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Interim Estimates of 2024–2025 COVID-19 Vaccine Effectiveness Among Adults Aged ≥18 Years — VISION and IVY Networks, September 2024–January 2025

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Abstract

COVID-19 vaccination averted approximately 68,000 hospitalizations during the 2023–24 respiratory season. In June 2024, CDC and the Advisory Committee on Immunization Practices (ACIP) recommended that all persons aged ≥6 months receive a 2024–2025 COVID-19 vaccine, which targets Omicron JN.1 and JN.1-derived sublineages. Interim effectiveness of 2024–2025 COVID-19 vaccines was estimated against COVID-19–associated emergency department (ED) or urgent care (UC) visits during September 2024–January 2025 among adults aged ≥18 years in one CDC-funded vaccine effectiveness (VE) network, against COVID-19–associated hospitalization in immunocompetent adults aged ≥65 years in two networks, and against COVID-19–associated hospitalization among adults aged ≥65 years with immunocompromising conditions in one network. Among adults aged ≥18 years, VE against COVID-19–associated ED/UC visits was 33% (95% CI = 28%–38%) during the first 7–119 days after vaccination. Among immunocompetent adults aged ≥65 years from two CDC networks, VE estimates against COVID-19–associated hospitalization were 45% (95% CI = 36%–53%) and 46% (95% CI = 26%–60%) during the first 7–119 days after vaccination. Among adults aged ≥65 years with immunocompromising conditions in one network, VE was 40% (95% CI = 21%–54%) during the first 7–119 days after vaccination. These findings demonstrate that vaccination with a 2024–2025 COVID-19 vaccine dose provides additional protection against COVID-19–associated ED/UC encounters and hospitalizations compared with not receiving a 2024–2025 dose and support current CDC and ACIP recommendations that all persons aged ≥6 months receive a 2024–2025 COVID-19 vaccine dose.

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Introduction

During September 24, 2023–August 11, 2024, approximately 800,000 COVID-19–associated hospitalizations occurred in the United States (*1*); adults aged ≥65 years accounted for 70% of these hospitalizations (*2*). During 2024, the SARS-CoV-2 Omicron JN.1 and JN.1-derived lineages predominated and were genomically divergent from the XBB lineages on which the 2023–2024 COVID-19 vaccines were based. On June 27, 2024, CDC's Advisory Committee on Immunization Practices (ACIP) recommended 2024–2025 COVID-19 vaccination with a Food and Drug Administration (FDA)–authorized or approved vaccine for all persons aged ≥6 months (*3*). In August 2024, FDA approved monovalent 2024–2025 COVID-19 vaccines by Moderna* and Pfizer-BioNTech† (based on the SARS-CoV-2 Omicron KP.2 lineage) and authorized a monovalent 2024–2025 COVID-19 vaccine by Novavax§ (based on the SARS-CoV-2 Omicron JN.1 lineage), for persons aged ≥12 years. For a majority of adults, 1 2024–2025 vaccine dose is recommended, although persons with moderate or severe immunocompromise and adults aged ≥65 years are recommended to receive additional doses, depending on their vaccination history and time since receipt of their most recent dose.¶

This analysis estimated 2024–2025 COVID-19 vaccine effectiveness (VE) against COVID-19–associated emergency department (ED) or urgent care (UC) visits in one CDC-funded VE network and VE against COVID-19–associated hospitalization in two CDC-funded VE networks during September 2024–January 2025** among adults aged ≥18 years.

Methods

Data Source

Methods for VE analyses in the Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network (VISION) and Investigating Respiratory Viruses in the Acutely Ill (IVY) network have been reported (*4*,*5*). VISION is a multisite, electronic health care records (EHR)–based network including 373 ED/UCs and 241 hospitals in eight states.†† Eligible patients are those who have received molecular (e.g., real-time reverse transcription–polymerase chain reaction [RT-PCR]) or antigen testing for SARS-CoV-2 during the 10 days preceding or ≤72 hours after an eligible ED/UC encounter or hospital

* https://www.fda.gov/vaccines-blood-biologics/spikevax
† https://www.fda.gov/vaccines-blood-biologics/comirnaty
§ https://www.fda.gov/vaccines-blood-biologics/coronavirus-covid-19-cber-regulated-biologics/novavax-covid-19-vaccine-adjuvanted
¶ https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

** The VISION analysis included ED/UC encounters and hospitalizations during September 1, 2024–January 21, 2025. The IVY network analysis included hospitalized patients admitted during September 1, 2024–January 30, 2025.
†† Sites from the CDC-funded VISION that contributed data for this analysis were HealthPartners (Minnesota and Wisconsin), Intermountain Health (Utah), Kaiser Permanente Northern California (California), Kaiser Permanente Northwest (Oregon and Washington), Regenstrief Institute (Indiana), and University of Colorado (Colorado).

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admission.[§§] COVID-19 vaccination history is ascertained from state or jurisdictional registries, EHRs and, in a subset of sites, medical claims data.[¶¶]

IVY is a multicenter, inpatient network of 26 hospitals in 20 U.S. states[***] and prospectively enrolls adults aged ≥18 years with COVID-19–like illness[†††] who receive molecular or antigen testing for SARS-CoV-2 within 10 days of illness onset and within 3 days of hospital admission. Nasal swabs are collected at enrollment for central RT-PCR testing for SARS-CoV-2 at Vanderbilt University Medical Center (Nashville, Tennessee); SARS-CoV-2–positive specimens are sent to the University of Michigan (Ann Arbor, Michigan) for whole genome sequencing to identify SARS-CoV-2 lineages. Demographic and clinical data are collected through EHR review and patient or proxy interview. COVID-19 vaccination history is ascertained from state or jurisdictional registries, EHRs, and plausible self-report based on known location and dates of vaccination.

In both analyses, persons who had received the 2024–2025 COVID-19 vaccine ≥7 days before the encounter index date (VISION) or illness onset date (IVY) were considered vaccinated. Those who had not received the 2024–2025 COVID-19 vaccine (regardless of previous COVID-19 vaccination or infection history) were considered not vaccinated and served as comparators.

Data Analysis

The VISION and IVY networks conducted separate VE analyses using test-negative designs (*4*,*5*). In both analyses, adults aged ≥18 years with COVID-19–like illness who 1) had a medical encounter at an ED/UC (VISION only) or 2) were hospitalized (VISION and IVY) at a participating facility were included. Case-patients were those who received a positive SARS-CoV-2 molecular or antigen test result, and control patients were those who received a negative SARS-CoV-2 molecular test result. Participants were excluded if they 1) had received a 2024–2025 COVID-19 vaccine <7 days or ≥120 days before their eligible ED/UC encounter or hospitalization, 2) had received a 2024–2025 COVID-19 vaccine dose <2 months after receiving a previous COVID-19 vaccine dose, or 3) were immunocompetent persons who had received more than 1 2024–2025 COVID-19 vaccine dose. COVID-19 case-patients were also excluded if they were co-infected with influenza or respiratory syncytial virus (RSV) at the time of their COVID-19–like illness encounter. Because of potential confounding from correlated vaccination behaviors, control patients with a positive or indeterminant influenza test result (adults ≥18 years) or a positive RSV test result (adults ≥60 years) were excluded from the primary analysis (*6*,*7*). Previous SARS-CoV-2 infections are incompletely documented in medical records; therefore, patients were included regardless of prior SARS-CoV-2 infections.

Odds ratios (OR) and 95% CIs were estimated using multivariable logistic regression, comparing persons who received a 2024–2025 COVID-19 vaccine dose with those who did not among case- and control patients, regardless of previous COVID-19 vaccination. VE models were adjusted a priori for age, sex, race and ethnicity, calendar time, and geographic

[§§] Eligible ED/UC encounters or hospital admissions were those for COVID-19–like illness, obtained using *International Classification of Diseases, Tenth Revision* (ICD-10) discharge codes. The specific codes used were COVID-19 pneumonia: J12.81 and J12.82; influenza pneumonia: J09.X1, J10.0*, J11.0*, and other viral pneumonia: J12*; bacterial and other pneumonia: J13, J14, J15*, J16*, J17, and J18*; influenza disease: J09*, J10.1, J10.2, J10.8*, J11.1, J11.2, and J11.8*; acute respiratory distress syndrome: J80; chronic obstructive pulmonary disease with acute exacerbation: J44.1; acute asthma exacerbation: J45.21, J45.22, J45.31, J45.32, J45.41, J45.42, J45.51, J45.52, J45.901, and J45.902; respiratory failure: J96.0*, J96.2*, R09.2, and J96.9*; other acute lower respiratory tract infections: B97.4, J20*, J21*, J22, J40, J44.0, J41*, J42, J43*, J47*, J85*, and J86*; acute and chronic sinusitis: J01* and J32*; acute upper respiratory tract infections: J00*, J02*, J03*, J04*, J05*, and J06*; acute respiratory illness signs and symptoms: R04.2, R05, R05.1, R05.2, R05.4, R05.8, R05.9, R06.00, R06.02, R06.03, R06.1, R06.2, R06.8, R06.81, R06.82, R06.89, R07.1, R09.0*, R09.1, R09.2, R09.3, and R09.8*; acute febrile illness signs and symptoms: R50*, R50.81, R50.9, and R68.83; acute nonrespiratory illness signs and symptoms: M79.10, M79.18, R10.0, R10.1*, R10.2, R10.3*, R10.81*, R10.84, R10.9, R11.0, R11.10, R11.11, R11.15, R11.2, R19.7, R21*, R40.0, R40.1, R41.82, R43*, R51.9, R53.1, R53.81, R53.83, R57.9, and R65*; febrile convulsions: R56.0; viral and respiratory diseases complicating pregnancy, childbirth, and puerperium: O98.5*, O98.8*, O98.9*, O99.5*. All ICD-10 codes with * include all child codes under the specific parent code.

[¶¶] National pharmacy chains were required to establish bidirectional linkage with jurisdictional immunization information systems (IISs) to support vaccine distribution early in the COVID-19 pandemic; thus, doses administered at pharmacies should be reported to IISs.

[***] Sites from the CDC-funded IVY network that contributed data for this analysis were Barnes-Jewish Hospital (St. Louis, Missouri), Baylor Scott & White Medical Center (Temple, Texas), Baylor University Medical Center (Dallas, Texas), Baystate Medical Center (Springfield, Massachusetts), Beth Israel Deaconess Medical Center (Boston, Massachusetts), Cleveland Clinic (Cleveland, Ohio), Emory University Medical Center (Atlanta, Georgia), Hennepin County Medical Center (Minneapolis, Minnesota), Henry Ford Health (Detroit, Michigan), Intermountain Medical Center (Murray, Utah), Johns Hopkins Hospital (Baltimore, Maryland), Montefiore Medical Center (New York, New York), Oregon Health and Science University Hospital (Portland, Oregon), Ronald Reagan UCLA Medical Center (Los Angeles, California), Stanford University Medical Center (Stanford, California), The Ohio State University Wexner Medical Center (Columbus, Ohio), UCHealth University of Colorado Hospital (Aurora, Colorado), University of Arizona Medical Center (Tucson, Arizona), University of Iowa Hospitals (Iowa City, Iowa), University of Miami Medical Center (Miami, Florida), University of Michigan Hospital (Ann Arbor, Michigan), University of Utah (Salt Lake City, Utah), University of Washington (Seattle, Washington), Vanderbilt University Medical Center (Nashville, Tennessee), Wake Forest University Baptist Medical Center (Winston-Salem, North Carolina), and Yale University (New Haven, Connecticut).

[†††] In the IVY network analysis, COVID-19–like illness was defined as one or more of the following signs and symptoms: fever, cough, dyspnea, new or worsening findings on chest imaging consistent with pneumonia, or hypoxemia defined as SpO2 <92% on room air or supplemental oxygen to maintain SpO2 ≥92%. For patients on chronic oxygen therapy, hypoxemia was defined as SpO2 below baseline or an escalation of supplemental oxygen to maintain a baseline SpO2.

region.[§§§] VE was calculated as (1 – adjusted OR) x 100% during the first 7–119 days since receipt of a 2024–2025 COVID-19 vaccine dose and separately during the first 7–59 days and 60–119 days since receipt of a dose. For ED/UC encounters, VE was estimated for persons aged ≥18 years, 18–64 years, and ≥65 years (Supplementary Table 1, https://stacks.cdc.gov/view/cdc/176586). Statistical power to estimate VE against hospitalization was limited in adults aged 18–64 years; therefore, VE against hospitalization was only estimated for adults aged ≥65 years in both networks. In the IVY network, VE against hospitalization was estimated in immunocompetent adults due to limited statistical power to assess VE for immunocompromised adults; in VISION, VE was estimated for all adults in the ED/UC setting and separately for adults with and without immunocompromising conditions in the hospital setting.[¶¶¶] The distribution of case- and control patients aged 5–17 years was explored in VISION; however, statistical power was limited in both the ED/UC and hospital settings, so frequencies are described without VE estimation (Supplementary Table 2; https://stacks.cdc.gov/view/cdc/176592).

Analyses were conducted using R software (version 4.3.2; R Foundation) for the VISION analysis and R software (version 4.4.0; R Foundation) for the IVY network analysis. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.[****]

[§§§] VISION regression models were adjusted for age, sex, race and ethnicity, calendar day, and geographic region with age and calendar day included as natural cubic splines. Geographic region was included in the model based on site-defined geographic cluster of the final discharge facility of the encounter. IVY network regression models were adjusted for age, sex, race and ethnicity, calendar time in biweekly intervals, and U.S. Department of Health and Human Services region.

[¶¶¶] Immunocompromising conditions were obtained from ICD-10 discharge codes. The specific codes used were hematologic malignancy: C81.*, C82.*, C83.*, C84.*, C85.*, C86.*, C88.*, C90.*, C91.*, C92.*, C93.*, C94.*, C95.*, C96.*, D46.*, D61.0*, D70.0, D61.2, D61.9, and D71.*; solid malignancy: C00.*, C01.*, C02.*, C03.*, C04.*, C05.*, C06.*, C07.*, C08.*, C09.*, C10.*, C11.*, C12.*, C13.*, C14.*, C15.*, C16.*, C17.*, C18.*, C19.*, C20.*, C21.*, C22.*, C23.*, C24.*, C25.*, C26.*, C30.*, C31.*, C32.*, C33, C34.*, C37, C38.*, C39.*, C40.*, C41.*, C43.*, C45.*, C46.*, C47.*, C48.*, C49.*, C50.*, C51.*, C52, C53.*, C54.*, C55, C56.*, C57.*, C58, C60.*, C61, C62.*, C63.*, C64.*, C65.*, C66.*, C67.*, C68.*, C69.*, C70.*, C71.*, C72.*, C73, C74.*, C75.*, C76.*, C77.*, C78.*, C79.*, C7A.*, C7B.*, C80.*, Z51.0, Z51.1*, and C4A.*; transplant: T86.0*, T86.1*, T86.2*, T86.3*, T86.4*, T86.5*, T86.81*, T86.85*, D47.Z1, Z48.2*, and Z94.*, and Z98.85; rheumatologic/inflammatory disorders: D86.*, E85.1, E85.2, E85.3, E85.4, E85.8*, E85.9, G35, J67.9, L40.54, L40.59, L93.0, L93.2, L94.*, M05.*, M06.*, M07.*, M08.*, M30.*, M31.3*, M31.5, M32.*, M33.*, M34.*, M35.3, M35.89, M35.9, M46.0*, M46.1, M46.8*, and M46.9*; other intrinsic immune condition or immunodeficiency: D27.9, D72.89, D80.*, D81.0, D81.1, D81.2, D81.4, D81.5, D81.6, D81.7, D81.8*, D81.9, D82.*, D83.*, D84.*, D89.0, D89.1, D89.3, D89.4*, D89.8*, D89.9, K70.3*, K70.4*, K72.*, K74.3, K74.4, K74.5, K74.6*, N04.*, and R18.0; HIV: B20.*, B21.*, B22.*, B23.*, B97.35, O98.7*, and Z21. All ICD-10 codes with * include all child codes under the specific parent code.

[****] 45 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.

Results

2024–2025 COVID-19 VE Against COVID-19–associated ED/UC Visits, VISION

Among adults aged ≥18 years in VISION, 137,543 ED/UC encounters met criteria for inclusion in the analyses, including 10,459 (8%) case-patients and 127,084 (92%) control patients (Table 1). Effectiveness of a 2024–2025 COVID-19 vaccination against a COVID-19–associated ED/UC visit was 33% (95% CI = 28%–38%) during the first 7–119 days after vaccination, 36% (95% CI = 29%–42%) during the first 7–59 days after vaccination, and 30% (95% CI = 22%–37%) during the 60–119 days after vaccination (Table 2).

