HHS Public Access

Author manuscript

Clin Infect Dis. Author manuscript; available in PMC 2024 March 21.

Published in final edited form as:

Clin Infect Dis. 2024 March 20; 78(3): 746–755. doi:10.1093/cid/ciad704.

Vaccine Effectiveness Against Pediatric Influenza-A–Associated Urgent Care, Emergency Department, and Hospital Encounters During the 2022–2023 Season: VISION Network

Katherine Adams[1], **Zachary A. Weber**[2], **Duck-Hye Yang**[2], **Nicola P. Klein**[3], **Malini B. DeSilva**[4], **Kristin Dascomb**[5], **Stephanie A. Irving**[6], **Allison L. Naleway**[6], **Suchitra Rao**[7], **Manjusha Gaglani**[8,9], **Brendan Flannery**[1], **Shikha Garg**[1], **Anupam B. Kharbanda**[10], **Shaun J. Grannis**[11,12], **Toan C. Ong**[13], **Peter J. Embi**[14], **Karthik Natarajan**[15,16], **Bruce Fireman**[3], **Ousseny Zerbo**[3], **Kristin Goddard**[3], **Julius Timbol**[3], **John R. Hansen**[3], **Nancy Grisel**[5], **Julie Arndorfer**[5], **Sarah W. Ball**[2], **Margaret M. Dunne**[2], **Lindsey Kirshner**[2], **Jessie R. Chung**[1], **Mark W. Tenforde**[1]

[1]Influenza Division, Centers for Disease Control and Prevention, Atlanta, Georgia, USA

[2]Department of Clinical Research, Westat, Rockville, Maryland, USA

[3]Kaiser Permanente Vaccine Study Center, Kaiser Permanente Northern California Division of Research, Oakland, California, USA

[4]Department of Research, HealthPartners Institute, Minneapolis, Minnesota, USA

[5]Division of Infectious Diseases and Clinical Epidemiology, Intermountain Healthcare, Salt Lake City, Utah, USA

[6]Department of Science Programs, Kaiser Permanente Center for Health Research, Portland, Oregon, USA

[7]Department of Pediatrics, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA

Correspondence: M. Tenforde, Influenza Division, Centers for Disease Control and Prevention, 1600 Clifton Road, Mailstop H24-7, Atlanta, GA 30329-4027 (pij6@cdc.gov).

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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 (CDC).

Potential conflicts of interest. N. P. K. reports research support from Sanofi Pasteur and Seqirus for unrelated adult influenza vaccine effectiveness studies, and from Pfizer, Merck, and GlaxoSmithKline for unrelated studies. S. R. received funds from GlaxoSmithKline. M. G. reports a research grant and contract for the CDC Ambulatory US Flu/COVID VE Network, a grant for HAIVEN Adult Inpatient Flu/COVID VE, a contract for SYNERGY FLU/COVID study, and subcontracts for the IVY COVID/FLU VE PHS project and RECOVER-PROTECT COVID Cohort studies. D.-H. Y., L. K., M. M. D., S. W. B., and Z. A. W. report payments made to Westat via CDC contract number 200-2019-F-06819. A. B. K., A. L. N., J. A., K. D., K. N., M. B. D., M. G., N. G., P. J. E., S. A. I, S. J. G., S. R., and T. C. O. report payments made to their institution by CDC via Westat. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

[8]Department of Pediatrics, Section of Pediatric Infectious Diseases, Baylor Scott & White Health and Baylor College of Medicine, Temple, Texas, USA

[9]Department of Medical Education, Texas A&M University College of Medicine, Temple, Texas, USA

[10]Department of Emergency Medicine, Children's Minnesota, Minneapolis, Minnesota, USA

[11]Center for Biomedical Informatics, Regenstrief Institute, Indianapolis, Indiana, USA

[12]School of Medicine, Indiana University, Indianapolis, Indiana, USA

[13]Department of Biomedical Informatics, University of Colorado Anschutz Medical Campus, Aurora, Colorado, USA

[14]Department of Biomedical Informatics, Vanderbilt University Medical Center, Nashville, Tennessee, USA

[15]Department of Biomedical Informatics, Columbia University Irving Medical Center, New York, New York, USA

[16]Medical Informatics Services, New York-Presbyterian Hospital, New York, New York, USA

Abstract

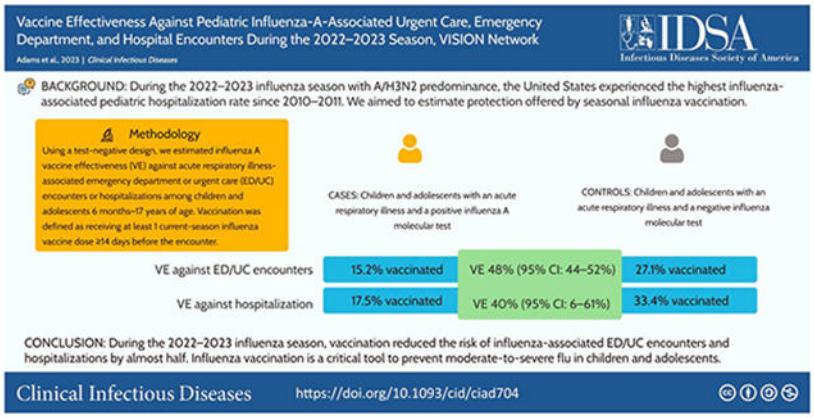
Background.—During the 2022–2023 influenza season, the United States experienced the highest influenza-associated pediatric hospitalization rate since 2010–2011. Influenza A/H3N2 infections were predominant.

Methods.—We analyzed acute respiratory illness (ARI)–associated emergency department or urgent care (ED/UC) encounters or hospitalizations at 3 health systems among children and adolescents aged 6 months–17 years who had influenza molecular testing during October 2022–March 2023. We estimated influenza A vaccine effectiveness (VE) using a test-negative approach. The odds of vaccination among influenza-A–positive cases and influenza-negative controls were compared after adjusting for confounders and applying inverse-propensity-to-be-vaccinated weights. We developed overall and age-stratified VE models.

Results.—Overall, 13 547 of 44 787 (30.2%) eligible ED/UC encounters and 263 of 1862 (14.1%) hospitalizations were influenza-A–positive cases. Among ED/UC patients, 15.2% of influenza-positive versus 27.1% of influenza-negative patients were vaccinated; VE was 48% (95% confidence interval [CI], 44–52%) overall, 53% (95% CI, 47–58%) among children aged 6 months–4 years, and 38% (95% CI, 30–45%) among those aged 9–17 years. Among hospitalizations, 17.5% of influenza-positive versus 33.4% of influenza-negative patients were vaccinated; VE was 40% (95% CI, 6–61%) overall, 56% (95% CI, 23–75%) among children ages 6 months–4 years, and 46% (95% CI, 2–70%) among those 5–17 years.

