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Vaccine Effectiveness Against Influenza A(H1N1), A(H3N2), and B–Associated Hospitalizations — United States, September 1, 2023–May 31, 2024

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Abstract

Background: The 2023–2024 influenza season included sustained elevated activity from December 2023–February 2024 and continued activity through May 2024. Influenza A(H1N1), A(H3N2), and B viruses circulated during the season.

Methods: During September 1, 2023–May 31, 2024, a multistate sentinel surveillance network of 24 medical centers in 20 U.S. states enrolled adults aged ≥ 18 years hospitalized with acute respiratory illness (ARI). Consistent with a test-negative design, cases tested positive for influenza viruses by molecular or antigen test, and controls tested negative for influenza viruses and SARS-CoV-2. Vaccine effectiveness (VE) against influenza-associated hospitalization was calculated as $(1 - \text{adjusted odds ratio for vaccination}) \times 100\%$.

Results: Among 7690 patients, including 1170 influenza cases (33% vaccinated) and 6520 controls, VE was 40% (95% CI: 31%–48%) with varying estimates by age (18–49 years: 53% [34%–67%]; 50–64 years: 47% [31%–60%]; ≥ 65 years: 31% [16%–43%]). Protection was similar among immunocompetent patients (40% [30%–49%]) and immunocompromised patients (32% [7–50%]). VE was statistically significant against influenza B (67% [35%–84%]) and A(H1N1) (36% [21%–48%]) and crossed the null against A(H3N2) (19% [–8%–39%]). VE was higher for patients 14–60 days from vaccination (54% [40%–65%]) than >120 days (18% [–1%–33%]).

Conclusions: During 2023–2024, influenza vaccination reduced the risk of influenza A(H1N1)– and influenza B–associated hospitalizations among adults; effectiveness was lower in patients vaccinated >120 days prior to illness onset compared with those vaccinated 14–60 days prior.

Summary

This manuscript provides differential VE against influenza-associated hospitalization during 2023–2024 for all three relevant subtypes/lineage (A/H1N1, A/H3N2, and B), relevant age groups, and based on time since vaccination for both virus types and groups.

Keywords

seasonal influenza; severe influenza; vaccine effectiveness; waning; hospitalization

Introduction

During the 2023–2024 Northern Hemisphere influenza season, influenza A(H1N1) and A(H3N2) circulated widely, and B viruses returned to widespread circulation for the first time since 2019–2020. In addition, the influenza season in the United States was relatively long, with an initial increase in activity in early November 2023, a peak in late December 2023, and sustained elevated activity through February 2024.¹ Although influenza A(H1N1)pdm09 (i.e., A[H1N1]) viruses predominated overall and especially earlier in the season, incidence of influenza A(H3N2) and influenza B (all from the Victoria lineage) increased as A(H1N1) decreased and accounted for substantial proportions of influenza viruses detected during the latter part of the 2023–2024 season.² Influenza A(H3N2) viruses overtook A(H1N1) as the predominant influenza virus in early April 2024.¹

The 2023–2024 Northern Hemisphere egg-based influenza vaccine was composed of an A/Victoria/4897/2022 (H1N1)pdm09-like virus, an A/Darwin/9/2021 (H3N2)-like virus, a B/Austria/1359417/2021 (B/Victoria lineage)-like virus, and a B/Phuket/3073/2013 (B/Yamagata lineage)-like virus. Two different influenza A viruses, an A/Wisconsin/67/2022 (H1N1)pdm09-like virus and an A/Darwin/6/2021 (H3N2)-like virus, were used for cell- and recombinant-based vaccines. Phylogenetic analysis showed that the vaccine viruses were antigenically similar to the vast majority of circulating influenza viruses during 2023–2024.¹

An influenza season with substantial numbers of all three influenza viruses and antigenic similarity between the vaccine viruses and circulating viruses thus offers an important opportunity to investigate differences in influenza virus-specific vaccine effectiveness (VE). Stratifying these results by the demographic and medical characteristics of hospitalized influenza patients and by the timing of vaccination during a long influenza season underscores the importance of well-timed vaccination and ongoing evaluation of virus-specific VE.

Methods

Study Population

Data were collected by the Investigating Respiratory Viruses in the Acutely Ill (IVY) Network from September 1, 2023, to May 31, 2024. The IVY Network is a multi-pathogen acute respiratory illness (ARI) surveillance program consisting of 26 hospitals from 20 US

states, funded by the Centers for Disease Control and Prevention (CDC) and coordinated from Vanderbilt University Medical Center. This program was determined to be a non-research public health surveillance activity by CDC and each participating site and was conducted in a manner consistent with applicable federal law and CDC policy.^a

To compare likelihood of influenza vaccination (exposure) among patients with influenza-associated hospitalization (outcome) vs control patients, patients who tested positive for influenza virus and negative for SARS-CoV-2 by local clinical testing and/or centralized RT-PCR testing were classified as case patients. Patients who tested negative for both influenza virus and SARS-CoV-2 by local clinical testing and centralized RT-PCR were classified as control patients. Patients were eligible for enrollment if they met the following criteria: (1) at least 18 years old, (2) presentation with one or more symptoms of ARI (fever, cough, shortness of breath, new hypoxemia, new pulmonary findings on chest imaging consistent with pneumonia), (3) hospitalization, and (4) a recent (within 10 days of symptom onset and within 3 days of hospital admission) molecular or antigen test for influenza virus, SARS-CoV-2, or respiratory syncytial virus (RSV). Each site followed standard protocols for eligibility assessment, data collection, and specimen collection, with eligible controls enrolled locally within two weeks of eligible influenza, SARS-CoV-2, and RSV cases to ensure comparability between cases and controls.^{3,4}

