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Influenza Vaccine Effectiveness Against Influenza A–Associated Emergency Department, Urgent Care, and Hospitalization Encounters Among US Adults, 2022–2023

Mark W. Tenforde¹, Zachary A. Weber², Duck-Hye Yang², Malini B. DeSilva³, Kristin Dascomb⁴, Stephanie A. Irving⁵, Allison L. Naleway⁵, Manjusha Gaglani^{6,7}, Bruce Fireman⁸, Ned Lewis⁸, Ousseny Zerbo⁸, Kristin Goddard⁸, Julius Timbol⁸, John R. Hansen⁸, Nancy Grisel⁴, Julie Arndorfer⁴, Charlene E. McEvoy³, Inih J. Essien³, Suchitra Rao⁹, Shaun J. Grannis^{10,11}, Anupam B. Kharbanda¹², Karthik Natarajan^{13,14}, Toan C. Ong⁹, Peter J. Embi¹⁵, Sarah W. Ball², Margaret M. Dunne², Lindsey Kirshner², Ryan E. Wiegand¹⁶, Monica Dickerson¹, Palak Patel¹, Caitlin Ray¹, Brendan Flannery¹, Shikha Garg¹, Katherine Adams¹, Nicola P. Klein⁸

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

²Department of Clinical Research, Westat, Rockville, Maryland

³Department of Research, HealthPartners Institute, Minneapolis, Minnesota

⁴Division of Infectious Diseases and Clinical Epidemiology, Intermountain Healthcare, Salt Lake City, Utah

⁵Department of Science Programs, Kaiser Permanente Center for Health Research, Portland, Oregon

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Correspondence: Mark W. Tenforde, MD, PhD, MPH, DTM&H, Influenza Division, Centers for Disease Control and Prevention, 1600 Clifton Rd NE, MS H24-7, Atlanta, GA 30329-4027 (pij6@cdc.gov); Nicola P. Klein, MD, PhD, Kaiser Permanente Vaccine Study Center, 1 Kaiser Plaza, 16th Floor, Oakland, CA 94612 (nicola.klein@kp.org).

Supplementary Data

Supplementary materials are available at *The Journal of Infectious Diseases* online (<http://jid.oxfordjournals.org/>). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

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⁶Section of Pediatric Infectious Diseases, Department of Pediatrics, Baylor Scott & White Health and Baylor College of Medicine, Temple, Texas

⁷Department of Medical Education, Texas A&M University College of Medicine, Temple, Texas

⁸Kaiser Permanente Vaccine Study Center, Kaiser Permanente Northern California Division of Research, Oakland, California

⁹Department of Pediatrics, University of Colorado Anschutz Medical Campus, Aurora, Colorado

¹⁰Center for Biomedical Informatics, Regenstrief Institute, Indianapolis, Indiana

¹¹School of Medicine, Indiana University, Indianapolis, Indiana

¹²Department of Pediatric Emergency Medicine, Children's Minnesota, Minneapolis, Minnesota

¹³Department of Biomedical Informatics, Columbia University Irving Medical Center, New York, New York

¹⁴Medical Informatics Services, NewYork-Presbyterian Hospital, New York, New York

¹⁵Department of Biomedical Informatics, Vanderbilt University Medical Center, Nashville, Tennessee

¹⁶Coronavirus and other Respiratory Viruses Division, Centers for Disease Control and Prevention, Atlanta, Georgia

Abstract

Background.—The 2022–2023 United States influenza season had unusually early influenza activity with high hospitalization rates. Vaccine-matched A(H3N2) viruses predominated, with lower levels of A(H1N1)pdm09 activity also observed.

Methods.—Using the test-negative design, we evaluated influenza vaccine effectiveness (VE) during the 2022–2023 season against influenza A–associated emergency department/urgent care (ED/UC) visits and hospitalizations from October 2022 to March 2023 among adults (aged 18 years) with acute respiratory illness (ARI). VE was estimated by comparing odds of seasonal influenza vaccination among case-patients (influenza A test positive by molecular assay) and controls (influenza test negative), applying inverse-propensity-to-be-vaccinated weights.

Results.—The analysis included 85 389 ED/UC ARI encounters (17.0% influenza A positive; 37.8% vaccinated overall) and 19 751 hospitalizations (9.5% influenza A positive; 52.8% vaccinated overall). VE against influenza A–associated ED/UC encounters was 44% (95% confidence interval [CI], 40%–47%) overall and 45% and 41% among adults aged 18–64 and 65 years, respectively. VE against influenza A–associated hospitalizations was 35% (95% CI, 27%–43%) overall and 23% and 41% among adults aged 18–64 and 65 years, respectively.

Conclusions.—VE was moderate during the 2022–2023 influenza season, a season characterized with increased burden of influenza and co-circulation with other respiratory viruses. Vaccination is likely to substantially reduce morbidity, mortality, and strain on healthcare resources.

Keywords

influenza; H3N2; vaccine effectiveness; test-negative design; clinical outcomes

After historically low influenza activity during the first year of the coronavirus disease 2019 (COVID-19) pandemic (ie, the 2020–2021 influenza season), increased and prolonged circulation of vaccine-mismatched influenza A(H3N2) viruses was observed during the 2021–2022 United States (US) influenza season, although the overall burden of illness was low [1, 2]. The 2022–2023 season was characterized by early and intense influenza activity and co-circulation of other respiratory viruses, including severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and respiratory syncytial virus (RSV) [3, 4]. A majority of influenza infections were caused by influenza A(H3N2) viruses belonging to the 3C.2a1b.2a.2 clade that were antigenically similar to the vaccine strain, with lower circulation of A(H1N1) pdm09 viruses and minimal B virus circulation [4].

Seasonal influenza vaccination is recommended annually in the US to protect against influenza-associated illness [5]. Vaccination remains the most effective way of preventing influenza illness and associated complications [5]. Prevention of influenza and other viral diseases through vaccination may substantially reduce the impact of serious respiratory infections on the healthcare system.