2024–2025 COVID-19 VE Against COVID-19–associated Hospitalization, VISION and IVY Networks Among Older Adults

Among adults aged ≥65 years without immunocompromising conditions in VISION, 26,219 hospitalizations met criteria for inclusion in analyses, including 2,248 (9%) case-patients and 23,971 (91%) control patients. VE of a 2024–2025 COVID-19 vaccine dose against COVID-19–associated hospitalization was 45% (95% CI = 36%–53%) a median interval of 53 days since receipt of a 2024–2025 COVID-19 vaccine dose (Table 3). Among adults aged ≥65 years with immunocompromising conditions in VISION, 8,192 hospitalizations met criteria for inclusion in analyses, including 598 (7%) case-patients and 7,594 (93%) control patients. VE was 40% (95% CI = 21%–54%), a median interval of 53 days after receipt of a 2024–2025 COVID-19 vaccination. Among adults aged ≥65 years without immunocompromising conditions in the IVY network, 1,929 met inclusion criteria, including 683 (35%) case-patients and 1,246 (65%) control patients. VE against COVID-19–associated hospitalization was 46% (95% CI = 26%–60%), a median of 60 days after receipt of a 2024–2025 COVID-19 vaccine dose.

Whole Genome Sequencing of SARS-CoV-2 Specimens, IVY Network

Among adults aged ≥18 years in the IVY network, 653 SARS-CoV-2–positive specimens collected during September 1, 2024–December 31, 2024 were successfully sequenced; 55 (8.4%) had JN.1-like spike proteins, 92 (14.1%) had KP.2-like proteins, 340 (52.1%) had KP.3-like proteins, 126 (19.3%) had XEC-like proteins, and 40 (6.1%) had other spike proteins.[††††] Similarly,

[††††] SARS-CoV-2 lineages during the period of this analysis were classified according to their clade assignment as follows: sequences with clades 24A and 23I were grouped together as JN.1-like lineages; clades 24G and 24B were grouped together as KP.2-like lineages; clades 24C and 24E were grouped together as KP.3-like lineages; clade 24F represented XEC lineage; and "Other" represents non-JN.1-derived or recombinant viruses detected during September 1–December 31, 2024.

TABLE 1. Characteristics of emergency department and urgent care encounters and hospitalizations among adults aged ≥18 years with COVID-19–like illness, by COVID-19 case status and CDC vaccine effectiveness network — VISION and IVY Networks,* September 2024–January 2025

Characteristic	VE network and setting, no. (column %)								
	VISION ED/UC encounters, all adults aged ≥18 years			VISION hospitalizations, all adults aged ≥65 years			IVY hospitalizations, immunocompetent adults aged ≥65 years		
	Total	COVID-19 case-patients	COVID-19 control patients	Total	COVID-19 case-patients	COVID-19 control patients	Total	COVID-19 case-patients	COVID-19 control patients
All encounters	**137,543**	**10,459**	**127,084**	**34,411**	**2,846**	**31,565**	**1,929**	**683**	**1,246**
2024–2025 COVID-19 vaccination status									
No 2024–2025 dose†	**118,517 (86)**	9,545 (91)	108,972 (86)	**27,623 (80)**	2,540 (89)	25,083 (79)	**1,635 (85)**	614 (90)	1,021 (82)
Received 2024–2025 dose									
7–119 days earlier	**19,026 (14)**	**914 (9)**	**18,112 (14)**	**6,788 (20)**	**306 (11)**	**6,482 (21)**	**294 (15)**	**69 (10)**	**225 (18)**
7–59 days earlier	**10,269 (7)**	480 (5)	9,789 (8)	**3,904 (11)**	179 (6)	3,725 (12)	**146 (8)**	41 (6)	105 (8)
60–119 days earlier	**8,757 (6)**	434 (4)	8,323 (7)	**2,884 (8)**	127 (4)	2,757 (9)	**148 (8)**	28 (4)	120 (10)
Median age, yrs (IQR)	**53 (34–72)**	58 (37–74)	53 (34–71)	**78 (72–84)**	79 (73–86)	78 (71–84)	**77 (71–84)**	78 (72, 85)	76 (70, 83)
Age group, yrs§									
18–64	**88,858 (65)**	6,113 (58)	82,745 (65)	—	—	—	—	—	—
≥65	**48,685 (35)**	4,346 (42)	44,339 (35)	**34,411 (100)**	2,846 (100)	31,565 (100)	**1,929 (100)**	683 (100)	1,246 (100)
Female sex	**83,641 (61)**	6,275 (60)	77,366 (61)	**18,274 (53)**	1,412 (50)	16,862 (53)	**1,050 (54)**	374 (55)	676 (54)
Race and ethnicity									
Black or African American, NH	**15,003 (11)**	794 (8)	14,209 (11)	**2,575 (7)**	156 (5)	2,419 (8)	**370 (19)**	120 (18)	250 (20)
White, NH	**83,282 (61)**	7,256 (69)	76,026 (60)	**25,811 (75)**	2,281 (80)	23,530 (75)	**1,223 (63)**	447 (65)	776 (62)
Hispanic or Latino, any race	**20,461 (15)**	1,255 (12)	19,206 (15)	**2,640 (8)**	183 (6)	2,457 (8)	**184 (10)**	59 (9)	125 (10)
Other, NH¶	**14,014 (10)**	897 (9)	13,117 (10)	**2,858 (8)**	188 (7)	2,670 (8)	**89 (5)**	34 (5)	55 (4)
Unknown**	**4,783 (3)**	257 (2)	4,526 (4)	**527 (2)**	38 (1)	489 (2)	**63 (3)**	23 (3)	40 (3)
HHS region††									
1	**0**	0	0	**0**	0	0	**614 (32)**	235 (34)	379 (30)
2	**0**	0	0	**0**	0	0	**104 (5)**	23 (3)	81 (7)
3	**0**	0	0	**0**	0	0	**21 (1)**	10 (2)	11 (1)
4	**0**	0	0	**0**	0	0	**279 (15)**	93 (14)	186 (15)
5	**45,211 (33)**	3,416 (33)	41,795 (33)	**13,844 (40)**	1,261 (44)	12,583 (40)	**248 (13)**	115 (17)	133 (11)
6	**0**	0	0	**0**	0	0	**144 (8)**	33 (5)	111 (9)
7	**0**	0	0	**0**	0	0	**52 (3)**	11 (2)	41 (3)
8	**33,345 (24)**	4,519 (43)	28,826 (23)	**6,217 (18)**	696 (24)	5,521 (17)	**254 (13)**	86 (13)	168 (14)
9	**48,738 (35)**	1,728 (17)	47,010 (37)	**12,574 (37)**	766 (27)	11,808 (37)	**154 (8)**	54 (8)	100 (8)
10	**10,249 (7)**	796 (8)	9,453 (7)	**1,776 (5)**	123 (4)	1,653 (5)	**59 (3)**	23 (3)	36 (3)
No. of organ systems with a chronic medical condition, median (IQR)§§	**0 (0–1)**	0 (0–1)	0 (0–1)	**3 (2–4)**	3 (2–4)	3 (2–4)	**3 (2, 4)**	2 (2, 3)	3 (2, 4)
Immunocompromised¶¶	—	—	—	**8,192 (24)**	598 (21)	7,594 (24)	—	—	—
Month/Yr. of COVID-19–associated ED/UC encounter or hospitalization									
Sep 2024	**28,086 (20)**	3,675 (35)	24,411 (19)	**7,723 (22)**	982 (35)	6,741 (21)	**508 (26)**	229 (34)	279 (22)
Oct 2024	**28,364 (21)**	1,927 (18)	26,437 (21)	**7,641 (22)**	557 (20)	7,084 (22)	**377 (20)**	147 (22)	230 (19)
Nov 2024	**28,040 (20)**	1,465 (14)	26,575 (21)	**7,751 (23)**	408 (14)	7,343 (23)	**312 (16)**	114 (17)	198 (16)
Dec 2024	**38,148 (28)**	2,712 (26)	35,436 (28)	**9,063 (26)**	771 (27)	8,292 (26)	**394 (20)**	125 (18)	269 (22)
Jan 2025	**14,905 (11)**	680 (7)	14,225 (11)	**2,233 (6)**	128 (4)	2,105 (7)	**338 (18)**	68 (10)	270 (22)

Abbreviations: ED = emergency department; EHR = electronic health care records; HHS = U.S. Department of Health and Human Services; IVY = Investigating Respiratory Viruses in the Acutely Ill; NH = non-Hispanic; UC = urgent care; VE = vaccine effectiveness; VISION = Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network.

* Sites from the CDC-funded VISION that contributed data for this analysis were HealthPartners (Minnesota and Wisconsin), Intermountain Health (Utah), Kaiser Permanente Northern California (California), Kaiser Permanente Northwest (Oregon and Washington), Regenstrief Institute (Indiana), and University of Colorado (Colorado). Sites from the CDC-funded IVY network that contributed data for this analysis were Barnes-Jewish Hospital (St. Louis, Missouri), Baylor Scott & White Medical Center (Temple, Texas), Baylor University Medical Center (Dallas, Texas), Baystate Medical Center (Springfield, Massachusetts), Beth Israel Deaconess Medical Center (Boston, Massachusetts), Cleveland Clinic (Cleveland, Ohio), Emory University Medical Center (Atlanta, Georgia), Hennepin County Medical Center (Minneapolis, Minnesota), Henry Ford Health (Detroit, Michigan), Intermountain Medical Center (Murray, Utah), Johns Hopkins Hospital (Baltimore, Maryland), Montefiore Medical Center (New York, New York), Oregon Health and Science University Hospital (Portland, Oregon), Ronald Reagan UCLA Medical Center (Los Angeles, California), Stanford University Medical Center (Stanford, California), The Ohio State University Wexner Medical Center (Columbus, Ohio), UCHealth University of Colorado Hospital (Aurora, Colorado), University of Arizona Medical Center (Tucson, Arizona), University of Iowa Hospitals (Iowa City, Iowa), University of Miami Medical Center (Miami, Florida), University of Michigan Hospital (Ann Arbor, Michigan), University of Utah (Salt Lake City, Utah), University of Washington (Seattle, Washington), Vanderbilt University Medical Center (Nashville, Tennessee), Wake Forest University Baptist Medical Center (Winston-Salem, North Carolina), and Yale University (New Haven, Connecticut).

† The "no 2024–2025 dose" group included all eligible persons who did not receive 2024–2025 COVID-19 vaccine dose, regardless of number of previous doses (if any) received.

See table footnotes continued on the next page.

TABLE 1. (*Continued*) Characteristics of emergency department and urgent care encounters and hospitalizations among adults aged ≥18 years with COVID-19–like illness, by COVID-19 case status and CDC vaccine effectiveness network — VISION and IVY Networks,* September 2024–January 2025

§ In VISION, a total of 18,289 eligible hospitalizations were reported in adults aged 18–64 years, including 804 (4%) case-patients and 17,485 (96%) control patients. Of the hospitalized case-patients, 35 (4%) had received a 2024–2025 COVID-19 vaccine. Of the hospitalized control patients, 1,277 (7%) had received a 2024–2025 COVID-19 vaccine. In IVY, a total of 1,446 eligible hospitalizations were reported in adults aged 18–64 years, including 342 (24%) case-patients and 1,104 (76%) control patients. Of the case-patients aged 18–64 years, 16 (5%) had received a 2024–2025 COVID-19 vaccine. Of the control patients aged 18–64 years, 69 (6%) had received a 2024–2025 COVID-19 vaccine.

¶ For VISION, "Other, non-Hispanic" race includes persons reporting non-Hispanic ethnicity and any of the following for race: American Indian or Alaska Native, Asian, Native Hawaiian or Pacific Islander, Middle Eastern or North African, other races not listed, and multiple races. Because of small numbers, these categories were combined. For IVY, "Other race, non-Hispanic" includes Asian, American Indian or Alaska Native, Native Hawaiian or other Pacific Islander and patients who self-reported their race and ethnicity as, "Other"; these groups were combined because of small counts.

** For VISION, "Unknown" includes persons with missing race and ethnicity in their EHR. For IVY, "Unknown" refers to patients who did not report their race and ethnicity.

†† In VISION, geographic region was included in the model based on site-defined geographic cluster of the final discharge facility of the encounter. In IVY, geographic region was included in the model based on HHS region. HHS regions are included to illustrate geographic spread across both networks. Regions are defined by HHS. States included in each region are available at https://www.hhs.gov/about/agencies/iea/regional-offices/index.html. VISION sites included were located as follows: *Region 5:* HealthPartners (Minnesota and Wisconsin) and Regenstrief Institute (Indiana); *Region 8*: Intermountain Healthcare (Utah) and University of Colorado (Colorado); *Region 9*: Kaiser Permanente Northern California (California); and *Region 10*: Kaiser Permanente Northwest (Oregon and Washington). IVY network sites were located as follows: *Region 1*: Baystate Medical Center (Springfield, Massachusetts), Beth Israel Deaconess Medical Center (Boston, Massachusetts), and Yale University (New Haven, Connecticut); *Region 2*: Montefiore Medical Center (New York, New York); *Region 3*: Johns Hopkins Hospital (Baltimore, Maryland); *Region 4*: Emory University Medical Center (Atlanta, Georgia), University of Miami Medical Center (Miami, Florida), Vanderbilt University Medical Center (Nashville, Tennessee), and Wake Forest University Baptist Medical Center (Winston-Salem, North Carolina); *Region 5*: Cleveland Clinic (Cleveland, Ohio), Hennepin County Medical Center (Minneapolis, Minnesota), Henry Ford Health (Detroit, Michigan), The Ohio State University Wexner Medical Center (Columbus, Ohio), and University of Michigan Hospital (Ann Arbor, Michigan); *Region 6*: Baylor Scott & White Medical Center (Temple, Texas) and Baylor University Medical Center (Dallas, Texas); *Region 7*: Barnes-Jewish Hospital (St. Louis, Missouri) and University of Iowa Hospitals (Iowa City, Iowa); *Region 8*: Intermountain Medical Center (Murray, Utah), UCHealth University of Colorado Hospital (Aurora, Colorado), and University of Utah (Salt Lake City, Utah); *Region 9*: Stanford University Medical Center (Stanford, California), Ronald Reagan UCLA Medical Center (Los Angeles, California), and University of Arizona Medical Center (Tucson, Arizona); and *Region 10*: Oregon Health and Science University Hospital (Portland, Oregon) and University of Washington (Seattle, Washington).

§§ VISION underlying medical condition categories included pulmonary, cardiovascular, cerebrovascular, neurologic or musculoskeletal, hematologic, endocrine, renal, and gastrointestinal. IVY network underlying medical condition categories included pulmonary, cardiovascular, neurologic, hematologic, endocrine, kidney, gastrointestinal, and autoimmune.

¶¶ Immunocompromised status is not evaluated for ED/UC encounters because of a higher likelihood of incomplete discharge diagnosis codes in this setting. In IVY, a total of 656 eligible hospitalizations were reported in adults aged ≥65 years with immunocompromise, including 178 (27%) case-patients and 478 (73%) control patients. Of the case-patients aged ≥65 years with immunocompromise, 24 (13%) had received a 2024–2025 COVID-19 vaccine. Of the control patients aged ≥65 years with immunocompromise, 102 (21%) had received a 2024–2025 COVID-19 vaccine. Immunocompromised adults were excluded from the IVY Network's VE analyses due to limited sample size.

among 6,491 SARS-CoV-2–positive specimens collected during the same period and sequenced by CDC as part of national genomic surveillance,[§§§§] 928 (14.3%) had JN.1-like spike proteins, 982 (15.1%) had KP.2-like proteins, 3,430 (52.8%) had KP.3-like proteins, 894 (13.8%) XEC-like proteins, and 257 (4.0%) had other spike proteins.

Discussion

During September 2024–January 2025, 2024–2025 COVID-19 vaccination provided additional protection against COVID-19–associated ED/UC encounters and hospitalizations among adults with and without immunocompromising conditions, compared with not receiving a 2024–2025 COVID-19 vaccine dose. These results support current CDC recommendations for 2024–2025 COVID-19 vaccination, irrespective of previous COVID-19 vaccination and infection history, and represent the added benefit of 2024–2025 COVID-19 vaccination above existing protection from previous vaccination or infection (*3*).

During the analytic period, the primary circulating SARS-CoV-2 lineages were descendants of the Omicron JN.1 lineage, including KP.2, KP.3, and XEC.[¶¶¶¶] XEC is closely related to the KP.2 and JN.1 strains in the 2024–2025 COVID-19 vaccines, which might account for the sustained protection from COVID-19 vaccination observed during the analysis period, despite the emergence and increasing prevalence of XEC. Starting in January 2025, prevalence of LP.8.1 (a JN.1 and KP.1.1 descendent) began to increase, accounting for 31% of sequences in CDC's national genomic surveillance as of February 15, 2025. The pace and frequency with which new SARS-CoV-2 lineages have become predominant underscores the need for ongoing monitoring of COVID-19 VE and genomic surveillance.