Centralized Viral Testing

In addition to clinical viral testing completed at hospital laboratories, personnel at each site collected nasal swab specimens at enrollment and sent them to Vanderbilt University Medical Center (VUMC) (Nashville, Tennessee, USA). Overnight shipments of specimens were received on dry ice and maintained at -80°C for a ≤ 14 days, thawed, and aliquoted into 2 ml cryovials. Aliquoted material was immediately returned to -80°C for long-term storage. At the time of thawing, a volume of specimen sufficient for pathogen testing was combined with lysis buffer and held at 4°C for <1 hour, followed by automated nucleic acid extraction. Specimens were received at the central laboratory in original containment. Research specimens were collected in 3 ml viral transport medium and processed at VUMC. Salvaged clinical residuals were received in containers used by the local site diagnostic laboratory and further processed (i.e., aliquoted) at VUMC, where they underwent testing for influenza virus, SARS-CoV-2, and RSV by reverse transcription polymerase chain reaction (RT-PCR). For specimens that tested positive for influenza virus by RT-PCR, an aliquot of primary specimen stored at -80°C was shipped overnight on dry ice to University of Michigan (Ann Arbor, Michigan, USA) for whole genome sequencing (WGS). We excluded SARS-CoV-2-positive patients from our control group to prevent the underestimation of influenza VE associated with the correlation of COVID-19 and influenza vaccination. As patients hospitalized with COVID-19 are less likely to be vaccinated against either disease, including SARS-CoV-2-positive patients as controls increases the number of unvaccinated control patients and thus lower VE estimates.⁴ RSV cases remained included as controls. Although RSV vaccination was also available during 2023–2024, there were

^a45 C.F.R. part 46.102(l)(2), 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

neither sufficient numbers of patients vaccinated for RSV (<12%) nor RSV cases among controls (<10%) to introduce meaningful bias based on correlated vaccination behaviors.⁴

Influenza Vaccination History

Vaccination status was determined by review of electronic medical records, Immunization Information System (IIS) searches, and self-report with date and location of administration. Patients were classified as vaccinated if they received one or more doses of the 2023–2024 seasonal influenza vaccine at least 14 days before the start of symptoms (i.e., illness onset). Patients were classified as unvaccinated if they received no doses of the 2023–2024 seasonal influenza vaccine.

Statistical Analysis

In our analysis, we excluded patients who: (1) received influenza testing before illness onset or more than 10 days after illness onset; (2) displayed first ARI symptoms after hospital admission or >14 days before hospital admission; (3) tested positive for SARS-CoV-2; (4) were controls enrolled outside the period of local influenza circulation (i.e., before the first influenza case or after the last influenza case at each hospital); (5) had unknown influenza vaccination status; (6) received an influenza vaccine <14 days prior to illness onset; or (7) were missing covariate data used in the VE model. For those that remained after exclusion, we compared patient characteristics by case status using Chi-square tests for categorical variables and Mann-Whitney U tests for continuous variables. We tested for differences in median vaccination date among age and immunocompetence groups using Kruskal-Wallis and Mann-Whitney U tests, respectively. We tested for differences in vaccination timing (September and earlier vs October and later) and influenza subtype by age group using Chi-square tests.

We used a test-negative design to estimate influenza VE. Our primary outcome was influenza-associated hospitalization, defined as hospital admission for symptomatic, laboratory-confirmed influenza virus infection. We first fit a multivariable logistic regression model to compare the odds of vaccination among cases and controls while accounting for relevant covariates. Models were adjusted for age group (18–49, 50–64, ≥65 years), sex (male/female), race/ethnicity (Non-Hispanic White, Non-Hispanic Black, Hispanic, Other, Unknown), HHS region (Regions 1–10), and biweekly period of enrollment. We then calculated VE for protection against influenza-associated hospitalization as $(1 - \text{adjusted odds ratio for vaccination}) \times 100\%$. We calculated point estimates and 95% confidence intervals for overall VE and VE stratified by influenza virus, age group, and immunocompetence status using this model.

We additionally calculated VE estimates by time since vaccination by substituting the exposure variable in our regression model with a time variable (unvaccinated, and vaccinated 14–60 days, 61–120 days or >120 days before illness onset for overall VE; unvaccinated, and vaccinated 14–120 days or >120 days before illness onset for subtype-specific VE) and compared intervals by VE 95% confidence interval overlap. Analyses were performed using SAS version 9.4 (Cary, North Carolina, USA)⁵ and R version 4.4.1 (R Core Team, Vienna, Austria).⁶

Results

Enrollment and Patient Characteristics

Overall, 13,041 patients were enrolled between September 1, 2023, and May 31, 2024. Of these, 5,351 were excluded from the analysis. Most excluded patients tested positive for SARS-CoV-2 (n=3,112, 58%), had incomplete data for influenza vaccination status (n=817, 15%), or received influenza testing before the illness-onset date or more than 10 days after the illness-onset date (n=693, 13%) (Figure 1). A total of 7,690 patients comprised the analytic data set, including 1,170 influenza cases and 6,920 controls.

Among 1,170 influenza-case patients, influenza type was determined by RT-PCR for 762 patients, including 465/762 (61%) with influenza A(H1N1) and 228/762 (30%) with influenza A(H3N2), and 69/762 (9%) with influenza B. Influenza A(H1N1) and A(H3N2) were distributed similarly across age groups, but most influenza B cases (49/69, 71%) were among patients aged 18–49 years (Supplementary Figure 1). Among the 465 patients with influenza A(H1N1) confirmed by RT-PCR, viral WGS identified a clade in 441 patients, of which 343 (78%) were genetic group 6B.1A.5a.2a.1 and 98 (22%) were genetic group 6B.1A.5a.2a. Among 228 patients with influenza A(H3N2), WGS identified a clade in 200 patients, of which all were genetic group 3C.2a1b.2a.2a.3a.1. Among 69 patients with influenza B, WGS identified a clade in 51 patients, of which all were genetic group V1A.3a.2.