Using data from a multistate vaccine effectiveness (VE) network, we assessed 2022–2023 influenza VE against influenza-associated emergency department or urgent care (ED/UC) visits and hospitalizations in adults. In addition, we describe characteristics and outcomes of vaccinated and unvaccinated patients hospitalized with influenza.

METHODS

Population, Settings, and Study Design

This study from the VISION Network included healthcare encounters between 16 October 2022 and 31 March 2023 in 3 large health systems with integrated clinical, laboratory, and vaccination data in 4 states (Kaiser Permanente Northern California [KPNC], Intermountain Healthcare [IH] in Utah, and HealthPartners [HP] in Minnesota and Wisconsin). VISION's study sites and methods used to evaluate influenza VE have been previously described [2]. In summary, using a test-negative case-control study design, among adults 18 years of age with an acute respiratory illness (ARI)-associated ED/UC encounter or hospitalization who underwent molecular testing for influenza (eg, reverse-transcription polymerase chain reaction), we estimated VE by comparing the odds of current-season influenza vaccination among those who tested positive for influenza A (case-patients) with those who tested negative for influenza A and B (controls). All influenza testing was clinician-initiated. Encounters were eligible if the patient received influenza testing within 10 days before or up to 72 hours after an ED/UC encounter date or date of hospital admission and also received SARS-CoV-2 molecular testing (in order to exclude controls with COVID-19, given the confounding bias due to the association between influenza and COVID-19 vaccination behaviors [2, 6, 7]). SARS-CoV-2-positive encounters (including coinfections

with influenza), as well as a small number of influenza B–positive encounters, were excluded from the analysis. In addition, patients with an influenza or COVID-19 discharge diagnosis without a positive test result were excluded. We defined ARI as having ≥ 1 *International Classification of Diseases, Tenth Revision (ICD-10)* discharge code during the index encounter, including acute respiratory clinical diagnoses (eg, influenza, pneumonia) or acute respiratory signs or symptoms (eg, shortness of breath, cough), as previously defined [2]. A patient could contribute >1 encounter if ED/UC encounters occurred >24 hours apart or hospitalizations >30 days apart; repeat ED/UC visits within 24 hours or readmissions that occurred within 30 days of discharge were combined into a single encounter.

Demographic characteristics (eg, age, sex, race, and ethnicity) and underlying medical conditions were extracted from the electronic health records (EHRs). Current-season influenza vaccination status was classified based on EHR (HP, IH, KPNC), immunization information systems (HP, IH), or claims record (KPNC) of ≥ 1 dose of influenza vaccine since 1 August 2022. Events among patients with documented vaccination <14 days before the index date were excluded. Index date was defined as the earlier of the associated influenza test or the ED/UC visit or admission date. We collected data on the date of vaccination and the type of influenza vaccine product received, including standard-dose egg- or cell culture–based, recombinant, adjuvanted, or high-dose inactivated vaccine (Supplementary Table 1). For hospitalizations, additional clinical outcome measures were collected, including length of stay, intensive care unit (ICU) admission, receipt of invasive mechanical ventilation (IMV), and death during hospitalization or within 28 days from the admission date.

ED/UC encounters and hospitalizations were restricted to the period when influenza began circulating across sites (starting 16 October 2022) until no influenza cases were identified for 2 or more consecutive weeks at a study site and care setting or 31 March 2023, whichever came first. Exclusion criteria for ED/UC encounters and hospitalizations are detailed in Supplementary Figures 1 and 2, respectively.

Statistical Analysis

Demographic and clinical characteristics by case and vaccination status were described using counts and percentages and standardized mean difference (SMD) across groups (by case/control status or by vaccination status). An SMD ≥ 0.20 was considered a meaningful difference indicating imbalance of means or proportions between comparison groups. VE was calculated as $(1 - \text{adjusted odds ratio}) \times 100\%$ using multivariable logistic regression by comparing the odds of influenza vaccination between case-patients and controls. Models were adjusted for prespecified confounders including age, study site, and calendar time, as well as any covariate with an SMD >0.20 . Age and calendar time were modeled as natural cubic spline variables. Also, inverse-propensity-to-be-vaccinated weights (IPVWs) were estimated via generalized boosted regression trees and used in logistic regression models to account for additional imbalances between vaccinated and unvaccinated groups [8].

VE against influenza A–associated ED/UC encounters and hospitalizations were estimated by care setting, by age group (18–64, ≥ 65 years), presence of 1 or more likely immunocompromising conditions (any, none) [9], and presence of medical conditions by

number of organ system categories (0–2 or 3 categories). Medical condition categories included pulmonary, cardiovascular, cerebrovascular, neurological or musculoskeletal, endocrine or metabolic, hematologic, renal, hepatic, and immune conditions (a list of *ICD-10* codes is provided in Supplementary Table 2). Sensitivity analyses included restricting to influenza A–positive case-patients with influenza-associated *ICD-10* discharge code (eg, influenza pneumonia) and restricting to the period from 16 October 2022 to 31 January 2023, when influenza circulation was observed across all study sites and healthcare settings.

As a secondary objective, to explore whether patient characteristics and in-hospital outcomes were different between vaccinated and unvaccinated influenza-positive cases, we compared proportions of patients with more severe clinical outcomes by influenza vaccination status stratified by age (18–64, 65 years) using counts and percentages and SMDs.

Analyses were conducted in SAS version 9.4 (SAS Institute) or R version 4.1.0 (R Foundation for Statistical Computing) software. The study was approved by institutional review boards at Westat and participating sites or under a reliance agreement with Westat and the Centers for Disease Control and Prevention.

