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Suspected *Legionella* Transmission from a Single Donor to Two Lung Transplant Recipients — Pennsylvania, May 2022

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Abstract

In July 2022, the Pennsylvania Department of Health received two reports of laboratory-confirmed Legionnaires disease in patients who had recently received lung transplants from the same donor at a single Pennsylvania hospital. The donor's cause of death was freshwater drowning in a river, raising suspicion of potential donor-derived transmission, because *Legionella* bacteria naturally live in fresh water. Further investigation of patients receiving other organs from the same donor did not identify additional legionellosis cases. Health care–associated infection caused by water exposure at the hospital was also evaluated as a potential source of infection and was found to be unlikely. Hospital water quality parameter measurements collected during May–June 2022 were within expected ranges and no water disruptions were noted, although no testing for *Legionella* was performed during this period. Notifiable disease data did not identify any other Legionnaires disease cases with exposure to this hospital within the 6 months before or after the two cases. Although laboratory testing did not confirm the source of recipient infections, available data suggest that the most likely source was the donor lungs. This cluster highlights the need for increased clinical awareness of possible infection with *Legionella* in recipients of lungs from donors who drowned in fresh water before organ recovery.

Investigation and Results

In July 2022, the Pennsylvania Department of Health (PADOH) received reports of two cases of laboratory-confirmed Legionnaires disease in patients with exposure to the same Philadelphia hospital. Further investigation confirmed that each of the two patients had undergone transplantation of a single lung from the same donor before disease onset. Because of the possibility of a transplant-associated infection with *Legionella*, the hospital notified the Organ Procurement and Transplantation Network (OPTN) and initiated an investigation by OPTN's ad hoc Disease Transmission Advisory Committee (DTAC). CDC, as a member of DTAC, led the investigation to determine whether the infections were transmitted through transplanted organs and to identify other patients who were potentially at risk.

The donor was a man aged 30–39 years who fell into a river and was submerged for ≥5 minutes. Despite resuscitation efforts, he sustained anoxic brain injury, which led to determination of brain death. Organ recovery occurred within 7 days of the drowning event. At the time, exposure to *Legionella* was not suspected, and no testing for *Legionella* was performed on any donor specimens before or after organ recovery.

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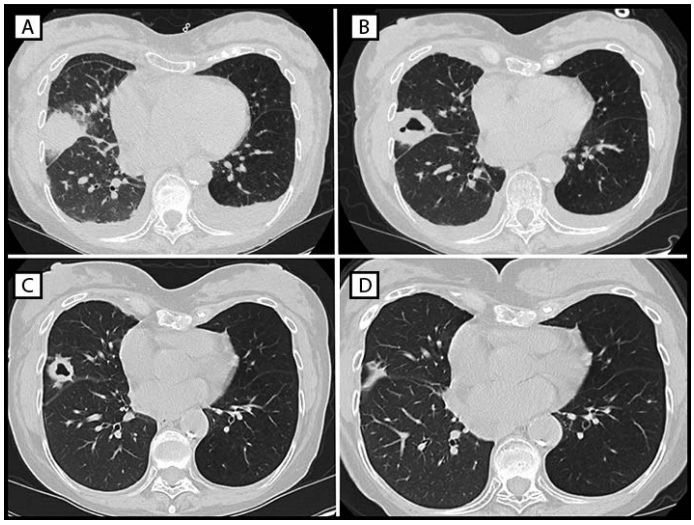
The first Legionnaires disease case was identified in a woman aged 70–79 years (patient A) who received a right lung transplant in May 2022. Nine days after transplantation, the patient's laboratory results revealed an elevated white blood cell count and acute anemia, which prompted imaging studies. A computed tomography (CT) scan was performed based on these blood test results. The CT scan identified dense consolidation in the middle lobe of the donor lung, which evolved into a cavitary lesion during the subsequent week (Figure). A bronchoalveolar lavage specimen collected during early June tested positive for *Legionella* species other than *Legionella pneumophila* by nucleic acid amplification. Doxycycline treatment was initiated immediately after *Legionella* was identified in the lavage specimen, and the patient fully recovered. No further testing was performed to identify the species or rule out the presence of multiple *Legionella* species.

The second case occurred in a man aged 60–69 years (patient B) who received a left lung transplant on the same day and from the same donor as did patient A. Patient B experienced multiple postoperative complications, including the need for extracorporeal membrane oxygenation and renal replacement therapy, and he received antibiotic treatment with doxycycline starting on postoperative day 15. Ground glass–appearing opacities (a nonspecific sign that might represent infection) were noted in the donor lung after a CT scan performed 24 days after transplantation. After the first case was disclosed, a sputum specimen was collected during early June and tested positive for *L. pneumophila* by culture at a commercial laboratory. Although the patient experienced an initial clinical recovery, after a prolonged hospital stay, he died approximately 6 months after the transplant surgery due to respiratory failure secondary to a mucous plug.

FIGURE. Computed tomography studies of the chest of patient A, who experienced infection with *Legionella* sp. (other than *Legionella pneumophila*) after receipt of a transplanted right lung from a donor who had drowned in fresh water, showing dense consolidative opacity with surrounding ground glass opacification (postoperative day 9) (A), thick-walled cavitation (postoperative day 16) (B), resolving lesion with thinning of cavity walls (postoperative day 29) (C), and continuing improvement (postoperative day 119) (D) — Philadelphia, Pennsylvania, May 2022



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Three additional recipients received transplanted organs from the same donor, including heart, liver, and right kidney. The heart, liver, and lung transplants occurred on the same day; the kidney transplant occurred 1 day later. The heart recipient had numerous nonspecific complications (none suggestive of legionellosis) after the transplant; no testing for *Legionella* was performed. The liver recipient had few postoperative complications, and a urinary antigen test result for *Legionella* was negative. The kidney recipient had few complications, but no evidence of postoperative infection; no testing for *Legionella* was performed. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.*

Public Health Response

After notification of the two cases of Legionnaires disease, the Philadelphia Department of Public Health (PDPH) and PADOH requested water quality parameter and testing records for *Legionella* from the transplant hospital. Records collected during May–June 2022 were reviewed, including water management program data from both the potable water system and multiple cooling towers operated by the hospital. The cooling tower records indicated operation consistent with a well-functioning water management program.† Potable water records collected during this period indicated that disinfectant was detected at all tested points of use. Routine testing of water samples for *Legionella* was not part of the facility's water management program.

CDC attempted to identify any remaining clinical specimens from the donor or the organ recipients for testing for *Legionella*; however, no relevant specimens were available. Specimens relevant to testing for *Legionella* are not required to be collected or saved from organ donors. CDC and PADOH attempted to retrieve clinical isolates or any remaining clinical specimens from either lung transplant recipient and were similarly unsuccessful. The specimens collected from the patients either did not result in isolates after testing or were discarded by the commercial testing laboratory before additional testing could be performed.

PDPH and PADOH conducted retrospective and prospective active case finding by reviewing reportable disease surveillance data to ascertain whether any other persons with cases of Legionnaires disease were exposed to the transplant hospital during this period. No cases were identified during the 6 months before or after the transplant events.

Discussion

Legionella bacteria are found naturally in freshwater environments, can survive under a wide range of environmental conditions, and typically grow best in warm water at temperatures of 77°F–113°F (25°C–45°C) (*1*). Exposure to water outside of human-made systems is not generally considered a risk factor for Legionnaires disease, which typically occurs after inhalation of water droplets containing *Legionella* (although aspiration is a recognized route of infection) (*2*). Before the cases described in this report were observed, infections with *Legionella* attributed to aspiration resulting from near-drowning incidents have been documented (*3*).

Legionnaires disease incidence has increased substantially during the past decade, reaching a peak of 2.71 cases per 100,000 persons in 2018 (*4*). Most cases are not associated with a known source, although approximately 18% have a reported health care facility–associated exposure (*5*). The Centers for Medicare & Medicaid Services requires that all acute care hospitals design and implement a water management program to reduce the growth and spread of *Legionella*.§ An effective water management program, along with strict adherence to infection control guidance, remain the best means to prevent health care–associated Legionnaires disease (*6*). Although solid organ transplantation is known to increase the risk for infection with *Legionella*, likely due to required immunosuppressive therapy, transmission via the organs themselves has not previously been reported (*2*). As with all infections in transplant recipients, prompt identification is critical to limit morbidity and mortality.

