno Lewin, MD³, Richard Contreras, MS³, Ousseny Zerbo, PhD⁴, Bruce Fireman⁴, John Hansen, MPH⁴, Julius Timbol, MS⁴, Tamara Sheffield, MD⁵, Daniel Bride, MS⁵, Julie Arndorfer, MPH⁵, Josh VanOtterloo, MSPH⁵, Charlene E. McEvoy, MD, MPH⁶, Omobosola O. Akinsete, MBBS, MPH⁶, Inih J. Essien, OD, MPH⁶, Brian E. Dixon, PhD, MPA^{7,12}, Colin Rogerson, MD, MPH^{7,8}, William F. Fadel, PhD^{7,12}, Thomas Duszynski, PhD¹², Allison L. Naleway, PhD⁹, Michelle A. Barron, MD¹³, Suchitra Rao, MBBS, MSCS¹⁴, David Mayer, BS¹⁰, Catia Chavez, MS¹⁰, Sarah W. Ball, ScD, MPH², Amanda B. Payne, PhD, MPH¹, Caitlin Ray, MPH¹, Monica Dickerson, BS¹, Varsha Neelam, MPH¹, Katherine Adams, MPH¹, Brendan Flannery, PhD¹, Jennifer DeCuir, MD, PhD^{1,11}, Shikha Garg, MD, MPH^{1,11}

¹National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia, United States

²Westat, Rockville, Maryland, United States

³Department of Research & Evaluation, Kaiser Permanente Southern California, Pasadena, California, United States

⁴Kaiser Permanente Vaccine Study Center, Kaiser Permanente Northern California Division of Research, Oakland, California, United States

⁵Division of Infectious Diseases and Clinical Epidemiology, Intermountain Health, Salt Lake City, Utah, United States

⁶HealthPartners Institute, Minneapolis, Minnesota, United States

⁷Center for Biomedical Informatics, Regenstrief Institute, Indianapolis, Indiana, United States

⁸School of Medicine, Indiana University, Indianapolis, Indiana, United States

Corresponding Author: Mark W Tenforde, MD, PhD, MPH, DTM&H, 1600 Clifton Road, Atlanta, GA 30329-4027, United States, pij6@cdc.gov. Alternative Corresponding Author: Shikha Garg, MD, MPH, 1600 Clifton Road, Atlanta, GA 30329-4027, United States, izj7@cdc.gov.

Disclaimer. The findings and conclusions of this report are those of the authors and do not necessarily reflect the official position of the Centers for Disease Control and Prevention. Preliminary vaccine effectiveness estimates were presented at a CDC Advisory Committee on Immunization Practices meeting on February 29, 2024 and published in CDC's Morbidity and Mortality Weekly Report.

⁹Kaiser Permanente Center for Health Research, Portland, Oregon, United States

¹⁰Department of Biomedical Informatics, University of Colorado Anschutz Medical Campus, Aurora, Colorado, United States

¹¹United States Public Health Service Commissioned Corps, Rockville, Maryland, United States

¹²Fairbanks School of Public Health, Indiana University, Indianapolis, Indiana, United States

¹³Department of Medicine, University of Colorado Anschutz Medical Campus, Aurora, Colorado, United States

¹⁴Department of Pediatrics, University of Colorado Anschutz Medical Campus, Aurora, Colorado, United States

Abstract

Background: The 2023–2024 influenza season had predominant influenza A(H1N1)pdm09 virus activity, but A(H3N2) and B viruses co-circulated. Seasonal influenza vaccine strains were well-matched to these viruses.

Methods: Using health care encounters data from health systems in 8 states, we evaluated influenza vaccine effectiveness (VE) against influenza-associated medical encounters from October 2023–April 2024. Using a test-negative design, we compared the odds of vaccination between patients with an acute respiratory illness (ARI) who tested positive (cases) versus negative (controls) for influenza by molecular assay, adjusting for confounders. VE was stratified by age group, influenza type (overall, influenza A, influenza B), and care setting (hospitalization, emergency department or urgent care [ED/UC] encounter).

Results: Overall, 74,000 encounters in children and adolescents aged 6 months–17 years (3,479 hospitalizations, 70,521 ED/UC encounters) and 267,606 in adults aged ≥ 18 years (66,828 hospitalizations, 200,778 ED/UC encounters) were included. Across care settings, among children and adolescents 15% (2,758/17,833) of cases versus 32% (18,240/56,167) of controls had received vaccination. Among adults, 25% (11,632/46,614) of cases versus 44% (97,811/220,992) of controls across care settings had received vaccination. VE was 58% (95% confidence interval [95% CI]: 44–69%) against hospitalization and 58% (95% CI: 56–60%) against ED/UC encounters for children and adolescents, and 39% (95% CI: 35–43) against hospitalization and 47% (95% CI: 46–49%) against ED/UC encounters for adults. Across age groups, VE was higher against influenza B than influenza A.

Conclusions: Influenza vaccines provided protection against influenza-associated illness across health care settings and age groups during the 2023–2024 influenza season.

Brief Summary:

During the 2023–2024 U.S. influenza season, vaccine effectiveness against influenza-associated hospitalizations and emergency department/urgent care encounters was 39% and 47% respectively, among adults and 58% against both among children.. VE against influenza B was higher than against influenza A viruses.

Keywords

influenza; vaccine effectiveness; vaccination; test-negative design

INTRODUCTION

During the 2023–2024 influenza season, the United States experienced at least 380,000 influenza-associated hospitalizations and 17,000 deaths [1]. The highest incidence of influenza-associated hospitalizations was observed among adults aged ≥ 65 years, followed by adults aged 50–64 years and children aged 0–4 years [2]. A mix of influenza virus types and sub-types circulated [3]. Through May 4, 2024, data from U.S. clinical and public health laboratories found that 71% of tested viruses were influenza A viruses (69% subtyped as H1N1pdm09 and 31% as H3N2) and 29% were influenza B/Victoria viruses. Antigenic characterization suggested that reference strains used in the 2023–2024 Northern Hemisphere vaccine were well matched to circulating influenza viruses [3].

Seasonal influenza vaccination is recommended in the United States for all people aged ≥ 6 months annually [4]. However, the United States has experienced a broad decline in vaccine uptake during recent seasons. In December 2023, the Centers for Disease Control and Prevention issued a health alert highlighting increased risk of influenza-associated illness due to low immunization rates [5]. The burden of influenza illness can be reduced substantially with increased vaccine uptake, even in seasons with low or moderate influenza vaccine effectiveness (VE) [6–8].

From a multi-site VE network, we evaluated the effectiveness of the 2023–2024 influenza vaccine in preventing influenza-associated hospitalizations and emergency department (ED) or urgent care (UC) encounters among children, adolescents, and adults.

METHODS

Population, settings, and study design.

Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network (VISION) is an electronic health record-based network that performs real-world evaluations of VE for respiratory viruses. This study included acute respiratory illness (ARI)-associated medical encounters among individuals aged ≥ 6 months. Seven sites in 8 states contributed encounter data (Kaiser Permanente Northern California, Kaiser Permanente Southern California, UCHHealth in Colorado, Regenstrief Institute in Indiana, HealthPartners in Minnesota and Wisconsin, Kaiser Permanente Northwest in Oregon and Washington, and Intermountain Healthcare in Utah). The study sampled ARI-associated encounters between October 15, 2023 and April 30, 2024.

As previously described [9], we used a test-negative design to evaluate influenza VE by comparing the odds of influenza vaccination in influenza-positive cases versus influenza-negative controls. We included children and adolescents (aged 6 months–17 years) and adults (aged ≥ 18 years) with ARI-associated ED/UC encounters or hospitalizations of ≥ 24 hours duration. ARI was defined by *International Classification of Diseases, Tenth*

Revision (ICD-10) codes for acute respiratory clinical diagnoses or acute respiratory signs or symptoms at the encounter (Supplementary Table 1). All patients received molecular testing for influenza as well as SARS-CoV-2 within 10 days before or up to 72 hours after the ED/UC visit or admission date. An individual could contribute more than one encounter; multiple ED and/or UC encounters within a 7-day period were combined into a single ED/UC encounter and hospitalizations within 30 days combined into a single hospitalization.

Baseline patient demographic and clinical information, including underlying medical conditions (Supplementary Table 2), was extracted from electronic health records (EHRs), along with in-hospital outcomes. Influenza vaccination status was ascertained from EHRs, state immunization information systems, and/or claims data. When available, information on vaccine type was collected. A patient was classified as vaccinated if they received ≥ 1 dose of a 2023–2024 influenza vaccine on or after August 1, 2023 and ≥ 14 days prior to the encounter index date (the earliest date of the most recent influenza test or the date of the ED/UC visit or hospital admission). A patient was considered unvaccinated if 2023–2024 influenza vaccination was not documented before the encounter index date. Certain children aged 6 months–8 years required 2 doses of influenza vaccine for the season based on their vaccination history [4]; partial versus full vaccination was not assigned for these children due to incomplete capture of vaccination history for past seasons.