COVID-19–associated hospitalization rates during the time frame of this analysis were relatively low compared with those during previous years, precluding estimation of VE against critical illness (i.e., intensive care unit admission, invasive mechanical ventilation, or death); VE against these outcomes has historically been higher and more sustained than that against less severe outcomes (*4*,*5*,*8*). Because of both lower hospitalization rates and lower vaccination rates,[*****] VE could not be estimated for children and adolescents aged

§§§§ CDC national SARS-CoV-2 genomic surveillance includes samples sequenced by CDC and national testing laboratories contracted by CDC.

¶¶¶¶ https://covid.cdc.gov/covid-data-tracker/#variant-proportions

***** https://www.cdc.gov/respvaxview/about

TABLE 2. Effectiveness of 2024–2025 COVID-19 vaccination against COVID-19–associated emergency department or urgent care encounters, by age group — VISION, September 2024–January 2025

Age group/COVID-19 vaccination dosage pattern	COVID-19 case patients No. (col %)	COVID-19 control patients No. (col %)	Median interval since last dose for vaccinated, days (IQR)	VE %* (95% CI)
≥18 yrs				
No 2024–2025 dose† (Ref)	9,545 (91)	108,972 (86)	998 (539–1,142)	Ref
Received 2024–2025 dose				
7–119 days earlier	914 (9)	18,112 (14)	55 (32–80)	33 (28–38)
7–59 days earlier	480 (5)	9,789 (8)	33 (20–46)	36 (29–42)
60–119 days earlier	434 (4)	8,323 (7)	82 (71–97)	30 (22–37)
18–64 yrs				
No 2024–2025 dose† (Ref)	5,860 (96)	76,792 (93)	1,042 (751–1,180)	Ref
Received 2024–2025 dose				
7–119 days earlier	253 (4)	5,953 (7)	53 (29–77)	30 (20–39)
7–59 days earlier	134 (2)	3,379 (4)	32 (20–45)	36 (23–46)
60–119 days earlier	119 (2)	2,574 (3)	81 (70–95)	21 (5–35)
≥65 yrs				
No 2024–2025 dose† (Ref)	3,685 (85)	32,180 (73)	750 (346–1,076)	Ref
Received 2024–2025 dose				
7–119 days earlier	661 (15)	12,159 (27)	57 (33–82)	35 (29–41)
7–59 days earlier	346 (8)	6,410 (14)	34 (21–47)	36 (28–44)
60–119 days earlier	315 (7)	5,749 (13)	83 (71–97)	34 (25–42)

Abbreviations: Ref = referent group; VE = vaccine effectiveness; VISION = Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network.

* VE was calculated by comparing the odds of 2024–2025 COVID-19 vaccination among case-patients and control patients using the following equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. The odds ratio was adjusted for age, sex, race and ethnicity, calendar day, and geographic region.

† The "no 2024–2025 dose" group included all eligible persons who did not receive a 2024–2025 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses (if any) received.

TABLE 3. Effectiveness of 2024–2025 COVID-19 vaccination against COVID-19–associated hospitalization among adults aged ≥65 years — VISION and IVY Networks, September 2024–January 2025

VE network/ Immunocompromise status/ COVID-19 vaccination dosage pattern	COVID-19 case-patients No. (col %)	COVID-19 control patients No. (col %)	Median interval since last dose for vaccinated, days (IQR)	VE %* (95% CI)
VISION, immunocompetent				
No 2024–2025 dose† (Ref)	2,016 (90)	19,198 (80)	775 (357–1,084)	Ref
Received 2024–2025 dose				
7–119 days earlier	232 (10)	4,773 (20)	53 (30–77)	45 (36–53)
7–59 days earlier	129 (6)	2,759 (12)	33 (20–46)	42 (30–52)
60–119 days earlier	103 (5)	2,014 (8)	81 (70–94)	48 (36–58)
VISION, immunocompromised				
No 2024–2025 dose† (Ref)	524 (88)	5,885 (78)	720 (343–1,064)	Ref
Received 2024–2025 dose				
7–119 days earlier	74 (12)	1,709 (22)	53 (31–78)	40 (21–54)
IVY network, immunocompetent				
No 2024–2025 dose† (Ref)	614 (90)	1,021 (82)	—§	Ref
Received 2024–2025 dose				
7–119 days earlier	69 (10)	225 (18)	60 (31–85)	46 (26–60)
7–59 days earlier	41 (6)	105 (9)	31 (20–45)	42 (14–61)
60–119 days earlier	28 (4)	120 (10)	85 (72–98)	47 (17–67)

Abbreviations: Ref = referent group; VE = vaccine effectiveness; VISION = Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network; IVY = Investigating Respiratory Viruses in the Acutely Ill.

* VE was calculated by comparing the odds of 2024–2025 COVID-19 vaccination in case-patients and control patients using the equation: (1 – adjusted odds ratio) x 100%. Odds ratios were estimated by multivariable logistic regression. For VISION, the odds ratio was adjusted for age, sex, race and ethnicity, calendar day, and geographic region. For IVY, the odds ratio was adjusted for age, sex, race and ethnicity, geographic region (U.S. Department of Health and Human Services region), and calendar time (biweekly intervals).

† The "no 2024–2025 dose" group included all eligible persons who did not receive a 2024–2025 COVID-19 vaccine dose, regardless of number of previous COVID-19 vaccine doses (if any) received.

§ Median interval from last dose for persons who received previous doses of COVID-19 vaccine but did not receive a 2024–2025 COVID-19 vaccine dose was not available in the IVY network.

5–17 years for either outcome or for adults aged 18–64 years against hospitalization. Analyses from previous years have indicated that COVID-19 vaccines provide similar protection across age groups. For the 2023–2024 COVID-19 vaccines, VE against ED/UC encounters during the first 60–179 days after vaccination was 24% (95% CI = -31% to 56%) for children aged 9 months–4 years, 50% (95% CI = 22%–68%) for children and adolescents aged 5 years–17 years, 24% (95% CI = 17%–31%) for adults aged 18–64 years, and 25% (95% CI = 20%–30%) for adults aged ≥65 years.†††††

Previous SARS-CoV-2 infection contributes protection against future disease, although protection wanes over time (*9*). An increase in SARS-CoV-2 circulation in the United States during late summer 2024, just before the 2024–2025 COVID-19 vaccines were approved and authorized, might have resulted in higher population-level immunity against JN.1-lineage strains, which could have resulted in lower measured VE than would have been detected in a population with less recent infection. Analyses did not account for previous SARS-CoV-2 infection or previous COVID-19 vaccination (e.g., original monovalent, bivalent, or 2023–2024 doses). VE should therefore be interpreted as the added benefit of 2024–2025 COVID-19 vaccination in a population with high levels of infection-induced immunity, vaccine-induced immunity, or both.

Limitations

The findings in this report are subject to at least four limitations. First, although case-patients were those who met a COVID-19–like illness definition and had a positive SARS-CoV-2 test result, they might have visited ED/UCs or been hospitalized for reasons other than COVID-19, which might have lowered VE estimates. Second, misclassification

††††† https://www.cdc.gov/acip/downloads/slides-2024-06-26-28/03-COVID-Link-Gelles-508.pdf

Summary

What is already known about this topic?

In June 2024, CDC's Advisory Committee on Immunization Practices (ACIP) recommended 2024–2025 COVID-19 vaccination for all persons aged ≥6 months to provide additional protection against severe COVID-19.

What is added by this report?

Vaccine effectiveness (VE) of 2024–2025 COVID-19 vaccine was 33% against COVID-19–associated emergency department (ED) or urgent care (UC) visits among adults aged ≥18 years and 45%–46% against hospitalizations among immunocompetent adults aged ≥65 years, compared with not receiving a 2024–2025 vaccine dose. VE against hospitalizations in immunocompromised adults aged ≥65 years was 40%.

What are the implications for public health practice?

These findings indicate that 2024–2025 COVID-19 vaccination provides additional protection against COVID-19–associated ED/UC encounters and hospitalization, versus no 2024–2025 vaccination and support CDC and ACIP recommendations that all persons aged ≥6 months receive 2024–2025 COVID-19 vaccination.

of vaccination status was possible, which would likely result in underestimation of VE if the misclassification was nondifferential. Third, lack of statistical power prevented estimation of VE in some strata, including younger age groups. Finally, although analyses were adjusted for some relevant confounders, residual confounding from other factors, such as behavioral modifications to prevent SARS-CoV-2 exposure and outpatient antiviral treatment for COVID-19, might remain.

Implications for Public Health Practice

In this analysis, receipt of a 2024–2025 COVID-19 vaccine dose provided additional protection against COVID-19–associated ED/UC visits and hospitalization among adults with and without immunocompromise. These results support CDC and ACIP recommendations for 2024–2025 COVID-19 vaccination (*3*). CDC continues to monitor VE of 2024–2025 COVID-19 vaccines.

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Interim Estimates of 2024–2025 Seasonal Influenza Vaccine Effectiveness — Four Vaccine Effectiveness Networks, United States, October 2024–February 2025

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Abstract

Annual influenza vaccination is recommended for all persons aged ≥6 months in the United States. Interim influenza vaccine effectiveness (VE) was calculated among patients with acute respiratory illness–associated outpatient visits and hospitalizations from four VE networks during the 2024–25 influenza season (October 2024–February 2025). Among children and adolescents aged <18 years, VE against any influenza was 32%, 59%, and 60% in the outpatient setting in three networks, and against influenza-associated hospitalization was 63% and 78% in two networks. Among adults aged ≥18 years, VE in the outpatient setting was 36% and 54% in two networks and was 41% and 55% against hospitalization in two networks. Preliminary estimates indicate that receipt of the 2024–2025 influenza vaccine reduced the likelihood of medically attended influenza and influenza-associated hospitalization. CDC recommends annual receipt of an age-appropriate influenza vaccine by all eligible persons aged ≥6 months as long as influenza viruses continue to circulate locally.

Introduction

Because of continual evolutionary changes in influenza viruses, CDC regularly monitors* influenza vaccine effectiveness (VE). Influenza vaccination prevents hundreds of thousands of outpatient medical visits, tens of thousands of hospitalizations, and thousands of deaths from influenza every year.† CDC's Advisory Committee on Immunization Practices recommends annual seasonal influenza vaccination for all persons aged ≥6 months (*1*). In March 2024, after the absence of detections of influenza B/Yamagata lineage viruses since 2020,§ the Food and Drug Administration recommended changing from a quadrivalent vaccine (including four influenza virus antigens) to a trivalent vaccine, containing three influenza virus antigens. During the 2024–25 influenza season, most influenza viruses detected in the United States were influenza A viruses (97% of positive specimens); among subtyped influenza A–positive specimens, 52% were influenza A(H3N2), and 47% were A(H1N1)pdm09 viruses.¶ This report provides interim estimates of effectiveness of any 2024–2025 influenza vaccine (i.e., trivalent inactivated influenza vaccine, trivalent recombinant influenza vaccine, or trivalent live attenuated influenza vaccine) against medically attended, laboratory-confirmed influenza for persons in the outpatient and inpatient settings from four U.S. VE surveillance networks.

Methods

Data Source and Collection

Analyses were conducted using data from four CDC-affiliated VE networks, all of which use a test-negative, case-control design to evaluate influenza VE: 1) Investigating Respiratory Viruses in the Acutely Ill (IVY), 2) the New Vaccine Surveillance Network (NVSN), 3) U.S. Flu Vaccine Effectiveness (U.S. Flu VE), and 4) the Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network (VISION). These analyses include child and adolescent and adult patients who received medical care (outpatient or inpatient) for an acute respiratory illness (ARI) during the 2024–25 influenza season. Case-patients were those persons with ARI who received a positive influenza molecular assay test result,** and control patients were those with ARI who received a negative influenza molecular assay test result.

The setting and age of enrolled patients differed by network (Box). IVY enrolled hospitalized patients aged

* https://www.cdc.gov/flu-vaccines-work/php/effectiveness-studies/index.html
† https://www.cdc.gov/flu-burden/php/data-vis-vac/index.html
§ https://www.fda.gov/vaccines-blood-biologics/lot-release/use-trivalent-influenza-vaccines-2024-2025-us-influenza-season
¶ https://www.cdc.gov/fluview/surveillance/2025-week-05.html
** To reduce potential case misclassification, all influenza case-patients received a positive reverse transcription–polymerase chain reaction test result from a clinical or surveillance respiratory laboratory specimen for IVY, NVSN, and U.S. Flu VE. For VISION, influenza case-patients received a positive molecular assay result from a clinical respiratory laboratory specimen.

BOX. Characteristics of four influenza vaccine effectiveness networks — United States, 2024–25 influenza season

1. Investigating Respiratory Viruses in the Acutely Ill Network

- **Population:** adults aged ≥18 years
- **Setting**: inpatient only
- **Inclusion dates**: October 1, 2024–February 4, 2025
- **Type of surveillance**: active
- **Medical centers included (state):** Baylor Scott & White Medical Center - Temple (Texas), Baylor Scott & White - Baylor University Medical Center (Texas), Baystate Medical Center (Massachusetts), Beth Israel Deaconess Medical Center (Massachusetts), Cleveland Clinic (Ohio), Emory University Medical Center (Georgia), Hennepin County Med. Ctr. (Minnesota), Henry Ford Health (Michigan), Intermountain Medical Center (Utah), Johns Hopkins Hospital (Maryland), Montefiore Medical Center (New York), The Ohio State University Wexner Medical Center (Ohio), Oregon Health and Science University Hospital (Oregon), Stanford University Medical Center (California), University of California, Los Angeles Medical Center (California), University of Colorado Hospital (Colorado), University of Iowa Hospitals (Iowa), University of Miami Medical Center (Florida), University of Michigan Hospital (Michigan), University of Utah (Utah), University of Washington (Washington), Vanderbilt University Medical Center (Tennessee), Wake Forest University Baptist Medical Center (North Carolina), Barnes-Jewish Hospital (Missouri), University of Arizona Medical Center (Arizona), and Yale University (Connecticut)
- **Determination of vaccination status**: influenza vaccination status was ascertained using jurisdictional immunization registries, electronic medical records, and by plausible patient or proxy report in the absence of source documentation
- **ARI definition**: one or more of the following: fever, cough, shortness of breath, new hypoxemia, or new pulmonary findings on chest imaging consistent with pneumonia
- **Influenza A subtype available**: yes

2. New Vaccine Surveillance Network

- **Population:** children and adolescents aged 6 months–17 years
- **Settings**: outpatient (outpatient clinics, urgent care clinics, and emergency departments); inpatient
- **Inclusion dates**: October 2, 2024–January 30, 2025
- **Type of surveillance**: primarily active*
- **Medical centers included (state)**: Vanderbilt University Medical Center (Tennessee), University of Rochester Medical Center (New York), Cincinnati Children's Hospital Medical Center (Ohio), Texas Children's Hospital (Texas), Seattle Children's Hospital (Washington), Children's Mercy Hospital (Missouri), and University of Pittsburgh Medical Center Children's Hospital of Pittsburgh (Pennsylvania)
- **Determination of vaccination status**: jurisdictional immunization registries, medical records or self-report.
- **ARI definition**: symptoms of acute respiratory illness (including cough, fever, or other symptoms) within 10 days of illness onset
- **Influenza A subtype available**: Yes

3. United States Flu Vaccine Effectiveness Network

- **Population:** children and adolescents aged 8 months–17 years; adults aged ≥18 years
- **Settings**: outpatient (outpatient clinics, urgent care clinics, and emergency departments)
- **Inclusion Dates**: October 1, 2024–January 17, 2025
- **Type of surveillance**: active
- **Medical centers included (state)**: Arizona State University Tempe, Phoenix Children's Hospital, Valleywise Health Medical Center (Arizona), University of Michigan and Henry Ford Health (Michigan), Washington University in St. Louis (Missouri), University Hospitals of Cleveland and Louis Stokes Cleveland Department of Veterans Affairs Medical Center (Ohio), University of Pittsburgh, University of Pittsburgh Medical Center (Pennsylvania), Baylor Scott & White Health (Texas), and Kaiser Permanente Washington (Washington)
- **Determination of vaccination status**: medical records/ jurisdictional immunization registries and self-report
- **ARI definition**: illness ≤7 days duration with new or worsening cough
- **Influenza A subtype available**: yes

4. Virtual SARS-CoV-2, Influenza and Other respiratory viruses Network

- **Population:** children and adolescents aged 6 months–17 years; adults aged ≥18 years
- **Settings**: outpatient (urgent care clinics and emergency departments); inpatient
- **Inclusion dates**: October 1, 2024–January 24, 2025
- **Type of surveillance**: passive
- **Medical centers included (state)**: HealthPartners (Minnesota and Wisconsin), Intermountain Health (Utah), Kaiser Permanente Northern California (California), Kaiser Permanente Southern California (California); Kaiser Permanente Center for Health Research (Oregon and Washington); Regenstrief Institute (Indiana); and UCHealth (Colorado)
- **Determination of vaccination status**: jurisdictional immunization registries, electronic health records, and claims data
- **ARI definition**: acute respiratory clinical diagnoses or respiratory signs or symptoms based on ICD-10 codes
- **Influenza A subtype available**: no

Abbreviations: ARI = acute respiratory illness; ICD-10 = *International Classification of Diseases, Tenth Revision.*
* For this analysis, 94% of New Vaccine Surveillance Network patients were enrolled through active surveillance.