Despite a lack of confirmatory clinical or genomic evidence, three factors suggest that the transplanted lungs were the likely source of infection in the two cases presented in this report. First, different *Legionella* species were identified in the two patients. This can potentially be explained by infections derived from the donor's exposure to river water, which might contain a larger diversity of *Legionella* species compared with potable water (*7*). Second, a review of records from the transplant facility indicated that water parameters were within expected ranges and the hospital did not report any disturbances to the building's water system, recent changes in water quality parameters, or other events that might have increased the risk for infection with *Legionella* during this period. Finally, no other cases of legionellosis were reported from this facility within the 12-month period surrounding the two reported cases and no other possible sources of exposure were identified. Given the tight clustering in time, identification of additional cases would be expected if the source was the hospital facility's water system or cooling towers.

Limitations

The findings in this report are subject to at least three limitations. First, clinical specimens were not available from the

* 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://www.cdc.gov/legionella/wmp/control-toolkit/index.html

§ https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/SurveyCertificationGenInfo/Policy-and-Memos-to-States-and-Regions-Items/Survey-And-Cert-Letter-17-30-

Summary

What is already known about this topic?

Legionnaires disease is a severe pneumonia caused by *Legionella* bacteria. Comorbidities, including recent organ transplantation, increase the risk for infection.

What is added by this report?

In June 2022, two cases of Legionnaires disease were reported in patients, each of whom had received a lung transplant from the same donor, who had drowned in a river. Epidemiologic, environmental, and laboratory evidence suggest that the source of infection was likely the transplanted lungs.

What are the implications for public health practice?

Clinicians caring for patients who received organs from donors who drowned in fresh water should consider infection with *Legionella* in patients who develop postoperative complications. Prompt diagnosis and treatment of Legionnaires disease increases the likelihood of a full recovery.

donor for testing for *Legionella*. As a result, the presence of infection with *Legionella* in the donor before organ donation could not be confirmed. Second, specimens from the patients were not available for additional laboratory analyses which might have better characterized the species and serotypes present. In addition, the heart and kidney transplant recipients did not receive any *Legionella*-specific testing. Finally, the transplant hospital's building water system and cooling towers were not tested for *Legionella* before or immediately after the surgical procedures. Although the hospital's water parameter data indicate a well-maintained system, presence of *Legionella* bacteria in the water system at the time of the transplants cannot be ruled out.

Implications for Public Health Practice

This report adds to the understanding of microbial risk assessment among recipients of organs from donors who died from drowning. Previous studies have documented bacterial and fungal pathogen transmission to transplant recipients when the donors have drowned, which have sometimes resulted in outcomes including bacterial and fatal fungal infections (*8*–*10*). The present findings suggest that clinicians caring for patients who receive organs from donors who experienced freshwater drowning also should maintain a higher index of suspicion for legionellosis, even in organ recipients without classic clinical symptoms. In such patients, posttransplant antimicrobials could be tailored to include agents that combat atypical waterborne organisms. When an unexpected donor-derived infection is suspected, providers are required to report the case to the United Network for Organ Sharing or OPTN for investigation by DTAC and to public health authorities for expedited evaluation and identification of potentially infected organs and tissues.[¶] Prompt assessment by astute clinicians can result in more rapid diagnosis and treatment of Legionnaires disease, which requires organism-specific testing, thereby increasing the likelihood of a full recovery.

[¶] https://optn.transplant.hrsa.gov/media/eavh5bf3/optn_policies.pdf

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Wastewater Surveillance Data as a Complement to Emergency Department Visit Data for Tracking Incidence of Influenza A and Respiratory Syncytial Virus — Wisconsin, August 2022–March 2023

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Abstract

Wastewater surveillance has been used to assist public health authorities in tracking local transmission of SARS-CoV-2. The usefulness of wastewater surveillance to track community spread of other respiratory pathogens, including influenza virus and respiratory syncytial virus (RSV), is less clear. During the 2022–23 respiratory diseases season, concentrations of influenza A virus and RSV in wastewater samples in three major Wisconsin cities were compared with emergency department (ED) visits associated with these pathogens. In all three cities, higher concentrations of influenza A virus and RSV in wastewater were associated with higher numbers of associated ED visits (Kendall's tau range = 0.50–0.63 for influenza-associated illness and 0.30–0.49 for RSV-associated illness). Detections of both influenza A virus and RSV in wastewater often preceded a rise in associated ED visits for each pathogen, and virus material remained detectable in wastewater for up to 3 months after pathogen-specific ED visits declined. These results demonstrate that wastewater surveillance has the potential to complement conventional methods of influenza and RSV surveillance, detecting viral signals earlier and for a longer duration than do clinical data. Continued use of wastewater surveillance as a supplement to established surveillance systems such as ED visits might improve local understanding and response to seasonal respiratory virus outbreaks.

Introduction

Wastewater surveillance has demonstrated benefit as a robust, highly adaptable platform for community-level surveillance for SARS-CoV-2 transmission (*1*). In considering expansion of wastewater surveillance to track other respiratory pathogens, influenza viruses and respiratory syncytial virus (RSV) are two potential candidates: both viruses are quantifiable in wastewater, associated with substantial morbidity and mortality each year, and spread during annual winter outbreaks that can vary in timing and duration (*2*,*3*). Wastewater surveillance, which is independent of health care access or testing biases, might help supplement outbreak data collected by traditional, clinical surveillance systems; data on usefulness of wastewater surveillance to track influenza and RSV, however, are limited. During the 2022–23 respiratory diseases season, the Wisconsin Department of Health Services tracked influenza A virus and RSV in Wisconsin's three largest cities using wastewater surveillance data. Wastewater surveillance data for influenza A virus and RSV were compared with influenza- and RSV-associated emergency department (ED) visits, both descriptively and with basic correlation statistics, to broadly ascertain whether wastewater surveillance might be a useful, complementary surveillance tool for ongoing and future use in Wisconsin.

Methods

Data Sources

During August 2022–March 2023, wastewater samples were collected at least once weekly from approximately 40 wastewater treatment plants (treatment plants) as part of Wisconsin's established wastewater surveillance system. Refrigerated samples were shipped overnight to either the Wisconsin State Laboratory of Hygiene or a University of Wisconsin-Milwaukee laboratory for processing; laboratories used different concentration and extraction methods, but all samples from a given treatment plant were processed by the same laboratory.* Established assays were used with CDC primers and probes† to quantify concentrations (in gene copies per liter [gc/L]) of influenza A virus and RSV in samples (*4*). Weekly geometric mean concentrations were calculated in instances when more than one wastewater sample was tested from the same city during the same surveillance week. Concentration values were converted to the log(10) scale; a value of 1 gc/L was added to all values to allow for log(10) transformation of zero values.

ED visits for influenza and RSV were reported to the Electronic Surveillance System for Early Notification of Community-Based Epidemics (ESSENCE), the primary surveillance system used by CDC's National Syndromic Surveillance Program. Among 139 EDs across Wisconsin, 129 (93%) report data to ESSENCE. ED visits with influenza or RSV diagnoses were identified using standard CDC definitions, which were based on the diagnosis code and clinical terms for influenza or RSV, respectively, in discharge notes.§ ED visit counts were summed for each surveillance week.

* https://doi.org/10.6084/m9.figshare.23669271
† https://www.cdc.gov/coronavirus/2019-ncov/downloads/lab/multiplex-primers-probes-printer.pdf
§ Diagnostic codes and clinical terms were based on *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM), *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM), and Systematized Nomenclature of Medicine–Clinical Terms (SNOMED CT). https://www.cdc.gov/ncird/surveillance/respiratory-illnesses/index.html#companion-guide

A valid comparison of the wastewater and ED visit surveillance systems required that the populations covered be geographically similar. Wastewater surveillance data reflect contributions from persons within a sewershed (the geographic area contributing wastewater to a sampling location). ED visit data included the residential zip codes of patients. To identify overlapping population groups, sewershed boundaries were examined, and four treatment plants with sewershed boundaries were identified by visual inspection that were best aligned with zip code boundaries. These four treatment plants serviced the three most populous cities in Wisconsin (one in Green Bay, one in Madison, and two in Milwaukee) and provided an average of 1.7–3.2 samples per week. Thus, only wastewater surveillance data from the four treatment plants servicing these three cities were included; ED visit data were only included in the analysis if they were 1) linked to patients with a Green Bay, Madison, or Milwaukee residential zip code, and 2) reported by a Wisconsin ED during August 2022–March 2023.