Exclusion criteria are shown in Supplementary Figure 1A and 1B. Encounters with no influenza molecular test result, a diagnosis of influenza without a confirmatory positive laboratory test, or that occurred 1–13 days after influenza vaccination were excluded. We also excluded encounters with a SARS-CoV-2 positive test or COVID-19 ICD-10 discharge diagnostic code to reduce potential bias in influenza VE estimates due to correlation between influenza and COVID-19 vaccination [10].

Statistical analysis.

Baseline patient characteristics were described using counts and percentages or medians and interquartile ranges. Standardized mean differences (SMDs) were calculated to compare patient characteristics by influenza vaccination status and case/control status. An SMD > 0.20 was interpreted as a meaningful difference in distribution between groups. VE against influenza-associated hospitalizations and ED/UC encounters was estimated from logistic regression models comparing the odds of influenza vaccination between cases and controls, adjusting for pre-specified potential confounders used in prior VISION analyses: site, calendar day, patient age (in years), sex, and race/ethnicity reported in the EHR [11, 12]. VE was calculated as $(1 - \text{adjusted odds ratio}) \times 100$. Calendar day and age were modeled as natural cubic splines with 4 degrees of freedom.

We estimated VE separately for children and adolescents and for adults by encounter setting (ED/UC encounters or hospitalizations). Results were further stratified by age group (6 months–4 years, 5–17 years, 18–49 years, 50–64 years, ≥ 65 years), by influenza virus type (A or B), by time since vaccination in a model with 4 exposure groups (unvaccinated and 14–59 days, 60–119 days, ≥ 120 days since vaccination), and by presence or absence of ≥ 1 likely immunocompromising conditions. Intervals for waning models were selected based

on distribution of time since vaccination and seasonal influenza circulation patterns for most influenza seasons where most infections occur over several months in the fall and winter. Among ARI-associated hospitalizations, we evaluated VE against critical in-hospital outcomes, defined as intensive care unit (ICU) admission and/or death. For this analysis, cases included patients hospitalized with influenza who experienced a critical outcome, and controls were all hospitalized controls [13]. We also estimated VE against ED and UC encounters separately. Finally, because of differences by care setting in the proportion of influenza A and B cases and timing of vaccination across age groups, we stratified type-specific VE by age group and time since vaccination.

SAS version 9.4 (SAS Institute, Inc.) or R version 4.1.0 (R Foundation for Statistical Computing) were used to conduct analyses. These activities were reviewed and approved by institutional review boards (IRBs) at Kaiser Permanente Northern California and Kaiser Permanente Southern California (45 C.F.R. part 46.101(c); 21 C.F.R. part 56). The Westat IRB determined that the activities are non-research. Patient informed consent was not required.

RESULTS

Overall Patient Population

A total of 79,374 ARI-associated hospitalizations and 308,389 ARI-associated ED/UC encounters were identified; 9,067 (11.4%) hospitalizations and 37,090 (12.0%) ED/UC encounters met ≥ 1 exclusion criterion (Supplementary Figure 1A and 1B). After exclusions, 70,307 (88.6%) hospitalizations and 271,299 (88.0%) ED/UC encounters were included in analyses. Among 70,307 hospitalizations, 3,500 individuals had >1 hospitalization during the study period. Among 271,299 ED/UC encounters, 15,707 individuals had >1 ED/UC encounter.

Influenza circulation

Influenza activity peaked in late December to early January (Supplementary Figures 2A–2D). Of influenza cases, 48,757 (75.7%) were influenza-A-positive, 15,862 (24.6%) were influenza-B-positive, with 172 (0.3%) mixed A and B infections. The proportion of influenza B cases was higher in children and adolescents (34.4% of cases) than in adults (20.9% of cases).

Pediatric patient characteristics by care setting

Of 3,479 ARI-associated hospitalizations in children and adolescents, 340 (9.8%) were influenza cases and 3,139 (90.2%) were test-negative controls; influenza positivity was 5.3% among children aged 6 months–4 years and 16.6% among those aged 5–17 years. Proportions of hospitalizations among patients with ≥ 1 documented underlying medical condition were similar for influenza cases (63.8%) and controls (65.1%) [Table 1]. Overall, 1,270 (36.5%) hospitalized patients had received influenza vaccination (18.5% of cases vs 38.5% of controls, SMD = 0.45). Among vaccinated patients, median time since vaccination was 96 days; 91 days for those aged 6 months–4 years and 110 days for those aged 5–17 years.

Among 70,521 ARI-associated ED/UC encounters in children and adolescents, 17,493 (24.8%) were cases and 53,028 (75.2%) were controls; influenza positivity was 14.8% among children aged 6 months–4 years and 32.9% among those aged 5–17 years (Table 1). Overall, 19,728 (28.0%) had received influenza vaccination prior to the encounter. Children aged 6 months–4 years were more likely to be vaccinated than those aged 5–17 years (34.3% vs 22.9%, SMD = 0.28). Cases were less likely to be vaccinated than controls (15.4% vs 32.1%, SMD = 0.40). Among vaccinated patients, median time since vaccination was 91 days; 86 days for those aged 6 months–4 years and 98 days for those aged 5–17 years.

Across care settings, 90.0% of vaccinated children with known vaccine product received standard-dose, egg-based inactivated vaccine, 6.8% received cell-culture-based vaccine, 2.9% live-attenuated influenza vaccine, and 0.2% another product type (Supplementary Table 3).

Pediatric vaccine effectiveness

VE against pediatric influenza-associated hospitalization was 58% (95% confidence interval [95% CI]: 44–69%); 71% (95% CI: 51–83%) for children aged 6 months–4 years and 49% (95% CI: 27–65%) for those aged 5–17 years (Figure 1). VE against influenza B viruses (85% [95% CI: 72–93%]) was higher than against influenza A viruses (44% [95% CI: 23–60%]). VE against ICU admission was 43% (95% CI: –6–70%).

Estimates of VE against influenza-associated ED/UC encounters were consistent with VE against hospitalization and ICU admission. Overall VE against ED/UC encounters was 58% (95% CI: 56–60%); 65% (95% CI: 62–68%) for children aged 6 months–4 years and 54% (95% CI: 51–57%) for children aged 5–17 years (Figure 1). VE against influenza B-associated ED/UC encounters (74% [95% CI: 72–77%]) was higher than against influenza A-associated illness (49% [95% CI: 46–51%]). VE in ED and UC settings was similar (59% and 58%, respectively).

Adult patient characteristics by care setting

Of 66,828 ARI-associated hospitalizations in adults, 5,721 (8.6%) were influenza cases and 61,107 (91.4%) were controls; influenza positivity was 11.3% among adults aged 18–64 years and 7.2% among adults aged ≥65 years (Table 2). Median age was 67 years for cases and 72 years for controls, and most patients had ≥1 documented underlying medical condition (86.4% of cases and 92.0% of controls). Among hospitalized adults, 32,455 (48.6%) were vaccinated, including 35.1% of cases versus 49.8% of controls (SMD = 0.30). Of those vaccinated, median time since vaccination was 107 days; 103 days for those aged 18–49 years, 103 days for those aged 50–64 years, and 109 days for those aged ≥65 years. Of hospitalized cases, 824 (14.4%) were admitted to an ICU and 190 (3.3%) died during hospitalization.

Among 200,778 ARI-associated ED/UC encounters in adults, 40,893 (20.4%) were influenza cases and 159,885 (79.6%) were controls; influenza positivity was 24.5% among adults aged 18–64 years and 11.4% among adults aged ≥65 years. Cases were younger on average than controls (median age 42 vs 54 years) and less likely to have ≥1 documented underlying medical condition (20.5% of cases vs 36.1% of controls, SMD = 0.35; Table

2). Overall, 76,988 (38.3%) were vaccinated (23.5% of cases vs 42.1% of controls, SMD = 0.40). Among vaccinated adults, median time since vaccination was 103 days; 98 days for those aged 18–49 years, 101 days for those aged 50–64 years, and 106 days for those aged ≥65 years.

Across sites, most (85.5%) vaccinated adults aged 18–64 years with known vaccine type received standard-dose, egg-based inactivated vaccine (Supplementary Table 3). Most (90.3%) older adults received a high-dose inactivated or adjuvanted vaccine, which are preferentially recommended products for older adults [14].