Conclusions.—During the 2022–2023 influenza season, vaccination reduced the risk of influenza-associated ED/UC encounters and hospitalizations by almost half (overall VE, 40–48%). Influenza vaccination is a critical tool to prevent moderate-to-severe influenza illness in children and adolescents.

Graphical Abstract



Keywords

influenza; pediatric; vaccine effectiveness; test-negative design

Seasonal influenza creates a substantial health burden among children and adolescents. Pediatric infections increase community and household transmission rates and can result in moderate and serious illness, particularly among children younger than 5 years of age or those with underlying medical conditions [1, 2]. During the 2022–2023 influenza season, the highest rate of pediatric influenza-associated hospitalizations since 2010–2011 was observed by the US Centers for Disease Control and Prevention (CDC) Influenza Hospitalization Surveillance Network [3]. Influenza-associated pediatric deaths reported to the CDC were also high during the 2022–2023 season, with 172 deaths reported as of 19 August 2023 [4, 5]. The 2022–2023 season was also characterized by unusually early activity and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and respiratory syncytial virus (RSV) co-circulation, which strained the US healthcare system [6-8].

Vaccination against seasonal influenza remains the most effective public health strategy to protect against influenza illness and severe complications and is recommended for nearly all children and adolescents starting at 6 months of age [9, 10]. Despite the documented benefits of seasonal influenza vaccination, pediatric vaccination has declined in the United States since the beginning of the coronavirus disease 2019 (COVID-19) pandemic [11]. Previous studies have shown that influenza vaccination can prevent influenza-associated symptomatic illnesses, outpatient visits, hospitalizations, critical illness, and deaths, but vaccine effectiveness (VE) varies by season and by match between vaccine and circulating strains [12-15]. During the 2022–2023 season, influenza A/H3N2 and A/H1N1pdm09 viruses predominated (70.8% and 29.2% of subtyped influenza A specimens reported by national public health laboratories, respectively), and circulating influenza viruses in the United States were antigenically similar to the influenza vaccine reference strains [5, 8].

To evaluate VE among children and adolescents aged 6 months–17 years during the 2022–2023 influenza season, we analyzed data from 3 large, integrated healthcare systems in the United States within the Virtual SARS-CoV-2, Influenza, and Other Respiratory Viruses Network (VISION Network), a multistate collaboration with the CDC.

METHODS

Setting and Design

Pediatric electronic health record (EHR) data were included from 55 hospitals and 107 emergency department (ED) or urgent care (UC) sites across 3 participating VISION partner healthcare systems: Kaiser Permanente Northern California, Intermountain Healthcare in Utah, and HealthPartners in Minnesota and Wisconsin. Methods used by the VISION Network to evaluate VE have been described [16]. This study protocol was reviewed and approved by Institutional Review Boards (IRBs) at participating sites or under a reliance agreement with the Westat IRB and by CDC.

A test-negative case-control study design was used to estimate seasonal influenza VE against influenza A virus illness among children and adolescents aged 6 months–17 years with acute respiratory illness (ARI)–associated ED/UC encounters or hospitalizations during the 2022–2023 influenza season. Influenza B viruses could not be assessed because of low levels of circulation during the season [5]. *International Classification of Diseases, 10th Revision* (ICD-10) discharge diagnosis codes were used to develop an ARI case definition, which included clinical diagnoses such as pneumonia or influenza, as well as signs and symptoms of ARI such as cough or shortness of breath (Supplementary Table 1). All eligible pediatric patients had an ARI-associated encounter with molecular testing for SARS-CoV-2 and influenza viruses within 10 days prior to or until 72 hours after the encounter. Influenza case-patients were defined as those with a positive influenza A molecular test, while influenza-negative patients were those with a negative test for influenza A and B.

Data Collection

Demographic and clinical data were extracted from EHRs using a standardized data dictionary. If a hospitalized patient was readmitted within 30 days of discharge or a repeat visit to an ED/UC occurred within 24 hours, these encounters were treated as a single event. Start dates varied by study setting due to low numbers of reported inpatient influenza cases. The ED/UC encounters were included at all sites starting on 16 October 2022 (ie, the beginning of the *Morbidity and Mortality Weekly Report* [MMWR] surveillance week occurring 2 weeks following the start of the US influenza season); hospitalizations were included starting on the date of the first influenza case in the study population at each site (date range = 19 October–6 November 2022) (Supplementary Table 2). Site- and setting-specific end dates used a threshold of when weekly influenza test positivity fell below 2%.

Study Population

Patients aged 6 months–17 years eligible to receive a seasonal influenza vaccine were included. Encounters were excluded if the patient did not receive both influenza and SARS-CoV-2 molecular tests within 10 days before or up to 72 hours after their ED/UC encounter or hospitalization date, if either test result was unknown or indeterminate, or if the patient tested positive for influenza B. Patients who received influenza vaccination 1–13 days prior to the index event date (ie, earliest date of most recent influenza test result or ED/UC encounter/hospital admission) were excluded from analysis. Encounters assigned an influenza-specific ICD-10 diagnostic code but which also had a negative influenza

molecular test were excluded because the influenza diagnosis occurred in the absence of laboratory confirmation. Additionally, patients with an ICD-10 code indicating COVID-19 (Supplementary Table 1) without molecular test confirmation or those with positive SARS-CoV-2 test results were excluded to reduce potential confounding due to correlation between influenza and COVID-19 vaccination decisions [17].

Vaccination Status Classification

Vaccination status was ascertained using EHR, state or local immunization information system, and claims data from the 2022–2023 influenza season. Patients were classified as vaccinated if they received 1 or more influenza vaccine doses beginning 1 August 2022, and at least 14 days prior to their index event date, and unvaccinated if no record of current season vaccination was found or if the vaccine administration date occurred after the index date. Since vaccination history prior to the 2022–2023 influenza season was not routinely available, we were unable to ascertain whether children aged 6 months–8 years were fully vaccinated [18].