RESULTS

Patient Characteristics

Overall, 85 389 ED/UC encounters and 19 751 ARI hospitalizations were included in analyses. Exclusions are shown in Supplementary Figures 1 and 2. Among ED/UC encounters that met inclusion criteria, 14 484 (17.0%) of patients tested positive for influenza A, with influenza cases peaking in November–December 2022 (Table 1 and Figure 1A). The median time between the ED/UC encounter date and most recent influenza test was 0 days (interquartile range [IQR], 0–0 days). ED/UC patients who tested positive for influenza were more likely to be 18–64 compared to 65 years of age (19.7% vs 11.9% positive, respectively; SMD, 0.275), and less likely to have a respiratory chronic condition or nonrespiratory chronic condition (all SMD >0.20); 37.8% of ED/UC patients were vaccinated for influenza (24.1% of 14 484 case-patients and 40.6% of 70 905 controls), with the overall percentage vaccinated increasing from 19.2% in October 2022 to 47.0% in March 2023 and ranging from 31.6% to 44.6% across sites (Table 1).

Among hospitalization episodes, 1874 (9.5%) patients tested positive for influenza A, with a similar peak in activity as seen in ED/UC settings (Table 2 and Figure 1B). The median time between the hospital admission date and most recent influenza test was 0 days (IQR, 0–1 days). Among 19 751 hospitalized patients, 52.8% were vaccinated for influenza (39.1% of 1874 case-patients and 54.3% of 17 877 controls), increasing from 29.8% in October 2022 to 62.3% in March 2023 and ranging from 40.5% to 58.6% across sites.

In both ED/UC encounters and hospitalizations, vaccine product was documented for 32 065 (75.1%) vaccinated patients; 10 792 (33.7%) received egg-based standard-dose inactivated vaccine, 14 786 (46.1%) high-dose vaccine, 5894 (18.4%) adjuvanted vaccine, and 593

(1.1%) a different product (Supplementary Table 1). Of those with known product type, most adults aged 18–64 years (94.2%) received a standard-dose inactivated vaccine, whereas most adults aged ≥ 65 years (92.1%) per recommendations received high-dose inactivated, adjuvanted, or recombinant vaccine [5].

Vaccine Effectiveness

In the ED/UC setting, 20.7% of unvaccinated patients versus 10.8% of vaccinated patients tested positive for influenza A (Table 1 and Figure 2). VE against influenza A–associated ED/UC encounters was 44% (95% confidence interval [CI], 40%–47%) overall. VE was similar in adults aged 18–64 and ≥ 65 years (45% [95% CI, 41%–48%] and 41% [95% CI, 36%–46%], respectively) as well as those without and with likely immunocompromising conditions (44% [95% CI, 41%–47%] and 38% [95% CI, 10%–58%], respectively). Estimates were 44% (95% CI, 41%–47%) among patients with <3 underlying medical condition categories and 51% (95% CI, 39%–61%) among those with ≥ 3 categories.

For ARI-associated hospitalizations, 12.2% of unvaccinated patients versus 7.0% of vaccinated patients tested positive for influenza (Table 2 and Figure 2). VE against influenza A–associated hospitalizations was 35% (95% CI, 27%–43%) overall. VE was 23% (95% CI, 4%–39%) in adults aged 18–64 years and 41% (95% CI, 33%–48%) in adults aged ≥ 65 years. Similar VE was observed among hospitalized adults without and with likely immunocompromising conditions. VE was 39% (95% CI, 23%–52%) and 36% (95% CI, 28%–44%) among adults with <3 and ≥ 3 categories of underlying medical condition, respectively.

In the first sensitivity analysis restricting case-patients to those with an influenza-related *ICD-10* discharge code, 11 922 (72.9%) case-patients across settings had 1 or more influenza-related *ICD-10* discharge codes. VE was 46% (95% CI, 43%–50%) against influenza A–associated ED/UC visits and 36% (95% CI, 27%–43%) against influenza A–associated hospitalizations; these estimates were similar (within 1%–2%) to the primary analyses (Figure 2). In the second sensitivity analysis using an earlier study end date of 31 January 2023, 29 641 (28%) patients were excluded who had encounter index dates during February–March 2023. VE was 43% (95% CI, 40%–46%) against influenza A–associated ED/UC visits and 36% (95% CI, 28%–43%) against influenza A–associated hospitalizations, similar to the primary analyses.

Baseline Characteristics and Outcomes of Vaccinated Versus Unvaccinated Hospitalized Influenza A Case-Patients

Of 1874 hospitalized influenza A cases, median age was 72 years; 733 (39.1%) had been vaccinated and 1141 (60.9%) were unvaccinated. Among 661 adults aged 18–64 years hospitalized with influenza A, 161 (24.4%) were vaccinated and 500 (75.6%) unvaccinated (Table 3). Within this age group, compared to unvaccinated, vaccinated case-patients were older and more likely to have underlying cardiovascular, endocrine or metabolic, renal, or immunocompromising conditions (all SMD >0.20). However, vaccinated case-patients were less likely to have an *ICD-10* discharge code for influenza disease or influenza pneumonia (89.4% vs 95.6%; SMD, 0.24) or to receive IMV during hospitalization (2.5% vs 7.0%;

SMD, 0.21) than unvaccinated case-patients. Other outcomes, including ICU admission and death, were similar between vaccinated and unvaccinated groups.

Among 1213 adults aged ≥ 65 years hospitalized with influenza A, 572 (47.2%) were vaccinated and 641 (52.8%) were unvaccinated. Baseline demographic characteristics and underlying medical conditions were similar across vaccinated and unvaccinated groups within this age strata (SMD, <0.20). The percentage experiencing severe in-hospital clinical outcomes including ICU admission, receipt of IMV, or death, was similar across vaccination groups.

DISCUSSION

During the 2022–2023 US influenza season, we observed moderate VE against influenza A–associated ED/UC encounters and hospitalizations, ranging from 35% to 44% across care settings. Similar VE was also observed among groups at higher risk for severe complications from influenza, including older adults, those with immunocompromising conditions, and those with multiple underlying chronic medical conditions. These estimates were higher than those from the VISION Network during the 2021–2022 season (25% for both ED/UC encounters and hospitalizations [2]) when most infections were caused by viruses from an A(H3N2) subclade that differed antigenically from the vaccine component. The Northern Hemisphere vaccine was updated with a new A(H3N2) component that was antigenically similar to circulating A(H3N2) viruses during the 2022–2023 season [10, 11]. This may have contributed to higher VE during the 2022–2023 season, although co-circulation of A(H1N1)pdm09 viruses may have also impacted VE.