Adult vaccine effectiveness

VE against influenza-associated hospitalization in adults was 39% (95% CI: 35–43%); 51% (95% CI: 42–60%) for adults aged 18–49 years, 40% (95% CI: 32–48%) for adults aged 50–64 years, and 36% (95% CI: 31–41%) for adults aged ≥65 years (Figure 2). VE against influenza B viruses (67% [95% CI: 54–76%]) was higher than against influenza A viruses (37% [95% CI: 32–41%]). VE against critical illness (ICU admission and/or death) was 41% (95% CI: 30–49%); 41% (95% CI: 31–50%) against ICU admission and 50% (95% CI: 31–65%) against in-hospital death.

As observed for pediatric patients, VE against ED/UC encounters was similar to VE against hospitalization and ICU admission among adult age groups. VE against influenza-associated ED/UC encounters was 47% (95% CI: 46–49%); 54% (95% CI: 53–56%) for ages 18–49 years, 44% (95% CI: 40–47%) for ages 50–64 years, and 37% (95% CI: 34–40%) for adults aged ≥65 years (Figure 2). VE against influenza -associated ED/UC encounters among adults was 75% (95% CI: 72–77%) for influenza B versus 41% (95% CI: 39–42%) for influenza A.

Vaccine effectiveness by time since vaccination

In analyses of time since vaccination, vaccination provided significant protection against hospitalizations and ED/UC visits through ≥120 days after vaccination (Figure 1–3, Supplementary Table 4). Among children, we observed no significant differences in VE against hospitalization at 14–59 days (50% [95% CI: 18–71%]) versus ≥120 days versus (67% [95% CI: 45–81%]) after vaccination (Figure 1). VE against ED/UC encounters was 63% (95% CI: 60–66%) at 14–59 days versus 56% (95% CI: 53–59%) at 60–119 and 57% (95% CI: 53–60%) ≥120 days after vaccination. Type-specific VE estimates stratified by age group and time since vaccination are shown in Figure 3B and Supplementary Table 4. For children and adolescents, VE against influenza A-associated encounters trended downward with greater time since vaccination, with most difference observed for encounters ≥60 days since vaccination, although no consistent trend was observed against influenza B-associated encounters.

Among hospitalized adults, VE at 14–59 days after vaccination (49% [95% CI: 42–55%]) was higher than at 60–119 and ≥120 days after vaccination (Figure 2). Against influenza-associated ED/UC encounters, VE was lower with increased time since vaccination (e.g., 57% [95% CI: 55–60%] at 14–59 days vs 48% [95% CI: 45–50%] at ≥120 days since vaccination). Within strata of time since vaccination, VE against influenza A- and B-

associated encounters tended to be lower in older compared to younger adults (Figure 3, Supplementary Table 4).

DISCUSSION

During the 2023–2024 U.S. influenza season, influenza vaccination reduced the risk of influenza-associated encounters across age groups and care settings, including against severe in-hospital outcomes. These findings support current recommendations for routine annual influenza vaccination beginning at 6 months of age [4].

Greatest vaccine protection was observed in children aged 6 months–4 years, which is notable given the elevated risk of severe influenza-associated outcomes among young children, including those with no underlying medical conditions [15]. VE among children and adolescents was generally higher than among adults, with more sustained protection. Overall and type-specific VE estimates were lowest among older adults. This could be due to a number of factors, such as primary reasons or thresholds for admission that may be age-related (e.g., due to exacerbation of chronic underlying medical condition after influenza virus infection versus primary viral lower respiratory tract disease), age-related changes including immunosenescence in older adults [16], or effects of repeat vaccination over multiple seasons on immune responses [17, 18]. Protection among older adults was less than for adults aged 18–64 despite preferential receipt of high-dose and adjuvanted influenza vaccines for older adults [4].

VE was consistently higher against influenza B vs influenza A-associated encounters. Following the emergence of influenza A(H1N1)pdm09 viruses in 2009, population immunity to A(H1N1)pdm09 viruses in younger age groups increased over several seasons. During that period, VE against A(H1N1)pdm09 was similar to VE against B/Yamagata and B/Victoria-associated outpatient illness, while VE against A(H3N2) has been lower, especially among older adults [19]. B/Yamagata viruses no longer circulate and influenza B/Victoria viruses have remained antigenically similar since the emergence of the V1.3 clade but had not circulated for 3 seasons. Lower baseline antibody levels in the population without boosting from natural infection may have resulted in relatively higher levels of protective antibody among vaccinated persons this season. In contrast, levels of protective antibodies against circulating A(H1N1)pdm09 viruses may have been more similar among vaccinated and unvaccinated individuals. Improved understanding of virus and antigen-specific vaccine responses may inform development of more effective influenza vaccines.

Protection was observed for more than 120 days after vaccination. Among adults, VE estimates were highest 14–59 days post-vaccination. The timing of influenza activity varies from season to season, and optimal timing for vaccination is difficult to predict [20]. CDC's Advisory Committee on Immunization Practices recommends that most people who require 1 vaccine dose in a season are offered vaccination in September or October, balancing factors including unpredictability of influenza activity, within-season waning of VE [21, 22], and programmatic considerations [4]. In addition to vaccination, other tools may reduce the risk of complications from influenza among older adults and others at increased risk for severe outcomes, such as timely influenza antiviral treatment [23].

This analysis was subject to several limitations. VE estimates were limited to influenza A- and B-associated encounters because VISION relies on clinician-driven testing and influenza A viruses were not consistently subtyped. During the 2023–2024 influenza season, influenza A(H1N1)pdm09 viruses co-circulated with A(H3N2) and B/Victoria viruses. Influenza A(H3N2) VE has historically been lower than for A(H1N1)pdm09 [19, 24, 25] and co-circulation likely influenced VE against influenza A-associated hospitalizations and ED/UC encounters. As influenza A(H3N2) activity peaked later than A(H1N1)pdm09 activity, declines in VE by time since vaccination may reflect both waning in vaccine-induced immune protection [26] and changes in the distribution of influenza A virus subtypes circulating. Second, we did not have information on influenza vaccination across multiple seasons to evaluate effects from current- and prior-season vaccination [17, 18] or VE in younger children based on partial versus full vaccination [4]. Third, we did not evaluate influenza VE by vaccine type which may impact immune responses and effectiveness [26–28]. Most younger adults received egg-based standard-dose inactivated vaccines whereas most older adults received high-dose inactivated or adjuvanted vaccines. Fourth, the study population may not be representative of the entire U.S. population. Fifth, although vaccination data was captured from a variety of data sources, under-capture of vaccine doses administered in cases or controls could result in vaccination exposure misclassification and potential bias in VE estimates.

Conclusions

Influenza vaccination provided protection against influenza-associated encounters for U.S. children, adolescents, and adults during the 2023–2024 influenza season including against severe in-hospital outcomes. Increased uptake of annual influenza vaccination should be strongly encouraged to decrease the burden of influenza illness and its sequelae.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Padma Koppolu, Brad Crane, Katie Allen, Ashley Wiensch, Aaron Buck, Sunita Thapa, Linda Fletcher, Sheryl Kane, Angela Cheung, Lindsey Kirshner, Elizabeth Bassett, Elizabeth Rowley, Yan Zhuang, and Sarah Reese.

Conflict of Interest Disclaimer:

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. During the conduct of the study, all Kaiser Permanente Southern California Department of Research and Evaluation and Kaiser Permanente Northern California Division of Research-affiliated authors reported receiving contractual support from the Centers for Disease Control and Prevention (CDC) via payments made to their respective institutions. Additionally, all authors affiliated with HealthPartners Institute, Intermountain Healthcare, Kaiser Permanente Center for Health Research, Regenstrief Institute, and University of Colorado Anschutz Medical Campus reported receiving contractual support from the CDC during the conduct of the study, via subcontracts from Westat, Inc. with payments made to their respective institutions. Unrelated to the submitted work, the following disclosures were reported from the past 36 months: SYT reports contracts from GlaxoSmithKline and Pfizer. NPK reports support from Sanofi Pasteur, Merck, Pfizer, Seqirus, and GlaxoSmithKline. TCO received consulting fees from Regenstrief Institute and support for travel from Patient-Centered Outcomes Research Institute (PCORI) and Regenstrief Institute and has a current patent, PCT/US2018/047961. SJG reports contracts with National Institutes of Health (NIH) National Center for Advancing Translational Sciences and NIH National Institute of Mental Health. BED reports a contract with Vaccine Safety

Datalink Project, Contract No. 75D30122D15424. WFF reports a contract with Vaccine Safety Datalink Project, Contract No. 75D30122D15424. CEM reports support from NIH, Department of Defense, PCORI, Astra Zeneca, and GlaxoSmithKline and is a member of the American Lung Association of Minnesota Board, Minnesota Department of Health Long COVID Advisory Committee, and Minnesota Department of Health Asthma Care Advisory Committee. TS is a member of CDC Advisory Committee on Immunization Practices Influenza Vaccine Work Group, chair of Utah Adult Immunization Coalition – volunteer vaccine quality improvement and advocacy group and a member of Utah Department of Health and Human Services Scientific Advisory Committee on Vaccines. OZ reports contract number R01AI168373 with the National Institute of Allergy and Infectious Diseases. LSS reports contracts with GlaxoSmithKline, Moderna, and Dynavax. SR reports support from Biofire and GlaxoSmithKline. MB was a speaker bureau participant – Innoviva Specialty Therapeutics -Oct 2023. No other disclosures were reported.