Statistical Analysis

We calculated the number of weekly cases of influenza and percent positivity by site and care setting (ED/UC or hospitalization). Demographic characteristics, stratified by vaccination status and influenza test results, were described using frequencies and proportions for binary or categorical variables and medians and interquartile ranges (IQRs) for continuous variables. Standardized mean differences (SMDs) were reported to allow comparison between groups, with an SMD of 0.20 or greater indicating a nonnegligible difference in distribution [19]. To characterize patterns in vaccination coverage across study months, frequencies and proportions of vaccinated patients were calculated and stratified by influenza test results. Vaccine effectiveness was estimated by comparing the odds of 2022–2023 seasonal influenza vaccination among influenza-A–positive patients versus influenza-negative patients, calculated as VE = (1 – adjusted odds ratio [OR]) × 100%. ORs were generated using multivariable logistic regression, adjusted for patient age, study site, and calendar day. Natural cubic splines were used for age and calendar day. To balance baseline site, demographic, and underlying medical condition characteristics, inverse probability of treatment (ie, vaccination) weighting was performed using generalized boosted regression trees and truncated at the 99th percentile. Unadjusted and adjusted VE estimates are presented for each setting (ED/UC encounters and hospitalizations), along with 95% confidence intervals (CIs). Vaccine effectiveness was not examined by subtype (A/H3N2 vs A/H1N1pdm09) because subtype information was not available for most influenza-A–positive cases.

To explore whether different inclusion criteria changed VE estimates among young children, 2 sensitivity analyses were performed. First, inclusion criteria for patients younger than 2 years of age, who may present more often with nonrespiratory signs or symptoms of influenza, were expanded to include ICD-10 codes indicating fever and COVID-19–like illness (CLI) (eg, diarrhea, myalgia, and nausea/vomiting; full expanded ICD-10 CLI definition in Supplementary Table 1) [20]. Second, influenza-positive cases were restricted to those with influenza-specific ICD-10 discharge codes for influenza pneumonia or

influenza disease (Supplementary Table 1). This latter analysis was done to remove patients in whom influenza was not identified as a contributing diagnosis during the encounter using a more specific case definition. All analyses were performed using SAS version 9.4 (SAS Institute) or R 4.2.1 (R Foundation for Statistical Computing).

RESULTS

Epidemic Curves

Pediatric influenza A cases among both ED/UC encounters and hospitalizations at participating sites peaked during the week ending 10 December 2022, and remained high until late December (Supplementary Figure 1). Site-level influenza test percent positivity for ED/UC encounters dropped below 2% after 21 January 2023 and through 4 March 2023. Among hospitalizations at sites with sufficient data to ascertain trends, influenza test percent positivity dropped below 2% after 4 February 2023. Of 507 influenza-A–positive cases with information on subtype (all from a single site), 419 (82.6%) were A/H3N2 and 88 (17.4%) were A/H1N1pdm09 viruses.

Acute Respiratory Illness Diagnoses by Case Status

Among influenza-positive cases across care settings (ED/UC encounters and hospitalizations), the most common ARI discharge diagnosis codes included those for influenza disease (63.0%) and upper respiratory tract infection (32.2%) (Supplementary Table 3). Among influenza-negative patients, the most common discharge codes were for upper respiratory tract infection (52.7%) and acute respiratory signs and symptoms (26.6%).

Emergency Department/Urgent Care Encounter Characteristics and Vaccine Effectiveness

Of 62 207 pediatric ARI-associated ED/UC encounters, 56 898 (91.5%) occurred during periods of local influenza circulation (ie, where percent positivity among those tested for influenza was >2%). Of these encounters, 12 111 (21.3%) were excluded, most commonly due to lack of influenza molecular testing (n = 7311), having a negative influenza test result and a positive SARS-CoV-2 test result (n = 1833), and influenza vaccination 1–13 days before the index date (n = 1583) (Supplementary Figure 2).

A total of 44 787 eligible ED/UC encounters were included in the analysis; 13 547 (30.2%) were influenza A case-patients and 31 240 (69.8%) were influenza-negative patients (Table 1). Overall, 10 517 (23.5%) ED/UC encounters occurred in vaccinated patients; 15.2% of influenza-positive patients versus 27.1% of influenza-negative patients had been vaccinated; and median time since vaccination was 52 days (IQR, 33–75 days). The proportion of vaccinated influenza-negative ED/UC encounter patients ranged across sites from 12.8% to 16.0% within the first week of data capture and increased to 33.3–44.1% during the final week, and was higher in 0–4-year-olds than in 5–17-year-olds (Supplementary Table 4). Among 6848 (65.1%) vaccinated patients with a documented influenza vaccine product, 95.6% received egg-based standard-dose quadrivalent inactivated influenza vaccine (IIV4), 2.0% received a live attenuated influenza vaccine (LAIV), and 2.4% received cell culture–based IIV4. The median patient age was 4 years (IQR, 2–8 years), with vaccination coverage highest in patients aged 6 months–4 years (27.9%) and lowest in those aged

9–17 years (17.9%). Of ED/UC encounters, 53.2% occurred in male patients, 56.5% of patients were White, and 69.9% were non-Hispanic. Of ED/UC patients, 9.8% had an underlying respiratory or non-respiratory medical condition, and 0.4% had a likely immunocompromising condition documented at the index encounter.

The adjusted VE against influenza-A–associated pediatric ED/UC encounters was 48% (95% CI, 44–52%) overall (Figure 1). Vaccine effectiveness was higher among younger patients: 53% (95% CI, 47–58%) for those aged 6 months–4 years, 46% (95% CI, 38–53%) among 5–8-year-olds, and 38% (95% CI, 30–45%) among 9–17-year-olds. Expanding the inclusion criteria to nonrespiratory signs and symptoms for patients aged 6 months–2 years or restricting influenza-positive patients to those with influenza pneumonia or influenza disease discharge codes produced similar VE estimates as the primary analysis (Supplementary Figures 4 and 5).

Hospitalizations Characteristics and Vaccine Effectiveness

Of 2632 pediatric ARI-associated hospitalizations identified, 2048 (77.8%) occurred during periods of local influenza circulation at participating VISION sites (Supplementary Figure 3). Of these, 186 (9.1%) were excluded from the primary analysis, most frequently due to influenza vaccination 1–13 days before the index date (n = 63), having a positive COVID-19 test result (n = 53), and having a negative influenza test result but an influenza disease/pneumonia or COVID-19 pneumonia diagnosis (n = 37).