≥18 years. NVSN enrolled child and adolescent patients (aged 6 months–17 years) in the outpatient setting,[††] as well as those admitted to a hospital. U.S. Flu VE enrolled child and adolescent (aged 8 months–17 years) and adult (≥18 years) patients in the outpatient setting. VISION included child and adolescent (aged 6 months–17 years) and adult (aged ≥18 years) patients in the outpatient setting and those admitted to a hospital.

Data Analysis

To assess effects of vaccination on likelihood of influenza illness, VE was estimated as (1 – adjusted odds ratio) × 100% using multivariable logistic regression, adjusting for geographic region, age, calendar time of illness, and other prespecified confounders.[§§] Patients were considered to be vaccinated if they received ≥1 dose of the 2024–2025 seasonal influenza vaccine ≥14 days before the date of ARI onset or clinical encounter.[¶¶] Patients were excluded[***] if they were vaccinated <14 days before the index date or had received a positive SARS-CoV-2 molecular assay test result (*2*). IVY, NVSN, and U.S. Flu VE calculated VE against influenza A virus subtypes A(H1N1)pdm09 and A(H3N2), when possible. VE point estimates for each network are reported, with 95% CIs included in the tables of this report; 95% CIs that exclude zero were considered statistically significant. For each network and patient age group, VE and 95% CIs were interpreted as the percentage of specific influenza outcomes prevented. SAS software (version 9.4; SAS Institute) and R (version 4.4; R Foundation) were used to conduct the analyses. IVY, NVSN, and U.S. Flu VE activities were reviewed by CDC, deemed not research, and were conducted consistent with applicable federal law and CDC policy.[†††] VISION activities were reviewed by CDC and conducted consistent with applicable federal law and CDC policy.[§§§]

Results

Data from the IVY network included 3,175 hospitalized adult patients aged ≥18 years with ARI (Table 1) (Supplementary Table 1, https://stacks.cdc.gov/view/cdc/176587). NVSN included 4,611 patients aged <18 years with ARI, including 2,969 seen in outpatient settings and 1,642 who were hospitalized. Among 3,344 patients with ARI in the outpatient setting included in the U.S. Flu VE network, 1,134 were patients aged <18 years, and 2,210 were adults. VISION data included 139,558 outpatient encounters (36,919 among patients aged <18 years and 102,639 among adults) and 32,671 hospitalized encounters (1,638 among patients aged <18 years and 31,033 among adults).

Influenza Vaccination Status Among Control Patients

Among control patients (i.e., those patients with ARI and a negative influenza test result) aged <18 years, the percentage vaccinated ranged from 22% (VISION) to 34% (NVSN) in outpatient settings, and from 27% (VISION) to 40% (NVSN) in the inpatient setting (Table 2). Among all adult control patients, the percentage vaccinated was 34% in outpatient settings (U.S. Flu VE and VISION) and ranged from 35% (IVY) to 39% (VISION) in the inpatient setting. Among control patients aged ≥65 years, 54% (VISION) to 59% (U.S. Flu VE) in outpatient settings and 45% (IVY) to 46% (VISION) in the inpatient setting were vaccinated.

VE against ARI in Outpatient and Inpatient Settings

Children and adolescents. Among persons aged <18 years, VE against any influenza-associated ARI was 32% (U.S. Flu VE), 59% (NVSN), and 60% (VISION) in outpatient settings and 63% (NVSN) and 78% (VISION) against influenza-associated hospitalization. Against influenza A(H1N1)pdm09, VE was 72% (NVSN) and 53% (U.S. Flu VE) in outpatient settings, and 63% (NVSN) against influenza-associated hospitalization. Against influenza A(H3N2), VE was 42% (NVSN) in outpatient settings and 55% (NVSN) against influenza-associated hospitalization. The estimate of VE in outpatient settings in the U.S. Flu VE network was not statistically significant (16%; 95% CI = –34% to 49%).

Adults. Among persons aged ≥18 years, VE against any influenza-associated ARI was 36% (U.S. Flu VE) and 54% (VISION) in outpatient settings and 41% (IVY) and 55% (VISION) against influenza-associated hospitalization. Effectiveness against influenza A(H1N1)pdm09 was 42% in outpatient settings (U.S. Flu VE) but was not statistically significant against influenza-associated hospitalization in the IVY network (39%; 95% CI = –14% to 67%). Effectiveness against influenza A(H3N2) was 51% (IVY) against influenza-associated hospitalization but was not statistically significant in the outpatient setting (25%; 95% CI = –6% to 48%, U.S. Flu VE network).

[††] Patients enrolled as outpatients in NVSN might have progressed to a more acute level of care, and those data might not be reflected in this analysis.
[§§] IVY, U.S. Flu VE, and VISION also adjusted for sex and race and ethnicity.
[¶¶] IVY, NVSN, and U.S. Flu VE used date of ARI onset. VISION used the earlier of outpatient visit date, hospital admission date, or influenza clinical testing date.
[***] VISION also excluded patients who received a negative influenza test but a clinical diagnosis of influenza, patients who received a clinical diagnosis of COVID-19, and influenza case-patients who received a positive molecular test for respiratory syncytial virus.
[†††] 45 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.
[§§§] 45 C.F.R. part 46, 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.

TABLE 1. Number and percentage of patients who received medical care for an acute respiratory illness, by medical care setting, age group, and influenza test result — four vaccine effectiveness networks, United States, 2024–25 influenza season

Network/ Patient age group	Outpatient setting*,†	Influenza test result, no. (%)		Inpatient setting	Influenza test result, no. (%)	
		Positive	Negative		Positive	Negative
IVY						
≥18 yrs	—	—	—	3,175	675 (21)	2,500 (79)
NVSN						
<18 yrs (6 mos–17 yrs)	2,969	482 (16)	2,487 (84)	1,642	119 (7)	1,523 (93)
U.S. Flu VE						
<18 yrs (8 mos–17 yrs)	1,134	217 (19)	917 (81)	—	—	—
≥18 yrs	2,210	475 (21)	1,735 (79)	—	—	—
VISION						
<18 yrs (6 mos–17 yrs)	36,919	9,563 (26)	27,356 (74)	1,638	157 (10)	1,481 (90)
≥18 yrs	102,639	26,011 (25)	76,628 (75)	31,033	2,959 (10)	28,074 (90)

Abbreviations: IVY = The Investigating Respiratory Viruses in the Acutely Ill Network; NVSN = New Vaccine Surveillance Network; U.S. Flu VE = U.S. Flu Vaccine Effectiveness Network; VE = vaccine effectiveness; VISION = Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network.

* Outpatient = outpatient clinics, urgent care, and emergency departments (NVSN and U.S. Flu VE); and urgent care and emergency departments (VISION).

† Patients enrolled as outpatients in NVSN might have progressed to a more acute level of care; those data might not be reflected in this analysis.

Among adults aged 18–64 years, VE against any influenza-associated ARI in outpatient settings was 37% (U.S. Flu VE) and 56% (VISION); VE against hospitalization was 48% (IVY) and 51% (VISION). Among adults aged ≥65 years, VE against any influenza-associated ARI was 51% (VISION) in outpatient settings and was 38% (IVY) and 57% (VISION) against hospitalization; VE was not statistically significant in the outpatient setting in the U.S. Flu VE network (VE = 18%; 95% CI = –69% to 60%).

Genetic Characterization of Influenza Viruses

As of February 3, 2025, a total of 286 influenza A(H3N2) viruses were genetically characterized, including 26 (9%) from patients in IVY, 200 (70%) from the U.S. Flu VE network, and 60 (21%) from NVSN; all belonged to the hemagglutinin (HA) clade 2a.3a.1, which includes the A(H3N2) strain selected for the 2024–2025 cell-grown influenza vaccine (A/Massachusetts/18/2022) (Supplementary Table 2, https://stacks.cdc.gov/view/cdc/176590) Among 158 sequenced A(H1N1)pdm09 viruses, five (3%) were from IVY, 80 (51%) were from the U.S. Flu VE network, and 73 (46%) were from NVSN. Among these, three from IVY, 55 from U.S. Flu VE, and 46 from NVSN belonged to HA clade 5a.2a, and two from IVY, 25 from U.S. Flu VE, and 27 from NVSN belonged to HA clade 5a.2a.1. The HA clade 5a.2a.1 includes the A(H1N1)pdm09 strain selected for the 2024–2025 cell-grown influenza vaccine (A/Wisconsin/67/2022).

TABLE 2. Number and percentage of children and adolescents* aged <18 years and adults aged ≥18 years receiving seasonal influenza vaccine, number and percentage with a positive or negative influenza test result, and vaccine effectiveness,† by influenza type and subtype§ — four vaccine effectiveness networks, United States, 2024–25 influenza season

Network (setting)	Influenza test result by influenza vaccination status, no. vaccinated/Total (%)		
	Influenza-positive	Influenza-negative	VE (95% CI)¶
All ages			
Any influenza**			
VISION (outpatient)	6,953/35,574 (20)	31,785/103,984 (31)	56 (54 to 58)
U.S. Flu VE (outpatient)	166/692 (24)	848/2,652 (32)	42 (29 to 54)
All children and adolescents aged <18 yrs			
Any influenza**			
NVSN†† (outpatient§§)	100/482 (21)	855/2,487 (34)	59 (47 to 68)
U.S. Flu VE (outpatient)	54/217 (25)	256/917 (28)	32 (1 to 54)
VISION (outpatient)	1,322/9,563 (14)	5,943/27,356 (22)	60 (56 to 63)
NVSN (inpatient)	28/119 (24)	613/1,523 (40)	63 (41 to 76)
VISION (inpatient)	16/157 (10)	406/1,481 (27)	78 (60 to 89)
Influenza A(H1N1)pdm09			
NVSN (outpatient)	32/224 (14)	855/2,487 (34)	72 (59 to 81)
U.S. Flu VE (outpatient)	9/50 (18)	256/917 (28)	53 (3 to 79)
NVSN (inpatient)	13/60 (22)	613/1,523 (40)	63 (30 to 81)
Influenza A(H3N2)			
NVSN (outpatient)	62/218 (28)	855/2,487 (34)	42 (19 to 58)
U.S. Flu VE (outpatient)	29/107 (27)	256/917 (28)	16 (–34 to 49)
NVSN (inpatient)	12/44 (27)	613/1,523 (40)	55 (14–77)¶¶
All adults aged ≥18 yrs			
Any¶ influenza			
U.S. Flu VE (outpatient**)	112/475 (24)	592/1,735 (34)	36 (16 to 51)
VISION (outpatient)	5,631/26,011 (22)	25,842/76,628 (34)	54 (52 to 56)
IVY (inpatient)	211/675 (31)	873/2,500 (35)	41 (28 to 52)
VISION (inpatient)	905/2,959 (31)	10,869/28,074 (39)	55 (51 to 59)
Influenza A(H1N1)pdm09			
U.S. Flu VE (outpatient)	36/118 (31)	592/1,735 (34)	42 (8 to 64)
IVY (inpatient)	12/50 (24)	873/2,500 (35)	39 (–14 to 67)
Influenza A(H3N2)			
U.S. Flu VE (outpatient)	56/230 (24)	592/1,735 (34)	25 (–6 to 48)
IVY (inpatient)	28/110 (26)	873/2,500 (35)	51 (22 to 69)

See table footnotes on the next page.

TABLE 2. (*Continued*) Number and percentage of children and adolescents* aged <18 years and adults aged ≥18 years receiving seasonal influenza vaccine, number and percentage with a positive or negative influenza test result, and vaccine effectiveness,† by influenza type and subtype§ — four vaccine effectiveness networks, United States, 2024–25 influenza season

Network (setting)	Influenza test result by influenza vaccination status, no. vaccinated/Total (%)		
	Influenza-positive	Influenza-negative	VE (95% CI)¶
Adults aged 18–64 yrs			
Any Influenza			
U.S. Flu VE (outpatient)	84/419 (20)	397/1,403 (28)	37 (16 to 53)
VISION (outpatient)	3,056/20,280 (15)	10,864/49,103 (22)	56 (53 to 58)
IVY (inpatient)	61/334 (18)	282/1,187 (24)	48 (28 to 63)
VISION (inpatient)	212/1,062 (20)	1,966/8,803 (22)	51 (41 to 59)
Adults aged ≥65 yrs			
Any influenza			
U.S. Flu VE (outpatient)	28/56 (50)	195/332 (59)	18 (–69 to 60)
VISION (outpatient)	2,575/5,731 (45)	14,978/27,525 (54)	51 (47 to 54)
IVY (inpatient)	150/341 (44)	591/1,313 (45)	38 (19 to 52)
VISION (inpatient)	693/1,897 (37)	8,903/19,271 (46)	57 (52 to 61)

Abbreviations: IVY = The Investigating Respiratory Viruses in the Acutely Ill Network; NVSN = New Vaccine Surveillance Network; OR = odds ratio; U.S. Flu VE = U.S. Flu Vaccine Effectiveness Network; VE = vaccine effectiveness; VISION = Virtual SARS-CoV-2, Influenza, and Other respiratory viruses Network.

* Aged 6 months–17 years (NVSN and VISION); 8 months–17 years (U.S. Flu VE).

† VE was estimated using the test-negative design comparing odds of receipt of 2024–2025 influenza vaccination among persons with an acute respiratory illness who received a positive influenza test result with those among persons who received a negative influenza or SARS-CoV-2 test result. ORs were estimated using logistic regression; VE was calculated as (1 − adjusted OR) × 100%. Firth logistic regression was used for estimates from IVY.

§ Subtype was not available for VISION.

¶ All networks were adjusted for geographic region, age, and calendar time. IVY, U.S. Flu VE, and VISION were adjusted for sex and race and ethnicity.

** As of February 1, 2025, most influenza viruses detected have been influenza A viruses (97% of positive specimens).

†† Patients enrolled as outpatients in NVSN might have progressed to a more acute level of care, and those data might not be reflected in this analysis.

§§ Outpatient = outpatient clinics, urgent care, and emergency departments (NVSN and U.S. Flu VE); or urgent care and emergency departments (VISION).

¶¶ Firth logistic regression was used for this estimate.

Discussion

These interim estimates of 2024–25 VE indicate that influenza vaccination was effective in preventing medically attended influenza-associated illness in children, adolescents, and adults in the United States. Among children and adolescents, VE against medically attended influenza ranged from 32% to 60% in outpatient settings and from 63% to 78% against influenza-associated hospitalization. Among adults, VE against medically attended influenza was 36% and 54% in two outpatient settings and 41% and 55% against influenza-associated hospitalization. Despite increased circulation of influenza A(H3N2) viruses, which are generally associated with lower VE (*3*), estimates from this influenza season were consistent with those from the 2023–24 season and seasons associated with higher VE over the last 15 years (*4*). These estimates are also similar to interim estimates from Canada for the 2024–25 influenza season, which estimated VE to be 54% overall (*5*), and estimates from South America for the 2024 southern hemisphere influenza vaccine, which estimated VE against influenza A to be 34% overall (*6*). Given the high levels of influenza activity and severity in the United States this season, increasing influenza vaccination could reduce influenza-associated illnesses, medical visits, hospitalizations and deaths.¶¶¶

The VE estimates and associated confidence levels included in this report might reflect regional variations in circulating viruses. In U.S. Flu VE, most subtyped influenza A specimens (67%) were influenza A(H3N2) compared with 48% in NVSN. The U.S. Flu VE network did not find statistically significant VE against influenza A(H3N2) in the outpatient setting among child and adolescent patients or among adult patients. The VE estimates against influenza A(H3N2) are similar to findings from the 2018–19 season (*7*) and to findings from Europe during the 2024–25 influenza season (*8*). To address evolutionary changes in the influenza virus, the composition of influenza vaccines is reviewed annually; influenza vaccines are updated to protect against the influenza viruses that data indicate are most likely to be circulating during the following influenza season. When circulating viruses are antigenically different from the vaccine viruses, influenza VE can be reduced.****

Limitations

The findings in this report are subject to at least four limitations. First, these VE estimates are preliminary, and end-of-season estimates might be different as influenza continues to spread during the 2024–25 season. Second, influenza vaccination status might be misclassified in some networks, which could affect VE estimates. Vaccines administered in pharmacies are routinely reported to jurisdictional immunization information systems (IISs), although vaccination clinics conducted in nontraditional settings such as workplaces might not be reported to IISs. Third, patients who had received ≥1 dose of the 2024–2025 influenza vaccine were considered vaccinated; however, children aged 6 months–8 years are recommended to receive 2 doses if they have not previously received ≥2 doses. Therefore, some children who were classified as vaccinated might not have been fully vaccinated, which could reduce VE estimates. Finally, the potential for unmeasured confounding exists, because networks did not control for variables such as

¶¶¶ https://www.cdc.gov/flu-burden/php/data-vis/2024-2025.html

**** https://www.cdc.gov/flu/vaccines/keyfacts.html

Summary

What is already known about this topic?

