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Large Community Outbreak of Legionnaires Disease Potentially Associated with a Cooling Tower — Napa County, California, 2022

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Abstract

Legionnaires disease is a serious infection acquired by inhalation of water droplets from human-made building water systems that contain *Legionella* bacteria. On July 11 and 12, 2022, Napa County Public Health (NCPH) in California received reports of three positive urinary antigen tests for *Legionella pneumophila* serogroup 1 in the town of Napa. By July 21, six Legionnaires disease cases had been confirmed among Napa County residents, compared with a baseline of one or two cases per year. NCPH requested assistance from the California Department of Public Health (CDPH) and CDC to aid in the investigations. Close temporal and geospatial clustering permitted a focused environmental sampling strategy of high-risk facilities which, coupled with whole genome sequencing results from samples and investigation of water system maintenance, facilitated potential linking of the outbreak with an environmental source. NCPH, with technical support from CDC and CDPH, instructed and monitored remediation practices for all environmental locations that tested positive for *Legionella.* The investigation response to this community outbreak illustrates the importance of interdisciplinary collaboration by public health agencies, laboratory support, timely communication with the public, and cooperation of managers of potentially implicated water systems. Timely identification of possible sources, sampling, and remediation of any facility testing positive for *Legionella* is crucial to interrupting further transmission.

Investigation and Results

Epidemiologic Investigation

Napa County Public Health (NCPH) defined a confirmed case as the diagnosis of Legionnaires disease based on the results of a urinary antigen test (UAT), polymerase chain reaction (PCR) test, or culture received by a person who lived, worked, or spent time in downtown Napa, with illness onset during or after June 2022. A suspected case was defined as community-acquired pneumonia of unknown origin identified among three categories of persons: 1) a hospitalized patient; 2) a resident of, worker in, or visitor to downtown Napa; or 3) a patient who did not receive testing for *Legionella* spp. during hospitalization.

During July 11–August 15, 2022, NCPH identified 17 Legionnaires disease cases, including 14 confirmed and three suspected cases (Table 1). Among these 17 cases, 16 persons were hospitalized, 10 were admitted to an intensive care

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unit, and five required intubation and mechanical ventilation; one patient died. Comorbidities included smoking, diabetes, hypertension, lung disease, and heart disease. Two patients were coinfected with SARS-CoV-2, the virus that causes COVID-19. The longest hospital stay was 36 days. All confirmed cases were diagnosed by UAT results. Lower respiratory tract specimens were collected from four patients with confirmed Legionnaires disease; *L. pneumophila* serogroup 1 was detected by PCR in two clinical specimens, one of which yielded an isolate, which is necessary for whole genome sequencing. Interviews with patients or their proxies revealed that 14 patients lived in downtown Napa, two visited downtown Napa, and one worked in downtown Napa.

Environmental Health Investigation

The search for potential environmental sources began with the delimitation of a high-risk zone, which was defined as the area within a 1.0-mile (1.6-km) radius from the center of a circle drawn around the cluster of patients' residences plotted on a point density heat map generated using ArcGIS Pro (version 3.0; Esri) (Figure). Aerial imagery, onsite visual inspections, and calls to businesses and cooling tower maintenance companies identified and confirmed the locations and uses of cooling towers.* Environmental sampling locations were selected on the basis of patient interviews, and a risk score analysis was derived from the geographic proximity of facilities with cooling towers and other aerosolizing devices to the patients' residences. A total of seven facilities with nine potential exposure sources (seven cooling towers, one decorative fountain, and one produce mister) were mapped within the high-risk zone (Figure) (Table 2). Cooling towers located at facilities A and B were the highest scoring devices in the risk score analysis.

Visual inspection, review of records, and sampling of devices within the high-risk zone revealed a lack of maintenance at most cooling towers. Many had low or no detectable chlorine at the time of sampling, because of lack of routine biocide application, improper distribution methods, or other problems with the system.† Facility A's cooling tower had a clog in the pipe leading to the chemical feed system that impeded the controller's ability to detect water flow, resulting in low or no injection of biocide into the tower. According to maintenance records, the clog was detected in early July, at approximately the same time that many case exposures occurred and was resolved in early August.

Public health investigators collected environmental samples from 11 potential sources. Seven samples tested positive for

* A cooling tower is a centralized heat-rejection system for buildings or industrial processes that uses water and fans to remove heat from the air.

† A typical cooling tower has an automated chemical feed system to inject water treatment chemicals. This system has two primary components: a pump that injects the chemicals (including biocides) and a controller that tells the system when and at what speed and volume to inject the chemicals.