Financial support.

This study was supported by the CDC through contract 75D30121D12779 to Westat and contracts 75D30123C17595 and 75D301123C018039 to Kaiser Foundation Hospitals.

References

- Centers for Disease Control and Prevention. Preliminary Estimated Flu Disease Burden 2023–2024 Flu Season. Available at: <https://www.cdc.gov/flu-burden/php/data-vis/2023-2024.html>. Accessed on: 27 Sept 2024.
- Centers for Disease Control and Prevention. FluView Interactive: Laboratory-confirmed influenza hospitalizations. Available at: <https://gis.cdc.gov/GRASP/Fluview/FluHospRates.html>. Accessed on: 2 Jul 2024.
- Centers for Disease Control and Prevention. Weekly U.S. Influenza Surveillance Report. Available at: <https://www.cdc.gov/flu/weekly/index.htm>. Accessed on: 2 Jul 2024.
- Grohskopf LA, Ferdinands JM, Blanton LH, Broder KR, Loehr J. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices — United States, 2024–25 Influenza Season. *MMWR Recomm Rep* 2024;73(No. RR-5):1–25.
- Centers for Disease Control and Prevention. Health Alert Network: Urgent Need to Increase Immunization Coverage for Influenza, COVID-19, and RSV and Use of Authorized/Approved Therapeutics in the Setting of Increased Respiratory Disease Activity During the 2023 – 2024 Winter Season. Available at: <https://emergency.cdc.gov/han/2023/han00503.asp>. Accessed on: 19 Jul 2024.
- Chung JR, Rolfes MA, Flannery B, Prasad P, O'Halloran A, Garg S, et al. Effects of Influenza Vaccination in the United States during the 2018–2019 Influenza Season. *Clin Infect Dis*. 2020;71:8.
- Rolfes MA, Flannery B, Chung J, O'Halloran A, Garg S, Belongia EA, et al. Effects of Influenza Vaccination in the United States during the 2017–2018 Influenza Season. *Clin Infect Dis*. 2019;69(11).
- Centers for Disease Control and Prevention. Past seasons estimated influenza disease burden averted by vaccination. Available at: <https://www.cdc.gov/flu/vaccines-work/past-burden-averted-est.html>. Accessed on: 16 Oct 2023.
- Tenforde MW, Weber ZA, DeSilva MB, Stenehjem E, Yang DH, Fireman B, et al. Vaccine effectiveness against influenza-associated urgent care, emergency department, and hospital encounters during the 2021–2022 season, VISION Network. *J Infect Dis*. 2023;228(2):185–95. [PubMed: 36683410]
- Doll MK, Pettigrew SM, Ma J, Verma A. Effects of Confounding Bias in Coronavirus Disease 2019 (COVID-19) and Influenza Vaccine Effectiveness Test-Negative Designs Due to Correlated Influenza and COVID-19 Vaccination Behaviors. *Clin Infect Dis*. 2022;75(1):e564–e71. [PubMed: 35325923]
- DeCuir J, Payne AB, Self WH, Rowley EAK, Dascomb K, DeSilva MB, et al. Interim Effectiveness of Updated 2023–2024 (Monovalent XBB.1.5) COVID-19 Vaccines Against COVID-19-Associated Emergency Department and Urgent Care Encounters and Hospitalization

- Among Immunocompetent Adults Aged ≥ 18 Years - VISION and IVY Networks, September 2023-January 2024. *MMWR Morb Mortal Wkly Rep.* 2024;73(8):180–8. [PubMed: 38421945]
12. Frutos AM, Price AM, Harker E, Reeves EL, Ahmad HM, Murugan V, et al. Interim Estimates of 2023–24 Seasonal Influenza Vaccine Effectiveness - United States. *MMWR Morb Mortal Wkly Rep.* 2024;73(8):168–74. [PubMed: 38421935]
 13. Tenforde MW, Self WH, Gaglani M, Ginde AA, Douin DJ, Talbot HK, et al. Effectiveness of mRNA Vaccination in Preventing COVID-19-Associated Invasive Mechanical Ventilation and Death - United States, March 2021-January 2022. *MMWR Morb Mortal Wkly Rep.* 2022;71(12):459–65. [PubMed: 35324878]
 14. Grohskopf LA, Blanton LH, Ferdinands JM, Chung JR, Broder KR, Talbot HK, et al. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices - United States, 2022–23 Influenza Season. *MMWR Recomm Rep.* 2022;71(1):1–28.
 15. Shang M, Blanton L, Brammer L, Olsen SJ, Fry AM. Influenza-Associated Pediatric Deaths in the United States, 2010–2016. *Pediatrics.* 2018;141(4).
 16. Haq K, McElhaney JE. Immunosenescence: Influenza vaccination and the elderly. *Curr Opin Immunol.* 2014;29:38–42. [PubMed: 24769424]
 17. Jones-Gray E, Robinson EJ, Kucharski AJ, Fox A, Sullivan SG. Does repeated influenza vaccination attenuate effectiveness? A systematic review and meta-analysis. *Lancet Respir Med.* 2023;11(1):27–44. [PubMed: 36152673]
 18. Kwong JC, Chung H, Jung JK, Buchan SA, Campigotto A, Campitelli MA, et al. The impact of repeated vaccination using 10-year vaccination history on protection against influenza in older adults: a test-negative design study across the 2010/11 to 2015/16 influenza seasons in Ontario, Canada. *Euro Surveill.* 2020;25(1).
 19. Belongia EA, Simpson MD, King JP, Sundaram ME, Kelley NS, Osterholm MT, et al. Variable influenza vaccine effectiveness by subtype: a systematic review and meta-analysis of test-negative design studies. *Lancet Infect Dis.* 2016;16(8):942–51. [PubMed: 27061888]
 20. Centers for Disease Control and Prevention. Flu Season. Available at: <https://www.cdc.gov/flu/about/season/index.html#:~:text=The%20exact%20timing%20and%20duration,last%20as%20late%20as%20May>. Accessed on: 19 Jul 2024.
 21. Ferdinands JM, Gaglani M, Martin ET, Monto AS, Middleton D, Silveira F, et al. Waning Vaccine Effectiveness Against Influenza-Associated Hospitalizations Among Adults, 2015–2016 to 2018–2019, United States Hospitalized Adult Influenza Vaccine Effectiveness Network. *Clin Infect Dis.* 2021;73(4):726–9. [PubMed: 33462610]
 22. Ray GT, Lewis N, Klein NP, Daley MF, Wang SV, Kulldorff M, et al. Intraseason Waning of Influenza Vaccine Effectiveness. *Clin Infect Dis.* 2019;68(10):1623–30. [PubMed: 30204855]
 23. Uyeki TM, Bernstein HH, Bradley JS, Englund JA, File TM, Fry AM, et al. Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza. *Clin Infect Dis.* 2019;68(6):e1–e47.
 24. Belongia EA, McLean HQ. Influenza Vaccine Effectiveness: Defining the H3N2 Problem. *Clin Infect Dis.* 2019;69(10):1817–23. [PubMed: 31102401]
 25. Flannery B, Kondor RJG, Chung JR, Gaglani M, Reis M, Zimmerman RK, et al. Spread of Antigenically Drifted Influenza A(H3N2) Viruses and Vaccine Effectiveness in the United States During the 2018–2019 Season. *J Infect Dis.* 2020;221(1):8–15. [PubMed: 31665373]
 26. Cowling BJ, Perera RAPM, Valkenburg SA, Leung NHL, Iuliano AD, Tam YH, et al. Comparative Immunogenicity of Several Enhanced Influenza Vaccine Options for Older Adults: A Randomized, Controlled Trial. *Clin Infect Dis.* 2020;71(7):1704–14. [PubMed: 31828291]
 27. Zhong S, Ng TWY, Skowronski DM, Iuliano AD, Leung NHL, Perera RAPM, et al. Influenza A(H3N2) Antibody Responses to Standard-Dose Versus Enhanced Influenza Vaccine Immunogenicity in Older Adults and Prior Season's Vaccine Status. *J Infect Dis.* 2024;229(5):1451–9. [PubMed: 37950884]