CDC routinely monitors influenza vaccine effectiveness (VE). Annual influenza vaccination is recommended for all eligible persons aged ≥6 months.

What is added by this report?

Interim 2024–2025 seasonal influenza VE estimates were derived from four U.S. VE networks. Among children and adolescents, VE was 32%, 59%, and 60% in outpatient settings (three networks) and 63% and 78% against influenza-associated hospitalization (two networks). Among adults, VE was 36% and 54% in outpatient settings (two networks) and 41% and 55% against influenza-associated hospitalization (two networks).

What are the implications for public health practice?

Vaccination with the 2024–2025 influenza vaccine reduced the risk for influenza-associated outpatient visits and hospitalization. These findings support recommendations that all eligible persons aged ≥6 months should receive an annual influenza vaccination. Vaccination should be offered as long as influenza viruses are circulating.

previous vaccination, previous influenza virus infection, or underlying medical conditions.

Implications for Public Health Practice

Vaccination is the best way to prevent influenza and influenza-associated hospitalization. Findings in this report show that vaccination with the 2024–2025 influenza vaccine reduced the likelihood of medically attended influenza and support CDC's recommendation that all persons aged ≥6 months be vaccinated against influenza (*1*). These findings also support the strong protective effect influenza vaccination has against influenza-associated hospitalization, demonstrating the importance of vaccination to reduce more severe influenza-associated complications. Eligible persons aged ≥6 months who have not received the 2024–2025 influenza vaccine should get vaccinated as long as influenza viruses circulate locally.

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Reports of Encephalopathy Among Children with Influenza-Associated Mortality — United States, 2010–11 Through 2024–25 Influenza Seasons

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Abstract

In late January 2025, CDC received anecdotal reports of children with influenza-associated acute necrotizing encephalopathy (ANE), a severe form of influenza-associated encephalopathy or encephalitis (IAE), including several fatal cases. In response, CDC examined trends in the proportions of cases with IAE among influenza-associated pediatric deaths reported during the 2010–11 through 2024–25 influenza seasons, including demographic and clinical characteristics of identified cases. CDC contacted state health departments to ascertain whether any pediatric influenza-associated deaths with IAE reported this season also had a diagnosis of ANE. Among 1,840 pediatric influenza-associated deaths during the 2010–11 through 2024–25 influenza seasons, 166 (9%) had IAE, ranging from 0% (2020–21 season) to 14% (2011–12 season); preliminary data for the 2024–25 season (through February 8, 2025) indicate that nine of 68 (13%) had IAE. Across seasons, the median age of patients with fatal IAE was 6 years; 54% had no underlying medical conditions, and only 20% had received influenza vaccination. Because no dedicated national surveillance for IAE or ANE exists, it is unknown if the numbers of cases this season vary from expected numbers. Health care providers should consider IAE in children with acute febrile illness and neurologic signs or symptoms lasting >24 hours. Evaluation should include testing for influenza and other viruses and neuroimaging; clinical management should include early antiviral treatment for suspected or confirmed influenza and supportive critical care management as needed. Influenza vaccination is recommended for all eligible persons aged ≥6 months as long as influenza viruses are circulating.

Introduction

Children of all ages, and especially those aged <5 years with certain underlying medical conditions, can experience severe or fatal complications associated with influenza virus infection (*1*), including pneumonia, myocarditis, pericarditis, and neurologic complications.* Influenza-associated encephalopathy or encephalitis (IAE) comprises a spectrum of neurologic syndromes that are triggered by influenza virus infection of the respiratory tract, resulting in a dysregulated host inflammatory response, leading to varying degrees of brain dysfunction, inflammation, or both (*2*,*3*). Acute necrotizing encephalopathy (ANE) is one of the most severe forms of encephalopathy and is a known complication of infection with influenza and other viruses (including SARS-CoV-2 and human herpesvirus 6) (*3*). The diagnosis of ANE is based on characteristic symmetric lesions affecting the bilateral thalami and other parts of the brain detected by head computed tomography or magnetic resonance imaging, in a child with febrile illness preceding or concurrent with the onset of neurologic signs or symptoms and rapid neurologic decline. In late January 2025, public health partners alerted CDC with anecdotal reports of pediatric hospitalizations with IAE, including several fatal cases with ANE. Data from CDC's U.S. Influenza-Associated Pediatric Mortality Surveillance System were reviewed to further investigate.

Methods

Data Source

The Influenza-Associated Pediatric Mortality Surveillance System† is a national surveillance system that collects data on all identified influenza-associated pediatric deaths, which have been nationally notifiable in the United States since 2004. An influenza-associated pediatric death is defined as the death of a person aged <18 years who has laboratory-confirmed influenza and a clinically compatible illness, with no period of complete recovery between illness and death.

Identification of Cases of IAE and ANE

State and local health departments report influenza-associated pediatric deaths to CDC and use a standardized case report form to collect information on demographic characteristics, influenza laboratory results, underlying medical conditions, clinical course, acute complications, and influenza vaccination status.§ Trends in the proportions of cases of encephalopathy or encephalitis (included as a checkbox in the acute complications section of the case report form) among influenza-associated pediatric deaths reported to CDC during the 2010–11 through 2024–25 seasons were examined, including the demographic

* https://www.idsociety.org/practice-guideline/influenza/

† https://www.cdc.gov/fluview/overview/index.html#cdc_generic_section_5-mortality-surveillance

§ Health departments verify vaccination status by reviewing medical records, contacting health care providers, or checking state vaccine registries.

and clinical characteristics of identified cases. For this analysis, a case of IAE was defined as the marking of the encephalopathy or encephalitis checkbox on the case report form. During the 2024–25 season, for any ANE cases that had not already been reported to CDC, state health departments were contacted to ascertain whether any reported pediatric influenza-associated deaths with IAE identified through routine surveillance also had a diagnosis of ANE, because information regarding ANE is not specifically collected on the case report form. SAS software (version 9.4; SAS Institute) was used to conduct all analyses. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.[¶]

Results

IAE Cases Reported During the 2010–11 Through 2024–25 U.S. Influenza Seasons

Among 1,840 pediatric influenza-associated deaths reported to CDC during the 2010–11 through 2024–25 influenza seasons, 166 (9%) had IAE, ranging from 0% (2020–21 season) to 14% (2011–12 season); preliminary data for the 2024–25 season (reported October 1, 2024–February 8, 2025) indicate that nine of 68 (13%) deaths had IAE (Table 1). By age group, IAE prevalence was highest among children aged 2–4 years (34 [10%] of 334 total fatal cases) and lowest among infants aged <6 months (eight [5%] of 148 fatal cases).

Characteristics of IAE Cases

Among the 166 fatal pediatric influenza-associated cases with IAE, the median age was 6 years (IQR = 2.5–10.5 years), 52% were female, and 40% were non-Hispanic White (Table 2). Overall, 119 (72%) patients had influenza A, and 46 (28%) had influenza B virus infection. Among 73 influenza A cases with available subtype, 41 (56%) had A(H1N1)pdm09 and 32 (44%) had A(H3N2). No underlying medical conditions were reported for more than one half of fatal cases (89; 54%); 32 patients (20%) had received ≥1 dose of current season influenza vaccine >2 weeks before illness onset, and 121 (73%) received influenza antiviral treatment. Overall, 155 (93%) patients required mechanical ventilation; other documented acute complications included acute respiratory distress syndrome (57; 34%), pneumonia (54; 33%), and sepsis (47; 28%). Among all fatal cases, 159 (96%) patients died during hospitalization, 2% died in the emergency department, and 2% died outside the hospital setting.

¶ 45 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.

TABLE 1. Pediatric influenza-associated deaths (N = 1,840) and deaths with influenza-associated encephalopathy or encephalitis (n = 166), by influenza season and age group — Influenza-Associated Pediatric Mortality Surveillance System, United States, 2010–11 through 2024–25* influenza seasons

Characteristic	No. of pediatric influenza-associated deaths[†]	No. of influenza-associated deaths with IAE diagnosis (row %)
Influenza season		
2010–11	124	12 (10)
2011–12	37	5 (14)
2012–13	171	10 (6)
2013–14	111	4 (4)
2014–15	148	15 (10)
2015–16	95	8 (8)
2016–17	110	9 (8)
2017–18	188	16 (9)
2018–19	145	13 (9)
2019–20	199	20 (10)
2020–21	1[§]	0 (—)
2021–22	49	5 (10)
2022–23	187	17 (9)
2023–24	207	23 (11)
2024–25*	68	9 (13)
Age group		
0–6 mos	148	8 (5)
6–23 mos	311	28 (9)
2–4 yrs	334	34 (10)
5–11 yrs	635	62 (10)
12–17 yrs	412	34 (8)
Total 0–17 yrs	**1,840**	**166 (9)**

Abbreviation: IAE = influenza-associated encephalopathy or encephalitis.
* Preliminary data through February 8, 2025.
† Data available at https://gis.cdc.gov/grasp/fluview/pedfludeath.html
§ Influenza activity was historically low during the COVID-19 pandemic. https://www.cdc.gov/mmwr/volumes/69/wr/mm6937a6.htm

IAE and ANE Cases During the 2024–25 Influenza Season

Nine pediatric influenza-associated deaths with IAE were reported to CDC during the 2024–25 season through February 8, 2025; four had documented ANE (two ANE deaths were proactively reported to CDC by state health departments, and two additional deaths were identified during CDC outreach to states). All four ANE deaths were aged <5 years; one child had underlying medical conditions, and all four had laboratory-confirmed influenza A(H1N1)pdm09. Two children with ANE had received influenza vaccination >2 weeks before illness onset; the others had not received influenza vaccination during the 2024–25 influenza season. Two children with ANE received oseltamivir treatment, two experienced seizures during hospitalization, and all four received mechanical ventilation.

Discussion

CDC has received recent anecdotal reports of critically ill children with influenza-associated ANE, including several deaths, during the 2024–25 influenza season. CDC does not

TABLE 2. Characteristics of children with influenza-associated mortality and influenza-associated encephalopathy or encephalitis (N = 166) — Influenza-Associated Pediatric Mortality Surveillance System, United States, 2010–11 through 2024–25* influenza seasons

Characteristic (no. with available information)	No. with IAE (%)
Total no. with IAE	**166 (100)**
Median age, yrs (IQR)	6.0 (2.5–10.5)
Sex (166)	
Male	80 (48)
Female	86 (52)
Race and ethnicity (166)†	
American Indian or Alaska Native	2 (1)
Asian or Pacific Islander	20 (12)
Black or African American	22 (13)
White	66 (40)
Hispanic or Latino	47 (28)
Unknown/Missing	9 (5)
Influenza type/Subtype (166)	
Influenza A	119 (72)
Known A subtype	73 (61)
A(H1N1)	41/73 (56)
A(H3N2)	32/73 (44)
Unknown A subtype	46 (39)
Influenza B	46 (28)
A/B not distinguished	1 (<1)
≥1 underlying medical condition (166)	
Yes	74 (45)
No	89 (54)
Unknown/Missing	3 (2)
Received current season influenza vaccine >14 days before illness onset (158)§	
Yes	32 (20)
No	96 (61)
Unknown/Missing	30 (19)
Receipt of antiviral treatment (166)	
Yes	121 (73)
No	45 (27)
Required mechanical ventilation (166)	
Yes	155 (93)
No	6 (4)
Unknown	5 (3)
Other acute complications (166)¶	
Pneumonia	54 (33)
Sepsis	47 (28)
ARDS	57 (34)
Location of death (166)	
Outside of hospital	3 (2)
Emergency department	4 (2)
Hospital	159 (96)

Abbreviations: ARDS = acute respiratory distress syndrome; IAE = influenza-associated encephalopathy or encephalitis.
* Data for the 2024-25 influenza season are preliminary through February 8, 2025.
† Persons of Hispanic or Latino (Hispanic) ethnicity might be of any race but are categorized as Hispanic; all racial groups listed here are non-Hispanic.
§ Eight children are excluded from this denominator because they were aged <6 months and not eligible for influenza vaccination.
¶ Some children had multiple complications, thus numbers reported are not mutually exclusive.

systematically collect data on either influenza-associated ANE or IAE cases; however, national pediatric influenza-associated mortality surveillance during the 2024–25 season (through February 8, 2025) detected IAE in 13% of cases; four of the children had a diagnosis of ANE. Because there is no dedicated U.S. surveillance for IAE (including ANE) among children, it is currently not known whether these reported cases vary from expected numbers. Enhanced surveillance to systematically identify and report pediatric IAE cases, including ANE, in the United States during the remainder of the 2024–25 season would improve understanding of the incidence of this influenza complication and the frequency of severe outcomes, including long-term neurologic sequelae or death. Thus, on February 24, 2025, CDC posted a national call for possible cases of pediatric IAE identified during this influenza season (October 1, 2024, through May 30, 2025) on the Epidemic Information Exchange (EPI-X). CDC can be contacted at severeflu@cdc.gov to begin the case reporting process; no case information, including protected health information, should be communicated over email. Additional information can be found at https://epix2.cdc.gov/v2/Reports/Display.aspx?id=541771.

IAE is not notifiable in the United States; however, in Japan, where encephalopathy and encephalitis due to an infection is notifiable, the number of cases among persons of all ages during 2010–2015 ranged from 64 to 105 per season. Seventy-four percent of cases were in persons aged <18 years, and IAE case-fatality among persons aged <18 years was 8% (*4*).

Three major IAE syndromes have been described. ANE is the most severe form and is associated with high rates of long-term neurologic sequalae and death, followed by acute encephalopathy with biphasic seizures and late reduced diffusion (a finding on magnetic resonance imaging that typically signifies tissue damage or abnormality), and clinically mild encephalitis or encephalopathy with a reversible splenial lesion (*2*). Other less commonly reported IAE syndromes include acute encephalopathy with refractory partial seizures and posterior reversible encephalopathy syndrome (*2*). Although no standardized IAE case definition currently exists, consensus definitions for infection-triggered encephalopathy syndromes have recently been published (*3*). Criteria for diagnosis of ANE, including influenza-associated ANE, are well characterized and include febrile illness preceding or concurrent with the onset of neurologic signs or symptoms, rapid neurologic decline, and neuroimaging demonstrating symmetric lesions affecting the bilateral thalami and other parts of the brain (*3*).

The following features that have been described in pediatric cases of IAE can be useful for surveillance purposes or clinical diagnosis, in conjunction with clinical judgment: 1) age <18 years; 2) laboratory-confirmed influenza virus infection; 3) diagnosis of encephalopathy or encephalitis or neurologic signs or symptoms, including seizures, altered mental status, delirium, decreased level of consciousness, lethargy, hallucinations, or personality changes lasting >24 hours; and 4) neuroimaging abnormalities (not always present) such as

Summary

What is already known about this topic?

Influenza-associated encephalopathy or encephalitis (IAE), including acute necrotizing encephalopathy (ANE), is a rare and potentially fatal complication of influenza. No national IAE surveillance exists.

What is added by this report?

During late January 2025, CDC received anecdotal reports of critically ill children with IAE, including deaths with ANE. Data from the Influenza-Associated Pediatric Mortality Surveillance System was investigated and revealed the median proportion of pediatric influenza deaths with IAE during the 2010–11 through 2024–25 influenza seasons was 9%. IAE was identified in 13% (nine of 68) of deaths during the 2024–25 influenza season (through February 8, 2025), including four with ANE.

What are the implications for public health practice?

It is not known whether cases observed in the 2024–25 season vary from expected numbers. Clinicians should consider IAE in children with influenza and abnormal neurologic signs or symptoms. Influenza vaccination is recommended for all persons aged ≥6 months while influenza viruses are circulating.

brain edema, inflammation, or brain lesions, or electroencephalographic abnormalities; in the absence of other known causes of disease (*3*–*5*).