From 19 October 2022 to 18 February 2023, 1862 ARI-associated hospitalizations were eligible for the analysis, including 263 (14.1%) influenza A case-patients and 1599 (85.9%) influenza-negative patients (Table 2). Of influenza-associated hospitalizations, 31.1% occurred among vaccinated patients (17.5% of influenza case-patients vs 33.4% of influenza-negative patients had been vaccinated), with a median time since vaccination of 54 days (IQR, 36–80 days). The proportion of vaccinated influenza-negative hospitalized pediatric patients ranged across sites from 11.7% to 22.3% during the first week of data capture and expanded to 36.4–66.7% during the last week (Supplementary Table 5). Among 397 (68.4%) patients with a documented influenza vaccine product, 95.7% received egg-based standard dose IIV4, 0.5% received LAIV, and 3.8% received cell culture–based IIV4. The median age was 2 years (IQR, 1–5 years), with the highest proportion vaccinated among children aged 6 months–4 years (34.2%) and lowest among those aged 9–17 years (22.3%). Of hospitalizations, 53.1% occurred in males, 59.2% were White, 75.1% were non-Hispanic, and a majority had 1 or more underlying medical conditions (57.4%). Among 67 (3.6%) hospitalized patients who received invasive mechanical ventilation, 11 (16.4%) tested positive for influenza and 21 (31.3%) were vaccinated. Among 207 (11.1%) hospitalized patients who were admitted to an intensive care unit, 28 (13.5%) tested positive for influenza and 76 (36.7%) were vaccinated. Among 7 (<1%) patients who died in the hospital, 1 patient (14.3%) tested positive for influenza and 3 patients (42.9%) were vaccinated.

The overall adjusted VE against influenza-A–associated pediatric hospitalizations was 40% (95% CI, 6–61%) (Figure 2). In models stratified by age group, the VE point estimate was higher among patients aged 6 months–4 years (56%; 95% CI, 23–75%) versus patients aged 5–17 years (46%; 95% CI, 2–70%), although estimate precision was limited and CIs

over-lapped across age groups. Both sensitivity analyses produced similar estimates to the primary analysis but with limited precision (Supplementary Figures 6 and 7).

DISCUSSION

During the 2022–2023 season with predominant vaccine-matched influenza A/H3N2 virus circulation, seasonal influenza vaccination reduced the risk of influenza-A–associated ED/UC visits and hospitalizations by almost half across ED/UC (48% VE) and inpatient (40% VE) settings. VISION Network VE estimates against both influenza-A–associated ED/UC encounters and hospitalizations in pediatric age groups were similar to early-season estimates from other US-based networks for the 2022–2023 influenza season [21, 22]. VISION Network estimates also fall within the range of estimates against ED and/or UC encounters (46–56%) and hospitalizations and critical illness (41–63%) observed during recent seasons [14, 23-26]. However, despite the protection offered by seasonal influenza vaccines, vaccination coverage among children and adolescents in our analysis was relatively low. These findings align with other data finding a low proportion of children and adolescents vaccinated during the 2022–2023 season compared with prior seasons [27, 28]. To maximize the clinical and public health benefits of vaccination, continued efforts to optimize influenza vaccine uptake among children and adolescents are needed.

Vaccine effectiveness against influenza-A–associated ED/UC encounters tended to be higher among younger children (6 months–4 years) than older children and adolescents (9–17 years). These results are notable considering our analysis of a single dose of current season influenza vaccine and low circulation of influenza during the past 2 seasons due to the COVID-19 pandemic. Prior exposure to influenza viruses among very young children may have been limited and reduced adaptive immune responses or influenced VE by other mechanisms [29-31]. While point estimates of VE against influenza-associated hospitalizations were higher in younger versus older age groups, this comparison was limited due to a smaller sample size.

Both influenza VE and coverage directly impact illnesses, medical visits, and hospitalizations averted by vaccination programs [15]. Lower vaccine coverage diminishes the potential vaccine impact on disease burden. Children and adolescents also experience high influenza attack rates and can accelerate disease transmission among households and close contacts [1, 2]. Pediatric influenza can additionally result in substantial burden through school absenteeism, economic and productivity loss for caregivers, and direct medical expenses (eg, medical visits, over-the-counter and prescription medications) [32-35]. The atypically early start of the 2022–2023 influenza season may have resulted in lower observed vaccine coverage, as activity started and peaked before many children and adolescents may have had an opportunity to get vaccinated. Vaccination during July and August can be considered for children needing 1 dose of vaccine; children aged 6 months–8 years requiring 2 doses to be fully vaccinated should receive the first dose as soon as possible, including July and August [10, 36].

This analysis is subject to several limitations. First, we were unable to assess VE by influenza A virus subtype (A/H3N2 or A/H1N1pdm09) because VISION relies on clinician-

driven testing and influenza subtype was not included in most molecular assays. Second, as influenza testing is clinician-driven and may be influenced by clinical presentation, illness severity, and prior testing, variation in testing practices across VISION sites may have occurred. To mitigate this bias, we used a specific definition of ARI for eligibility, and all included patients had both influenza and SARS-CoV-2 testing performed. Among pediatric ARI encounters, 87.2% of ED/UC encounters and 98.8% of hospitalizations included molecular influenza testing, suggesting adequate capture of influenza using our ARI definition. Furthermore, our sensitivity analyses using different inclusion criteria produced estimates similar to our primary analysis. Third, selection bias may have been introduced if care-seeking differs between those with influenza-associated ARI and those with non-influenza ARI. However, others have found that this potential bias in influenza VE test-negative studies using an ARI definition is unlikely to be meaningful [37]. Fourth, influenza vaccination history across seasons was not routinely collected for the determination of partially or fully vaccinated children. However, our VE estimates for younger age groups are similar to other studies of known fully vaccinated pediatric patients [26, 38]. Additionally, the 2022–2023 influenza season began in early October 2022, reducing the opportunity for young children to receive 2 doses of vaccine 4 weeks apart and be fully vaccinated 2 weeks past the second dose. Fifth, although we captured encounters from geographically diverse health systems across 4 states, patients included in this analysis may not represent the overall US population and patients seeking care in other health systems.

CONCLUSIONS

In this analysis, receipt of the 2022–2023 seasonal influenza vaccine reduced the risk of influenza-A–associated ED or UC visits and hospitalizations by almost half. Influenza vaccination remains a critical public health tool for the prevention and mitigation of serious illness among children and adolescents and can reduce strain on healthcare resources, especially during periods of high co-circulation of influenza, SARS-CoV-2, RSV, and other respiratory viruses.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Financial support.

This work was supported by Centers for Disease Control and Prevention (contract number 75D30120C07986 to Westat, Inc, and contract number 75D30120C07765 to Kaiser Foundation Hospitals).

References

1. Committee on Infectious Diseases of the American Academy of Pediatrics. Recommendations for prevention and control of influenza in children, 2022–2023. Pediatrics 2022; 150:e2022059275. [PubMed: 36065750]
2. Grohskopf LA, Blanton LH, Ferdinands JM, 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; 71:1–28.

3. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases. FluView interactive: laboratory-confirmed influenza hospitalizations, 2023. Available at: https://gis.cdc.gov/GRASP/Fluview/FluHospRates.html. Accessed 9 May 2023.
4. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases (NCIRD). Pediatric flu deaths top 100 this season; most unvaccinated, 2023. Available at: https://www.cdc.gov/flu/spotlights/2022-2023/pediatric-flu-deaths.htm. Accessed 10 February 2023.
5. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases (NCIRD). Weekly U.S. Influenza Surveillance Report, 2023. Available at: https://www.cdc.gov/flu/weekly/index.htm. Accessed 19 August 2023.
6. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases. RESP-NET interactive dashboard, 2023. Available at: https://www.cdc.gov/surveillance/resp-net/dashboard.html. Accessed 9 May 2023.
7. US Department of Health and Human Services (HHS). Letter to U.S. governors from HHS Secretary Xavier Becerra on COVID-19, flu, and RSV resources. Available at: https://www.hhs.gov/about/news/2022/12/02/letter-us-governors-from-hhs-secretary-xavier-becerra-covid-19-flu-rsv-resources.html. Accessed 2 December 2022.
8. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases. FluView summary ending on April 22, 2023. Available at: https://www.cdc.gov/flu/weekly/weeklyarchives2022-2023/week16.htm. Accessed 9 May 2023.
9. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases. Flu shots for children, 2019. Available at: https://www.cdc.gov/vaccines/parents/diseases/flu.html. Accessed 2 August 2019.
10. Committee on Infectious Diseases. Recommendations for prevention and control of influenza in children, 2023–2024. Pediatrics 2023; 152:e2023063772. [PubMed: 37641879]
11. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases (NCIRD). Weekly flu vaccination dashboard, 2023. Available at: https://www.cdc.gov/flu/fluvaxview/dashboard/vaccination-dashboard.html. Accessed 28 April 2023.
12. Hood N, Flannery B, Gaglani M, et al. Influenza vaccine effectiveness among children: 2011–2020. Pediatrics 2023; 151:e2022059922. [PubMed: 36960655]
13. Boddington NL, Pearson I, Whitaker H, Mangtani P, Pebody RG. Effectiveness of influenza vaccination in preventing hospitalization due to influenza in children: a systematic review and meta-analysis. Clin Infect Dis 2021; 73:1722–32. [PubMed: 33772586]
14. Olson SM, Newhams MM, Halasa NB, et al. Vaccine effectiveness against life-threatening influenza illness in US children. Clin Infect Dis 2022; 75:230–8. [PubMed: 35024795]
15. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases (NCIRD). Past seasons estimated influenza disease burden averted by vaccination, 2023. Available at: https://www.cdc.gov/flu/vaccines-work/past-burden-averted-est.html. Accessed 2 February 2023.
16. Thompson MG, Stenehjem E, Grannis S, et al. Effectiveness of COVID-19 vaccines in ambulatory and inpatient care settings. N Engl J Med 2021; 385:1355–71. [PubMed: 34496194]
17. 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:e564–71. [PubMed: 35325923]
18. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases (NCIRD). Seasonal influenza vaccine dosage & administration, 2020. Available at: https://www.cdc.gov/flu/about/qa/vaxadmin.htm. Accessed 16 November 2020.
19. Cohen J. Statistical power analysis for the behavioral sciences. New York: Academic Press, 2013.
20. Uyeki TM, Bernstein HH, Bradley JS, 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; 68:895–902. [PubMed: 30834445]
21. Centers for Disease Control and Prevention, Advisory Committee on Immunization Practices. Preliminary 2022–23 influenza vaccine effectiveness: CDC networks, 2023. Available at: https://www.cdc.gov/vaccines/acip/meetings/slides-2023-02-22-24.html. Accessed 9 May 2023.

22. McLean HQ, Petrie JG, Hanson KE, et al. Interim estimates of 2022–23 seasonal influenza vaccine effectiveness—Wisconsin, October 2022–February 2023. MMWR Morb Mortal Wkly Rep 2023; 72:201–5. [PubMed: 36821715]
23. Campbell AP, Ogokeh C, Lively JY, et al. Vaccine effectiveness against pediatric influenza hospitalizations and emergency visits. Pediatrics 2020; 146:e20201368. [PubMed: 33020249]
24. Campbell AP, Ogokeh C, Weinberg GA, et al. Effect of vaccination on preventing influenza-associated hospitalizations among children during a severe season associated with B/Victoria viruses, 2019–2020. Clin Infect Dis 2021; 73:e947–54. [PubMed: 33502489]
25. Sahni LC, Naioti EA, Olson SM, et al. Sustained within-season vaccine effectiveness against influenza-associated hospitalization in children: evidence from the New Vaccine Surveillance Network, 2015–2016 through 2019–2020. Clin Infect Dis 2023; 76:e1031–9. [PubMed: 35867698]
26. Feldstein LR, Ogokeh C, Rha B, et al. Vaccine effectiveness against influenza hospitalization among children in the United States, 2015–2016. J Pediatric Infect Dis Soc 2021; 10:75–82. [PubMed: 32108879]
27. White EB, O'Halloran A, Sundaresan D, et al. High influenza incidence and disease severity among children and adolescents aged <18 years—United States, 2022–23 season. MMWR Morb Mortal Wkly Rep 2023; 72:1108–14. [PubMed: 37824430]
28. Irving SA, Groom HC, Belongia EA, et al. Influenza vaccination coverage among persons ages six months and older in the Vaccine Safety Datalink in the 2017–18 through 2022–23 influenza seasons. Vaccine 2023; 41:7138–7146. doi:10.1016/j.vaccine.2023.10.023 [PubMed: 37866991]
29. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases (NCIRD). 2020–2021 Flu season summary, 2021. Available at: https://www.cdc.gov/flu/season/faq-flu-season-2020-2021.htm. Accessed 20 October 2023.
30. Centers for Disease Control and Prevention, National Center for Immunization and Respiratory Diseases (NCIRD). 2021–2022 Flu season summary, 2023. Available at: https://www.cdc.gov/flu/season/faq-flu-season-2021-2022.htm. Accessed 17 July 2023.
31. Sakleshpur S, Steed AL. Influenza: toward understanding the immune response in the young. Front Pediatr 2022; 10:953150. [PubMed: 36061377]
32. McLean HQ, Peterson SH, King JP, Meece JK, Belongia EA. School absenteeism among school-aged children with medically attended acute viral respiratory illness during three influenza seasons, 2012–2013 through 2014–2015. Influenza Other Respir Viruses 2017; 11:220–9. [PubMed: 27885805]
33. Li S, Leader S. Economic burden and absenteeism from influenza-like illness in healthy households with children (5–17 years) in the US. Respir Med 2007; 101:1244–50. [PubMed: 17156991]
34. Ortega-Sanchez IR, Molinari NA, Fairbrother G, et al. Indirect, out-of-pocket and medical costs from influenza-related illness in young children. Vaccine 2012; 30: 4175–81. [PubMed: 22546332]
35. Putri W, Muscatello DJ, Stockwell MS, Newall AT. Economic burden of seasonal influenza in the United States. Vaccine 2018; 36:3960–6. [PubMed: 29801998]
36. Fiore AE, Shay DK, Broder K, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP), 2009. MMWR Recomm Rep 2009; 58:1–52.
37. Jackson ML, Phillips CH, Benoit J, et al. The impact of selection bias on vaccine effectiveness estimates from test-negative studies. Vaccine 2018; 36:751–7. [PubMed: 29254838]
38. Chung JR, Flannery B, Gaglani M, et al. Patterns of influenza vaccination and vaccine effectiveness among young US children who receive outpatient care for acute respiratory tract illness. JAMA Pediatr 2020; 174:705–13. [PubMed: 32364599]