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TABLE 1. Selected characteristics of patients with confirmed* and suspected† Legionnaires disease — Napa County, California, 2022

Characteristic	Legionnaires disease cases, no. (%)	
	Confirmed, n = 14*	Suspected, n = 3†
Age, yrs, mean (range)	62.6 (47–83)	62.7 (—§)
Age, yrs, median	64	—§
Male sex	12 (86)	1 (33)
Hospitalized (% of total cases)	**13 (93)**	**3 (100)**
ICU admission	10 (71)	0 (—)
Intubated	5 (36)	0 (—)
Residence zone		
High-risk¶	11 (79)	3 (100)
Low-risk**	3 (21)	0 (—)
Total living in or with visits to high-risk zone	14 (100)	3 (100)
Hospital length of stay, days, mean (range)	10.4 (2–36)	5.7 (3–9)
Days from onset to diagnosis, days, mean (range)	8.8 (4–13)	NA
Comorbidities		
Coronary heart disease	5 (36)	0 (—)
SARS-CoV-2 coinfection	2 (14)	0 (—)
Current or former smoker	11 (79)	2 (67)
Diabetes	4 (29)	0 (—)
Hypertension	5 (36)	1 (33)
Lung disease	6 (43)	0 (—)

Abbreviations: ICU = intensive care unit; NA = not applicable.

* Legionnaires disease was confirmed among 14 patients based on the results of a urinary antigen test, polymerase chain reaction test, or culture received by those who lived, worked, or spent time in downtown Napa, with illness onset during or after June 2022.

† Community-acquired pneumonia of unknown origin was identified among three categories of persons: 1) a hospitalized patient; 2) a resident of, worker in, or visitor to downtown Napa; or 3) a patient who did not receive testing for *Legionella* spp. during hospitalization.

§ Data suppressed for patient privacy.

¶ The area within a 1.0-mile (1.6-km) radius from the center of a circle surrounding the patients' residences plotted on a point density heat map generated using ArcGIS Pro (version 3.0; Esri).

** Areas not within the high-risk zone.

Legionella (six for *L. pneumophila* only and one for both *L. pneumophila* and *Legionella anisa*); all positive samples were collected within the high-risk zone.

Laboratory Investigation

L. pneumophila culture–positive clinical and environmental specimens underwent sequence-based typing at CDC and whole genome sequencing followed by single-nucleotide polymorphism (SNP) analysis at the California Department of Public Health (CDPH). Sequence-based typing generates an allelic profile based on the combination of allele numbers at seven loci (*1*). Each unique allelic profile corresponds to a sequence type (ST). Nested sequence-based typing, a culture-independent variation of sequence-based typing, was performed on the PCR-positive clinical specimen from which no isolate was recovered. In SNP analysis, whole genome sequencing data generated from isolates are aligned to a reference genome, and the variation from the reference is used to infer relatedness among isolates, visualized in a phylogenetic tree. A smaller number of SNP differences indicates closer relatedness (*2*).

The identified *L. pneumophila* STs from environmental samples included ST1, ST10, ST35, and ST296 (Table 2). ST35 was detected in the clinical isolate via sequence-based typing. Nested sequence-based typing performed on the PCR-positive, culture-negative clinical specimen also detected ST35. The only environmental sample that yielded ST35 was collected from the facility A cooling tower. No SNP differences between the clinical isolate and the facility A cooling tower isolate were identified, indicating that they were highly related, whereas other environmental isolates were genetically distant from facility A's cooling tower isolate (Supplementary Figure, https://stacks.cdc.gov/view/cdc/136165). This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.§

Public Health Response

A coordinated public communication strategy was implemented. An outbreak alert was sent to local health care providers, requesting *Legionella* testing for hospitalized patients with community-acquired pneumonia or those failing outpatient treatments. CDPH notified other local health departments, and a public press release encouraged persons with symptoms consistent with Legionnaires disease to seek care. A public-facing webpage with information about the outbreak was created on the Napa County website.¶