Statistical Analyses

Data on wastewater surveillance viral concentrations and ED visits were paired by surveillance week, and Kendall's tau (a nonparametric measure of correlation) was used to assess statistical agreement between the surveillance systems. Kendall's tau, which has been applied in previous wastewater surveillance literature, was used to quantify the relationship between the two data sources; higher values indicate a stronger correlation. R software (version 4.1.3; R Foundation) was used to conduct all statistical analyses. This activity was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.¶

¶ 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.

Results

A total of 6,271 influenza-associated ED visits and 1,518 RSV-associated ED visits were reported during August 2022–March 2023 (Table). According to both wastewater surveillance and ED data in each of the three cities, RSV peaked in early November, and influenza peaked approximately 1 month later (Figure 1). Wastewater samples from the three cities often tested positive for viral material in advance of rises in ED visit counts. Both influenza A virus and RSV detection persisted in sewersheds for up to 3 months after the associated ED visit trajectories had subsided. For both viruses, positive correlations were observed between paired wastewater surveillance and ED data in all three cities (Figure 2). Correlation values were higher for influenza than for RSV in all three cities. For Green Bay, Madison, and Milwaukee, Kendall's tau values for influenza were 0.50, 0.52, and 0.63, respectively, and 0.37, 0.49, and 0.30, respectively, for RSV.

Discussion

This analysis, which compared the results of wastewater surveillance and surveillance of ED visits for tracking influenza and RSV in three major Wisconsin cities during August 2022–March 2023, found a positive correlation between wastewater surveillance and ED visit data, findings that are consistent with previous analyses (*2*,*5*–*7*). The additional information concerning community levels of influenza and RSV circulation provided by wastewater surveillance might be beneficial for public health preparedness and response; for example, during the early stage of an epidemic wave (when case-based surveillance data are limited), it could be helpful to know when viral concentrations in wastewater start to increase. In addition, wastewater data might serve as supplementary input to forecasting models (*3*).

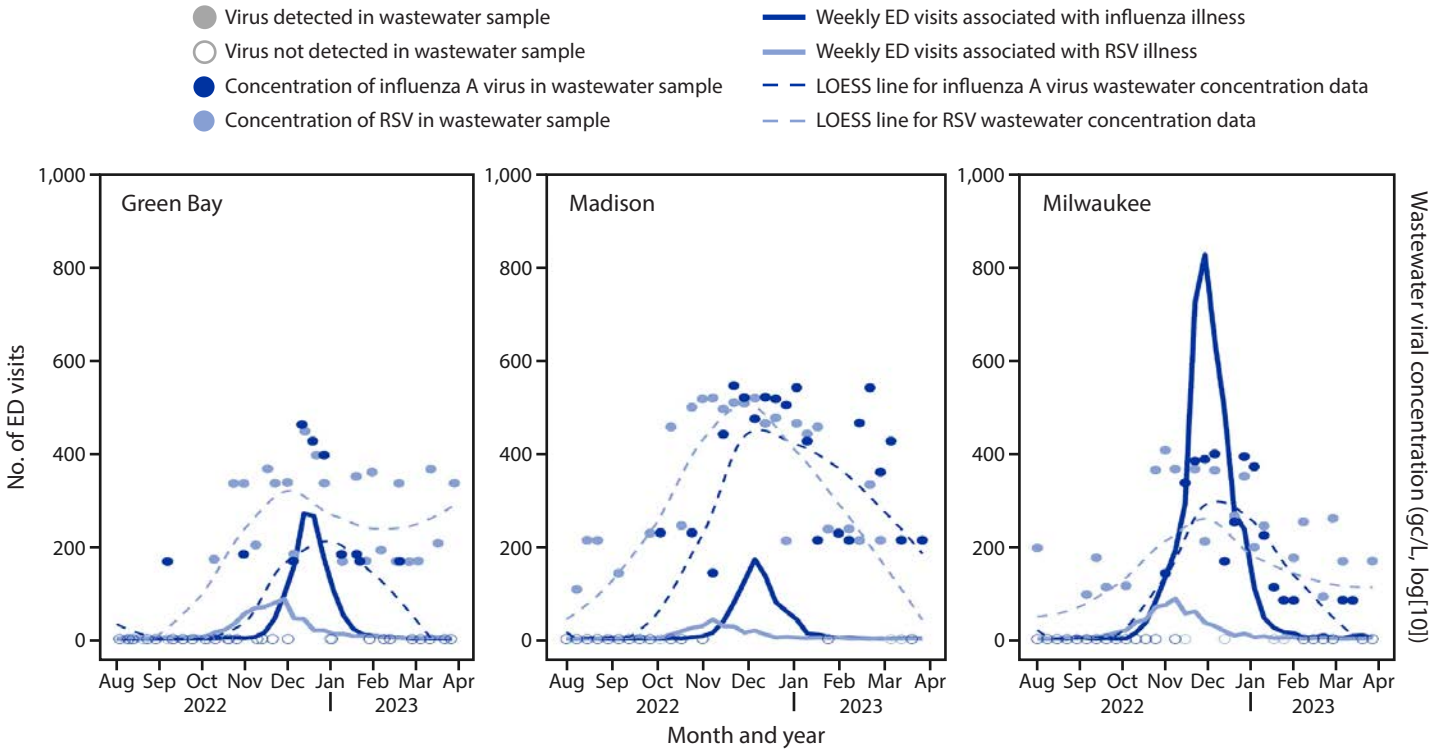
TABLE. Emergency department–based and wastewater-based surveillance for influenza and respiratory syncytial virus — Green Bay, Madison, and Milwaukee, Wisconsin, August 2022–March 2023

Characteristic	City			
	Green Bay	Madison	Milwaukee	Total
Emergency department influenza data				
No. of visits with illness meeting syndromic case definition*	1,251	805	4,215	**6,271**
Median age, yrs (IQR)	20 (6–44)	21 (7–45)	28 (14–48)	**26 (10–46)**
Emergency department RSV data				
No. of visits meeting syndromic case definition*	641	269	608	**1,518**
Median age, yrs (IQR)	2 (0–6)	1 (0–4)	3 (1–34)	**2 (0–9)**
Wastewater data				
No. of wastewater treatment plants serving city	1	1	2	**4**
Estimated population served by all wastewater treatment plants	189,000	345,000	1,085,941	**1,619,941**
Total no. of wastewater samples collected	61	78	111	**250**
Average no. of wastewater samples collected per wk	1.7	2.2	3.2	**2.4**

Abbreviation: RSV = respiratory syncytial virus.

* Diagnostic codes and clinical terms were based on *International Classification of Diseases, Tenth Revision, Clinical Modification* (ICD-10-CM), *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM), and Systematized Nomenclature of Medicine–Clinical Terms (SNOMED CT). https://www.cdc.gov/ncird/surveillance/respiratory-illnesses/index.html#companion-guide

FIGURE 1. Respiratory syncytial virus–associated and influenza-associated emergency department visits* and wastewater concentrations† for respiratory syncytial virus and influenza A virus — three Wisconsin cities, August 2022–March 2023§



Abbreviations: ED = emergency department; LOESS = locally estimated scatterplot smoothing; RSV = respiratory syncytial virus.
* Collected from the Electronic Surveillance System for the Early Notification of Community-Based Epidemics (ESSENCE) and based on CDC-provided definitions.
† Wastewater concentration values were log(10) and denoted in gene copies per L (gc/L); a value of 1 gc/L was added to all wastewater concentrations to allow for log(10) transformation of previously zero values.
§ LOESS lines are overlaid to display general trend in wastewater concentration data.