Findings from this analysis were consistent with other VE estimates from North America and Europe for the 2022–2023 influenza season. A test-negative design study from the US state of Wisconsin found VE against influenza A–associated outpatient illness of 54% (95% CI, 23%–73%) among persons aged 6 months to 64 years, similar to estimates we observed among adults aged 18–64 years in ED/UC settings (45%) [12]. Another study based in the US of hospitalized adults ≥ 18 years of age found VE against influenza A–associated hospitalizations of 37% (compared to 35% in our study), with VE against A(H3N2) and A(H1N1)pdm09 subtype viruses of 29% and 47%, respectively [13]. Using data from community-based sentinel surveillance practitioners, a study in Canada reported influenza VE against medically attended A(H3N2)-associated illness [14]. Influenza A(H3N2) VE estimates of 58% (95% CI, 33%–73%) for adults 20–64 years of age and 59% (95% CI, 15%–80%) for adults ≥ 65 years of age were higher than influenza A VE estimates we observed within ED/UC settings but with overlapping CIs. Studies in multiple European countries reported interim 2022–2023 influenza VE findings in primary care, ED, and hospital settings [15]. Across all ages and care settings, influenza A VE ranged from 27% to 44%. Primary care or ED setting VE estimates ranged from 29% to 44%, with estimates for VE against influenza A–associated hospitalization ranging from 27% to 33%.

Influenza VE can be interpreted as the incremental benefit from vaccination in the background of complex immune histories from prior influenza infection and vaccination. During the 2010–2011 through 2019–2020 influenza seasons, an estimated 9.3–41.0 million

symptomatic influenza illnesses occurred annually in the US [16], suggesting that a large proportion of people are infected over multiple seasons of exposure. If infections differentially occur among unvaccinated individuals, these people may have stronger infection-induced immunity over time that impacts future VE [17]. Preexisting immunity from natural infection or influenza vaccination, coupled with timing of these immunizing exposures, may further impact the quality of immune responses and associated VE [18, 19]. Even in seasons with moderate VE like the 2022–2023 season, however, vaccination is likely to have a substantial public health impact by preventing millions of medical visits, tens of thousands of hospitalizations, and thousands of deaths [20–22]. This reduction in medically attended illness and associated morbidity and mortality is especially critical to reduce burden on healthcare resources should influenza, SARS-CoV-2, RSV, and other respiratory viruses continue to co-circulate in high numbers. Although we did not evaluate incidence of medically attended influenza in vaccinated and unvaccinated individuals, in the setting of high influenza activity, it is likely that only a modest number of individuals would need to receive influenza vaccination to prevent a medically attended influenza-related encounter [20].

Influenza vaccination does not produce long-lasting immunity to prevent infection, but there may be additional benefits related to immune responses that attenuate illness severity following infection [23]. Studies of COVID-19 have demonstrated greater vaccine protection against severe illness including hospitalization and ICU admission or death compared to mild-to-moderate illness, as well as lower severity of hospitalized COVID-19 among vaccinated patients [24–26]. However, influenza VE studies over the past decade have generally found similar VE against mild-to-moderate outpatient illness and influenza-associated hospitalization [27, 28]. These studies have frequently compared estimates across different VE networks or healthcare systems with differing enrollment criteria or ability to control for confounding, which limits interpretation of findings. In our study, we also found similar VE within the same health systems across ambulatory and inpatient settings. This lack of gradient in VE may be related to increased hospital-based testing, including multipathogen testing that recognizes any symptomatic influenza illness regardless of severity. In addition, ambulatory and hospitalized patients with ARI differed in important demographic and clinical characteristics, complicating direct comparison. However, among patients hospitalized with influenza, the proportion experiencing critical outcomes (ICU admission, IMV, and death) was generally similar between vaccine breakthrough and unvaccinated case-patients, especially in older adults. Future studies and population-based cohorts are warranted to improve understanding of the overall impact of vaccination.

This study was subject to several limitations. Due to a lack of subtype data for most influenza cases, we were unable to generate influenza A(H3N2)- and A(H1N1)pdm09-specific VE estimates. VE against all influenza A viruses may be impacted by the relative proportion of cases by subtype. Second, VE by age group cannot be directly compared as most young adults received standard-dose inactivated vaccines and most older adults received enhanced products such as high-dose inactivated or adjuvanted vaccines. Despite most vaccinated older adults receiving enhanced vaccine products, VE was similar compared to younger adults who mostly received standard-dose inactivated vaccines. Third, encounters and hospitalizations in 3 healthcare systems are not representative of all encounters among

US adults. Fourth, unmeasured or residual confounding is possible after application of IPVWs and adjustment for measured confounders. For example, we did not capture preventive behaviors such as masking. Fifth, we did not account for influenza vaccination during prior seasons or prior infection history. Finally, VE estimates rely on clinical influenza testing rather than systematic testing in patients with ARI, and bias may be introduced if patients who receive influenza clinical testing differ from those who do not. This was likely to be minimal in this study, however, as >80% of patients with ARI encounters received influenza testing.