Group	No. of vaccinated influenza-positive case patients/total No. cases (%)	No. of vaccinated influenza-negative patients/total No. controls (%)	Unadjusted VE (95% CI)	Adjusted VE (95% CI)[a]
All pediatric ED/UC encounters	2058/13547 (15.2)	8459/31240 (27.1)	52 (49–54)	48 (44–52)
Age 6 months-4 years	701/3971 (17.7)	5874/19602 (30.0)	50 (45–54)	53 (47–58)
Age 5-8 years	586/4099 (14.3)	1365/5979 (22.8)	44 (37–49)	46 (38–53)
Age 9-17 years	771/5477 (14.1)	1220/5659 (21.6)	40 (34–46)	38 (30–45)

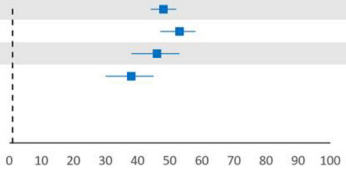


Figure 1.

Influenza VE against influenza-A–associated ED or UC visits among children and adolescents 6 months–17 years of age, October 2022–March 2023. Abbreviations: CI, confidence interval; ED, emergency department; UC, urgent care; VE, vaccine effectiveness. [a]Adjusted for age (natural cubic spline), study site, and date of encounter (natural cubic splines) and applied inverse-probability-to-be-vaccinated weights.

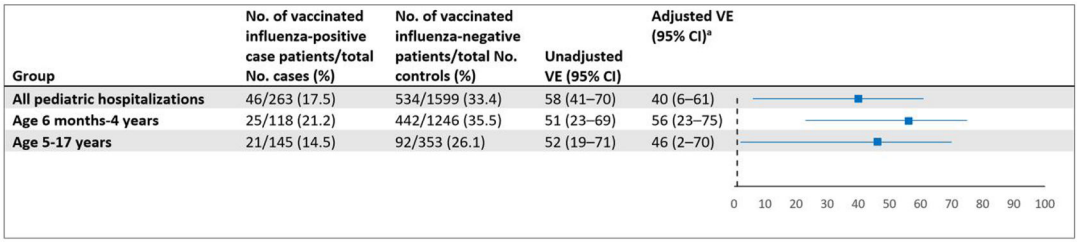


Figure 2.

Influenza VE against influenza-A–associated hospitalizations among children and adolescents 6 months–17 years of age, October 2022–February 2023. Abbreviations: CI, confidence interval; VE, vaccine effectiveness. [a]Adjusted for age (natural cubic spline), study site, and date of encounter (natural cubic splines) and applied inverse-probability-to-be-vaccinated weights.

Clin Infect Dis. Author manuscript; available in PMC 2024 March 21.

Table 1.

Characteristics of Emergency Department or Urgent Care Encounters With Acute Respiratory Illness Among Children and Adolescents 6 Months–17 Years of Age by Influenza Vaccination Status and Influenza Test Result, October 2022–March 2023

		Influenza Vaccination Status			Influenza Test Result		
Characteristic	**Total, No. (Col. %)**	**Unvaccinated, No. (Row %)**	**Vaccinated, No. (Row %)**	**SMD**	**Negative, No. (Row %)**	**Positive, No. (Row %)**	**SMD**
All ED/UC events	44 787	34 270 (76.5)	10 517 (23.5)	…	31 240 (69.8)	13 547 (30.2)	…
Influenza vaccination status							
Unvaccinated	34 270 (76.5)	34 270 (100.0)	0 (0.0)	…	22 781 (66.5)	11 489 (33.5)	0.294
Vaccinated	10 517 (23.5)	0 (0.0)	10 517 (100.0)	…	8459 (80.4)	2058 (19.6)	…
Median days since vaccination (IQR)	52 (33, 75)		52 (33, 75)	…	51 (32, 77)	52 (35, 70)	…
Vaccine type							
Egg-based standard dose IIV4	6545 (62.2)	0 (0.0)	6545 (100.0)	…	5224 (79.8)	1321 (20.2)	0.139
LAIV	138 (1.3)	0 (0.0)	138 (100.0)	…	88 (63.8)	50 (36.2)	…
Cell culture–based IIV4	165 (1.6)	0 (0.0)	165 (100.0)	…	124 (75.2)	41 (24.8)	…
Unknown/missing	3669 (34.9)	0 (0.0)	3669 (100.0)	…	3023 (82.4)	646 (17.6)	…
Month of encounter							
October 2022	4652 (10.4)	4005 (86.1)	647 (13.9)	0.314	4287 (92.2)	365 (7.8)	0.818
November 2022	17 375 (38.8)	13 882 (79.9)	3493 (20.1)	…	12 140 (69.9)	5235 (30.1)	…
December 2022	14 991 (33.5)	11 187 (74.6)	3804 (25.4)	…	7798 (52.0)	7193 (48.0)	…
January 2023	4750 (10.6)	3174 (66.8)	1576 (33.2)	…	4099 (86.3)	651 (13.7)	…
February 2023	2684 (6.0)	1798 (67.0)	886 (33.0)	…	2590 (96.5)	94 (3.5)	…
March 2023	335 (0.7)	224 (66.9)	111 (33.1)	…	326 (97.3)	9 (2.7)	…
Sites							
Site 1	3773 (8.4)	2929 (77.6)	844 (22.4)	0.023	2142 (56.8)	1631 (43.2)	0.263
Site 2	23 762 (53.1)	18 207 (76.6)	5555 (23.4)	…	17 704 (74.5)	6058 (25.5)	…
Site 3	17 252 (38.5)	13 134 (76.1)	4118 (23.9)	…	11 394 (66.0)	5858 (34.0)	…
Median age (IQR), y	4 (2, 8)	5 (2, 9)	3 (1, 7)	…	3 (1, 6)	7 (4, 11)	…
Age group							
6 m–4 y	23 573 (52.6)	16 998 (72.1)	6575 (27.9)	0.264	19 602 (83.2)	3971 (16.8)	0.724
5–8 y	10 078 (22.5)	8127 (80.6)	1951 (19.4)	…	5979 (59.3)	4099 (40.7)	…
9–17 y	11 136 (24.9)	9145 (82.1)	1991 (17.9)	…	5659 (50.8)	5477 (49.2)	…