Influenza vaccination was less likely among influenza case patients (391/1170; 33%) compared with control patients (2779/6520; 43%) ($P<.001$) (Table 1). Case patients, compared with control patients, were younger (median age: 62 vs 65 years, $P<.001$), more likely to be non-Hispanic Black (28% vs 22%; $P<.001$), less likely to be immunocompromised (18% vs 25%, $P<.001$) and less likely to have had ≥ 1 hospitalization in the previous year (50% vs 61%, $P<.001$). Patients who received influenza vaccination, compared with unvaccinated patients, were older (median age: 69 vs 61 years, $P<.001$), more likely to be non-Hispanic White (64% vs 50%; $P<.001$), more likely to be immunocompromised (28% vs 21%; $P<.001$), and more likely to have had ≥ 1 hospitalization in the previous year (65% vs 56%; $P<.001$) (Supplementary Table 1). Patients aged ≥ 65 years (compared with other age groups) were vaccinated a median 5 days earlier in the year and were more likely to be vaccinated before October (Figure 2). Immunocompromised patients (compared with immunocompetent patients) were also vaccinated slightly earlier in the year (Supplementary Figure 2).

VE Against Influenza-associated Hospitalization

The overall VE against influenza-associated hospitalization was 40% (95% confidence interval [CI]: 31%–48%). Stratified by age group, VE declined with age and was 53% (95% CI: 34%–67%) among adults aged 18–64 years, 47% (95% CI: 31%–60%) among adults aged 50–64 years, and 31% (16%–43%) among adults aged ≥ 65 years (Figure 3). By immunocompromised status, VE was 40% (95% CI: 30%–49%) for immunocompetent patients and 32% (95% CI: 7%–59%) for immunocompromised patients. Stratified by virus subtype, VE against influenza-associated hospitalization was 36% (95% CI: 21%–48%) for

influenza A(H1N1), 19% (95% CI: -8%–39%) for influenza A(H3N2) and 68% (95% CI: 35%–84%) for influenza B (Figure 4). VE against influenza A(H1N1)–associated hospitalizations was consistent across patients aged 18–49 years (VE: 40% [95% CI: -4%–65%]), 50–64 years (VE: 38% [95% CI: 8%–58%]) and ≥65 years (VE: 35% [95% CI: 14%–51%]). However, VE against influenza A(H3N2)–associated hospitalizations crossed the null for all three age groups (18–49 years: 40% [95% CI: -20%–70%]); 50–64 years: 30% [95% CI: -23%–60%]; ≥65 years: 2% [95% CI: -47%–35%]).

Differences in VE Based on Time Since Vaccination

VE against all influenza–associated hospitalizations differed by days elapsed between vaccination and enrollment, with the highest VE among those vaccinated 14–60 days prior to illness onset (VE: 54% [95% CI: 40%–65%]) and a significant decrease among patients vaccinated >120 days prior to onset (VE: 18% [95% CI: -1%–33%]) (Figure 5). Among patients vaccinated 14–120 days prior to onset (median: 68 days [IQR: 42–93 days]), VE was significant against influenza A(H1N1) (42% [95% CI: 32%–55%]), and B (VE: 72% [95% CI: 29%–89%]) but not influenza A(H3N2) (V28% [95% CI: -4%–49%]). Among patients vaccinated >120 days prior to onset (median: 159 days [IQR: 140–188 days]), VE crossed the null against A(H1N1) (13% [95% CI: -24%–39%]), A(H3N2) (-2% [95% CI: -52%–31%]), and B (62% [95% CI: -2%–86%]).

Discussion

During the 2023–2024 US influenza season, when influenza vaccine strains were antigenically similar to circulating viruses, influenza vaccination reduced the risk of influenza–associated hospitalization among vaccinated adults. Our findings are consistent with 2023–2024 mid-season estimates from the United States^{7,8} and Canada⁹, and both mid-season estimates^{10–12} and final-season estimates¹³ from Europe. The overall VE reported here (40% [95% CI: 31%–48%]) was also similar to that reported in the same network during the previous season (37% [95% CI: 27%–46%]), which also had a well-matched influenza vaccine.¹⁴ In addition, patients aged ≥65 years had the lowest VE point estimate, although most US adults aged ≥65 years receive a higher-dose or adjuvanted vaccine whereas most children, adolescents and working-age adults receive a standard-dose, egg-based inactivated influenza vaccine.^{15,16} Estimates from this analysis document overall protection from influenza vaccination against influenza-associated hospitalizations during a season marked by both co-circulation of influenza A (H1N1), A (H3N2) and B viruses and prolonged virus circulation that translated to a median time since vaccination of 104 days among patients in this analysis.

Vaccination was associated with reduced risk of hospitalization for influenza A(H1N1) and influenza B but not influenza A(H3N2). Low VE against influenza A(H3N2) has already been observed during the 2023–2024 season in this network and others^{7,8,9} as well as during several recent influenza seasons in this network^{4,14} and others^{17–19}, and intra-season antigenic drift (i.e., mutation) from the vaccine strain has been offered as an explanation for reduced VE during some previous seasons.^{18,19} However, during the 2023–2024 influenza season, when the vaccine was antigenically similar to the circulating influenza viruses, the

overall low VE against A(H3N2)–associated hospitalization may have been attributable to other reasons, such as egg adaptation mutations in A(H3N2) during vaccine manufacturing²⁰ or influenza A(H3N2) accounting for a larger proportion of total influenza cases during the second half of the influenza season.¹