Progression to severe neurologic impairment and death from IAE can occur rapidly after onset of influenza symptoms; thus, prompt recognition and intervention are crucial, including neurocritical supportive care for patients with increased intracranial pressure and management of multiorgan failure. Early initiation of antiviral treatment is recommended for children at increased risk for influenza-associated complications, although whether antiviral treatment is beneficial for management of IAE is unknown. Notably, one study reported that oseltamivir treatment was associated with a reduced risk for neuropsychiatric events among patients with influenza (*6*). Although there are currently no international evidence-based guidelines for standardized clinical management of patients with IAE, high-dose pulse methylprednisolone, plasma exchange, therapeutic hypothermia, and immune therapy such as gamma globulin, anakinra (an interleukin-1 receptor antagonist), and tocilizumab (an interleukin-6 receptor blocker) have been used (*6*–*8*). In one study, use of the nonsteroidal anti-inflammatory drug diclofenac sodium (but not acetaminophen) was associated with increased mortality in IAE cases (*5*). Additional studies are needed to identify optimal strategies for clinical management of IAE.

Limitations

The findings in this report are subject to at least four limitations. First, diagnoses of encephalopathy or encephalitis are currently captured in checkboxes on the pediatric influenza-associated mortality case report form; these data might have over- or underestimated the true prevalence of IAE. Second, data on IAE prevalence among pediatric influenza-associated deaths during the 2024–25 season are preliminary and based on small numbers; results might change as additional data become available. Third, the prevalence of IAE among pediatric influenza-associated deaths is likely not representative of overall pediatric IAE prevalence in the United States, especially less severe IAE cases. Finally, given the lack of established surveillance for IAE in the United States, it was not possible to ascertain whether anecdotal reports of pediatric IAE (including influenza-associated ANE) hospitalizations and deaths during the current influenza season are within or above expected ranges.

Implications for Public Health Practice

Health care providers should consider IAE in children with febrile illness and clinically compatible neurologic signs or symptoms, including but not limited to seizures, altered mental status, delirium, decreased level of consciousness, lethargy, hallucinations, or personality changes lasting >24 hours. Influenza-associated ANE should be considered in children with signs or symptoms of IAE, as well as rapid neurologic decline and neuroimaging demonstrating symmetric lesions affecting the bilateral thalami and other parts of the brain. Comprehensive assessment and management should include testing for influenza and other viruses, neuroimaging, early initiation of antiviral treatment if influenza is confirmed or suspected (i.e., providers should not wait for laboratory confirmation of influenza before initiating antiviral treatment), and supportive critical care management as needed for patients with IAE. Use of standardized criteria by health care providers for IAE case identification and establishment of a mechanism for public health reporting will improve understanding of the incidence and impact of this serious influenza complication. CDC has posted a national call for possible pediatric IAE cases identified during this influenza season on EPI-X and can be contacted at severeflu@cdc.gov.

Influenza vaccination is an important tool for preventing influenza and its associated complications (*1*). U.S. influenza activity is currently elevated, and influenza viruses could continue circulating into the spring; thus, health care providers should provide a strong recommendation for influenza

vaccination for all eligible persons aged ≥6 months who have not yet been vaccinated this season to prevent influenza illness and its associated severe and potentially fatal complications (*9*).

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Trends in Cervical Precancers Identified Through Population-Based Surveillance — Human Papillomavirus Vaccine Impact Monitoring Project, Five Sites, United States, 2008–2022

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Abstract

In 2006, human papillomavirus (HPV) vaccine was first recommended in the United States to prevent cancers and other diseases caused by HPV; vaccination coverage increased steadily through 2021, and increasing numbers of young women had received HPV vaccine as children or adolescents. Since 2008, CDC has monitored incidence of precancerous lesions (cervical intraepithelial neoplasia [CIN] grades 2–3 and adenocarcinoma in situ [AIS], collectively CIN2+), which are detected through cervical cancer screening and can be used as an intermediate outcome for monitoring vaccination impact, via the five-site Human Papillomavirus Vaccine Impact Monitoring Project. This analysis describes trends in incidence of CIN2+ and CIN3+ (i.e., CIN grade 3 and AIS) lesions during 2008–2022. Among women aged 20–24 years who were screened for cervical cancer, rates during 2008–2022 decreased for CIN2+ by 79%, and for CIN3+ by 80%. In the same period, CIN3+ rates among screened women aged 25–29 years decreased by 37%. These data are consistent with considerable impact of HPV vaccination for preventing cervical precancers among women in the age groups most likely to have been vaccinated, and support existing recommendations to vaccinate children at the routinely recommended ages as a cancer prevention measure.

Introduction

Human papillomavirus (HPV) causes approximately 10,800 cervical cancers in the United States each year; cervical cancer is the most common HPV-attributable cancer among women (*1*). HPV-attributable cancers take many years to develop (median age at diagnosis = 50 years),* whereas screen-detected cervical precancers (cervical intraepithelial neoplasia [CIN] grades 2–3 and adenocarcinoma in situ [AIS], collectively CIN2+) can develop within a few years after infection (*2*). Screening with the Papanicolaou (Pap) test and treatment of precancerous abnormalities have been the mainstay of secondary prevention of cervical cancer for decades; screening with a test for high-risk HPV, usually as a co-test with a Pap test, has been increasingly used during the past decade (*2*,*3*). Recommended screening intervals have increased, from annually to every 3 years (cytology only) or every 5 years (incorporating an HPV test). In 2006, HPV vaccine was first recommended in the United States by CDC's Advisory Committee on Immunization Practices to prevent cancers and other diseases caused by HPV† (*2*). Routine vaccination was first recommended for girls and women; in 2011, boys and men were included in the vaccination program. Currently, routine vaccination is recommended for all children at age 11–12 years (may commence at age 9 years), with catch-up vaccination through age 26 years (*2*). Since 2019, shared clinical decision-making has been recommended for consideration of vaccination of adults aged 27–45 years. Two doses of HPV vaccine are recommended if the series is started at age <15 years; otherwise, 3 doses are recommended. Coverage with ≥1 HPV vaccine dose among adolescents aged 13–17 years steadily increased through 2021 then plateaued, with most recent coverage of 76.8% in 2023 (*4*). CDC has monitored CIN2+ incidence since 2008 via the Human Papillomavirus Vaccine Impact Monitoring Project (HPV-IMPACT) (*5*,*6*). This analysis describes trends in CIN2+ and CIN3+ (i.e., CIN grade 3 and AIS) incidence during 2008–2022.

Methods

Surveillance System

HPV-IMPACT has conducted population-based CIN2+ surveillance in five sites since 2008.§ Participating sites conduct active surveillance of all histopathology laboratories serving catchment area residents to identify histologically confirmed CIN2+ diagnoses.

Populations and Screening Estimation

The number of women aged 20–64 years in the HPV-IMPACT catchment areas was obtained from U.S. Census

* https://www.cdc.gov/cancer/hpv/diagnosis-by-age.html

† https://www.cdc.gov/acip-recs/hcp/vaccine-specific/hpv.html

§ This report includes data submitted through August 2024. HPV-IMPACT sites are Alameda County, California; New Haven County, Connecticut; Monroe County, New York; Davidson County, Tennessee; and 28 zip codes in metropolitan Portland, Oregon. Originally, the California site included portions of Alameda County but was expanded retroactively to include the full county. Additional information about the surveillance system is available at https://www.cdc.gov/hpv-impact/about/index.html.

Bureau data, stratified by 5-year age group.[¶] The proportions of women screened (i.e., who had a Pap or HPV test in the preceding year), by 5-year age group, were estimated[**] using standardized data sources and methods for all sites[††] (*5*,*6*). To account for variations in screening by insurance coverage, estimates are weighted averages of proportions screened among privately insured,[§§] publicly insured,[¶¶] and uninsured women.[***] Annual age-specific numbers of women screened were estimated by multiplying age-specific proportions screened by age-specific populations of women.

Statistical Analysis

For the years 2008–2022, annual age-specific CIN2+ and CIN3+ incidence and 95% CIs were calculated using the estimated number of women screened as the denominator to control for changes in screening frequency; incidence is still affected by changes in screening test sensitivity and vaccination coverage. Incidence calculations were performed using SAS (version 9.4; SAS Institute). Age-specific trend analyses were conducted separately for CIN2+ and CIN3+ using Joinpoint software (version 5.3.0.0; National Cancer Institute).[†††] Overall trends for 2008–2022 were reported as average annual percent change (AAPC), and segment-specific trends were reported as annual percent change (APC).[§§§] Because health care disruptions due to the COVID-19 pandemic might have resulted in deviations in incidence in 2020 from the underlying trend, data from 2020 were excluded from trend analyses.[¶¶¶] This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.[****]

Results

During 2008–2022, a total of 39,977 CIN2+ cases were reported; 13,027 (32.6%) were CIN3+. CIN2+ cases per 100,000 screened women decreased 11.0% annually for women aged 20–24 years; the incidence in 2022 was 79.5% lower than that in 2008 (Table) (Figure) (Supplementary Table, https://stacks.cdc.gov/view/cdc/176064). Among screened women aged 25–29 years, CIN2+ incidence increased 3.1% annually during 2008–2016, and decreased 4.3% annually during 2016–2022, but AAPC was stable. Among women aged 30–34 years and 35–39 years, CIN2+ incidence trended upward during 2008–2016 and then downward during 2016–2022; AAPCs for the entire period were positive but small. Among those in age groups 40–49 and 50–64 years, CIN2+ incidence increased significantly during 2008–2022.

Trends for CIN3+ were generally similar to those for CIN2+; among women aged 20–24 years, the incidence in 2022 was 80.3% lower than that in 2008. One notable difference for CIN3+ compared with CIN2+ was an overall decreasing trend among screened women aged 25–29 years (AAPC = –3.5%); the CIN3+ incidence in 2022 was 37.2% lower than that in 2008.

Discussion

These data from HPV-IMPACT provide an updated view into the epidemiology of cervical precancers in the United States during an era of increasing HPV vaccination coverage among young women and changing cervical cancer screening practices among all age groups. Among women aged 20–24 years who were screened, CIN2+ incidence decreased 79% from 2008 to 2022, and CIN3+ incidence decreased 80%. Among screened women aged 25–29 years, CIN3+ incidence decreased 37%.

[¶] For the California, Connecticut, New York, and Tennessee sites, 2022 annual U.S. Census Bureau county estimates were used. The Connecticut site transitioned from counties to planning regions in 2022, but HPV-IMPACT maintained the original catchment area for the period of this report; the 2021 county U.S. Census Bureau population was used as a proxy for the 2022 population. For the Oregon site, annual demographic projections based on U.S. Census Bureau data were used.

[**] Estimation is necessary because no national or catchment area–specific registries for cervical cancer screening exist in the United States, and surveillance of cervical cytology laboratories is outside the scope of HPV-IMPACT surveillance.

[††] Methodology was similar to that used for the California site in previous reports, but with data sources standardized for all sites. For U.S. Census Bureau American Community Survey Public Use Microdata Areas corresponding to each catchment area, the proportion of women with public, private, or no insurance was obtained for the years 2008–2022 (https://www.census.gov/programs-surveys/acs/). Total proportion screened was a weighted average of the proportion screened for each of the three insurance categories.

[§§] The age-specific proportions of privately insured women who were screened were estimated using claims data from the Merative MarketScan Commercial Database. The data were used to obtain claims for Pap or HPV testing at the Metropolitan Statistical Area level for each site, 2008–2022. Pap or HPV testing claims among persons who also had a claim for hysterectomy were excluded.

[¶¶] The age-specific proportions of publicly insured women who were screened were estimated using claims data from the Merative MarketScan Multi-State Medicaid Database. The data were analyzed for Pap or HPV testing obtained nationally during 2008–2022. Pap or HPV testing claims among women who also had a claim for hysterectomy were excluded. For each site, these claims were adjusted based on the ratio between site-specific commercial claims and national commercial claims.

[***] The age-specific proportions of uninsured women who were screened were estimated by applying a multiplier to the proportions screened among all insured women, as estimated from claims data. The ratio of proportion screened among uninsured to insured was estimated by region, using data from the Behavioral Risk Factor Surveillance System, averaged across years 2008–2020 (https://www.cdc.gov/brfss/index.html). This ratio was then multiplied by the annual proportions screened for insured females.

[†††] https://surveillance.cancer.gov/joinpoint

[§§§] Joinpoint models were selected using weighted Bayesian information criterion. Up to two joinpoints were allowed; at least two observations were required between joinpoints or from a joinpoint to either end. If joinpoints were identified, segment-specific trends (APC) were reported. Trends were considered to increase when AAPC or APC >0 or decrease when AAPC or APC <0 and if the empirical quantile 95% CI did not include 0; otherwise, trends were considered stable.

[¶¶¶] Analyses were also performed with 2020 data included.

[****] 45 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.

TABLE. Average annual percent change and annual percent change for cervical precancers per 100,000 screened women* — Human Papillomavirus Vaccine Impact Monitoring Project,† five sites, United States, 2008–2022

Age group, yrs	CIN2+§ cases per 100,000 screened women (95% CI)		CIN3+¶ cases per 100,000 screened women (95% CI)	
	AAPC**	APC**	AAPC**	APC**
20–24	−11.0 (−12.8 to −10.2)††	2008–2012: −5.9 (−9.0 to 0.2) 2012–2022: −12.9 (−16.7 to −11.8)††	−10.2 (−13.0 to −9.0)††	2008–2013: −7.9 (−10.7 to −2.9)†† 2013–2018: −18.0 (−28.1 to −13.7)†† 2018–2022: −2.7 (−14.2 to 13.4)
25–29	−0.2 (−2.5 to 2.3)	2008–2016: 3.1 (1.1 to 16.7)†† 2016–2022: −4.3 (−14.6 to −0.7)††	−3.5 (−5.4 to −2.1)††	2008–2016: 0.7 (−1.2 to 4.4) 2016–2022: −8.8 (−16.2 to −5.3)††
30–34	2.4 (1.3 to 3.5)††	2008–2012: 2.6 (−6.5 to 7.7) 2012–2016: 12.3 (7.1 to 18.8)†† 2016–2022: −3.8 (−7.0 to −1.6)††	1.0 (−0.1 to 2.1)	2008–2012: 2.3 (−6.5 to 6.9) 2012–2016: 12.6 (7.4 to 18.8)†† 2016–2022: −6.8 (−10.0 to −4.4)††
35–39	3.0 (2.0 to 3.9)††	2008–2012: 3.0 (−4.4 to 7.4) 2012–2016: 12.1 (7.3 to 18.1)†† 2016–2022: −2.7 (−5.8 to −0.6)††	2.6 (0.1 to 6.0)††	2008–2017: 5.2 (2.1 to 29.3)†† 2017–2022: −2.0 (−13.7 to 3.9)
40–49	4.4 (2.2 to 7.5)††	2008–2017: 7.5 (5.5 to 26.6)†† 2017–2022: −0.8 (−11.9 to 4.0)	3.9 (2.0 to 5.8)††	2008–2022: 3.9 (2.0 to 5.8)††
50–64	5.2 (4.1 to 7.0)††	2008–2010: 1.9 (−6.2 to 13.8) 2010–2016: 12.8 (−4.7 to 21.9) 2016–2022: −0.7 (−4.7 to 4.6)	4.2 (2.1 to 7.3)††	2008–2017: 7.2 (5.0 to 27.5)†† 2017–2022: −0.9 (−11.6 to 4.2)

Abbreviations: AAPC = average annual percent change; APC = annual percent change; CIN = cervical intraepithelial neoplasia; HPV-IMPACT = Human Papillomavirus Vaccine Impact Monitoring Project.

* Denominators are the estimated number of screened women aged 20–24, 25–29, 30–34, 35–39, 40–49, or 50–64 years living in the catchment areas.

† HPV-IMPACT sites are Alameda County, California; New Haven County, Connecticut; Monroe County, New York; Davidson County, Tennessee; and 28 zip codes in metropolitan Portland, Oregon.

§ CIN2+ includes grades 2 or worse and adenocarcinoma in situ.

¶ CIN3+ includes grade 3 and adenocarcinoma in situ.

** Data from 2020 were excluded from trend analyses. Analyses were also performed with 2020 data included. Most AAPCs were similar (within approximately 0.3) and did not change statistical significance. The CIN2+ AAPC among age group 50–64 years increased from 5.2 to 6.5, and the increase in CIN3+ among age group 35–39 years was similar but not statistically significant. There were also some changes in the years of identified joinpoints that would not change overall interpretations.