In summary, during the 2022–2023 US influenza season, we observed moderate VE against influenza-associated ED/UC encounters and hospitalizations. With high levels of circulation of influenza and other respiratory viruses, influenza vaccination is a critical tool to reduce serious illness and minimize strain on healthcare resources as well as individual and societal impacts of influenza.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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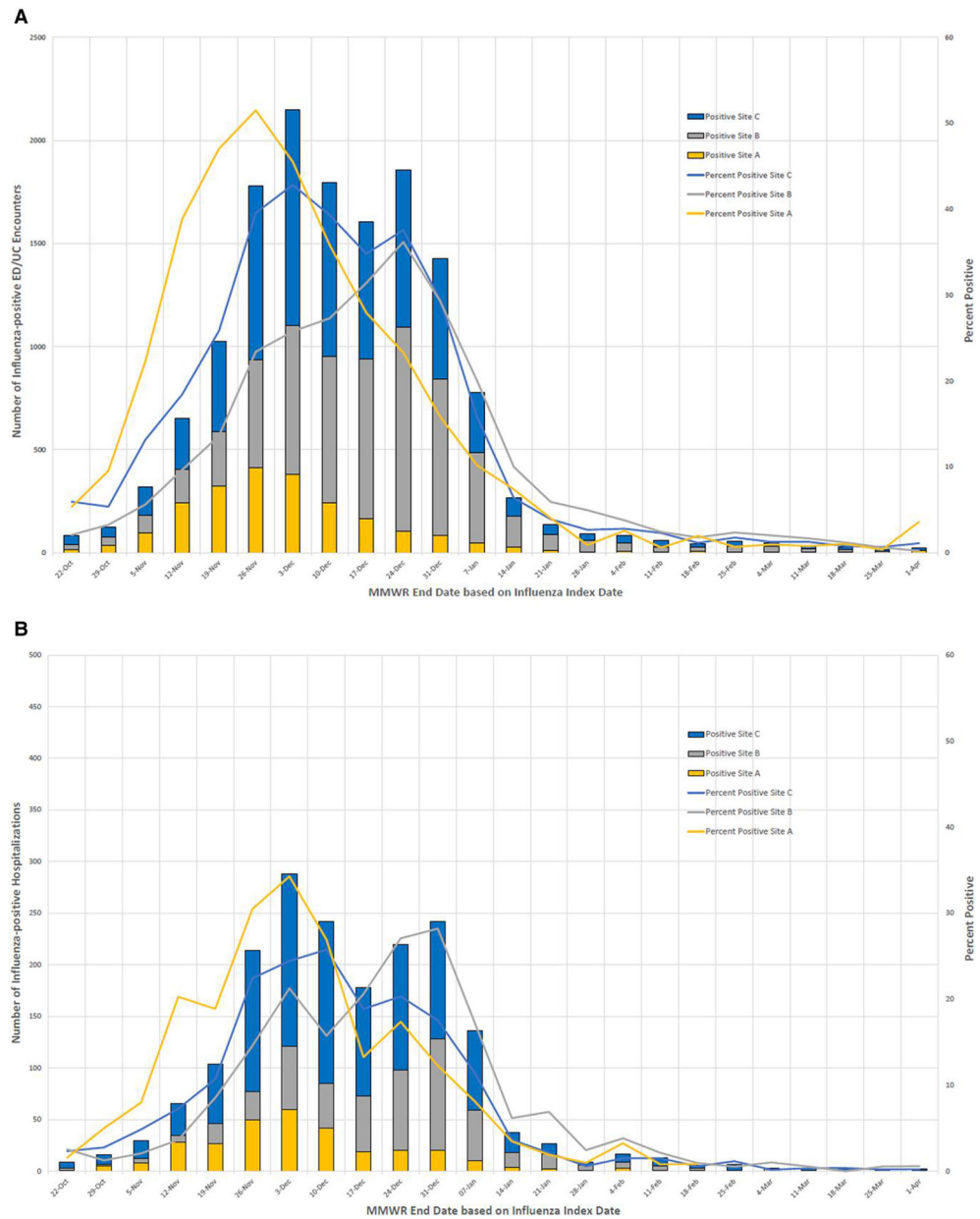


Figure 1.
A, Influenza-positive emergency department/urgent care encounters and percent positivity by week; **B**, Influenza-positive hospitalizations and percent positivity by week.
 Abbreviations: EC/UC, emergency department/urgent care; MMWR, *Morbidity and Mortality Weekly Report* calendar week.

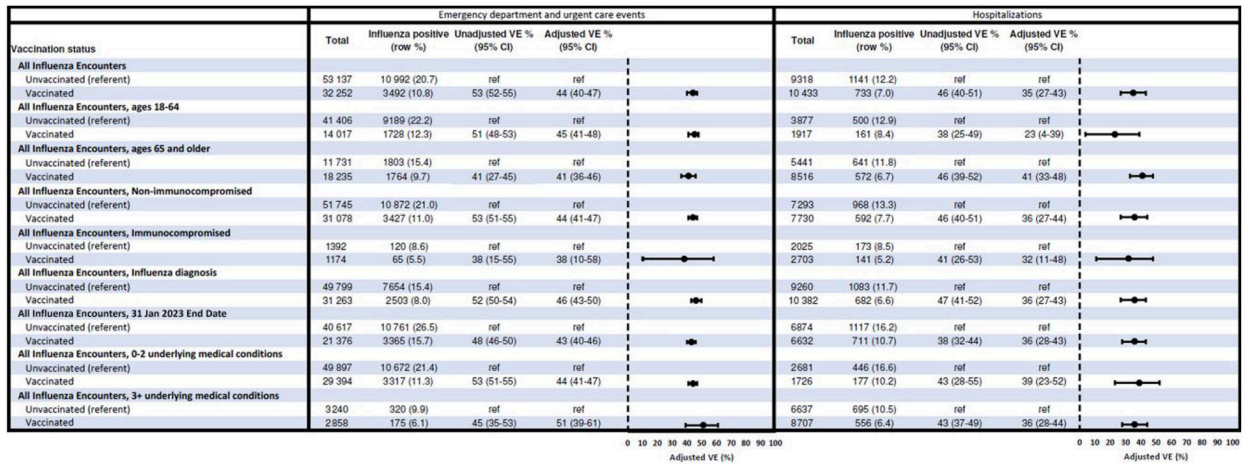


Figure 2. Vaccine effectiveness against influenza-associated emergency department/urgent care visits or hospitalizations. Abbreviations: CI, confidence interval; Ref, reference group; VE, vaccine effectiveness.

Characteristics of Acute Respiratory Illness-Associated Emergency Department/Urgent Care Encounters by Influenza Vaccination and Test Status, VISION Network

Table 1.