VE against influenza A(H3N2) was lowest among patients aged ≥ 65 years. Influenza A(H3N2) first appeared in 1968 and reduced VE against influenza A(H3N2) among older adults has often been attributed to the lack of early-in-life exposure (i.e., immune imprinting).²¹ In a similar analysis during the 2023–2024 season, influenza A(H3N2) was not more common than influenza A(H1N1) among cases patients aged ≥ 65 years compared with those 18–64 years, with A(H3N2) accounting for about a third of influenza A cases in both groups. However, influenza A(H3N2) accounted for a larger proportion of circulating virus later during the season (compared with earlier)¹, and patients aged ≥ 65 years were more likely to be vaccinated before October, which could have led to some additional waning in the already-low protection against A(H3N2) in this age group. In addition, our finding of poor VE against A(H3N2)–associated *hospitalization* specifically mirrors the rise in influenza–associated hospitalizations typically observed at the population level among adults aged ≥ 65 years during A(H3N2)–predominant influenza seasons.²² During the 2022–2023 influenza season, VE against A(H3N2)–associated hospitalization (7%) for patients aged ≥ 65 years in this network was substantially lower than that for medically attended (i.e., outpatient) A(H3N2) infection for the same group in Canada (59%),^{14,23} potentially suggesting that poor VE against A(H3N2)–associated hospitalization for older adults could be associated with an elevated inflammatory response to A(H3N2) resulting in severe disease.²² In contrast, VE against influenza B–associated hospitalizations was high, which has been observed in this network during past seasons²⁵, as well as in other networks earlier this season^{7,8} (United States), during the previous season (Europe),²⁶ and across multiple previous seasons (Canada).²⁷ High VE against influenza B, which reflects B/Victoria lineages only since the absence of B/Yamagata from 2022 onwards²⁸, typically has been associated with the relative stability of the virus and ability to successfully match the vaccine strain.²⁶

During an influenza season with a well-matched vaccine, we observed reduced VE against influenza A(H1N1)–associated hospitalizations among patients vaccinated >120 days prior to enrollment, and a signal of potentially further reduced protection against A(H3N2) even though VE already crossed the null at 14–120 days. This finding suggests that declining protection during the season can occur even when little or no antigenic drift (i.e., genetic mutation) of the virus has occurred. Our findings are similar to those of Young et al.’s meta-analysis of waning comprising influenza seasons from 2009–2016²⁹, and Ferdinands et al.’s analysis of waning across four US influenza seasons (2015–2019) when antigenic drift was also minimal.³⁰ In particular, the roughly 30 percentage point absolute differences in VE against influenza A–associated hospitalizations among patients vaccinated 14–120 days (median: 68 days) prior to enrollment and >120 days (median: 159 days) prior to enrollment align with Ferdinands et al.’s estimate of an 8–11 percentage point absolute decline in VE per month since vaccination (i.e., a 24–33 point decline over three months). We observed more modest waning (compared to A[H1N1] or A[H3N2]) using our sample of B/Victoria cases. Although Ferdinands et al. found similar levels of waning across influenza

A(H1N1), A(H3N2), and B/Yamagata– associated hospitalizations³⁰, the modest decrease in VE we observed against influenza B–associated hospitalizations is similar to the findings of Domnich et al.'s 2018–2023 multi-season analysis in Italy,³¹ where B/Victoria virus predominated among influenza B cases.

Although sample size did not permit us to explore more detailed timelines of waning or differences in subtype-specific waning by age group, during previous influenza seasons waning VE has generally been observed to begin sooner after vaccination for influenza A(H3N2) compared with other subtypes^{25,26} and to be more pronounced among older adults and children compared to working-age adults.^{25,27} These observations and the generally greater opportunities for waning during long influenza seasons have raised the question of whether vaccination should be delayed for some populations until later in the influenza season (e.g., after October 1) to maximize protection³³, although current recommendations are for vaccination to be offered to most adults in September or October.³⁴ However, the benefit of protection later into the season relative to the potential for unvaccinated people to become infected early in the season may change for each influenza season, and it remains difficult to predict the length of the season or intra-season variability in the subtype composition of circulating influenza viruses.^{33,35}

These findings must be interpreted considering several limitations. First, sample size limited VE estimation or precision for some subgroups, particularly for influenza B–associated hospitalizations. Second, data on the type of influenza vaccine received were not collected, precluding comparative effectiveness analyses by vaccine type. Third, although our analysis showed evidence of waning VE, further analyses are needed to identify specific trajectories of waning during seasons with different subtype composition and genetic similarities between the vaccine and circulating viruses. Finally, although the analysis controlled for several relevant potential confounders, residual confounding is possible.

Conclusions

During the 2023–2024 US influenza season, characterized by a period of sustained elevated activity, long-term activity, and antigenic similarity between the vaccine and circulating viruses, we observed statistically significant protection from vaccination against influenza-associated hospitalizations overall, for patients aged ≥ 65 years and for immunocompromised patients. Analyses by virus subtype and time since vaccination showed reduced protection among patients who had influenza A(H3N2) and among patients vaccinated >120 days prior to enrollment, the latter of which was likely attributable to waning immune response rather than antigenic drift of the circulating viruses. These findings highlight the ongoing challenges surrounding influenza VE and suggest that further research is needed to better understand optimal timing for seasonal influenza vaccination.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Disclosure of Potential Conflicts of Interest