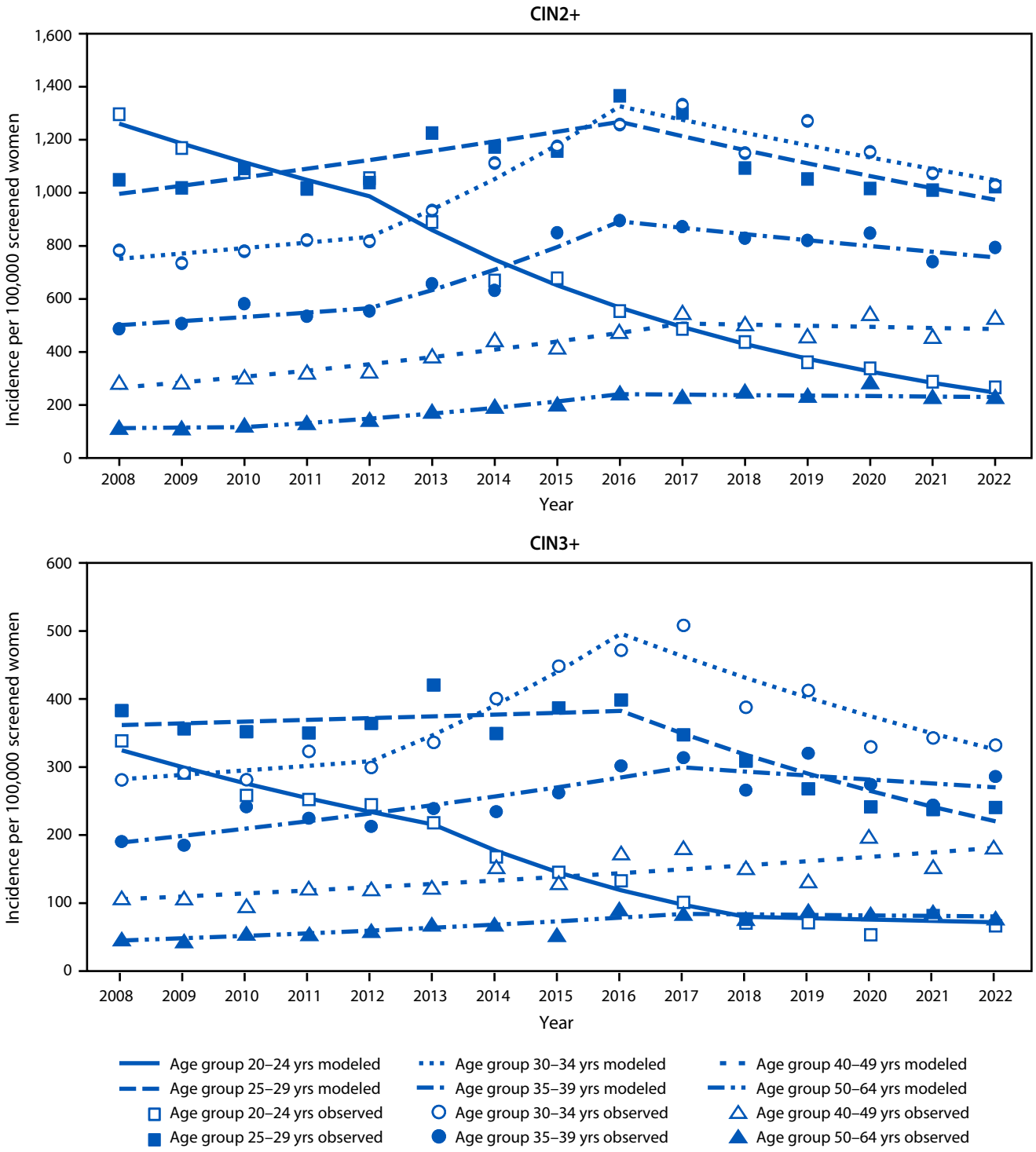
†† Denotes APC or AAPC is significantly different from zero at the alpha = 0.05 level.

The data are consistent with a considerable impact from the U.S. HPV vaccination program on cervical precancers, with the largest decreases in the youngest age group for which benefit of vaccination would first be observed.

Data from HPV-IMPACT previously indicated decreasing CIN2+ and CIN3+ incidence among women aged 18–20 and 21–24 years during 2008–2015 (*6*). As vaccinated women age into older age groups, declines in cervical precancers are expected. For example, before 2014, women aged 20–24 years could only have been vaccinated in the catch-up vaccination age range (13–26 years), whereas during 2018–2022, all women aged 20–24 years would have been eligible for vaccination at the routine age (11–12 years) in 2006. Vaccination at the routine age is more effective because vaccination is likely to occur before exposure to HPV through sexual contact. The declines in precancers mirror reported U.S. trends in vaccine-type HPV prevalence in self-collected cervicovaginal swabs, in which declines in quadrivalent HPV-type prevalence among adolescents and women aged 14–19 years were followed by declines among women aged 20–24 years (*2*). This report includes the first U.S. data showing significant decreases in cervical precancers in an older age group: CIN3+ incidence among screened women aged 25–29 years decreased compared with incidence during the beginning of the surveillance period. Most women aged 25–29 years in 2022 had been eligible for vaccination at age 11–12 years. The decrease in CIN3+ incidence before CIN2+ could be because CIN3+ (compared with CIN2+ lesions) are more frequently positive for HPV16 or HPV18, and therefore, a higher proportion are preventable by quadrivalent HPV vaccination (*5*,*7*).

HPV-IMPACT previously reported increasing trends in precancer incidence among women in age groups 25–39 years during 2008–2015 (*6*). Increases were attributed to longer screening intervals (all ages) and increasing use of HPV testing (age ≥30 years), which are more sensitive for detection of CIN2+ than Pap tests; HPV testing has increased during the surveillance period (*3*). Continued HPV-IMPACT surveillance indicated that increasing CIN2+ incidence among several age groups from 25 to 64 years reversed or leveled during 2016–2017. By 2022, incidence among women aged 25–29 years had decreased to near 2008 levels (CIN2+) or below (CIN3+). These findings are consistent with model predictions that changing from Pap to HPV testing would cause transient increases in detected precancer and cancer, followed by decreases (*8*). Although some women in age groups 30–34 years and older would have been vaccinated, less impact is expected among women in this age group at this time because they were only eligible for catch-up vaccination, at ages when many women are already sexually experienced and therefore likely to have been infected with HPV.

FIGURE. Incidence (cases per 100,000 screened women)* of cervical precancers† — Human Papillomavirus Vaccine Impact Monitoring Project,§ five sites, United States, 2008–2022¶



Abbreviations: CIN = cervical intraepithelial neoplasia; HPV-IMPACT = Human Papillomavirus Vaccine Impact Monitoring Project.

* Denominators are the estimated number of screened women aged 20–24, 25–29, 30–34, 35–39, 40–49, or 50–64 years living in the catchment areas.

† CIN2+ includes grades 2 or worse and adenocarcinoma in situ; CIN3+ includes grade 3 and adenocarcinoma in situ.

§ HPV-IMPACT sites are Alameda County, California; New Haven County, Connecticut; Monroe County, New York; Davidson County, Tennessee; and 28 zip codes in metropolitan Portland, Oregon.

¶ Trend lines were modeled using Joinpoint software (version 5.3.0.0; National Cancer Institute). Data from 2020 were excluded from trend analyses.

Summary

What is already known about this topic?

Since 2006, when human papillomavirus (HPV) vaccine was first recommended in the United States to prevent cancers and other diseases caused by HPV, vaccination coverage has increased, and many young women vaccinated as children or adolescents have become age-eligible for cervical cancer screening. CDC monitors cervical precancer incidence through the Human Papillomavirus Vaccine Impact Monitoring Project.

What is added by this report?

During 2008–2022, cervical precancer incidence decreased 79% and higher-grade precancer incidence decreased 80% among screened women aged 20–24 years, the age group most likely to have been vaccinated.

What are the implications for public health practice?

Observed declines in cervical precancers are consistent with HPV vaccination impact and support Advisory Committee on Immunization Practices recommendations to vaccinate children against HPV at age 11–12 years with catch-up through age 26 years.

Limitations

The findings in this report are subject to at least four limitations. First, numbers of women screened for cervical cancer were estimated using claims and survey data; inaccuracies could lead to under- or overestimates of precancer rates among screened women. Second, changes in screening and management guidelines and uncertainty in histologic classification could have affected CIN2+ and CIN3+ case detection. Third, data are limited to ecologic trends, and interpretations inferring relationships between vaccination and precancer incidence lack causal certainty; however, trend analyses such as these are routinely used to evaluate the impact of vaccination programs,[††††] and no other plausible explanations for the decreases in precancers have been identified. Finally, because one site's catchment area expanded and the overall program standardized its screening estimation methods, numbers are not directly comparable with those reported in previous publications from this project.

Implications for Public Health Practice

These data are consistent with continuing impact of the U.S. HPV vaccination program on reducing cervical precancers (including CIN3+, the outcome most proximal to cervical cancer), and are consistent with both declines in vaccine-type HPV prevalence and early observations of reductions in cervical cancer among young women (*2*,*9*,*10*). The data also suggest that precancer incidence in age groups ≥25 years, which were previously observed to increase through 2015, have begun to decrease. HPV vaccination[§§§§] and guidelines-based cervical cancer screening[¶¶¶¶] are important tools for cervical cancer prevention.

[††††] https://www.cdc.gov/mmwr/preview/mmwrhtml/su6004a9.htm

[§§§§] https://www.cdc.gov/hpv/vaccines/index.html

[¶¶¶¶] https://www.cdc.gov/cervical-cancer/screening/

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Avian Influenza A(H5) Subtype in Wastewater — Oregon, September 15, 2021–July 11, 2024

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Abstract

Wastewater surveillance is an important tool in the surveillance of emerging pathogens and has been leveraged during the highly pathogenic avian influenza (HPAI) A(H5N1) virus outbreak in cattle and poultry in the United States. Interpretation of avian influenza A(H5) subtype detections in wastewater requires an understanding of human and animal contributors to the sewershed because current testing does not distinguish between human and animal sources. Potential animal contributors include wild birds, farms with poultry or dairy cattle outbreaks, and dairy processing facilities. Retrospective analysis of 551 influenza A virus–positive wastewater surveillance samples from 20 sites in Oregon during September 15, 2021–July 11, 2024, revealed 21 avian influenza A(H5) subtype detections across 12 communities. Avian influenza A(H5) subtype detections in wastewater began approximately 6 weeks before Oregon's first HPAI outbreak in domestic poultry, 7 weeks before Oregon's first avian influenza A(H5) detection in wild birds, and 2 years before the first HPAI A(H5N1) outbreak in dairy cattle in the United States (Oregon has not detected HPAI A(H5N1) in dairy cattle or milk). No association was found between detection of avian influenza A(H5) in a community's wastewater and history of an HPAI A(H5) outbreak among poultry in the county or presence of dairy processing facilities or dairy farms within the sewershed. Avian influenza A(H5) was detected most frequently in two communities with important wild bird habitats. Animal inputs, including from wild birds, should be considered when interpreting avian influenza A(H5) subtype detections in wastewater.

Introduction

In January 2022, highly pathogenic avian influenza (HPAI) A(H5N1) clade 2.3.4.4b virus, originating in Europe, was first detected in wild birds in the United States (*1*). Since then, clade 2.3.4.4b has rapidly become enzootic in wild birds throughout North America and has demonstrated the ability to efficiently infect domestic poultry and some mammals (*1*). The first commercial poultry outbreak of HPAI A(H5N1) clade 2.3.4.4b in the United States occurred in February 2022 and, as of December 5, 2024, more than 112 million domestic birds in 49 states had been affected nationally (*2*). The first outbreak of HPAI A(H5N1) in U.S. dairy cattle occurred in March 2024 and, as of December 5, 2024, a total of 718 herds in 15 states had been affected nationally (*3*).

As part of the United States' response to HPAI A(H5N1) outbreaks in animals and human cases and exposures, CDC is collaborating with state and local health departments to use wastewater surveillance to monitor influenza A virus and the avian influenza A(H5) subtype (*4*). Wastewater surveillance strengthens traditional case-based surveillance methods by providing community-level data independent of symptom status, health care–seeking behavior, and testing access, and can be quickly leveraged to detect emerging pathogens (*4*,*5*). However, interpretation of avian influenza A(H5) subtype detections in wastewater requires an understanding of human and animal contributors to the sewershed because current polymerase chain reaction (PCR)–based avian influenza A(H5) testing does not distinguish between human and animal sources (*4*). Potential animal contributors to wastewater include wild birds, farms with poultry or dairy cattle outbreaks, and dairy processing facilities (*4*,*6*).

In Oregon, clade 2.3.4.4b was first detected in wild birds and poultry in May 2022 and, as of December 5, 2024, a total of 44 HPAI outbreaks among poultry and none among dairy cattle have been identified (*2*,*3*). This report describes detections of the avian influenza A(H5) virus subtype in wastewater before and after HPAI was detected in wild birds and poultry in Oregon and dairy cattle in the United States.

Methods

Data Source and Study Design

Oregon tested wastewater seasonally for influenza viruses during September 15, 2021–June 24, 2022, and August 28, 2022–April 30, 2023, and has conducted year-round wastewater surveillance for influenza viruses since October 1, 2023. All influenza A virus–positive wastewater samples from a sample of 20 Oregon communities were retrospectively tested for the avian influenza A(H5) subtype. Communities were selected for geographic representativeness, migratory bird stopover activity, historic detections of avian influenza in wild birds, and the presence of licensed Grade A dairy processors* and farms within the sewershed.

* Presence defined as a facility that produces Grade A milk under sufficiently sanitary conditions to qualify for human consumption. Grade A milk requires pasteurization and may be sold in all 50 states.

Specimen Collection and Laboratory Testing

As part of Oregon's routine influenza A virus wastewater surveillance, 24-hour composite samples are collected from wastewater treatment facility influents 1–2 times weekly (*5*), filtered and then stabilized in DNA/RNA Shield (Zymo Research, https://www.zymoresearch.com). All wastewater samples are collected in duplicate, with the second filtered sample being archived at −112°F (−80°C). For this study, RNA was extracted from archived wastewater samples that previously tested positive for influenza A virus (*5*). Samples were analyzed for the avian influenza A(H5) subtype by digital reverse transcription PCR using the QIAcuity Eight instrument with the QIAcuity 26k 8-well Nanoplate (containing 26,000 partitions per sample) and the QIAcuity OneStep Advanced Probe Kit (QIAcuity, https://www.qiagen.com), per the manufacturer's instructions. Primers (forward primer: TATAGARGGAGGATGGCAGG and reverse primer: ACDGCCTCAAAYTGAGTGTT) and probe (AGGGGAGTGGKTACGCTGCRGAC) were used (*6*). The one-step PCR cycling conditions were as follows: reverse transcription at 122°F (50°C) for 40 minutes; enzyme inactivation at 203°F (95°C) for 2 minutes; and 40 cycles that consisted of denaturation at 203°F (95°C) for 5 seconds followed by annealing and extension at 140°F (60°C) for 30 seconds. After PCR cycling, the 26,000 partitions were imaged on the HEX channel. Data from digital PCR imaging were analyzed using consistent thresholds, and quality control was ensured with positive (controlled at 100 or more positive partitions) and no-template[†] (controlled at zero positive partitions) controls. All samples and quality controls were analyzed in duplicate.

Statistical Analyses

The Fisher's exact test was used to examine the association between avian influenza A(H5) subtype detections in wastewater and the presence of Grade A dairy processing facilities or dairy farms within the sewershed and reported poultry outbreaks within the county; p-values <0.05 were considered statistically significant. RStudio software was used to conduct all analyses (version 4.3.1; RStudio, Inc.). This activity was reviewed by Oregon Health Authority, deemed not research, and was conducted consistent with federal law and CDC policy.[§]

Results

Regional Characterization

Among 551 influenza A virus–positive samples during September 15, 2021–July 11, 2024, 21 (3.8%) tested positive for the avian influenza A(H5) subtype (Figure 1) in 12 of 20 communities (Figure 2). The highest number of detections (five of 34) occurred in Ontario (Malheur County); the largest proportion of detections (three of 14) was in Newport (Lincoln County). Eight of 12 communities with avian influenza A(H5) subtype detections are within counties that previously had an outbreak of HPAI in poultry. Only four of 12 communities with avian influenza A(H5) subtype detections had a licensed Grade A dairy processing facility or dairy farm within the sewershed. The avian influenza A(H5) subtype was not detected in wastewater from the two sewersheds with the highest number of licensed Grade A dairy processing facilities (Portland [seven]) and Grade A dairy farms (Tillamook [13]). No association between avian influenza A(H5) subtype detections in wastewater and location within a county with a history of poultry outbreak ($p = 0.65$) or location of licensed grade A dairy processing facilities or dairy farms within the sewershed ($p = 0.65$) was identified.

Longitudinal Characterization

The avian influenza A(H5) subtype was detected during multiple weeks of each of the three influenza seasons during the study as well as during the summer of 2024 (Figure 1). The avian influenza A(H5) subtype was first detected in Oregon wastewater on March 21, 2022, approximately 7 weeks before avian influenza A(H5) was detected in wild birds (Figure 1) and approximately 6 weeks before HPAI was detected in poultry in Oregon (Figure 1).