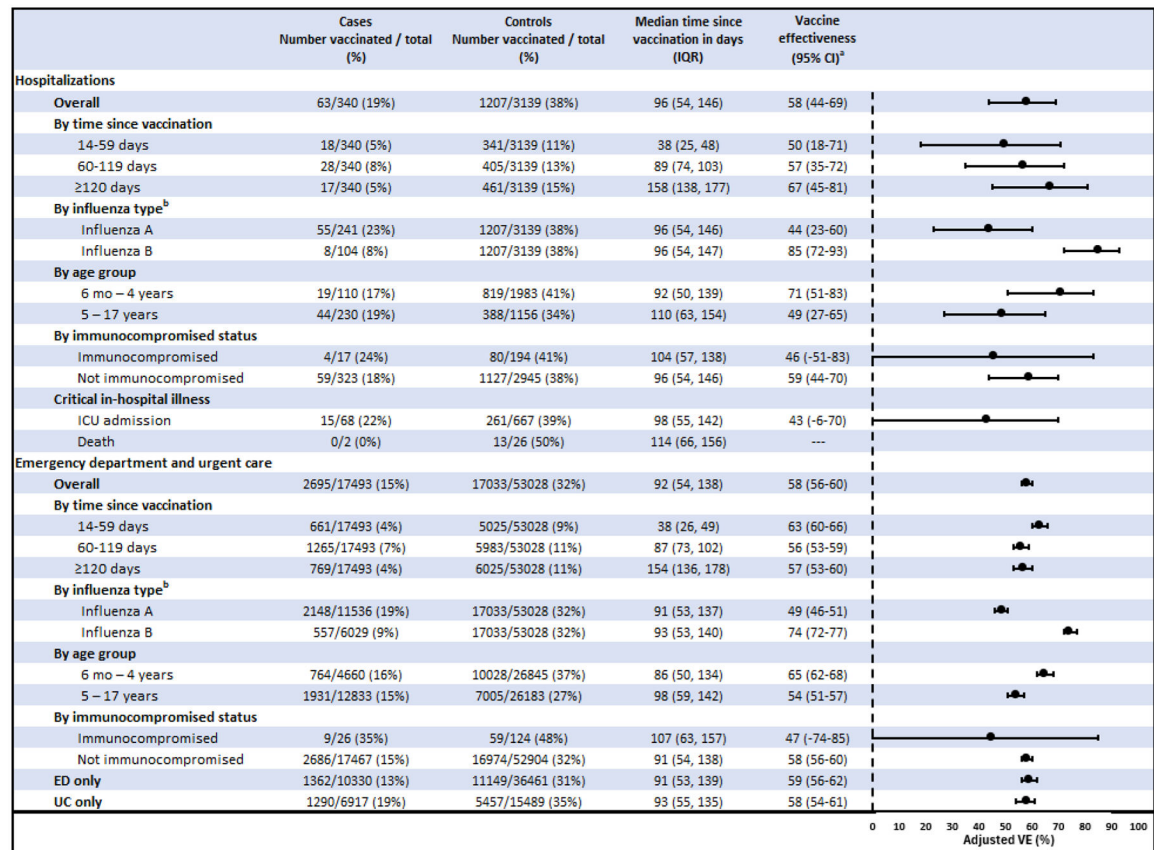
28. Izurieta HS, Lu M, Kelman J, Lu Y, Lindaas A, Loc J, et al. Comparative Effectiveness of Influenza Vaccines Among US Medicare Beneficiaries Ages 65 Years and Older During the 2019–2020 Season. *Clin Infect Dis*. 2021;73(11):e4251–e9. [PubMed: 33211809]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

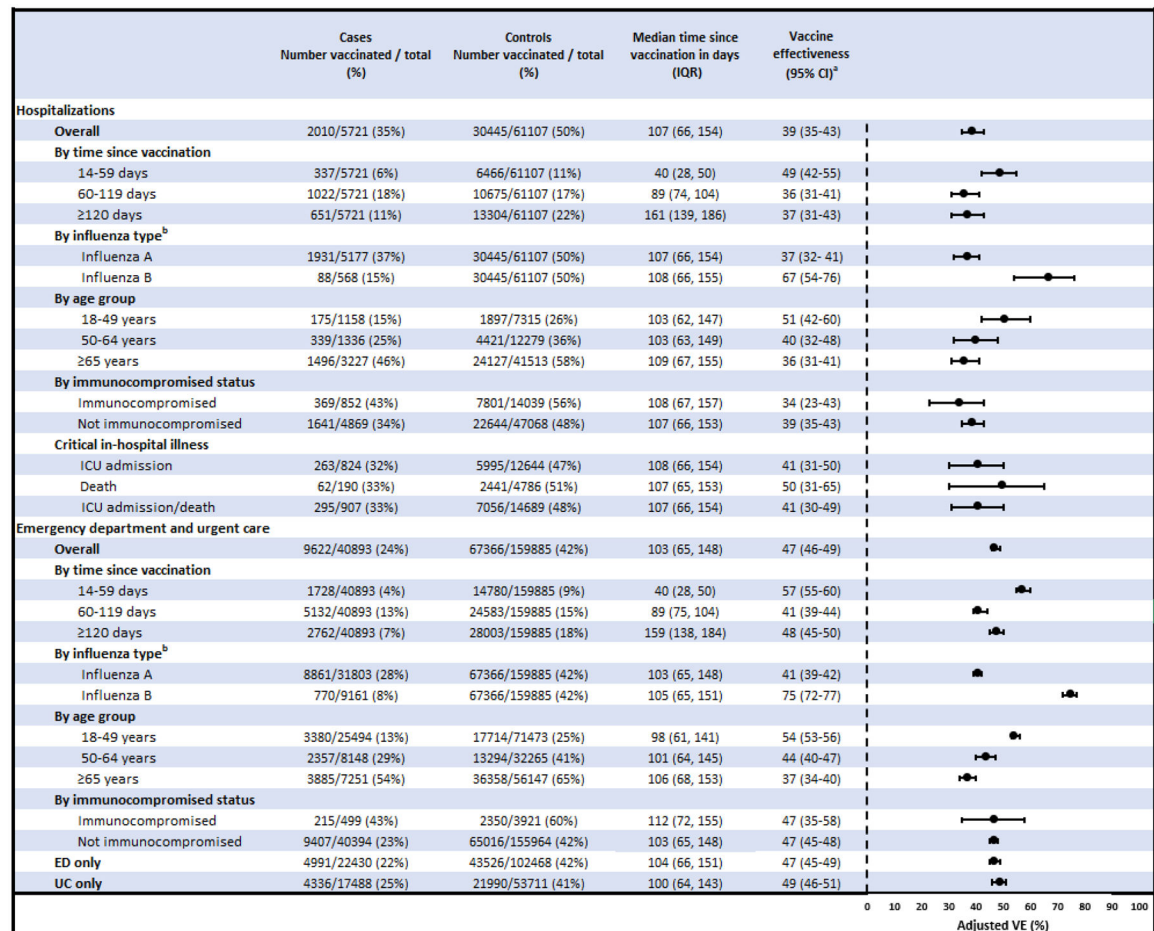
**Figure 1.**

Influenza vaccine effectiveness against influenza-associated hospitalizations and emergency department / urgent care encounters in children and adolescents aged 6 months-17 years.

Abbreviations: CI = confidence interval; ED = emergency department; ICU = intensive care unit; UC = urgent care

^a Vaccine effectiveness was estimated using logistic regression models comparing the odds of vaccination between cases and controls; models adjusted for site, calendar day, patient age, sex, and race/ethnicity with calendar day and age treated as natural cubic splines with 4 degrees of freedom.

^b Influenza A and B coinfections were included in both influenza A and influenza B case counts.

**Figure 2.**

Vaccine effectiveness against influenza-associated hospitalizations and emergency department / urgent care encounters in adults aged ≥18 years.

Abbreviations: CI = confidence interval; ED = emergency department; ICU = intensive care unit; UC = urgent care.

^a Vaccine effectiveness was estimated using logistic regression models comparing the odds of vaccination between cases and controls; models adjusted for site, calendar day, patient age, sex, and race/ethnicity with calendar day and age treated as natural cubic splines with 4 degrees of freedom.