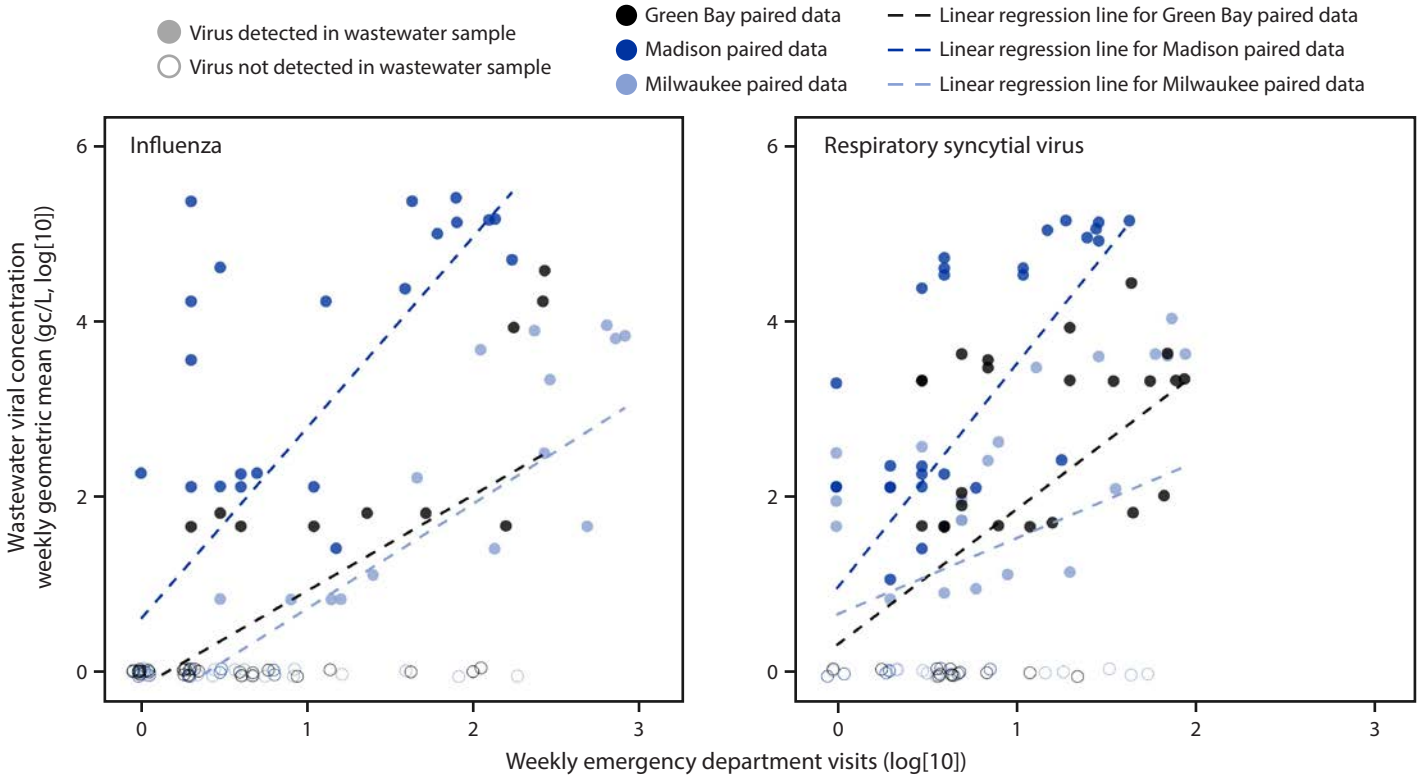
These findings are consistent with data from other reports showing that influenza virus and RSV are detected by wastewater surveillance in advance of rising clinical cases. Recent studies in Australia (*2*) and Canada (*8*) found that increasing concentrations of influenza virus and RSV in wastewater were strongly associated with increases in clinical cases 12–17 days later. Simple visual examination of the data in this current analysis suggested that influenza virus and RSV were generally detected in wastewater before significant increases in numbers of ED visits. However, this work was unable to determine the consistency or reliability of this lead time across cities or pathogens; for example, weekly aggregated data were too sparse to accurately calculate any time-shifted correlation coefficients. Future work could prioritize data collection and quantity in late summer and early fall seasons in anticipation of respiratory illness outbreaks to better ascertain these lead time values. Any advance warning provided by wastewater surveillance might provide health care and public health systems time to scale up capacity, ensure availability of treatment (e.g., antivirals), and promote preventive measures in advance of a clinical surge.

The observed persistence of influenza A virus and RSV detections in wastewater surveillance after the prevalence of ED visits declined likely reflects asymptomatic and mild illness outside the outbreak's peak, as well as possible prolonged viral shedding; influenza A virus genetic material has been found in stool samples of infected persons for up to 3 weeks after infection (*9*). A better understanding of this persistence might reassure public health authorities that continued detection of viral material in wastewater (beyond an observed decline in clinical cases) is not necessarily indicative of a resurgent wave of disease, but rather an inherent characteristic of this type of surveillance.

Limitations

The findings in this report are subject to at least four limitations. First, wastewater surveillance does not reflect disease patterns among residents not served by municipal wastewater infrastructure and thus would not be representative of households using septic systems. Similarly, wastewater surveillance would likely fail to collect data from diapered children, that

FIGURE 2. Correlation* between weekly emergency department visits and wastewater surveillance for influenza† and respiratory syncytial virus§ — three Wisconsin cities, August 2022–March 2023



* For visual ease of comparison, data from both surveillance systems were transformed to the log(10) scale, and a value of 1 was added to all datapoints in both datasets (e.g., 1 case or 1 gc/L) to allow for log(10) transformation of previously zero values. Values along the 0 gc/L, log(10) line are jittered slightly to display the density of points. Linear regression lines are overlaid to display general trend in relationships between paired data.
† Kendall's tau values = 0.50 (Green Bay), 0.52 (Madison), and 0.63 (Milwaukee).
§ Kendall's tau values = 0.37 (Green Bay), 0.49 (Madison), and 0.30 (Milwaukee).

might be important in surveillance for RSV, which predominates among young children. Second, surveillance data in both systems were based on weekly numbers, which might obscure nuanced outbreak or cluster patterns in a community. Third, the seasonal outbreak dynamics of influenza and RSV vary from year to year, and because this analysis only includes a small data set from one respiratory season, results presented here might not reflect disease patterns in all years. Finally, variability in wastewater concentrations for each community, and thus differences in temporal patterns between wastewater and ED data, could be attributable to a number of factors independent of the incidence in each community (e.g., wastewater temperature and pH and the presence of external chemical inhibitors) (*10*).

Implications for Public Health

The positive correlation between wastewater surveillance and ED visit data for both influenza and RSV, along with the detection of the two pathogens in wastewater before increases in associated ED visits, suggests that wastewater surveillance might help supplement established clinical surveillance for these viruses. Public health practitioners should be aware of the long persistence of viral detection in wastewater surveillance. Incorporation of, and continued research into, the capabilities of wastewater surveillance might improve local public health agencies' understanding of and response to seasonal respiratory virus disease outbreaks.

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Summary

What is already known about this topic?

Wastewater surveillance is useful for tracking community SARS-CoV-2 levels, but its usefulness for tracking influenza and respiratory syncytial virus (RSV) is less understood.

What is added by this report?

During August 2022–March 2023, influenza and RSV were tracked using wastewater surveillance and emergency department (ED) visits in three Wisconsin cities. A positive correlation between the two surveillance systems was observed. Wastewater surveillance detected increases in influenza and RSV that preceded increases in ED visits by weeks and persisted beyond declines in associated ED visits for up to 3 months.

What are the implications for public health practice?

Incorporating wastewater surveillance into established surveillance systems might improve local preparedness and response to seasonal respiratory virus disease outbreaks.