James D. Chappell reports research funding from Merck to study RSV epidemiology in hospitalized children with acute respiratory illness, outside the submitted work. Manju Gaglani reports funding from CDC for the US Flu VE Network and SYNERGY study, CDC-Abt Associates for RECOVER-PROTECT cohort studies, and CDC-Westat for the VISION study, outside the submitted work. Michelle Ng Gong reports being an advisor to trial design for Regeneron, participating as a DSMB member for Best, receiving grants from NHLBI as a HART co-investigator and ASP Steering Committee, and institutional payments from Wolters Kluwer as Section editor for UpToDate, outside the submitted work. Carlos G. Grijalva has served as consultant for Merck and GSK, and received research support from CDC, NIH, FDA, AHRQ and SyneosHealth, outside the submitted work. Natasha B. Halasa reports receiving a grant from Merck and participating on an advisory board for CSL-Seqirus, outside the submitted work. Akram Khan has received research support from 4D Medical, Roche Pharmaceuticals, Dompe Pharmaceuticals, Eli Lilly, Direct Biologics and NIH, NHLBI, BARDA, outside the submitted work. Adam S. Luring reports research support from NIAID, CDC, MDHHS, NSF and consulting fees from Roche related to a clinical trial of baloxavir, outside of the submitted work. Ithan D. Peltan reports research support from NIGMS and, unrelated to the present manuscript, research support from NHLBI and NIGMS and funding to his institution from Bluejay Diagnostics and Novartis, outside the submitted work. Mayur Ramesh served on an advisory Board for Moderna and Pfizer, and was an unbranded speaker for AstraZeneca, outside the submitted work. Ivana A. Vaughn receives funding through her institution from eMaxHealth, Lilly USA, Evidera PPD, outside the submitted work.

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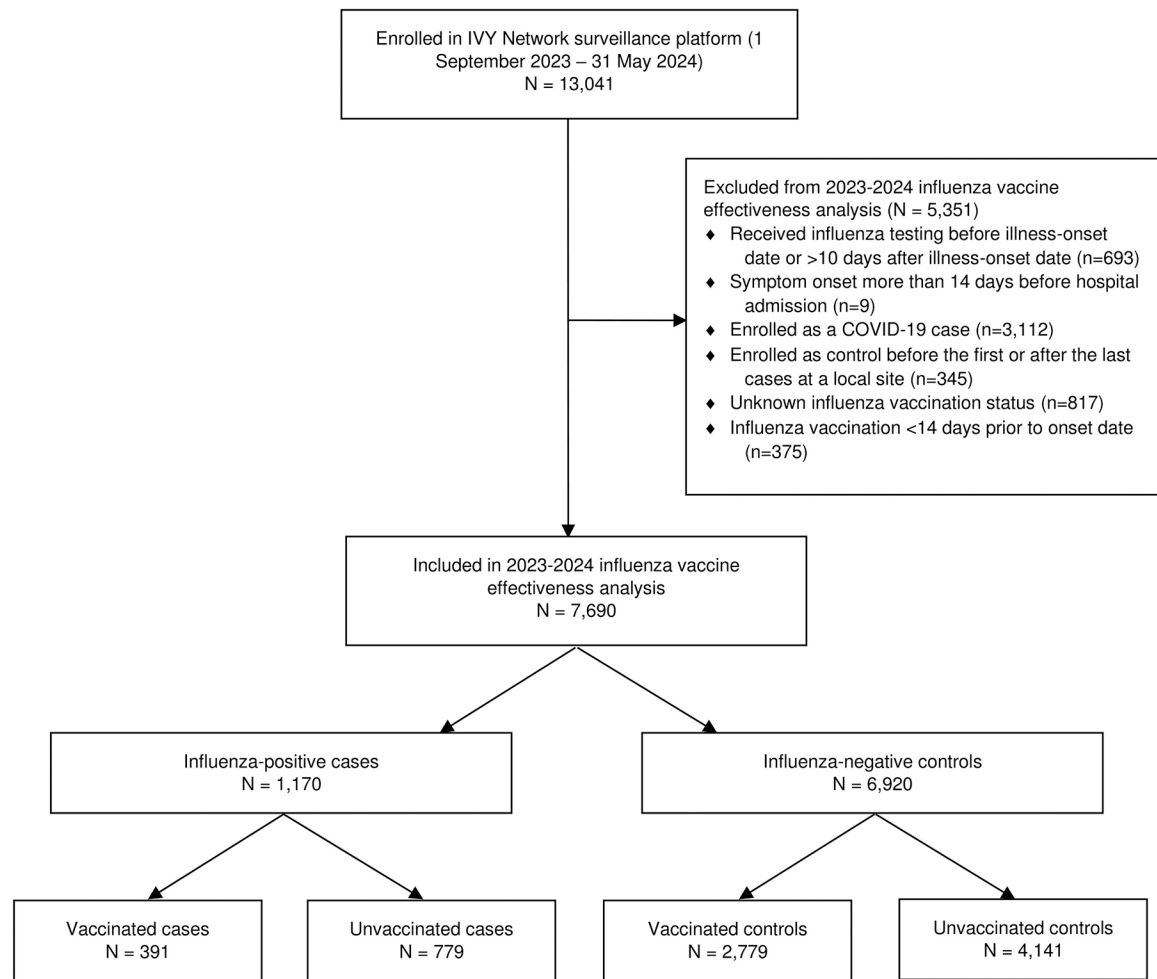


Figure 1.

Consort diagram of patient exclusions. No patients were found to be missing covariate data used in the VE model.