^b Influenza A and B coinfections were included in both influenza A and influenza B case counts.

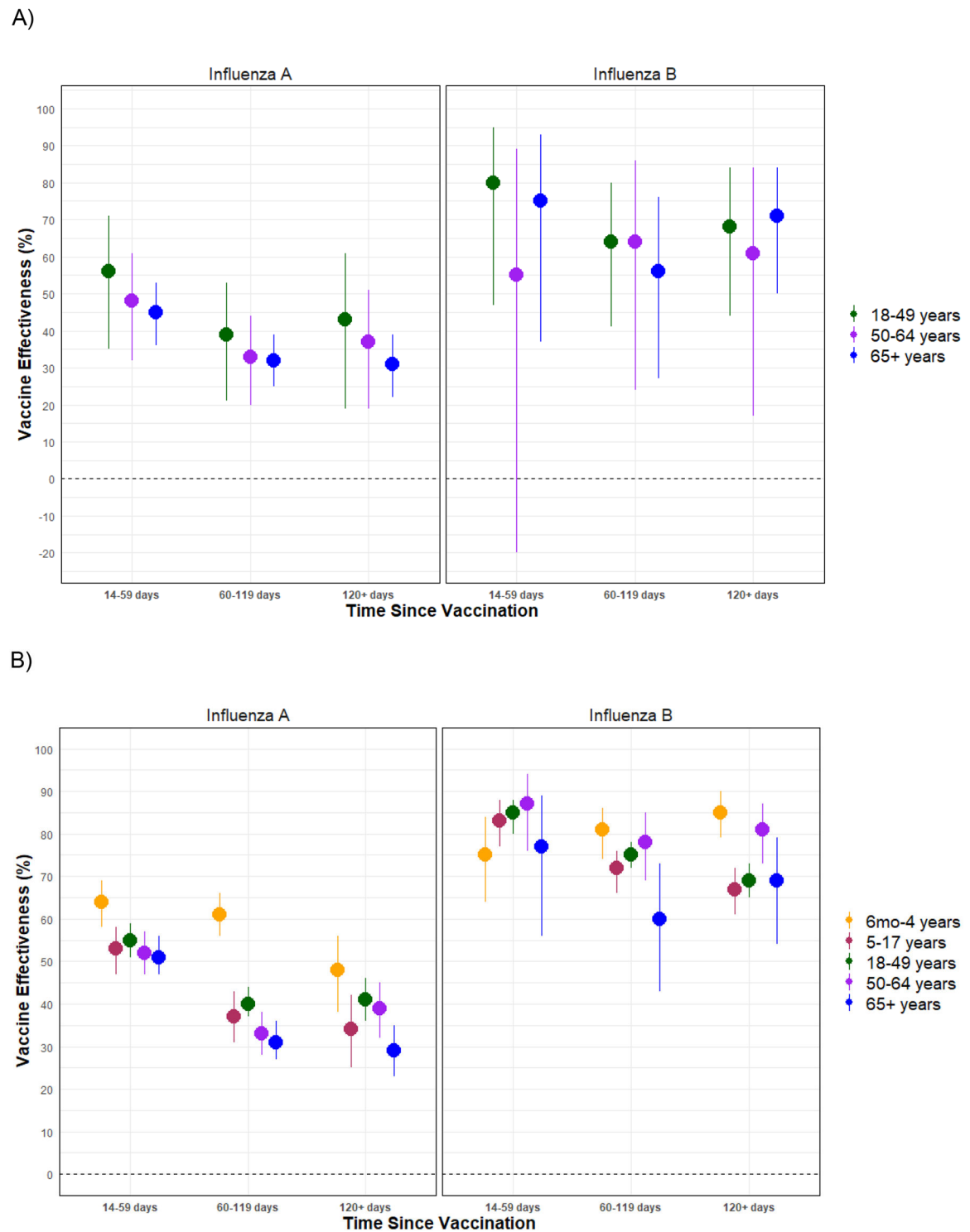


Figure 3.

A) Influenza vaccine effectiveness^a by time since vaccination by influenza type and age group^b among adult inpatient encounters B) Influenza vaccine effectiveness by time since vaccination by influenza type and age group among emergency department / urgent care encounters.

^a Forest plots depict vaccine effectiveness point estimates (circles) and 95% confidence intervals (vertical lines).

^b Inpatient vaccine effectiveness estimates not shown for children aged 6 months-4 years or 517 years because of imprecision.

Table 1.

Characteristics of acute respiratory illness-associated hospitalizations and emergency department / urgent care encounters in children aged 6 months-17 years by influenza vaccination and test status.

		Influenza vaccination status			Influenza test result		
	Total (col %)	Unvaccinated (row %)	Vaccinated (row %)	SMD ^a	Negative (row %)	Positive (row %)	SMD ^a
Hospitalizations							
All hospitalizations	3479	2209	1270		3139	340	
Influenza vaccination status							
Unvaccinated	2209 (63.5)	2209 (100.0)	0 (0.0)		1932 (87.5)	277 (12.5)	0.453
Vaccinated	1270 (36.5)	0 (0.0)	1270 (100.0)		1207 (95.0)	63 (5.0)	
Month of encounter							
October 2023	185 (5.3)	161 (87.0)	24 (13.0)	0.390	181 (97.8)	4 (2.2)	0.640
November 2023	546 (15.7)	386 (70.7)	160 (29.3)		522 (95.6)	24 (4.4)	
December 2023	753 (21.6)	511 (67.9)	242 (32.1)		641 (85.1)	112 (14.9)	
January 2024	529 (15.2)	345 (65.2)	184 (34.8)		444 (83.9)	85 (16.1)	
February 2024	501 (14.4)	288 (57.5)	213 (42.5)		446 (89.0)	55 (11.0)	
March 2024	506 (14.5)	282 (55.7)	224 (44.3)		460 (90.9)	46 (9.1)	
April 2024	459 (13.2)	236 (51.4)	223 (48.6)		445 (96.9)	14 (3.1)	
Sites							
Site A	29 (0.8)	22 (75.9)	7 (24.1)	0.277	26 (89.7)	3 (10.3)	0.251
Site B	357 (10.3)	238 (66.7)	119 (33.3)		310 (86.8)	47 (13.2)	
Site C	854 (24.5)	511 (59.8)	343 (40.2)		768 (89.9)	86 (10.1)	
Site D	83 (2.4)	49 (59.0)	34 (41.0)		80 (96.4)	3 (3.6)	
Site E	1128 (32.4)	656 (58.2)	472 (41.8)		1042 (92.4)	86 (7.6)	
Site F	845 (24.3)	620 (73.4)	225 (26.6)		755 (89.3)	90 (10.7)	
Site G	183 (5.3)	113 (61.7)	70 (38.3)		158 (86.3)	25 (13.7)	
Median age (Q1, Q3), years	3 (2, 7)	4 (2, 7)	3 (1, 6)		3 (1, 6)	7 (4, 10)	
Age group							
6 months-4 years	2093 (60.2)	1255 (60.0)	838 (40.0)	0.189	1983 (94.7)	110 (5.3)	0.649
5-17 years	1386 (39.8)	954 (68.8)	432 (31.2)		1156 (83.4)	230 (16.6)	
Sex							
Female	1556 (44.7)	989 (63.6)	567 (36.4)	0.003	1400 (90.0)	156 (10.0)	0.026
Male	1923 (55.3)	1220 (63.4)	703 (36.6)		1739 (90.4)	184 (9.6)	
Race/ethnicity							
White Non-Hispanic	1309 (37.6)	881 (67.3)	428 (32.7)	0.301	1182 (90.3)	127 (9.7)	0.178