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Interim Effectiveness Estimates of 2023 Southern Hemisphere Influenza Vaccines in Preventing Influenza-Associated Hospitalizations — REVELAC–i Network, March–July 2023

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Abstract

Evaluations of vaccine effectiveness during the March–September Southern Hemisphere influenza season can provide valuable information for countries currently experiencing the influenza season and preceding the October–May Northern Hemisphere influenza season. Since 2013, multiple countries have participated in the Network for the Evaluation of Vaccine Effectiveness in Latin America and the Caribbean–influenza (la Red para la Evaluación de Vacunas en Latino América y el Caribe—influenza [REVELAC–i]) to estimate and monitor vaccine effectiveness (VE) in preventing severe acute respiratory infection (SARI)–associated hospitalization. Based on data contributed by Argentina, Brazil, Chile, Paraguay, and Uruguay on 2,780 SARI patients hospitalized during March 27–July 9, 2023, the adjusted VE against SARI hospitalization associated with any influenza virus during the 2023 Southern Hemisphere season was 51.9% (95% Confidence Interval [CI] 39.2%–62.0%), including 55.2% (95% CI: 41.8%–65.5%) against the predominating A(H1N1)pdm09. These early, interim estimates, provided before the expected end of seasonal influenza virus circulation, suggest that vaccination substantially reduced the risk for severe influenza illnesses, underscoring the benefits of influenza vaccination. In anticipation of Northern Hemisphere influenza virus circulation, the World Health Organization and CDC recommend that health authorities encourage health care providers to administer annual influenza vaccination to all eligible persons, particularly emphasizing the importance of vaccination for persons at increased risk for severe outcomes (e.g., very young children, persons with preexisting health conditions [including pregnant women], and older adults).

Introduction

In Latin American and Caribbean countries, influenza viruses have been associated with 716,000–829,000 respiratory hospitalizations and 41,007–71,710 deaths each year (*1*). Despite a history of high influenza vaccination coverage in the region, declines in coverage since 2019 have been observed. Systematic monitoring of influenza and COVID-19 vaccine effectiveness (VE), as is conducted through the Pan American Health Organization's Network for the Evaluation of Vaccine Effectiveness in Latin America and the Caribbean–influenza (la Red para la Evaluación de Vacunas en Latino América y el Caribe—influenza [REVELAC–i])[†] can be helpful in supporting public messaging to improve vaccination coverage (*2*). In addition, VE estimates from countries in the Southern Hemisphere during the March–September influenza season can provide insight into the effectiveness of vaccines for use during the subsequent October–May Northern Hemisphere influenza season (*3*).

Methods

VE against influenza-associated hospitalization was estimated using a test-negative case-control study design to compare the odds of vaccination between hospitalized patients with a positive influenza test result (test-positive patients [case-patients]) and influenza test-negative hospitalized control patients. Patients meeting criteria for severe acute respiratory infection (SARI), defined as acute respiratory infection with a history of fever or documented temperature of ≥100.4°F [≥38°C] and cough, with onset during the preceding 10 days resulting in hospitalization, were identified through sentinel SARI surveillance using a standardized protocol (*4*). Respiratory specimens were collected and tested for influenza virus type and subtype by reverse transcription–polymerase chain reaction (RT-PCR) in national reference laboratories.

During March 27–July 9, 2023, midseason data were available and were pooled from 486 sentinel hospitals, including 11 in Argentina, 455 in Brazil, eight in Chile, two in Paraguay, and 10 in Uruguay. Because influenza was circulating in the Southern Hemisphere earlier than usual and before the start of influenza vaccination campaigns, the VE evaluation began 2 weeks after each country's annual national influenza vaccination campaign.[§] Participating countries used a Southern Hemisphere formulation of

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[†] https://www.paho.org/en/network-evaluation-vaccine-effectiveness-latin-america-and-caribbean-influenza-revelac-i

[§] Argentina: March 17; Brazil's Amazonas and Para states: March 11; other Brazil states: April 10; Chile: March 15; Paraguay: April 10; and Uruguay: April 18.

egg-based influenza vaccines; the egg-based trivalent formulation contained antigens from an A/Sydney/5/2021 (H1N1) pdm09-like virus, A/Darwin/9/2021 (H3N2)–like virus, and B/Austria/1359417/2021 (B/Victoria lineage)–like virus, with the egg-based quadrivalent formulation also containing B/Phuket/3073/2013 (B/Yamagata lineage)–like virus (*5*).

The evaluation population was restricted to SARI patients in three mutually exclusive target groups for vaccination based on national immunization policies. The criteria for each group varied slightly by country, but included 1) young children, 2) persons with preexisting conditions, and 3) older adults.[¶] Case-patients were defined as SARI patients with a positive RT-PCR influenza test result. Control patients were defined as SARI patients with negative RT-PCR test results for both influenza and SARS-CoV-2. Patient vaccination status was ascertained via linkage to national electronic immunization records using unique patient identifiers.

Patients who received ≥1 dose of the 2023 season influenza vaccine ≥14 days before symptom onset were considered vaccinated; those who did not receive any influenza vaccine during the 2023 season before symptom onset were considered unvaccinated. Patients vaccinated <14 days before symptom onset or who had positive SARS-CoV-2 RT-PCR test results were excluded from the evaluation to avoid the risk for confounding (*6*).

VE was estimated using mixed effects logistic models adjusting for age in years (fit as cubic spline), week of symptom onset (fit as cubic spline), and presence of at least one preexisting condition, and accounting for country as a random effect. Analyses were stratified by influenza type and subtype (when available) and presented when data were sufficient (at least five patients contributing to all strata) or when the 95% CI of the VE estimate was <140%. P-values <0.05 and 95% CIs that did not include zero were considered statistically significant. This activity was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.[**]

Results

During March 27–July 9, 2023, a total of 3,974 SARI hospitalizations among persons prioritized to receive influenza vaccination in Argentina, Brazil, Chile, Paraguay, and Uruguay were identified. Among these, 1,194 were excluded due to a positive SARS-CoV-2 test result (405), influenza test result missing (278), vaccinated <14 days before symptom onset (163), receipt of the 2022 influenza vaccine <120 days before 2023 vaccine availability (164), respiratory specimen collected >10 days after symptom onset (82), missing vaccine or demographic information (83), or a duplicated report (19). After these exclusions, 2,780 SARI patients remained in the final analytic sample for the three vaccination target groups, including 1,262 (45.4%) young children, 388 (14.0%) persons with preexisting conditions, and 1,130 (40.6%) older adults (Table 1). Overall, 88 (3.2%) SARI patients were from Argentina, 918 (33.0%) from Brazil, 1,158 (41.7%) from Chile, 167 (6.0%) from Paraguay, and 449 (16.1%) from Uruguay. Influenza viruses were detected among 900 (32.4%) SARI patients, including 815 (90.6%) influenza type A and 85 (9.4%) type B viruses, with a higher percentage of specimens testing positive during earlier surveillance weeks than during the average 2011–2019 circulation (Figure). Among 673 (82.6%) of the 815 influenza A viruses that were subtyped, 668 (99.3%) were A(H1N1)pdm09 and five (0.07%) were A(H3N2); all 85 B lineages were B/Victoria. Influenza detections varied by target group: nearly one half (547; 48.4%) were detected in older adults with SARI, approximately one third (139; 35.8%) in persons with preexisting conditions, and 214 (17.0%) in young children (p-value <0.001). Overall, 23.9% of SARI patients were vaccinated. Although this proportion did not vary by target group, significant differences in vaccination prevalence were observed among SARI patients by country, ranging from 9.4% in Uruguay to 37.0% in Chile.

Among SARI patients, 15.3% of case-patients had received a 2023 seasonal influenza vaccine, compared with 28.0% of control patients (Table 2). Overall adjusted VE against influenza-associated SARI hospitalization was 51.9%. VE among young children was 70.2%, and among older adults was 37.6% When limited to influenza A(H1N1)pdm09, which predominated during the 2023 Southern Hemisphere season, VE against SARI hospitalization was 55.2%, similar to overall estimates and consistent among target populations. Estimated VE for influenza B (Victoria) was not statistically significant (95% CI included zero) (Table 2), and insufficient numbers of vaccinated case-patients with influenza A(H3N2) precluded estimation of virus-specific VE.

As of August 15, 2023, a total of 1,031 influenza viruses had been genetically characterized by CDC, and the five countries' laboratories reported the isolates to the Global Initiative on Sharing All Influenza Data.[††] The majority of viruses were characterized as belonging to the same genetic clades as the 2023 Southern Hemisphere vaccine components: among

[¶] Young children were defined as the following age groups: Argentina = 6 months–2 years; Paraguay = 6 months–3 years; Chile and Uruguay = 6 months–5 years; and Brazil = 6 months–6 years. Older adults were defined as aged ≥ 60 years (Brazil and Paraguay) and aged ≥65 years (Argentina, Chile, and Uruguay). The preexisting conditions tracked by REVELAC–i are asthma, cancer, hypertension, diabetes, cardiovascular disease, respiratory disease (excluding asthma), obesity, and immunocompromise.