Characteristic	Total, No. (Column %)	Influenza Vaccination Status			Influenza Test Result		
		Unvaccinated, No. (Row %)	Vaccinated, No. (Row %)	SMD ^a	Negative, No. (Row %)	Positive, No. (Row %)	SMD ^a
All ED/UC events	85 389 (100.0)	53 137 (62.2)	32 252 (37.8)	...	70 905 (83.0)	14 484 (17.0)	...
Influenza vaccination status							
Unvaccinated	53 137 (62.2)	53 137 (100.0)	0 (0.0)	...	42 145 (79.3)	10 992 (20.7)	0.357
Vaccinated	32 252 (37.8)	0 (0.0)	32 252 (100.0)	...	28 760 (89.2)	3492 (10.8)	...
Month of encounter							
October 2022	5488 (6.4)	4436 (80.8)	1052 (19.2)	0.357	5214 (95.0)	274 (5.0)	1.129
November 2022	19 094 (22.4)	13 487 (70.6)	5607 (29.4)	...	13 992 (73.3)	5102 (26.7)	...
December 2022	23 075 (27.0)	14 687 (63.6)	8388 (36.4)	...	15 634 (67.8)	7441 (32.2)	...
January 2023	14 336 (16.8)	8007 (55.9)	6329 (44.1)	...	13 027 (90.9)	1309 (9.1)	...
February 2023	11 559 (13.5)	6244 (54.0)	5315 (46.0)	...	11 326 (98.0)	233 (2.0)	...
March 2023	11 837 (13.9)	6276 (53.0)	5561 (47.0)	...	11 712 (98.9)	125 (1.1)	...
Site							
Site A	10 315 (12.1)	6361 (61.7)	3954 (38.3)	0.261	8092 (78.4)	2223 (21.6)	0.148
Site B	39 687 (46.5)	27 163 (68.4)	12 524 (31.6)	...	33 712 (84.9)	5975 (15.1)	...
Site C	35 387 (41.4)	19 613 (55.4)	15 774 (44.6)	...	29 101 (82.2)	6286 (17.8)	...
Age, y, median (IQR)	53 (33–71)	43 (29–62)	68 (50–79)	...	55 (35–72)	43 (28–64)	...
Age group, y							
18–64	55 423 (64.9)	41 406 (74.7)	14 017 (25.3)	0.754	44 506 (80.3)	10 917 (19.7)	0.275
65	29 966 (35.1)	11 731 (39.1)	18 235 (60.9)	...	26 399 (88.1)	3567 (11.9)	...
Sex							
Female	50 409 (59.0)	31 129 (61.8)	19 280 (38.2)	0.024	41 896 (83.1)	8513 (16.9)	0.006
Male	34 980 (41.0)	22 008 (62.9)	12 972 (37.1)	...	29 009 (82.9)	5971 (17.1)	...
Race							
White	58 323 (68.3)	35 215 (60.4)	23 108 (39.6)	0.203	49 286 (84.5)	9037 (15.5)	0.161
Black	6936 (8.1)	5037 (72.6)	1899 (27.4)	...	5536 (79.8)	1400 (20.2)	...
Other ^b	9761 (11.4)	5592 (57.3)	4169 (42.7)	...	7980 (81.8)	1781 (18.2)	...

Characteristic	Total, No. (Column %)	Influenza Vaccination Status			Influenza Test Result		
		Unvaccinated, No. (Row %)	Vaccinated, No. (Row %)	SMD ^a	Negative, No. (Row %)	Positive, No. (Row %)	SMD ^a
Unknown	10 369 (12.1)	7293 (70.3)	3076 (29.7)	...	8103 (78.1)	2266 (21.9)	...
Ethnicity							
Hispanic	15 376 (18.0)	10 762 (70.0)	4614 (30.0)	0.158	12 209 (79.4)	3167 (20.6)	0.117
Non-Hispanic	70 013 (82.0)	42 375 (60.5)	27 638 (39.5)	...	58 696 (83.8)	11 317 (16.2)	...
Any medical condition							
Yes	28 482 (33.4)	15 839 (55.6)	12 643 (44.4)	0.199	25 418 (89.2)	3064 (10.8)	0.330
No	56 907 (66.6)	37 298 (65.5)	19 609 (34.5)	...	45 487 (79.9)	11 420 (20.1)	...
Respiratory condition							
Yes	20 049 (23.5)	11 141 (55.6)	8908 (44.4)	0.156	17 915 (89.4)	2134 (10.6)	0.266
No	65 340 (76.5)	41 996 (64.3)	23 344 (35.7)	...	52 990 (81.1)	12 350 (18.9)	...
Nonrespiratory condition							
Yes	16 762 (19.6)	9220 (55.0)	7542 (45.0)	0.150	15 110 (90.1)	1652 (9.9)	0.270
No	68 627 (80.4)	43 917 (64.0)	24 710 (36.0)	...	55 795 (81.3)	12 832 (18.7)	...
Immunosuppressive condition							
Yes	2566 (3.0)	1392 (54.2)	1174 (45.8)	0.059	2381 (92.8)	185 (7.2)	0.139
No	82 823 (97.0)	51 745 (62.5)	31 078 (37.5)	...	68 524 (82.7)	14 299 (17.3)	...

Abbreviations: ED/UC, emergency department/urgent care; IQR, interquartile range; SMD, standardized mean difference.

^aAn absolute SMD >0.20 indicates a nonnegligible difference in variable distributions between ED/UC encounters for vaccinated versus unvaccinated patients or for patients with positive influenza test results versus patients with negative influenza test results. For influenza vaccination status, SMD was calculated by comparing the vaccinated category versus unvaccinated.

^bOther race defined as any 1 of the following responses: Asian, Hawaiian or other Pacific Islander, American Indian or Alaska Native, other, multiple races.

Characteristics of Acute Respiratory Illness-Associated Hospitalizations by Influenza Vaccination and Test Status, VISION Network

Table 2.