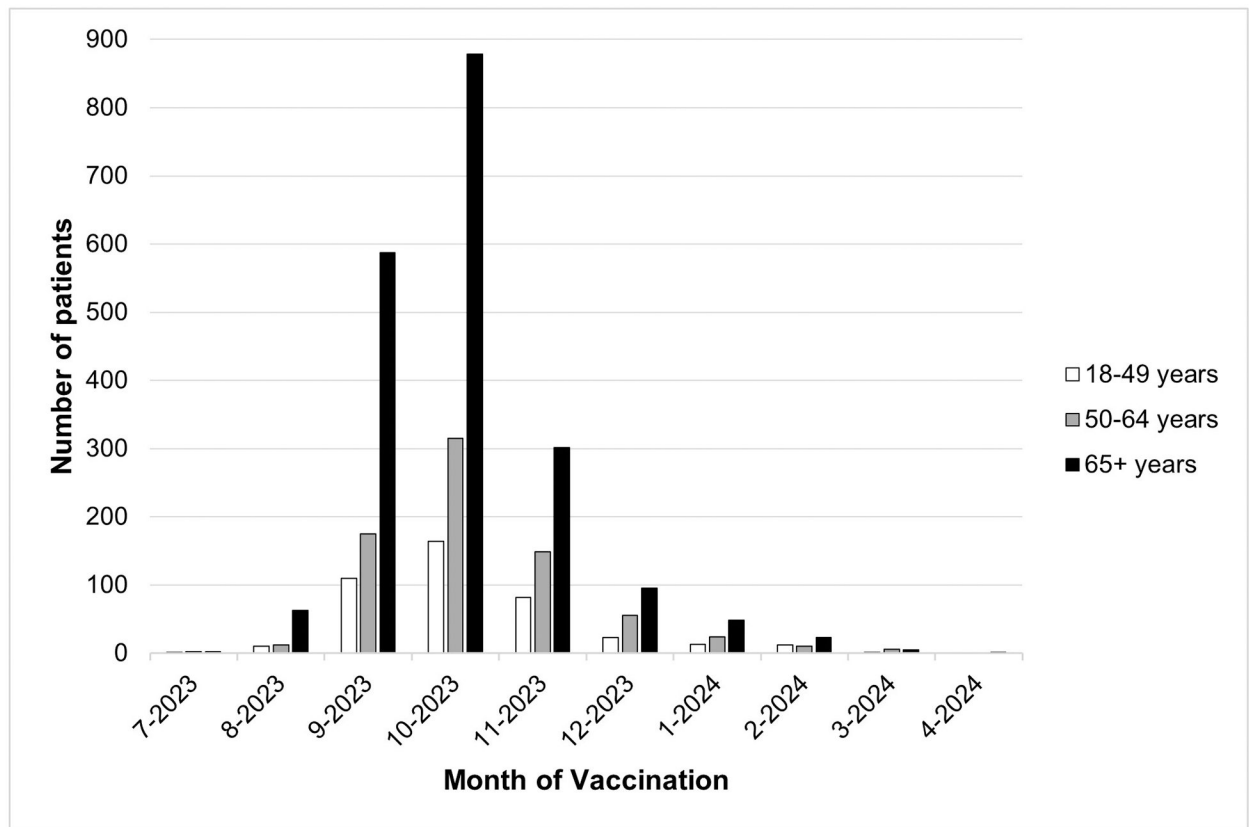


Figure 2.

Month of vaccination among cases and controls, by age group—IVY Network, September 1, 2023–May 31, 2024. Vaccination occurred slightly earlier in the year among patients aged ≥ 65 years (median: 10/11/2023 [IQR: 9/26/2023–10/30/2023]) than those aged 18–49 years (median: 10/15/2023 [IQR: 9/27/2023–11/7/2023]) or aged 50–64 years (median: 10/16/2023 [IQR: 9/30/2023–11/9/2023]) ($p < 0.001$). Patients aged ≥ 65 years were more likely to get an influenza vaccine in September or earlier compared to October or later than patients under 65 years old ($p < 0.001$).

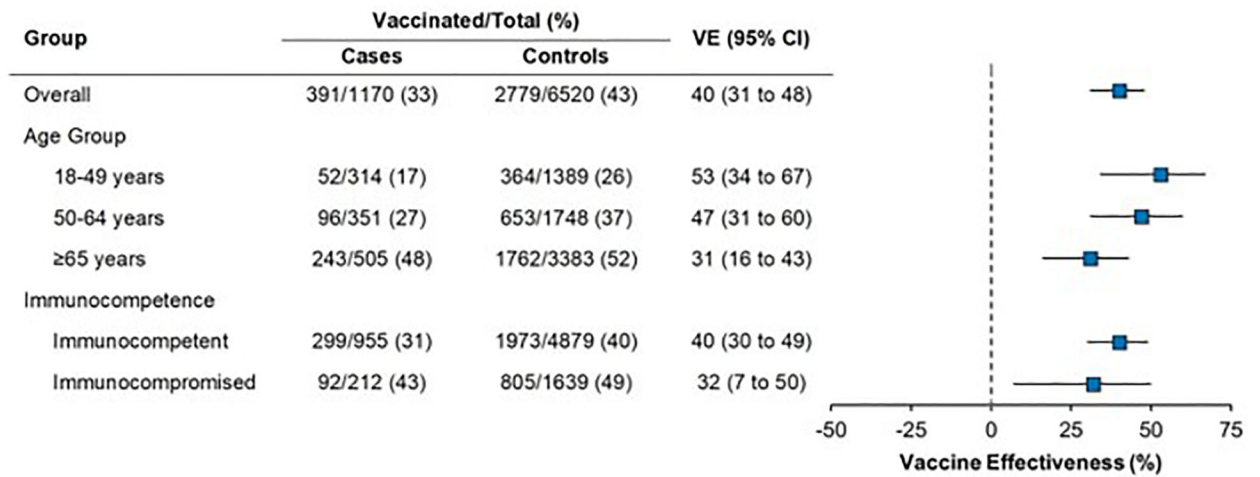


Figure 3. Influenza vaccine effectiveness (VE) against influenza-associated hospitalizations overall, by age group, and by immunocompromised status—IVY Network, September 1, 2023–May 31, 2024.