Discussion

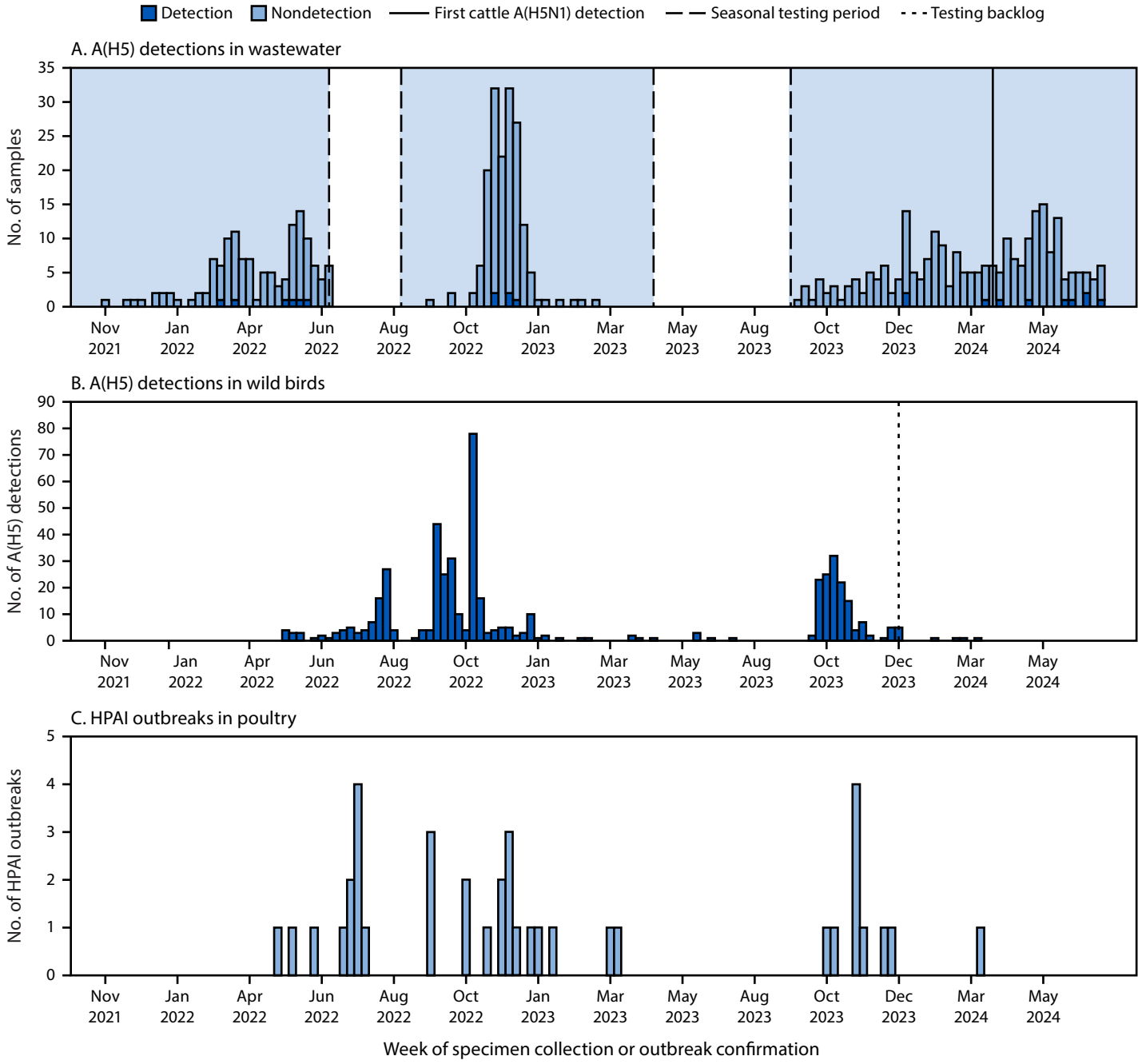
Wastewater surveillance in Oregon first detected the avian influenza A(H5) subtype on March 21, 2022, 6 weeks before HPAI A(H5) was identified in an Oregon domestic poultry outbreak, 7 weeks before avian influenza A(H5) was identified through Oregon wild bird surveillance, and 2 years before HPAI A(H5N1) was detected in dairy cattle in the United States (*1*). In this retrospective analysis, avian influenza A(H5) subtype detections in wastewater were not associated with poultry outbreaks or the presence of licensed dairy processing facilities or farms within the sewershed. Importantly, many avian influenza A(H5) detections occurred before the spillover of the virus into dairy cattle, estimated to have occurred during November 2023–January 2024,[¶] and no HPAI A(H5N1) outbreaks in dairy cattle have been identified in Oregon (*4*). These results do not support poultry or licensed dairy farm or processing facilities as the etiology of the avian influenza A(H5)

[†] A no-template control is a PCR reaction that does not contain a DNA or RNA template. This control checks for false positives that might occur because of cross-contamination.

[§] 45 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.

[¶] https://virological.org/t/preliminary-report-on-genomic-epidemiology-of-the-2024-h5n1-influenza-a-virus-outbreak-in-u-s-cattle-part-1-of-2/970

FIGURE 1. Number of detections of avian influenza A(H5) in wastewater (A)* and wild birds (B)† and highly pathogenic avian influenza outbreaks in poultry (C)§ — Oregon, September 15, 2021–July 11, 2024¶



Abbreviation: HPAI = highly pathogenic avian influenza.

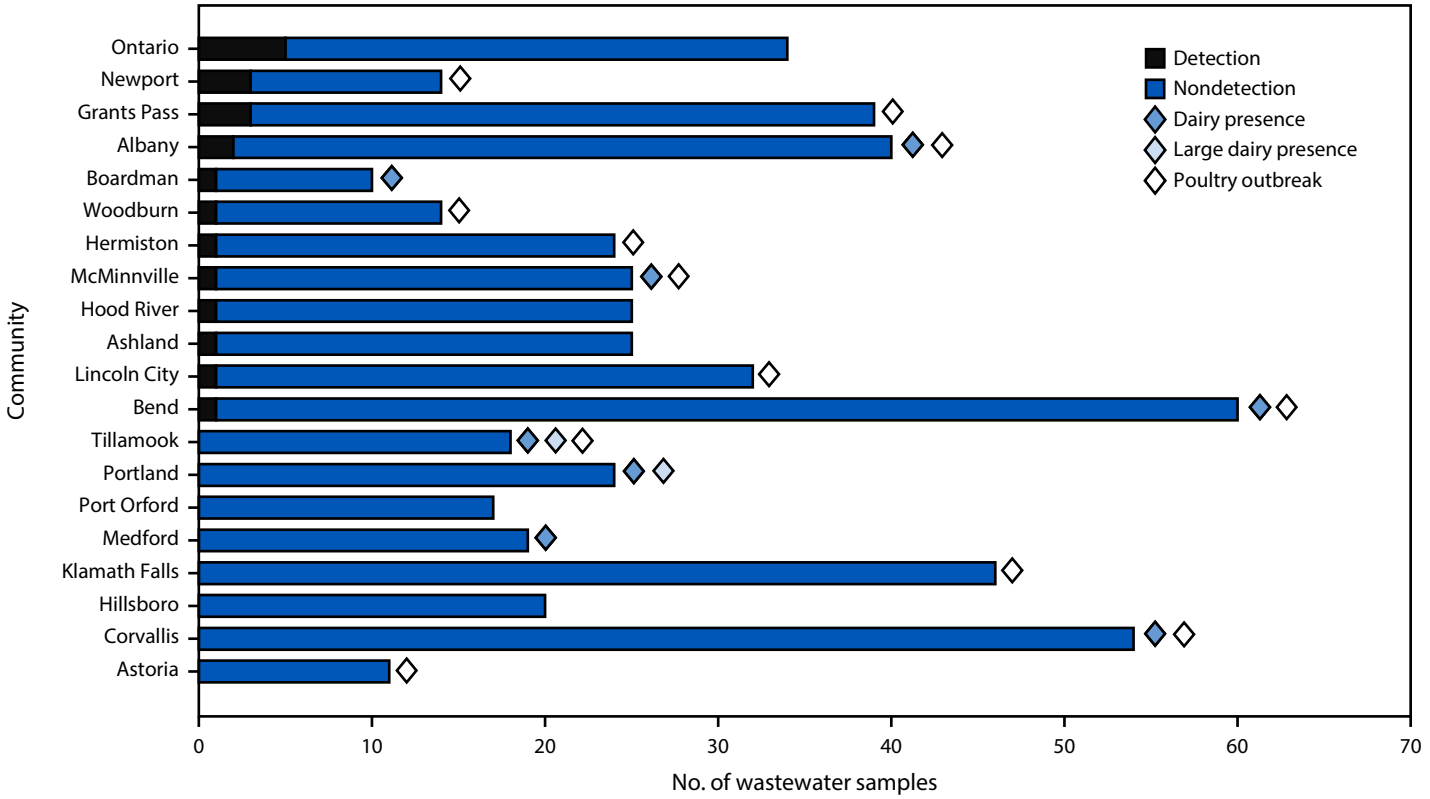
* During June 2022–August 2023, influenza testing of wastewater was only conducted seasonally.

† U.S. Department of Agriculture Animal and Plant Health Inspection Service has a backlog in testing wild bird samples, which might result in underrepresentation of the number of samples testing positive for avian influenza A(H5) after December 2023. https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/wild-birds

§ https://www.aphis.usda.gov/livestock-poultry-disease/avian/avian-influenza/hpai-detections/commercial-backyard-flocks

¶ The first cattle HPAI A(H5N1) detection in the United States was not in Oregon. Oregon has not detected HPAI A(H5N1) in dairy cattle or milk.

FIGURE 2. Number of wastewater samples tested for avian influenza A(H5), communities within a county that have experienced a highly pathogenic avian influenza A(H5) outbreak, and sewershed dairy presence* or large dairy presence† — Oregon, September 15, 2021–July 11, 2024



* Community with a licensed Grade A dairy processor (a facility that produces milk under sufficiently sanitary conditions to qualify for human consumption) or dairy farm within the sewershed.
† The sewersheds with the largest number of dairy farms (Tillamook [13]) and dairy processors (Portland [seven]).

subtype in Oregon wastewater and suggest that noncattle animals, suspected to be wild birds, are a significant animal contributor to wastewater within the state.

Oregon is located along the Pacific Flyway, a major north-south route for migratory birds in the Americas that extends from Alaska to Patagonia. An estimated 1 billion birds traverse the Pacific Flyway yearly, and Oregon contains many important stopover sites (*7*). Animal input can enter wastewater via stormwater in combined (i.e., open) sewersheds or via leaking pipes within separate (i.e., closed) sewersheds, as well as through the dumping of animal products into the sewer system (*6*,*8*). Surveillance programs that sample from wastewater clarifiers might also capture excreta from wild birds that have been observed using clarifiers and lagoons as resting habitats. The two communities in Oregon with the most avian influenza A(H5) subtype detections contain important habitats for migratory wild birds, including seasonal wetlands (Ontario) and estuaries of major rivers (Newport) (*7*,*9*). Avian influenza A(H5) subtype detections occurred in both combined and separate sewersheds.

Limitations

The findings in this report are subject to at least two limitations. First, avian influenza A(H5) testing was performed retrospectively on samples that had tested positive for influenza A virus as part of Oregon's routine influenza wastewater surveillance, which, before October 2023, occurred only during the influenza season. This approach limits the ability to describe seasonal avian influenza A(H5) subtype wastewater trends. Second, the testing methods used do not distinguish between animal sources or high- and low-pathogenic avian influenza A(H5) viruses (*10*).

Implications for Public Health Practice

The timing and spatial clustering of avian influenza A(H5) subtype detections in Oregon wastewater suggest that noncattle animals, suspected to be wild birds, are important

Summary

What is already known about this topic?

Highly pathogenic avian influenza A(H5N1) outbreaks have emerged in U.S. cattle and poultry. Wastewater surveillance detects influenza A(H5) subtype but does not currently distinguish between human and animal sources.

What is added by this report?

During September 15, 2021–July 11, 2024, retrospective analysis of wastewater surveillance data revealed 21 avian influenza A(H5) subtype detections across 12 Oregon communities. No association was found between detections in a community's wastewater and history of a poultry outbreak or presence of dairy processing facilities or dairy farms within the sewershed. Avian influenza A(H5) was detected most frequently in two communities with important wild bird habitats.

What are the implications for public health practice?

Wastewater surveillance was an early indicator of avian influenza emergence in Oregon. Nonhuman and noncattle animal inputs, including wild birds, are an essential consideration when interpreting A(H5) subtype detections in wastewater.

contributors of the virus to Oregon's wastewater. Oregon's first avian influenza A(H5) subtype detections in wastewater did not occur until after the introduction of the 2.3.4.4b clade into wild birds in North America and preceded Oregon's first HPAI poultry outbreaks and avian influenza A(H5) detections through wild bird surveillance by more than 6 weeks. The first avian influenza A(H5) subtype detection in Oregon wastewater occurred almost 2 years before the multistate outbreak of HPAI A(H5N1) in dairy cattle, excluding cattle as a potential source for subtype detections before November 2023. On the basis of the results of this retrospective study, continued intermittent detections of the avian influenza A(H5) subtype in wastewater are anticipated, even in the absence of outbreaks in dairy cattle or occurrence of human cases. Wild birds, in which HPAI A(H5) is now enzootic, are an important consideration when interpreting avian influenza A(H5) subtype detections in wastewater. Wastewater surveillance, with consideration of all animal contributors and in conjunction with other surveillance metrics, has the potential to strengthen ongoing avian influenza surveillance efforts.

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Oregon's wastewater treatment facilities staff members.

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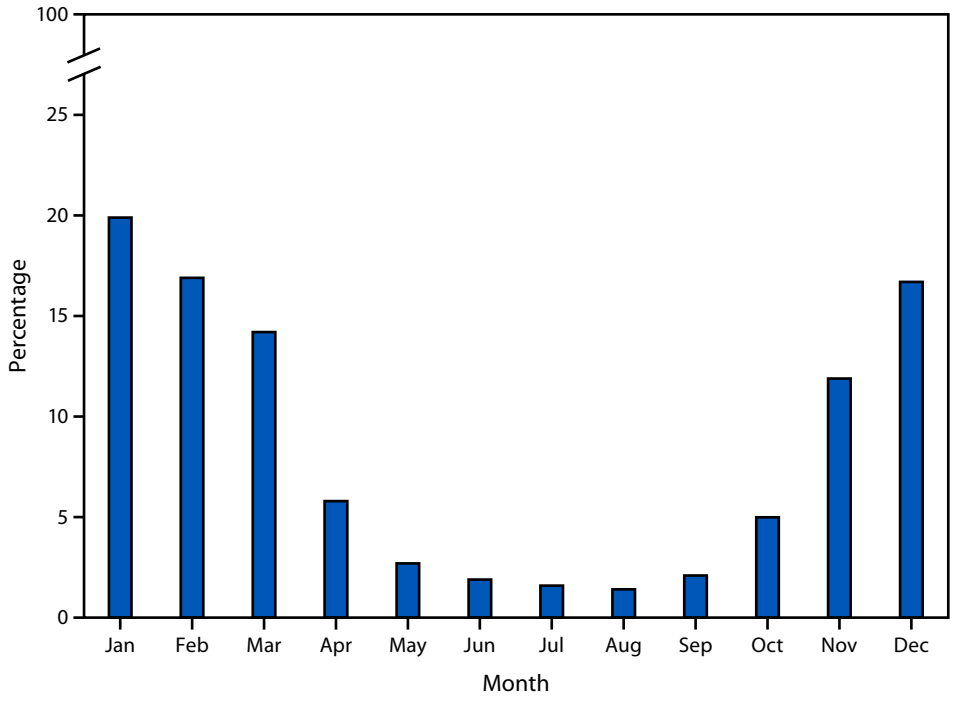
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage Distribution of Deaths Attributed to Excessive Cold or Hypothermia,* by Month — United States, 2023



* Deaths attributed to excessive cold or hypothermia were identified using the *International Classification of Diseases, Tenth Revision* underlying cause of death code X31 (Exposure to excessive natural cold) and multiple cause of death code T68 (Hypothermia).

In 2023, a total of 1,024 deaths were attributed to excessive cold or hypothermia. The majority of deaths occurred during January–February and November–December, with the highest percentage occurring in January (19.9%).

Supplementary Table: https://stacks.cdc.gov/view/cdc/175597

Source: National Center for Health Statistics, National Vital Statistics System, Mortality Data, 2023. https://www.cdc.gov/nchs/nvss/deaths.htm

Reported by: Matthew F. Garnett, MPH, Mgarnett@cdc.gov.

For more information on this topic, CDC recommends the following link: https://www.cdc.gov/winter-weather/prevention/index.html.

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