		Influenza vaccination status			Influenza test result		
	Total (col %)	Unvaccinated (row %)	Vaccinated (row %)	SMD ^a	Negative (row %)	Positive (row %)	SMD ^a
Black Non-Hispanic	365 (10.5)	259 (71.0)	106 (29.0)		316 (86.6)	49 (13.4)	
Other Non-Hispanic ^b	464 (13.3)	215 (46.3)	249 (53.7)		431 (92.9)	33 (7.1)	
Hispanic	1100 (31.6)	697 (63.4)	403 (36.6)		996 (90.5)	104 (9.5)	
Unknown	241 (6.9)	157 (65.1)	84 (34.9)		214 (88.8)	27 (11.2)	
Any medical condition	2259 (64.9)	1383 (61.2)	876 (38.8)	0.135	2042 (90.4)	217 (9.6)	0.026
Respiratory condition	1593 (45.8)	960 (60.3)	633 (39.7)	0.128	1465 (92.0)	128 (8.0)	0.184
Non-respiratory condition	1195 (34.3)	715 (59.8)	480 (40.2)	0.114	1055 (88.3)	140 (11.7)	0.157
Immunocompromising condition	211 (6.1)	127 (60.2)	84 (39.8)	0.036	194 (91.9)	17 (8.1)	0.051
ICU admission							
Yes	735 (21.1)	459 (62.4)	276 (37.6)	0.025	667 (90.7)	68 (9.3)	0.035
No	2701 (77.6)	1725 (63.9)	976 (36.1)		2431 (90.0)	270 (10.0)	
Unknown	43 (1.2)	25 (58.1)	18 (41.9)		41 (95.2)	2 (4.7)	
Invasive mechanical ventilation							
Yes	336 (9.7)	229 (68.2)	107 (31.8)	0.108	309 (92.0)	27 (8.0)	0.053
No	2518 (72.4)	1519 (60.3)	999 (39.7)		2282 (90.6)	236 (9.4)	
Unknown	625 (18.0)	461 (73.8)	164 (26.2)		548 (87.7)	77 (12.3)	
In-hospital death							
Yes	28 (0.8)	15 (53.6)	13 (46.4)	0.055	26 (92.9)	2 (7.1)	0.038
No	3450 (99.2)	2194 (63.6)	1256 (36.4)		3112 (90.2)	338 (9.8)	
Unknown	1 (0.0)	0 (0.0)	1 (100.0)		1 (100.0)	0 (0.0)	
Emergency department / urgent care encounters							
All encounters	70521	50793	19728		53028	17493	
Influenza vaccination status							
Unvaccinated	50793 (72.0)	50793 (100.0)	0 (0.0)		35995 (70.9)	14798 (29.1)	0.400
Vaccinated	19728 (28.0)	0 (0.0)	19728 (100.0)		17033 (86.3)	2695 (13.7)	
Month of encounter							
October 2023	3069 (4.4)	2625 (85.5)	444 (14.5)	0.287	2943 (95.9)	126 (4.1)	0.603
November 2023	10345 (14.7)	8139 (78.7)	2206 (21.3)		8872 (85.8)	1473 (14.2)	
December 2023	15918 (22.6)	11986 (75.3)	3932 (24.7)		10217 (64.2)	5701 (35.8)	
January 2024	11011 (15.6)	7922 (71.9)	3089 (28.1)		7322 (66.5)	3689 (33.5)	

		Influenza vaccination status			Influenza test result		
	Total (col %)	Unvaccinated (row %)	Vaccinated (row %)	SMD ^a	Negative (row %)	Positive (row %)	SMD ^a
February 2024	11631 (16.5)	8116 (69.8)	3515 (30.2)		8116 (69.8)	3515 (30.2)	
March 2024	10709 (15.2)	7029 (65.6)	3680 (34.4)		8529 (79.6)	2180 (20.4)	
April 2024	7838 (11.1)	4976 (63.5)	2862 (36.5)		7029 (89.7)	809 (10.3)	
Sites							
Site A	4866 (6.9)	3428 (70.4)	1438 (29.6)	0.378	3314 (68.1)	1552 (31.9)	0.289
Site B	2175 (3.1)	1641 (75.4)	534 (24.6)		1718 (79.0)	457 (21.0)	
Site C	16425 (23.3)	11076 (67.4)	5349 (32.6)		13614 (82.9)	2811 (17.1)	
Site D	1756 (2.5)	1238 (70.5)	518 (29.5)		1484 (84.5)	272 (15.5)	
Site E	22008 (31.2)	14757 (67.1)	7251 (32.9)		16491 (74.9)	5517 (25.1)	
Site F	13132 (18.6)	11302 (86.1)	1830 (13.9)		9213 (70.2)	3919 (29.8)	
Site G	10159 (14.4)	7351 (72.4)	2808 (27.6)		7194 (70.8)	2965 (29.2)	
Median age (Q1, Q3), years	5 (2,10)	6 (2, 10)	4 (2, 8)		4 (2, 9)	7 (4, 11)	
Age group							
6 months–4 years	31505 (44.7)	20713 (65.7)	10792 (34.3)	0.282	26845 (85.2)	4660 (14.8)	0.508
5–17 years	39016 (55.3)	30080 (77.1)	8936 (22.9)		26183 (67.1)	12833 (32.9)	
Sex							
Female	32837 (46.6)	23968 (73.0)	8869 (27.0)	0.045	24436 (74.4)	8401 (25.6)	0.039
Male	37684 (53.4)	26825 (71.2)	10859 (28.8)		28592 (75.9)	9092 (24.1)	
Race/ethnicity							
White Non-Hispanic	24595 (34.9)	18263 (74.3)	6332 (25.7)	0.312	18480 (75.1)	6115 (24.9)	0.092
Black Non-Hispanic	8476 (12.0)	7073 (83.4)	1403 (16.6)		6123 (72.2)	2353 (27.8)	
Other Non-Hispanic ^b	8012 (11.4)	4700 (58.7)	3312 (41.3)		6127 (76.5)	1885 (23.5)	
Hispanic	24257 (34.4)	17179 (70.8)	7078 (29.2)		18161 (74.9)	6096 (25.1)	
Unknown	5181 (7.3)	3578 (69.1)	1603 (30.9)		4137 (79.8)	1044 (20.2)	
Any medical condition	7352 (10.4)	4879 (66.4)	2473 (33.6)	0.093	6324 (86.0)	1028 (14.0)	0.214
Respiratory condition	5733 (8.1)	3760 (65.6)	1973 (34.4)	0.092	5152 (89.9)	581 (10.1)	0.261
Non-respiratory condition	1817 (2.6)	1224 (67.4)	593 (32.6)	0.037	1345 (74.0)	472 (26.0)	0.010
Immunocompromising condition	150 (0.2)	82 (54.7)	68 (45.3)	0.036	124 (82.7)	26 (17.3)	0.020

Abbreviations: ICU = intensive care unit; SMD = standardized mean difference

^a An absolute SMD >0.20 indicates a nonnegligible difference in variable distributions between hospitalizations for vaccinated versus unvaccinated encounters or for encounters with positive influenza test results versus negative influenza test results.

^b Other race defined as any one of the following responses: Asian, Hawaiian or other Pacific Islander, American Indian or Alaska Native, other, multiple races.

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Table 2.

Characteristics of acute respiratory illness-associated hospitalizations and emergency department / urgent care encounters in adults aged ≥ 18 years by influenza vaccination and test status.

		Influenza vaccination status			Influenza test result		
	Total (col %)	Unvaccinated (row %)	Vaccinated (row %)	SMD ^a	Negative (row %)	Positive (row %)	SMD ^a
Hospitalizations							
All hospitalizations	66828	34373	32455		61107	5721	
Influenza vaccination status							
Unvaccinated	34373 (51.4)	34373 (100.0)	0 (0.0)		30662 (89.2)	3711 (10.8)	0.300
Vaccinated	32455 (48.6)	0 (0.0)	32455 (100.0)		30445 (93.8)	2010 (6.2)	
Month of encounter							
October 2023	3261 (4.9)	2342 (71.8)	919 (28.2)	0.271	3215 (98.6)	46 (1.4)	0.602
November 2023	8807 (13.2)	5291 (60.1)	3516 (39.9)		8343 (94.7)	464 (5.3)	
December 2023	12072 (18.1)	6476 (53.6)	5596 (46.4)		10355 (85.8)	1717 (14.2)	
January 2024	12251 (18.3)	6155 (50.2)	6096 (49.8)		10687 (87.2)	1564 (12.8)	
February 2024	10340 (15.5)	5033 (48.7)	5307 (51.3)		9334 (90.3)	1006 (9.7)	
March 2024	10541 (15.8)	4896 (46.4)	5645 (53.6)		9910 (94.0)	631 (6.0)	
April 2024	9556 (14.3)	4180 (43.7)	5376 (56.3)		9263 (96.9)	293 (3.1)	
Sites							
Site A	3817 (5.7)	1789 (46.9)	2028 (53.1)	0.512	3447 (90.3)	370 (9.7)	0.171
Site B	6260 (9.4)	3951 (63.1)	2309 (36.9)		5637 (90.0)	623 (10.0)	
Site C	15215 (22.8)	6472 (42.5)	8743 (57.5)		14139 (92.9)	1076 (7.1)	
Site D	2144 (3.2)	1066 (49.7)	1078 (50.3)		2027 (94.5)	117 (5.5)	
Site E	11741 (17.6)	3818 (32.5)	7923 (67.5)		10859 (92.5)	882 (7.5)	
Site F	20825 (31.2)	13554 (65.1)	7271 (34.9)		18815 (90.3)	2010 (9.7)	
Site G	6826 (10.2)	3723 (54.5)	3103 (45.5)		6183 (90.6)	643 (9.4)	
Median age (Q1, Q3), years	72 (60, 81)	67 (55, 77)	76 (66, 83)		72 (61, 81)	67 (54, 78)	
Age group							
18–64 years	22088 (33.1)	15256 (69.1)	6832 (30.9)	0.513	19594 (88.7)	2494 (11.3)	0.239
≥ 65 years	44740 (66.9)	19117 (42.7)	25623 (57.3)		41513 (92.8)	3227 (7.2)	
Sex							
Female	35394 (53.0)	18183 (51.4)	17211 (48.6)	0.003	32214 (91.0)	3180 (9.0)	0.058
Male	31434 (47.0)	16190 (51.5)	15244 (48.5)		28893 (91.9)	2541 (8.1)	