[**] 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://gisaid.org/

TABLE 1. Seasonal vaccination status and influenza test results and among hospitalized patients with severe acute respiratory illness, by selected characteristics — REVELAC–i Network, March–July 2023

Characteristic	SARI patients					
	Total, no.	Vaccinated* no. (row %)	p-value†	Influenza test result, no. (%)		p-value†
				Positive	Negative	
Overall	**2,780**	**664 (23.9)**	—	**900 (32.4)**	**1,880 (67.6)**	—
Country						
Argentina	88	24 (27.3)	<0.001	22 (25.0)	66 (75.0)	<0.001
Brazil	918	150 (16.3)		438 (47.7)	480 (52.3)	
Chile	1,158	428 (37.0)		301 (26.0)	857 (74.0)	
Paraguay	167	20 (12.0)		42 (25.1)	125 (74.9)	
Uruguay	449	42 (9.4)		97 (21.6)	352 (78.4)	
Target group§						
Young children	1,262	305 (24.2)	0.76	214 (17.0)	1,048 (83.0)	<0.001
Persons with preexisting conditions	388	87 (22.4)		139 (35.8)	249 (64.2)	
Older adults	1,130	272 (24.1)		547 (48.4)	583 (51.6)	
Preexisting conditions¶						
One or more condition	1,624	374 (23.0)	0.21	677 (41.7)	947 (58.3)	<0.001
No preexisting condition	1,156	290 (25.1)		223 (19.3)	993 (80.7)	
Sex						
Female	1,480	347 (23.4)	0.56	512 (34.6)	968 (65.4)	0.01
Male	1,300	317 (24.4)		388 (29.9)	912 (70.1)	
Influenza test result						
Negative	1,880	526 (28.0)	—	—	1,880 (100)	—
Positive (all)	900	138 (15.3)		900 (100)	—	
Influenza A	815	128 (15.7)		815 (100)	—	
Influenza A/H1N1	668	102 (15.3)		668 (100)	—	
Influenza A/H3N2	5	0 (—)		5 (100)	—	
Influenza B	85	10 (11.8)		85 (100)	—	

Abbreviations: RT-PCR = reverse transcription–polymerase chain reaction; SARI = severe acute respiratory infection.

* Patients who received ≥1 dose of the 2023 season influenza vaccine ≥14 days before symptom onset were considered vaccinated; patients who did not receive any influenza vaccine during the 2023 season by the time of symptom onset were considered unvaccinated. Patients vaccinated 0–14 days before symptom onset or with positive SARS-CoV-2 RT-PCR test results were excluded from the evaluation to avoid the risk of confounding.

† A Pearson's chi-square test was used to ascertain whether there were differences in the numbers of persons who were vaccinated and unvaccinated or who received positive and negative influenza test results.

§ Target groups are presented as mutually exclusive groups of persons considered at high risk for severe outcomes associated with influenza infection. Within countries, young children were defined as the following age groups: Argentina = 6 months–2 years; Paraguay = 6 months–3 years; Chile and Uruguay = 6 months–5 years; and Brazil = 6 months–6 years. Older adults were defined as aged ≥60 years (Brazil and Paraguay) and aged ≥65 years (Argentina, Chile, and Uruguay). The preexisting conditions tracked by REVELAC–i are asthma, cancer, hypertension, diabetes, cardiovascular disease, respiratory disease (excluding asthma), obesity, and immunocompromise.

¶ Number of all SARI patients with preexisting conditions, including young children and older adults.

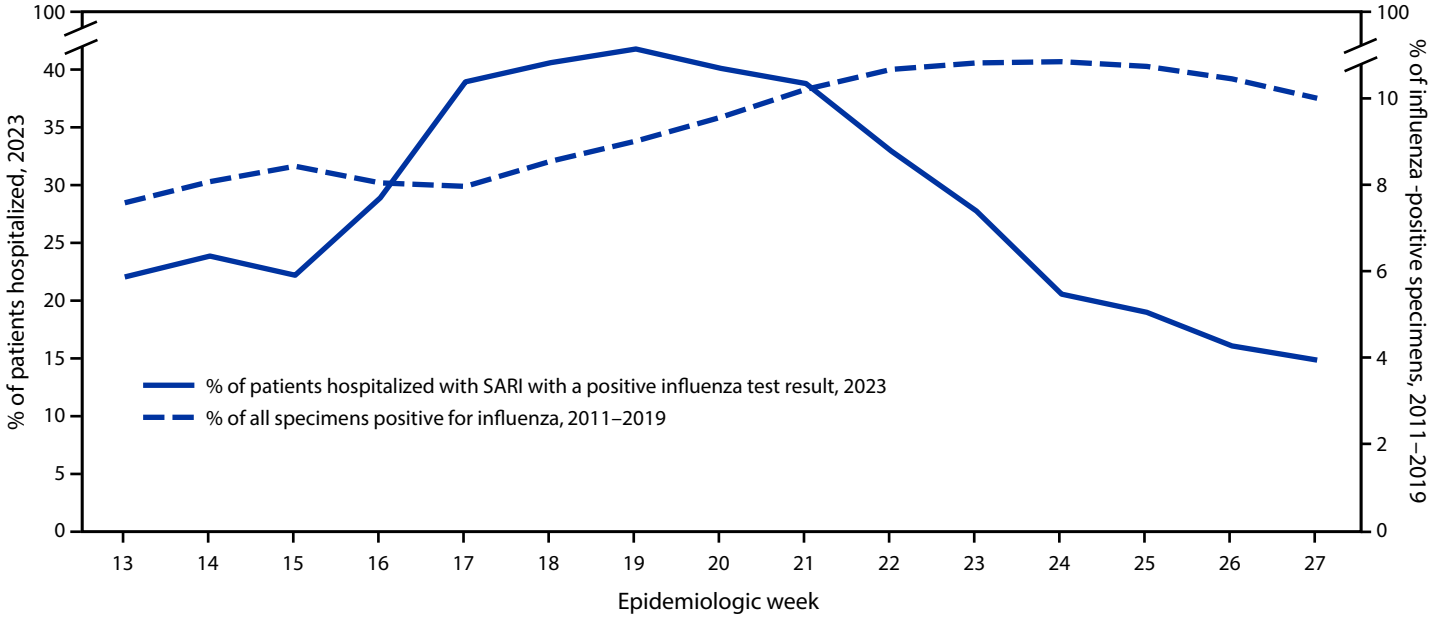
570 A(H1N1)pdm09 viruses, 309 (54.2%) belonged to subclade 5a.2a.1, 259 (45.4%) to subclade 5a.2a, and two (0.4%) to subclade 5a.1. Among six A(H3N2) viruses, three belonged to clade 3C.2a1b.2a.2 subclade 2a.1b and three to subclade 2b. All B/Victoria viruses belonged to subclade V1A.3a.2.

Discussion

This interim evaluation of the 2023 Southern Hemisphere influenza vaccine formulation was conducted using data from five Southern Hemisphere countries and suggests that the current season's trivalent and quadrivalent inactivated influenza vaccines are effective in reducing influenza-associated hospitalization. In particular, interim VE estimates indicate a significant reduction in hospitalization associated with the predominant influenza A(H1N1)pdm09 virus among young children and older adults. Vaccination is one of the most effective ways to prevent influenza and severe associated outcomes. Health authorities worldwide should encourage influenza vaccination for persons at increased risk for severe disease, including young children, persons with preexisting health conditions, and older adults, as well as those at increased risk for exposure to or transmission of influenza virus, such as health care personnel (*3*,*7*).

Despite the encouraging influenza VE, fewer than 30% of persons identified through REVELAC–i were vaccinated against influenza before their illness onset. The current findings were consistent with an interim report from Peru, where unadjusted VE against RT-PCR–confirmed influenza illness was 62%, but only one in five persons with medically attended respiratory illness had sought vaccination during 2023 (*8*), which is lower than the historical norm (*2*). Evaluations of influenza illness and vaccine knowledge, attitudes, and practices and deployment of World Health Organization (WHO) influenza post-introduction evaluations might help health

FIGURE. Percentage of patients hospitalized with severe acute respiratory infection with positive influenza virus test results,* by epidemiologic week, among 2011–2019 sentinel surveillance reports and hospitalized patients (N = 2,780) — REVELAC–i Network, Argentina, Brazil, Chile, Paraguay, and Uruguay, March–July 2023



Abbreviation: SARI = severe acute respiratory infection.
* By reverse transcription–polymerase chain reaction testing at national reference laboratories.