Characteristic	Total, No. (Col. %)	Influenza Vaccination Status			Influenza Test Result		
		Unvaccinated, No. (Row %)	Vaccinated, No. (Row %)	SMD	Negative, No. (Row %)	Positive, No. (Row %)	SMD
Sex							
Female	20 943 (46.8)	16 134 (77.0)	4809 (23.0)	0.027	14 487 (69.2)	6456 (30.8)	0.026
Male	23 844 (53.2)	18 136 (76.1)	5708 (23.9)	…	16 753 (70.3)	7091 (29.7)	…
Race							
American or Alaska Indian	397 (0.9)	320 (80.6)	77 (19.4)	0.240	304 (76.6)	93 (23.4)	0.175
Asian	3451 (7.7)	2231 (64.6)	1220 (35.4)	…	2399 (69.5)	1052 (30.5)	…
Black	3337 (7.5)	2854 (85.5)	483 (14.5)	…	2019 (60.5)	1318 (39.5)	…
Hawaiian or Pacific Islander	1042 (2.3)	839 (80.5)	203 (19.5)	…	777 (74.6)	265 (25.4)	…
Multiracial	1046 (2.3)	786 (75.1)	260 (24.9)	…	721 (68.9)	325 (31.1)	…
White	25 312 (56.5)	19 195 (75.8)	6117 (24.2)	…	18 232 (72.0)	7080 (28.0)	…
Other	624 (1.4)	485 (77.7)	139 (22.3)	…	350 (56.1)	274 (43.9)	…
Unknown	9578 (21.4)	7560 (78.9)	2018 (21.1)	…	6438 (67.2)	3140 (32.8)	…
Ethnicity							
Hispanic	13 489 (30.1)	10 752 (79.7)	2737 (20.3)	0.118	9192 (68.1)	4297 (31.9)	0.05
Non-Hispanic	31 298 (69.9)	23 518 (75.1)	7780 (24.9)	…	22 048 (70.4)	9250 (29.6)	…
Underlying medical condition[a]							
Yes	4402 (9.8)	3243 (73.7)	1159 (26.3)	0.051	3524 (80.1)	878 (19.9)	0.169
No	40 385 (90.2)	31 027 (76.8)	9358 (23.2)	…	27 716 (68.6)	12 669 (31.4)	…
Respiratory condition[a]							
Yes	3353 (7.5)	2477 (73.9)	876 (26.1)	0.041	2815 (84.0)	538 (16.0)	0.206
No	41 434 (92.5)	31 793 (76.7)	9641 (23.3)	…	28 425 (68.6)	13 009 (31.4)	…
Nonrespiratory condition[a]							
Yes	1464 (3.3)	1022 (69.8)	442 (30.2)	0.066	1089 (74.4)	375 (25.6)	0.041
No	43 323 (96.7)	33 248 (76.7)	10 075 (23.3)	…	30 151 (69.6)	13 172 (30.4)	…
Immunocompromising condition[b]							
Yes	170 (0.4)	105 (61.8)	65 (38.2)	0.046	151 (88.8)	19 (11.2)	0.062
No	44 617 (99.6)	34 165 (76.6)	10 452 (23.4)	…	31 089 (69.7)	13 528 (30.3)	…

Abbreviations: Col., column; ED, emergency department; IIV4, quadrivalent inactivated influenza vaccine; IQR, interquartile range; LAIV, live attenuated influenza vaccine; SMD, standardized mean difference; UC, urgent care.

[a] Underlying medical conditions include respiratory (asthma, chronic obstructive pulmonary disease, apnea, and other pulmonary conditions) and nonrespiratory underlying conditions (cardiovascular, cerebrovascular, neurological, musculoskeletal, hematologic, endocrine/metabolic, renal, gastrointestinal, hepatic, clinical obesity, clinical underweight, premature birth, developmental delays, and technology dependence).

[b] Immunocompromising conditions include hematological malignancy, solid malignancy, organ transplant, rheumatologic/inflammatory disorders, and other intrinsic immune conditions or immunodeficiency.

Table 2.

Characteristics of Hospitalizations With Acute Respiratory Illness Among Children and Adolescents 6 Months–17 Years of Age by Influenza Vaccination Status and Influenza Test Result, October 2022–February 2023

		Influenza Vaccination Status			Influenza Test Result		
Characteristic	**Total, No. (Col. %)**	**Unvaccinated, No. (Row %)**	**Vaccinated, No. (Row %)**	**SMD**	**Negative, No. (Row %)**	**Positive, No. (Row %)**	**SMD**
All hospitalizations	1862	1282 (68.9)	580 (31.1)	…	1599 (85.9)	263 (14.1)	…
Influenza vaccination status							
Unvaccinated	1282 (68.9)	1282 (100.0)	0 (0.0)	…	1065 (83.1)	217 (16.9)	0.371
Vaccinated	580 (31.1)	0 (0.0)	580 (100.0)	…	534 (92.1)	46 (7.9)	…
Median days since vaccination (IQR)	54 (36, 80)	…	54 (36, 80)	…	54 (35, 80)	56 (41, 74)	…
Vaccine type							
Egg-based standard dose IIV4	380 (65.5)	0 (0.0)	380 (100.0)	…	347 (91.3)	33 (8.7)	0.165
LAIV	2 (0.3)	0 (0.0)	2 (100.0)	…	2 (100.0)	0 (0.0)	…
Cell culture–based IIV4	15 (2.6)	0 (0.0)	15 (100.0)	…	14 (93.3)	1 (6.7)	…
Unknown/missing	183 (31.6)	0 (0.0)	183 (100.0)	…	171 (93.4)	12 (6.6)	…
Month of encounter							
October 2022	67 (3.6)	49 (73.1)	18 (26.9)	0.267	62 (92.5)	5 (7.5)	0.732
November 2022	751 (40.3)	559 (74.4)	192 (25.6)	…	673 (89.6)	78 (10.4)	…
December 2022	606 (32.5)	410 (67.7)	196 (32.3)	…	449 (74.1)	157 (25.9)	…
January 2023	327 (17.6)	203 (62.1)	124 (37.9)	…	306 (93.6)	21 (6.4)	…
February 2023	111 (6.0)	61 (55.0)	50 (45.0)	…	109 (98.2)	2 (1.8)	…
Sites							
Site 1	20 (1.1)	15 (75.0)	5 (25.0)	0.205	14 (70.0)	6 (30.0)	0.133
Site 2	1088 (58.4)	788 (72.4)	300 (27.6)	…	944 (86.8)	144 (13.2)	…
Site 3	754 (40.5)	479 (63.5)	275 (36.5)	…	641 (85.0)	113 (15.0)	…
Median age (IQR), y	2 (1, 5)	3 (1, 5)	2 (1, 4)	…	2 (1, 4)	5 (2, 9)	…
Age group							
6 m–4 y	1364 (73.3)	897 (65.8)	467 (34.2)	0.246	1246 (91.3)	118 (8.7)	0.731
5–8 y	296 (15.9)	228 (77.0)	68 (23.0)	…	220 (74.3)	76 (25.7)	…
9–17 y	202 (10.8)	157 (77.7)	45 (22.3)	…	133 (65.8)	69 (34.2)	…
Sex							