		Influenza vaccination status			Influenza test result		
	Total (col %)	Unvaccinated (row %)	Vaccinated (row %)	SMD ^a	Negative (row %)	Positive (row %)	SMD ^a
Race/ethnicity							
White Non-Hispanic	43712 (65.4)	22176 (50.7)	21536 (49.3)	0.236	40245 (92.1)	3467 (7.9)	0.115
Black Non-Hispanic	7499 (11.2)	4852 (64.7)	2647 (35.3)		6738 (89.9)	761 (10.1)	
Other Non-Hispanic ^b	5673 (8.5)	2417 (42.6)	3256 (57.4)		5170 (91.1)	503 (8.9)	
Hispanic	8874 (13.3)	4188 (47.2)	4686 (52.8)		7991 (90.0)	883 (10.0)	
Unknown	1070 (1.6)	740 (69.2)	330 (30.8)		963 (90.0)	107 (10.0)	
Any medical condition	61189 (91.6)	30454 (49.8)	30735 (50.2)	0.222	56246 (91.9)	4943 (8.1)	0.183
Respiratory condition	32449 (48.6)	15376 (47.4)	17073 (52.6)	0.158	30046 (92.6)	2403 (7.4)	0.144
Non-respiratory condition	58024 (86.8)	28276 (48.7)	29748 (51.3)	0.282	53401 (92.0)	4623 (8.0)	0.181
Immunocompromising condition	14891 (22.3)	6721 (45.1)	8170 (54.9)	0.135	14039 (94.3)	852 (5.7)	0.207
ICU admission							
Yes	13468 (20.2)	7210 (53.5)	6258 (46.5)	0.041	12644 (93.9)	824 (6.1)	0.167
No	52983 (79.3)	27002 (51.0)	25981 (49.0)		48106 (90.8)	4877 (9.2)	
Unknown	377 (0.6)	161 (42.7)	216 (57.3)		357 (94.7)	20 (8.6)	
Invasive mechanical ventilation							
Yes	8133 (12.2)	4643 (57.1)	3490 (42.9)	0.188	7527 (92.5)	606 (7.5)	0.046
No	41874 (62.7)	18604 (44.4)	23270 (55.6)		38369 (91.6)	3505 (8.4)	
Unknown	16821 (25.2)	11126 (66.1)	5695 (33.9)		15211 (90.4)	1610 (9.6)	
In-hospital death							
Yes	4976 (7.4)	2473 (49.7)	2503 (50.3)	0.020	4786 (96.2)	190 (3.8)	0.198
No	61852 (92.6)	31900 (51.6)	29952 (48.4)		56321 (91.1)	5531 (8.9)	
Emergency department / urgent care encounters							
All encounters	200778	123790	76988		159885	40893	
Influenza vaccination status							
Unvaccinated	123790 (61.7)	123790 (100.0)	0 (0.0)		92519 (74.7)	31271 (25.3)	0.404
Vaccinated	76988 (38.3)	0 (0.0)	76988 (100.0)		67366 (87.5)	9622 (12.5)	
Month of encounter							
October 2023	8201 (4.1)	6328 (77.2)	1873 (22.8)	0.229	7802 (95.1)	399 (4.9)	0.570
November 2023	25799 (12.8)	17518 (67.9)	8281 (32.1)		22281 (86.4)	3518 (13.6)	
December 2023	43346 (21.6)	27772 (64.1)	15574 (35.9)		29578 (68.2)	13768 (31.8)	

		Influenza vaccination status			Influenza test result		
	Total (col %)	Unvaccinated (row %)	Vaccinated (row %)	SMD ^a	Negative (row %)	Positive (row %)	SMD ^a
January 2024	39815 (19.8)	24571 (61.7)	15244 (38.3)		29024 (72.9)	10791 (27.1)	
February 2024	30919 (15.4)	18506 (59.9)	12413 (40.1)		24608 (79.6)	6311 (20.4)	
March 2024	29140 (14.5)	16540 (56.8)	12600 (43.2)		25044 (85.9)	4096 (14.1)	
April 2024	23558 (11.7)	12555 (53.3)	11003 (46.7)		21548 (91.5)	2010 (8.5)	
Sites							
Site A	13675 (6.8)	8245 (60.3)	5430 (39.7)	0.437	10592 (77.5)	3083 (22.5)	0.246
Site B	32700 (16.3)	24310 (74.3)	8390 (25.7)		24372 (74.5)	8328 (25.5)	
Site C	43299 (21.6)	24105 (55.7)	19194 (44.3)		36951 (85.3)	6348 (14.7)	
Site D	8134 (4.1)	4581 (56.3)	3553 (43.7)		7104 (87.3)	1030 (12.7)	
Site E	56000 (27.9)	28791 (51.4)	27209 (48.6)		44326 (79.2)	11674 (20.8)	
Site F	27367 (13.6)	21174 (77.4)	6193 (22.6)		21374 (78.1)	5993 (21.9)	
Site G	19603 (9.8)	12584 (64.2)	7019 (35.8)		15166 (77.4)	4437 (22.6)	
Median age (Q1, Q3), years	51 (34, 69)	42 (30, 60)	66 (47, 77)		54 (35, 71)	42 (31, 59)	
Age group							
18–64 years	137380 (68.4)	100635 (73.3)	36745 (26.7)	0.749	103738 (75.5)	33642 (24.5)	0.402
≥65 years	63398 (31.6)	23155 (36.5)	40243 (63.5)		56147 (88.6)	7251 (11.4)	
Sex							
Female	120659 (60.1)	73753 (61.1)	46906 (38.9)	0.028	97042 (80.4)	23617 (19.6)	0.060
Male	80119 (39.9)	50037 (62.5)	30082 (37.5)		62843 (78.4)	17276 (21.6)	
Race/ethnicity							
White Non-Hispanic	104840 (52.2)	63354 (60.4)	41486 (39.6)	0.219	85359 (81.4)	19481 (18.6)	0.134
Black Non-Hispanic	20641 (10.3)	14820 (71.8)	5821 (28.2)		16390 (79.4)	4251 (20.6)	
Other Non-Hispanic ^b	20051 (10.0)	10406 (51.9)	9645 (48.1)		15997 (79.8)	4054 (20.2)	
Hispanic	49402 (24.6)	30847 (62.4)	18555 (37.6)		37765 (76.4)	11637 (23.6)	
Unknown	5844 (2.9)	4363 (74.7)	1481 (25.3)		4374 (74.8)	1470 (25.2)	
Any medical condition	66039 (32.9)	34218 (51.8)	31821 (48.2)	0.291	57641 (87.3)	8398 (12.7)	0.350
Respiratory condition	35631 (17.7)	18906 (53.1)	16725 (46.9)	0.167	31697 (89.0)	3934 (11.0)	0.291
Non-respiratory condition	42677 (21.3)	20330 (47.6)	22347 (52.4)	0.304	37154 (87.1)	5523 (12.9)	0.253

		Influenza vaccination status			Influenza test result		
	Total (col %)	Unvaccinated (row %)	Vaccinated (row %)	SMD ^a	Negative (row %)	Positive (row %)	SMD ^a
Immunocompromising condition	4420 (2.2)	1855 (42.0)	2565 (58.0)	0.120	3921 (88.7)	499 (11.3)	0.092

Abbreviations: ICU = intensive care unit; SMD = standardized mean difference

^a An absolute SMD >0.20 indicates a nonnegligible difference in variable distributions between hospitalizations for vaccinated versus unvaccinated encounters or for encounters with positive influenza test results versus negative influenza test results.

^b Other race defined as any one of the following responses: Asian, Hawaiian or other Pacific Islander, American Indian or Alaska Native, other, multiple races.