TABLE 2. Interim 2023 southern hemisphere seasonal influenza vaccine effectiveness against all influenza types A and B and against virus type A(H1N1)pdm09 — REVELAC–i Network, March–July 2023

Influenza type/Target group§	Influenza test-positive case-patients*		Influenza test-negative control patients		Vaccine effectiveness†	
	Total	Vaccinated no. (%)	Total	Vaccinated no. (%)	Unadjusted % (95% CI)	Adjusted† % (95% CI)
Influenza A and B						
Overall	900	138 (15.3)	1,880	526 (28.0)	53.3 (42.4 to 62.4)	51.9 (39.2 to 62.0)
Older adults	547	96 (17.6)	583	176 (30.2)	50.8 (34.1 to 63.3)	37.6 (13.1 to 55.2)
Children	214	19 (8.9)	1,048	286 (27.3)	74.0 (57.3 to 85.0)	70.2 (50.3 to 82.1)
Persons with preexisting conditions	139	23 (16.5)	249	64 (25.7)	42.7 (0.3 to 67.8)	38.0 (−10.8 to 65.3)
Influenza A/H1N1						
Overall	668	102 (15.3)	1,880	526 (28.0)	53.6 (41.2 to 63.6)	55.2 (41.8 to 65.5)
Older adults	422	70 (16.6)	583	176 (30.2)	54.0 (36.6 to 66.8)	42.7 (18.5 to 59.8)
Children	120	10 (8.3)	1,048	286 (27.3)	75.8 (52.9 to 88.9)	75.3 (52.1 to 87.3)
Persons with preexisting conditions	126	22 (17.5)	249	64 (25.7)	38.9 (−7.6 to 66.1)	43.0 (−6.7 to 69.5)
Influenza B						
Overall	85	10 (11.8)	1,880	526 (28.0)	65.7 (32.6 to 84.3)	46.2 (−7.9 to 73.2)

* Reverse transcription polymerase–chain reaction testing for influenza was conducted at national reference laboratories.
† Vaccine effectiveness was estimated using mixed effects logistic models adjusting for age in years (fit as cubic spline), week of onset of symptoms (fit as cubic spline), and presence of at least one preexisting condition and accounting for country as a random effect.
§ Within counties, young children were defined as the following age groups: Argentina = 6 months–2 years; Paraguay = 6 months–3 years; Chile and Uruguay = 6 months–5 years; and Brazil = 6 months–6 years. Older adults were defined as aged ≥60 years (Brazil and Paraguay) and aged ≥65 years (Argentina, Chile, and Uruguay).

authorities understand the reasons for reduced vaccination coverage since the COVID-19 pandemic and optimize influenza vaccination coverage in the future.[§§]

Although the timing and intensity of influenza epidemics in one hemisphere are not necessarily predictive of subsequent epidemics in the opposite hemisphere, this report might help health officials in Northern Hemisphere jurisdictions prepare for a potentially early influenza season and highlight the benefits of vaccination. In recent weeks, most influenza detections in the United States have identified A(H1N1) pdm09 and B/Victoria viruses (*9*). This is a similar pattern to that identified among the evaluated Southern Hemisphere

[§§] https://apps.who.int/iris/handle/10665/70436

Summary

What is already known about this topic?

Effectiveness of seasonal influenza vaccine varies by season and circulating virus type.

What is added by this report?

The 2023 Southern Hemisphere seasonal influenza vaccine reduced the risk for influenza-associated hospitalizations by 52%. Circulating influenza viruses were genetically similar to those targeted by the 2023–24 Northern Hemisphere influenza vaccine formulation. This vaccine might offer similar protection if these viruses predominate during the coming Northern Hemisphere influenza season.

What are the implications for public health practice?

Vaccination remains one of the most effective ways to protect against influenza-associated complications. In anticipation of Northern Hemisphere influenza virus circulation, CDC recommends that health authorities encourage U.S. health care providers to administer seasonal influenza vaccine to all eligible persons aged ≥6 months.

countries, providing an encouraging outlook for vaccine protection from current influenza A(H1N1)pdm09 and influenza B/Victoria, because the Northern Hemisphere vaccine formulation contains antigenically similar A/Victoria/4897/2022 (H1N1)pdm09–like virus for egg-based vaccines and A/Wisconsin/67/2022 (H1N1)pdm09–like virus for cell-based vaccines. Nevertheless, whether influenza A(H1N1)pdm09 will remain the predominant virus in the United States during the October 2023–May 2024 Northern Hemisphere influenza season is unclear.

In advance of the WHO Vaccine Composition Meeting in September 2023, these data suggest that the influenza A/Sydney/5/2021 (H1N1)pdm09–like and B/Austria/1359417/2021 (B/Victoria lineage) viruses in the Southern Hemisphere vaccine formulation confer protection against influenza hospitalization; however, for the A/Darwin/9/2021 (H3N2)–like virus, VE estimates from other countries in the Southern Hemisphere, such as South Africa, which has a more substantial influenza A(H3N2) cocirculation, will be needed (*10*). Influenza B/Yamagata lineage has not circulated globally since 2020, and ongoing monitoring will be needed to determine if B/Yamagata antigens should remain in future influenza vaccine formulations.

Limitations

The findings in this report are subject to at least five limitations. First, the VE estimates are preliminary and represent only a 3-month period with a smaller analytic sample, resulting in some VE estimates with wide CIs. Second, nearly 25% of the 1,194 otherwise eligible patients were missing RT-PCR results for influenza and were excluded from analysis. Although the REVELAC–i protocol indicates RT-PCR testing for all patients meeting SARI criteria, limited hospital resources for surveillance specimen collection during high-incidence periods might result in incomplete testing. Third, although statistical models accounted for important sources of confounding, the potential for unmeasured confounding associated with the likelihood of hospitalization or propensity for vaccination remains. Fourth, VE estimates from the Southern Hemisphere are important for supporting routine influenza vaccination programs, but these results might not be generalizable to other countries in the region with different vaccine target groups, timing of vaccination campaigns, or viral clade circulation. Finally, this analysis was unable to disaggregate previously unvaccinated children aged 6 months–9 years who received 2 doses of influenza vaccine from those receiving only 1 dose; thus, it is possible that influenza VE among young children restricted to those who received 2 doses of influenza vaccines would have been higher than VE among those with only a first, priming dose (*3*).

Implications for Public Health Practice

Preliminary REVELAC–i data from five Southern Hemisphere countries suggest that influenza vaccines were effective in preventing more than one half of influenza-associated hospitalizations among young children, persons with preexisting conditions, and older adults. The 2023–24 Northern Hemisphere influenza vaccine formulation contains antigenically similar A/Victoria/4897/2022 (H1N1)pdm09–like virus (egg-based vaccines) and A/Wisconsin/67/2022 (H1N1)pdm09–like virus (cell-based vaccines) and might offer similar protection against influenza A(H1N1)pdm09 if these viruses predominate during the 2023–24 Northern Hemisphere influenza season. Evaluating influenza VE through integrated regional networks such as REVELAC–i provides valuable information that can guide public health practice. CDC and WHO recommend that health officials should encourage all eligible persons aged ≥6 months to seek influenza vaccination in accordance with national recommendations and to take other measures, including avoiding close contact with persons who are ill, to protect against influenza and potentially severe associated outcomes (*3*,*7*). Persons in the Northern Hemisphere who are at increased risk for influenza-associated complications, including children aged <2 years; persons with asthma; obesity; neurologic or neurodevelopmental conditions; blood disorders; chronic lung conditions; or endocrine, kidney, liver, metabolic, or heart diseases; who have had a stroke; or have a weakened immune system are especially encouraged to receive an influenza vaccination by September or October (*7*).