Characteristic	Total, No. (Col. %)	Influenza Vaccination Status			Influenza Test Result		
		Unvaccinated, No. (Row %)	Vaccinated, No. (Row %)	SMD	Negative, No. (Row %)	Positive, No. (Row %)	SMD
Female	873 (46.9)	596 (68.3)	277 (31.7)	0.025	751 (86.0)	122 (14.0)	0.012
Male	989 (53.1)	686 (69.4)	303 (30.6)	…	848 (85.7)	141 (14.3)	…
Race							
American or Alaska Indian	20 (1.1)	14 (70.0)	6 (30.0)	0.298	17 (85.0)	3 (15.0)	0.145
Asian	176 (9.5)	92 (52.3)	84 (47.7)	…	157 (89.2)	19 (10.8)	…
Black	99 (5.3)	82 (82.8)	17 (17.2)	…	84 (84.8)	15 (15.2)	…
Hawaiian or Pacific Islander	64 (3.4)	48 (75.0)	16 (25.0)	…	52 (81.2)	12 (18.8)	…
Multiracial	50 (2.7)	40 (80.0)	10 (20.0)	…	42 (84.0)	8 (16.0)	…
White	1103 (59.2)	764 (69.3)	339 (30.7)	…	949 (86.0)	154 (14.0)	…
Other	5 (0.3)	4 (80.0)	1 (20.0)	…	5 (100.0)	0 (0.0)	…
Unknown	345 (18.5)	238 (69.0)	107 (31.0)	…	293 (84.9)	52 (15.1)	…
Ethnicity							
Hispanic	464 (24.9)	330 (71.1)	134 (28.9)	0.061	386 (83.2)	78 (16.8)	0.125
Non-Hispanic	1398 (75.1)	952 (68.1)	446 (31.9)	…	1213 (86.8)	185 (13.2)	…
Underlying medical condition[a]							
Yes	1069 (57.4)	718 (67.2)	351 (32.8)	0.092	927 (86.7)	142 (13.3)	0.08
No	793 (42.6)	564 (71.1)	229 (28.9)	…	672 (84.7)	121 (15.3)	…
Respiratory condition[a]							
Yes	911 (48.9)	622 (68.3)	289 (31.7)	0.026	802 (88.0)	109 (12.0)	0.176
No	951 (51.1)	660 (69.4)	291 (30.6)	…	797 (83.8)	154 (16.2)	…
Nonrespiratory condition[a]							
Yes	361 (19.4)	223 (61.8)	138 (38.2)	0.159	298 (82.5)	63 (17.5)	0.13
No	1501 (80.6)	1059 (70.6)	442 (29.4)	…	1301 (86.7)	200 (13.3)	…
Immunocompromising condition[b]							
Yes	60 (3.2)	29 (48.3)	31 (51.7)	0.162	53 (88.3)	7 (11.7)	0.038
No	1802 (96.8)	1253 (69.5)	549 (30.5)	…	1546 (85.8)	256 (14.2)	…
Invasive mechanical ventilation							
Yes	67 (3.6)	46 (68.7)	21 (31.3)	0.002	56 (83.6)	11 (16.4)	0.035
Unvaccinated	…	…	…	…	37 (80.4)	9 (19.6)	0.365

Characteristic	Total, No. (Col. %)	Influenza Vaccination Status			Influenza Test Result		
		Unvaccinated, No. (Row %)	Vaccinated, No. (Row %)	SMD	Negative, No. (Row %)	Positive, No. (Row %)	SMD
Vaccinated	…	…	…	…	19 (90.5)	2 (9.5)	…
No	1795 (96.4)	1236 (68.9)	559 (31.1)	…	1543 (86.0)	252 (14.0)	…
Unvaccinated	…	…	…	…	1028 (83.2)	208 (16.8)	0.372
Vaccinated	…	…	…	…	515 (92.1)	44 (7.9)	…
ICU admission							
Yes	207 (11.1)	131 (63.3)	76 (36.7)	0.09	179 (86.5)	28 (13.5)	0.018
Unvaccinated	…	…	…	…	113 (86.3)	18 (13.7)	0.024
Vaccinated	…	…	…	…	66 (86.8)	10 (13.2)	…
No	1655 (88.9)	1151 (69.5)	504 (30.5)	…	1420 (85.8)	235 (14.2)	…
Unvaccinated	…	…	…	…	952 (82.7)	199 (17.3)	0.421
Vaccinated	…	…	…	…	468 (92.9)	36 (7.1)	…
Death							
Yes	7 (0.4)	4 (57.1)	3 (42.9)	0.032	6 (85.7)	1 (14.3)	0.001
Unvaccinated	…	…	…	…	3 (75.0)	1 (25.0)	1.414
Vaccinated	…	…	…	…	3 (100.0)	0 (0.0)	…
No	1855 (99.6)	1278 (68.9)	577 (31.1)	…	1593 (85.9)	262 (14.1)	…
Unvaccinated	…	…	…	…	1062 (83.1)	216 (16.9)	0.368
Vaccinated	…	…	…	…	531 (92.0)	46 (8.0)	…

Abbreviations: Col., column; ICU, intensive care unit; IIV4, quadrivalent inactivated influenza vaccine; IQR, interquartile range; LAIV, live attenuated influenza vaccine; SMD, standardized mean difference.

[a]Underlying medical conditions include respiratory (asthma, chronic obstructive pulmonary disease, apnea, and other pulmonary conditions) and nonrespiratory underlying conditions (cardiovascular, cerebrovascular, neurological, musculoskeletal, hematologic, endocrine/metabolic, renal, gastrointestinal, hepatic, clinical obesity, clinical underweight, premature birth, developmental delays, and technology dependence).

[b]Immunocompromising conditions include hematological malignancy, solid malignancy, organ transplant, rheumatologic/inflammatory disorders, and other intrinsic immune conditions or immunodeficiency.