Characteristic	Total, No. (Column %)	Influenza Vaccination Status			Influenza Test Result		
		Unvaccinated, No. (Row %)	Vaccinated, No. (Row %)	SMD ^a	Negative, No. (Row %)	Positive, No. (Row %)	SMD ^a
All hospitalizations	19 751 (100.0)	9318 (47.2)	10 433 (52.8)	...	17 877 (90.5)	1874 (9.5)	...
Influenza vaccination status							
Unvaccinated	9318 (47.2)	9318 (100.0)	0 (0.0)	...	8177 (87.8)	1141 (12.2)	0.307
Vaccinated	10 433 (52.8)	0 (0.0)	10 433 (100.0)	...	9700 (93.0)	733 (7.0)	...
Month of encounter							
October 2022	1165 (5.9)	818 (70.2)	347 (29.8)	0.352	1131 (97.1)	34 (2.9)	1.168
November 2022	3791 (19.2)	2169 (57.2)	1622 (42.8)	...	3203 (84.5)	588 (15.5)	...
December 2022	4654 (23.6)	2215 (47.6)	2439 (52.4)	...	3667 (78.8)	987 (21.2)	...
January 2023	3896 (19.7)	1672 (42.9)	2224 (57.1)	...	3677 (94.4)	219 (5.6)	...
February 2023	3169 (16.0)	1283 (40.5)	1886 (59.5)	...	3135 (98.9)	34 (1.1)	...
March 2023	3076 (15.6)	1161 (37.7)	1915 (62.3)	...	3064 (99.6)	12 (0.4)	...
Site							
Site A	2238 (11.3)	1140 (50.9)	1098 (49.1)	0.318	1936 (86.5)	302 (13.5)	0.170
Site B	5098 (25.8)	3034 (59.5)	2064 (40.5)	...	4592 (90.1)	506 (9.9)	...
Site C	12 415 (62.9)	5144 (41.4)	7271 (58.6)	...	11 349 (91.4)	1066 (8.6)	...
Age, y, median (IQR)	74 (62–83)	68 (55–79)	77 (68–84)	...	74 (62–83)	72 (59–81)	...
Age group, y							
18–64	5794 (29.3)	3877 (66.9)	1917 (33.1)	0.524	5133 (88.6)	661 (11.4)	0.141
65	13 957 (70.7)	5441 (39.0)	8516 (61.0)	...	12 744 (91.3)	1213 (8.7)	...
Sex							
Female	10 479 (53.1)	4908 (46.8)	5571 (53.2)	0.015	9427 (90.0)	1052 (10.0)	0.068
Male	9272 (46.9)	4410 (47.6)	4862 (52.4)	...	8450 (91.1)	822 (8.9)	...
Race							
White	13 614 (68.9)	6258 (46.0)	7356 (54.0)	0.190	12 344 (90.7)	1270 (9.3)	0.099
Black	1606 (8.1)	976 (60.8)	630 (39.2)	...	1421 (88.5)	185 (11.5)	...
Other ^b	2712 (13.7)	1132 (41.7)	1580 (58.3)	...	2490 (91.8)	222 (8.2)	...
Unknown	1819 (9.2)	952 (52.3)	867 (47.7)	...	1622 (89.2)	197 (10.8)	...

Characteristic	Total, No. (Column %)	Influenza Vaccination Status			Influenza Test Result		
		Unvaccinated, No. (Row %)	Vaccinated, No. (Row %)	SMD ^a	Negative, No. (Row %)	Positive, No. (Row %)	SMD ^a
Ethnicity							
Hispanic	2617 (13.2)	1340 (51.2)	1277 (48.8)	0.063	2333 (89.1)	284 (10.9)	0.060
Non-Hispanic	17 134 (86.8)	7978 (46.6)	9156 (53.4)	...	15 544 (90.7)	1590 (9.3)	...
Any medical condition							
Yes	19 353 (98.0)	9032 (46.7)	10 321 (53.3)	0.140	17 545 (90.7)	1808 (9.3)	0.103
No	398 (2.0)	286 (71.9)	112 (28.1)	...	332 (83.4)	66 (16.6)	...
Respiratory condition
Yes	15 904 (80.5)	7324 (46.1)	8580 (53.9)	0.092	14 566 (91.6)	1338 (8.4)	0.239
No	3847 (19.5)	1994 (51.8)	1853 (48.2)	...	3311 (86.1)	536 (13.9)	...
Nonrespiratory condition							
Yes	18 746 (94.9)	8613 (45.9)	10 133 (54.1)	0.212	17 031 (90.9)	1715 (9.1)	0.151
No	1005 (5.1)	705 (70.1)	300 (29.9)	...	846 (84.2)	159 (15.8)	...
Immunosuppressive condition							
Yes	4728 (23.9)	2025 (42.8)	2703 (57.2)	0.098	4414 (93.4)	314 (6.6)	0.197
No	15 023 (76.1)	7293 (48.5)	7730 (51.5)	...	13 463 (89.6)	1560 (10.4)	...
IMV							
Yes	1673 (8.5)	919 (54.9)	754 (45.1)	0.094	1579 (94.4)	94 (5.6)	0.151
No	18 078 (91.5)	8399 (46.5)	9679 (53.5)	...	16 298 (90.2)	1780 (9.8)	...
ICU admission							
Yes	3504 (17.7)	1663 (47.5)	1841 (52.5)	0.005	3276 (93.5)	228 (6.5)	0.172
No	16 247 (82.3)	7655 (47.1)	8592 (52.9)	...	14 601 (89.9)	1646 (10.1)	...
Death							
Yes	1172 (5.9)	514 (43.9)	658 (56.1)	0.034	1114 (95.1)	58 (4.9)	0.149
No	18 579 (94.1)	8804 (47.4)	9775 (52.6)	...	16 763 (90.2)	1816 (9.8)	...

Abbreviations: ICU, intensive care unit; IMV, invasive mechanical ventilation; IQR, interquartile range; SMD, standardized mean difference.

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

^bOther race defined as any 1 of the following responses: Asian, Hawaiian or other Pacific Islander, American Indian or Alaska Native, other, multiple races.