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Notes from the Field:

Online Weight Loss Supplements Labeled as Tejocote (*Crataegus mexicana*) Root, Substituted with Yellow Oleander (*Cascabela thevetia*) — United States, 2022

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In the United States, dietary supplements are regulated by the Food and Drug Administration (FDA).* Regulations mandate that all ingredients used to manufacture dietary supplements be tested for identity and be free from reasonably anticipated contaminants. Despite these regulations, misbranded dietary supplements are frequently found to contain potentially dangerous substances (*1*). Tejocote (*Crataegus mexicana*) root, a supplement promoted online through social media for weight loss, is readily available from online retailers. Recent DNA fingerprinting of a product labeled as containing tejocote root under the brand name Alipotec determined that the product was 100% yellow oleander (*Cascabela thevetia*) (*2*). Yellow oleander contains the cardenolide thevetin B, which has the same clinical effects as other cardenolides, such as digoxin, and can be highly toxic.

Investigation and Outcomes

On September 8, 2022, an emergency physician called the New Jersey Poison Information and Education System (NJPIES) regarding a child aged 23 months who had consumed Eva Nutrition Mexican Tejocote Root and developed nausea and vomiting. The product was marketed as a weight loss supplement and purchased by the patient's mother. The patient was experiencing age-specific bradycardia (heart rate = 90 bpm; normal range = 98–135 bpm) and was hypotensive (blood pressure = 71/60 mm Hg). Electrocardiogram (ECG) results demonstrated sinus bradycardia, frequent premature ventricular complexes, and scooped ST segments consistent with cardenolide toxicity. At the direction of NJPIES, a serum digoxin assay was obtained with a reported level of 0.5 ng/L, which NJPIES interpreted as being attributable to cross-reactivity with a nondigoxin cardiac glycoside. After receiving treatment with 40 mg of digoxin-specific antibody fragments (FAB, a digoxin overdose antidote), the patient's ECG and blood pressure normalized. A repeat ECG 12 hours later again demonstrated evidence of cardenolide toxicity. The patient received a second dose of FAB, and the ECG results returned to normal.

Preliminary Conclusions and Actions

Because of the public health concerns of this likely mislabeled product, 10 products labeled as tejocote and marketed as weight loss supplements were purchased by NJPIES online during December 2022. Each product was listed on a separate page, although some carried the same or similar labels. Products were shipped directly to Flora Research Laboratories (Grants Pass, Oregon), which specializes in the analysis of chemical constituents found in dietary supplements. Using ultra-high pressure liquid chromatography–accurate mass-time of flight mass spectrometry analysis, researchers compared the purchased supplements with authenticated tejocote root procured and authenticated results with an ethnobotanist (Trish Flaster, Botanical Liaisons, personal communication, December 2022). Nine of 10 products labeled as tejocote were yellow oleander, with no evidence of tejocote root (Table).

These readily available dietary supplements, upon testing, appeared to be mislabeled. Instead, they contained a toxic substance of concern to both clinicians and public health officials. FDA recently released a consumer warning about toxic yellow oleander purported to be Nuez de la India in certain botanical weight loss products.† Clinicians need to be aware that persons with signs and symptoms of cardiac glycoside exposure might have been exposed to products labeled as tejocote, Nuez de la India, or other supplements marketed for weight loss and might benefit from treatment with a similar approach to that used in cases of nondigoxin cardiac glycoside exposures. Persons who are exposed to yellow oleander with evidence of toxicity might have a positive serum digoxin result on immune assays caused by cross-reactivity and might respond to FAB, as did the patient in this report. However, higher doses of FAB might be required for the reversal of yellow oleander toxicity than that typically used in cases of digoxin toxicity (*3*). Serum digoxin assays are not reliable for detection of thevetin B and cardiac glycosides other than digoxin. Laboratory-reported digoxin levels do not accurately reflect serum levels of other cardiac glycosides (*4,5*). For public health officials, this is concerning because these supplements contain a highly toxic substance and are readily available from multiple retailers. Future prevention efforts need to include reporting products such as these to FDA and alerting retailers who might be unknowingly selling these hazardous products. Clinicians will need to ask persons seeking care with evidence of cardiac glycoside toxicity about the use of weight loss supplements and consider FAB for treatment.

* https://www.ecfr.gov/current/title-21/chapter-I/subchapter-B/part-111

† https://www.fda.gov/food/alerts-advisories-safety-information/fda-expands-warning-consumers-about-toxic-yellow-oleander-purported-be-nuez-de-la-india-certain?utm_medium=email&utm_source=govdelivery

TABLE. Results of testing* for presence of yellow oleander and tejocote root in 10 products labeled as containing tejocote — United States, January–May 2023

Product description	Yellow oleander detection	Tejocote root detection
Alipotec tejocote root pieces	Positive	Negative
Alipotec tejocote root pieces	Positive	Negative
Alipotec tejocote root capsules	Positive	Negative
Elv Alipotec Mexican tejocote root pieces	Positive	Negative
Eva Nutrition Mexican tejocote root pieces	Positive	Negative
Eva Nutrition Mexican tejocote root pieces	Positive	Negative
Niwali tejocote Mexican root pieces	Positive	Negative
Science Alpha Mexican tejocote root pieces	Positive	Negative
Tejocote seed liquid drops	Negative	Negative
Tejocotex tejocote root pieces	Positive	Negative

* Ultra-high pressure liquid chromatography–accurate mass-time of flight mass spectrometry analysis.

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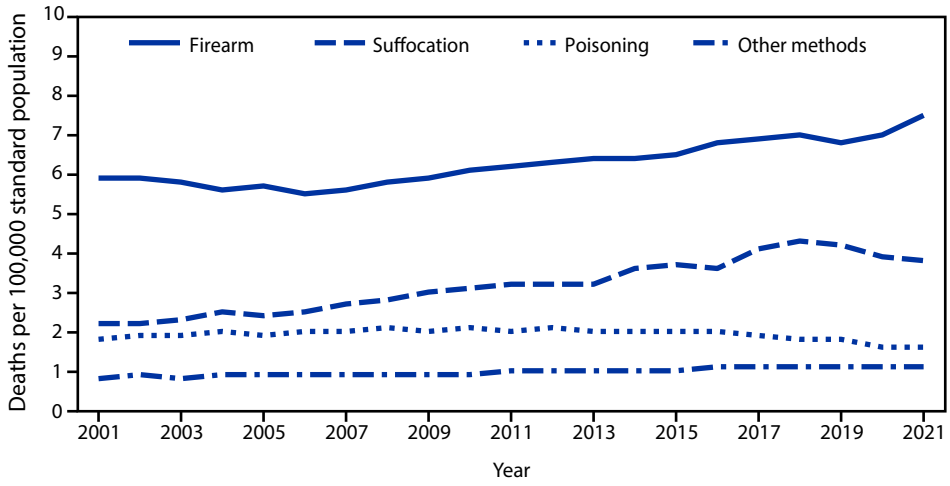
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Age-Adjusted Suicide Rates,* by Method of Suicide† — National Vital Statistics System, United States, 2001–2021



* Deaths per 100,000 population are age-adjusted to the 2000 U.S. standard population.
† Suicides were identified using *International Classification of Diseases, Tenth Revision* codes U03, X60–X84, and Y87.0. Specific methods of suicide were identified using underlying cause-of-death codes X72–X74 (firearm), X70 (suffocation), and X60–X69 (poisoning). Other methods include suicides involving means other than firearm, suffocation, or poisoning.

During 2001–2021, age-adjusted suicide rates involving firearms, suffocation, and other methods generally increased, and those involving poisoning decreased. Rates of firearm-related suicide were stable from 2001 (5.9 deaths per 100,000 population) to 2006 (5.5), and then increased through 2021 (7.5). Rates of suffocation-related suicide increased from 2.2 deaths in 2001 to 4.3 in 2018, and then decreased slightly through 2021 (3.8). After a period of increasing and then stable rates during 2001–2016, suicide rates attributed to poisoning decreased from 2.0 in 2016 to 1.6 in 2021. Firearm-related suicide had the highest rates during the period.

Source: National Center for Health Statistics, National Vital Statistics System, Mortality Data, 2001–2021. https://www.cdc.gov/nchs/nvss/deaths.htm

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For more information on this topic, CDC recommends the following link: https://www.cdc.gov/suicide

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