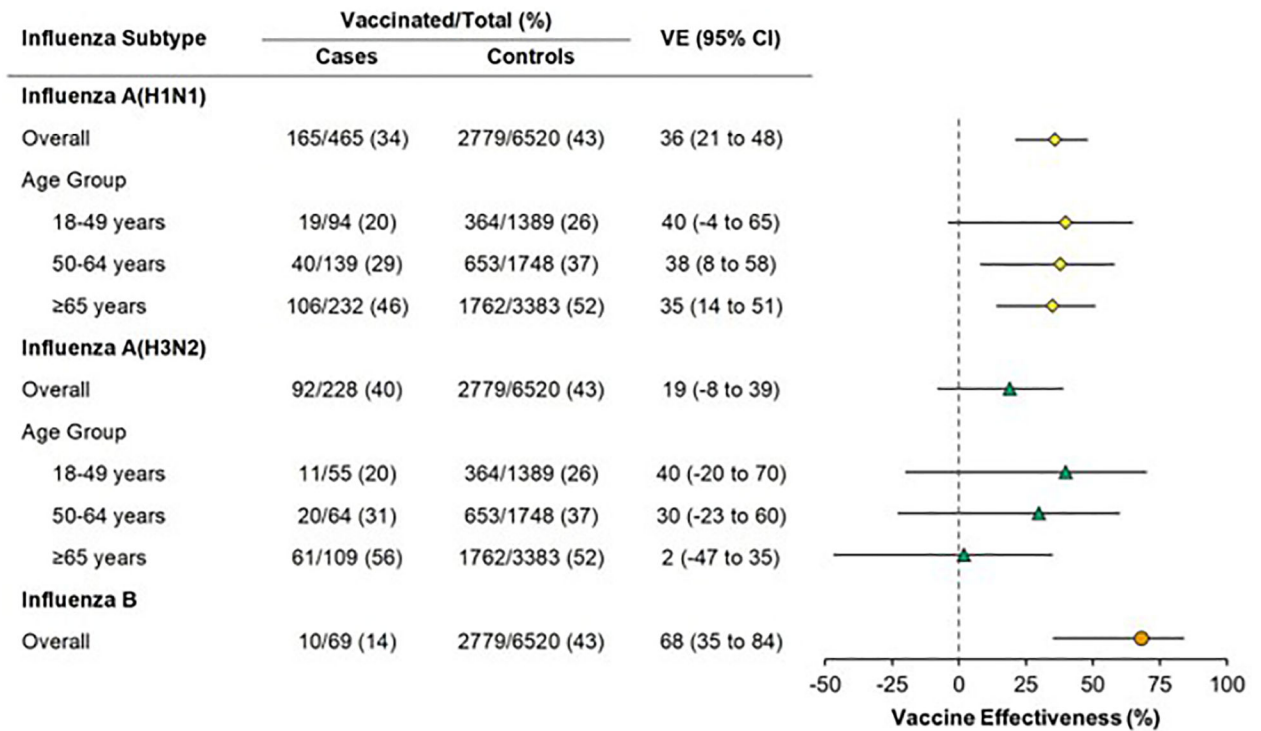


Figure 4.

Influenza vaccine effectiveness (VE) against influenza A(H1N1)-associated hospitalizations overall and by age group (diamond), influenza A(H3N2)-associated hospitalizations overall and by age group (triangle), and against influenza B-associated hospitalizations overall (circle)—IVY Network, September 1, 2023–May 31, 2024.

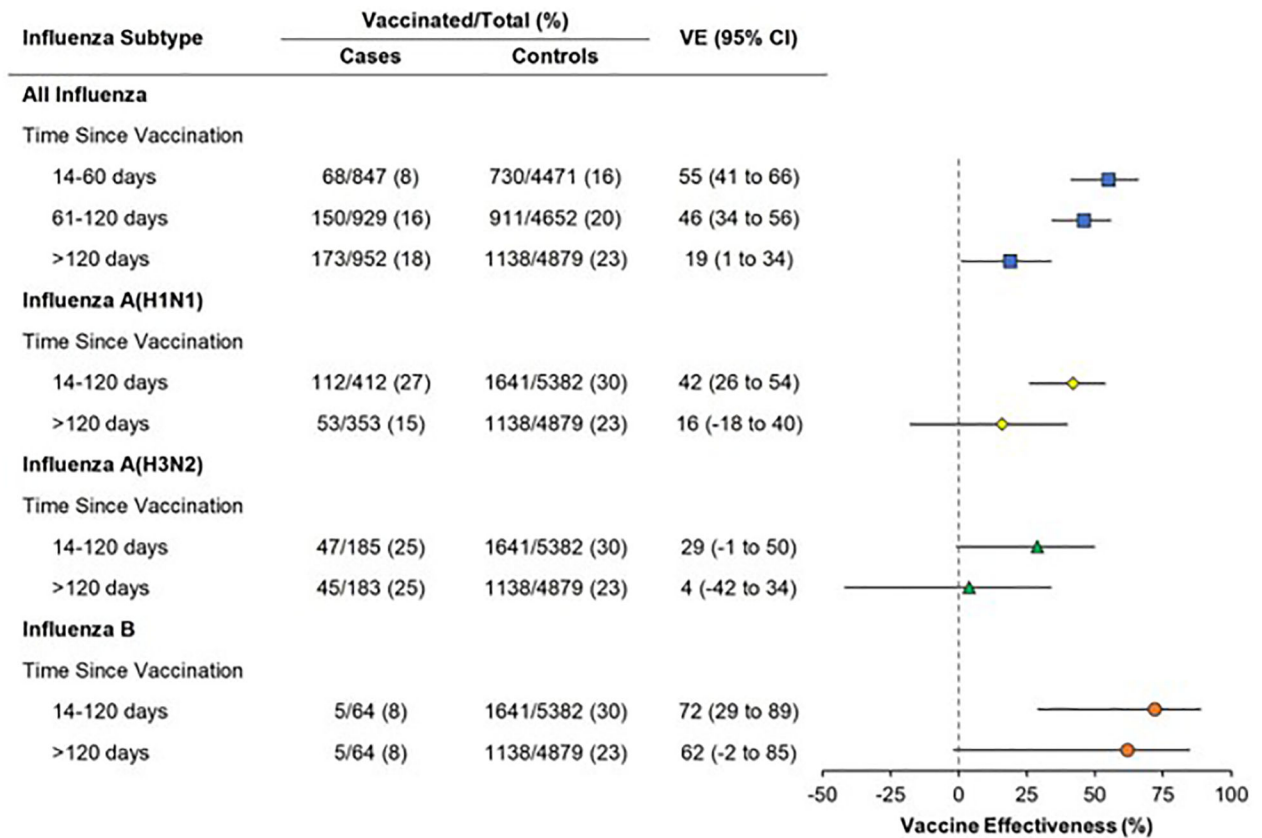


Figure 5.