Table 3. Baseline Characteristics and In-Hospital Outcomes Among Vaccinated Versus Unvaccinated Influenza-Positive Patients, by Age Group

Characteristic	Age 18–64 y			Age 65 y		
	Vaccinated, No. (Column %)	Unvaccinated, No. (Column %)	SMD ^a	Vaccinated, No. (Column %)	Unvaccinated, No. (Column %)	SMD ^a
Total	161	500	...	572	641	...
Demographic characteristics						
Age, y						
18–49	49 (30.4)	243 (48.6)	0.378
50–64	112 (69.6)	257 (51.4)
65–74	173 (30.2)	252 (39.3)	0.191
75–84	246 (43.0)	241 (37.6)	...
85	153 (26.7)	148 (23.1)	...
Sex						
Male	52 (32.3)	221 (44.2)	0.247	262 (45.8)	287 (44.8)	0.021
Female	109 (67.7)	279 (55.8)	...	310 (54.2)	354 (55.2)	...
Race/Ethnicity						
Black, NH	21 (13.0)	76 (15.2)	0.210	32 (5.6)	56 (8.7)	0.174
Hispanic	30 (18.6)	96 (19.2)	...	71 (12.4)	87 (13.6)	...
Other, NH ^b	27 (16.8)	50 (10.0)	...	51 (8.9)	69 (10.8)	...
White, NH	82 (50.9)	272 (54.4)	...	416 (72.7)	423 (66.0)	...
Unknown	1 (0.6)	6 (1.2)	...	2 (0.3)	6 (0.9)	...
Clinical characteristics						
Influenza pneumonia or disease diagnosis						
Yes	144 (89.4)	478 (95.6)	0.236	538 (94.1)	605 (94.4)	0.014
No	17 (10.6)	22 (4.4)	...	34 (5.9)	36 (5.6)	...
Respiratory condition						
Yes	112 (69.6)	340 (68.0)	0.034	424 (74.1)	462 (72.1)	0.046
No	49 (30.4)	160 (32.0)	...	148 (25.9)	179 (27.9)	...
Cardiological condition						
Yes	95 (59.0)	237 (47.4)	0.234	481 (84.1)	516 (80.5)	0.094
No	66 (41.0)	263 (52.6)	...	91 (15.9)	125 (19.5)	...

Characteristic	Age 18–64 y			Age 65 y		
	Vaccinated, No. (Column %)	Unvaccinated, No. (Column %)	SMD ^a	Vaccinated, No. (Column %)	Unvaccinated, No. (Column %)	SMD ^a
Cerebrovascular condition						
Yes	3 (1.9)	19 (3.8)	0.117	33 (5.8)	31 (4.8)	0.042
No	158 (98.1)	481 (96.2)	...	539 (94.2)	610 (95.2)	...
Neurological and/or musculoskeletal condition						
Yes	37 (23.0)	99 (19.8)	0.078	215 (37.6)	253 (39.5)	0.039
No	124 (77.0)	401 (80.2)	...	357 (62.4)	388 (60.5)	...
Hematologic condition						
Yes	14 (8.7)	28 (5.6)	0.120	41 (7.2)	42 (6.6)	0.024
No	147 (91.3)	472 (94.4)	...	531 (92.8)	599 (93.4)	...
Endocrine condition						
Yes	109 (67.7)	268 (53.6)	0.292	455 (79.5)	479 (74.7)	0.115
No	52 (32.3)	232 (46.4)	...	117 (20.5)	162 (25.3)	...
Renal condition						
Yes	38 (23.6)	68 (13.6)	0.259	240 (42.0)	242 (37.8)	0.086
No	123 (76.4)	432 (86.4)	...	332 (58.0)	399 (62.2)	...
Gastrointestinal and hepatic condition						
Yes	10 (6.2)	28 (5.6)	0.026	36 (6.3)	33 (5.1)	0.049
No	151 (93.8)	472 (94.4)	...	536 (93.7)	608 (94.9)	...
Any immunocompromising condition						
Yes	39 (24.2)	65 (13.0)	0.291	102 (17.8)	108 (16.8)	0.026
No	122 (75.8)	435 (87.0)	...	470 (82.2)	533 (83.2)	...
In-hospital treatment and outcomes						
Any influenza antiviral therapy received						
Yes	146 (90.7)	441 (88.2)	0.081	527 (92.1)	592 (92.4)	0.008
No	15 (9.3)	59 (11.8)	...	45 (7.9)	49 (7.6)	...
ICU admission during encounter						
Yes	21 (13.0)	77 (15.4)	0.068	67 (11.7)	63 (9.8)	0.061
No	140 (87.0)	423 (84.6)	...	505 (88.3)	578 (90.2)	...
IMV						
Yes	4 (2.5)	35 (7.0)	0.214	25 (4.4)	30 (4.7)	0.015

Characteristic	Age 18–64 y			Age 65 y		
	Vaccinated, No. (Column %)	Unvaccinated, No. (Column %)	SMD ^a	Vaccinated, No. (Column %)	Unvaccinated, No. (Column %)	SMD ^a
No	157 (97.5)	465 (93.0)	...	547 (95.6)	611 (95.3)	...
Death						
Yes	6 (3.7)	12 (2.4)	0.077	23 (4.0)	17 (2.7)	0.076
No	155 (96.3)	488 (97.6)	...	549 (96.0)	624 (97.3)	...
Length of stay > 5 d						
Yes	43 (26.7)	119 (23.8)	0.067	161 (28.1)	174 (27.1)	0.022
No	118 (73.3)	381 (76.2)	...	411 (71.9)	467 (72.9)	...

Abbreviations: ICU, intensive care unit; IMV, invasive mechanical ventilation; NH, non-Hispanic; SMD, standardized mean difference.

^a An absolute SMD >0.20 indicates a nonnegligible difference in variable distributions between hospitalizations for vaccinated versus unvaccinated patients.

^b Other race defined as any 1 of the following responses: Asian, Hawaiian or other Pacific Islander, American Indian or Alaska Native, other, multiple races.