Influenza vaccine effectiveness (VE) against influenza-associated hospitalizations among patients vaccinated 14–60, 61–120, and >120 days prior to enrollment, overall (square) and against hospitalizations associated with influenza A(H1N1) (diamond), influenza A(H3N2) (triangle), and influenza B (circle) among patients vaccinated 14–120 and >120 days prior to enrollment—IVY Network, September 1, 2023–May 31, 2024.

Table 1.
Characteristics of Influenza-positive Patients (Cases) and Influenza-negative Patients (Controls)

	Overall	Influenza-Positive Case Patients	Influenza-Negative and SARS-CoV-2-Negative Control Patients	P
No. (%) (row percentage)	7690 (100)	1170 (15.2)	6520 (84.8)	
HHS region				
1	1359 (17.7)	213 (18.2)	1146 (17.6)	<0.001
2	540 (7.0)	63 (5.4)	477 (7.3)	
3	135 (1.8)	16 (1.4)	119 (1.8)	
4	1197 (15.6)	139 (11.9)	1058 (16.2)	
5	1123 (14.6)	234 (20.0)	889 (13.6)	
6	774 (10.1)	150 (12.8)	624 (9.6)	
7	219 (2.8)	37 (3.2)	182 (2.8)	
8	1413 (18.4)	184 (15.7)	1229 (18.8)	
9	673 (8.8)	87 (7.4)	586 (9.0)	
10	257 (3.3)	47 (4.0)	210 (3.2)	
Vaccination characteristics				
Vaccinated for influenza	3170 (41.2)	391 (33.4)	2779 (42.6)	<0.001
Days from influenza vaccination to illness onset, median (IQR)	104 (60–150)	108 (73–144)	103 (58–151)	<0.001
14–60 days from vaccination	798 (10.4)	68 (5.8)	730 (11.2)	<0.001
61–120 days from vaccination	1061 (13.8)	150 (12.8)	911 (14.0)	
121+ days from vaccination	1311 (17.0)	173 (14.8)	1138 (17.5)	
Demographic characteristics				
Age, median (IQR), years	65 (52–75)	62 (48–72)	65 (53–75)	<0.001
Age group				
18–49 years	1703 (22.2)	314 (26.8)	1389 (21.3)	<0.001
50–64 years	2099 (27.3)	351 (30.0)	1748 (26.8)	
≥65 years	3888 (50.6)	505 (43.2)	3383 (51.9)	
Female	3930 (51.1)	621 (53.1)	3309 (50.8)	0.143
Race/ethnicity				
White, non-Hispanic	4290 (55.8)	571 (48.8)	3719 (57.0)	<0.001
Black, non-Hispanic	1771 (23.0)	330 (28.2)	1441 (22.1)	
Hispanic, any race	1042 (13.6)	177 (15.1)	865 (13.3)	
Other race, non-Hispanic	327 (4.3)	50 (4.3)	277 (4.3)	
Health status indicators				
Insured	7333 (95.4)	1090 (93.2)	6243 (95.8)	<0.001
Current tobacco smoking	1514 (19.7)	279 (23.9)	1235 (18.9)	<0.001
≥1 Hospitalization in prior year	4568 (59.4)	588 (50.3)	3980 (61.0)	<0.001
Chronic respiratory condition	3339 (43.4)	504 (43.1)	2835 (43.5)	0.794

	Overall	Influenza-Positive Case Patients	Influenza-Negative and SARS-CoV-2-Negative Control Patients	P
Immunocompromised ^a	1854 (24.1)	215 (18.4)	1639 (25.2)	<0.001
Number of chronic underlying medical conditions categories ^b				
0	556 (7.2)	111 (9.5)	445 (6.8)	<.001
1	1477 (19.2)	261 (22.3)	1216 (18.7)	
2	2024 (26.3)	322 (27.5)	1702 (26.1)	
3	1867 (24.3)	262 (22.4)	1605 (24.6)	
≥4	1765 (23.0)	214 (18.3)	1551 (23.8)	
Admission Characteristics				
Days from illness onset to influenza testing, median (IQR)	2 (0–3)	2 (1–4)	2 (0–3)	<.001
Days from illness onset to hospitalization, median (IQR)	2 (0–3)	2 (1–4)	1 (0–3)	<0.001

^a Any of: solid tumor or hematologic malignancy with immunosuppressive treatment in the previous 30 d, solid organ transplant with use of immunosuppressive medication in the previous 30 days, received bone marrow transplant/hematopoietic stem cell transplant within 2 y of transplantation or receipt of immunosuppressive therapy with the previous 30 days, not including CART-cell therapy, HIV infection with CD4 count <200 cells/mm³ in the past 1 y or diagnosed with AIDS, congenital immunodeficiency syndrome, or current use of immunosuppressive therapy in the past 30 d for a condition other than malignancy, solid organ transplant, or bone marrow transplant/ hematopoietic stem cell transplant.

^b Individual conditions were grouped into 7 categories: cardiovascular, neurologic, pulmonary, gastrointestinal, endocrine, renal, and hematologic. Participants were classified by the number of categories in which conditions were documented (0, 1, 2 or ≥3).