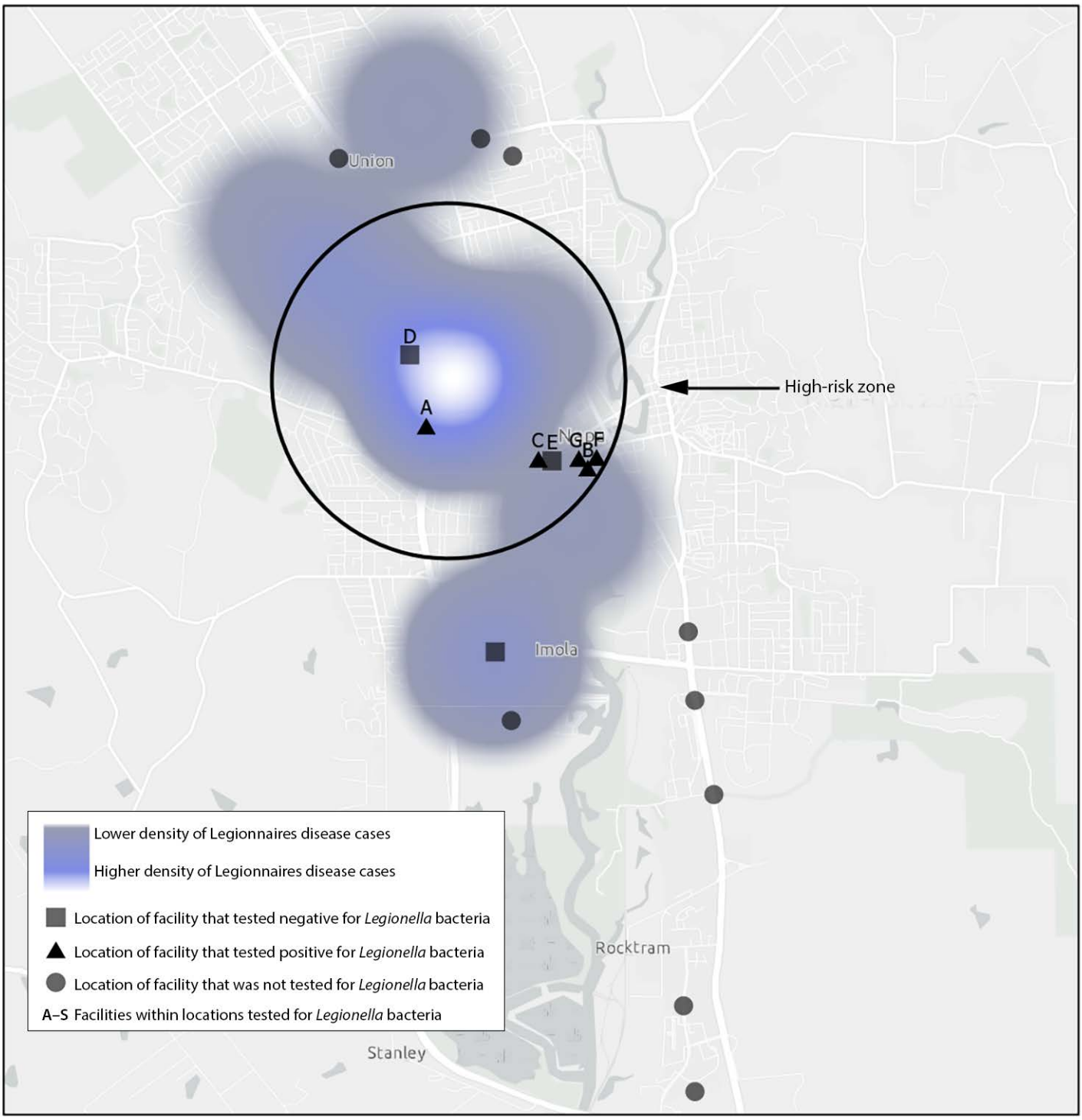
The heat map and high-risk zone definition served as the basis for prioritizing environmental testing resources to devices most likely to have generated aerosols to which patients in this cluster were exposed. Facilities where *Legionella* was detected were notified to immediately begin remediation of their cooling towers.** One facility that did not respond to oral and written communications received a legal order to shut down its cooling tower until remediation was completed. NCPH tracked remediation efforts and, when available, inspected remediation logs and maintenance records. The last Legionnaires disease case was detected on August 15, by which time most facilities had initiated or completed remediation. Facilities with cooling towers outside the high-risk zone were informed of the outbreak and best practices for cooling tower maintenance.

§ 45 C.F.R. part 46 102(1)(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.countyofnapa.org/3370/Legionnaires-Disease

** Cleaning and disinfection procedures for cooling towers associated with an outbreak are available in the cooling tower module of the CDC *Legionella* Control Toolkit. https://www.cdc.gov/legionella/wmp/control-toolkit/cooling-towers.html

FIGURE. Point density heat map of residences of patients with Legionnaires disease — Napa County, California, 2022*



Sources: County of Napa; California State Parks; Esri; HERE technologies; Garmin International; SafeGraph; GeoTechnologies, Inc.; Ministry of Economy, Trade, and Industry of Japan/National Aeronautics and Space Administration; United States Geological Survey; Bureau of Land Management; Environmental Protection Agency; National Park Service; United States Department of Agriculture.

* The high-risk zone is defined as the area within a 1.0-mile (1.6-km) radius from the center of a circle surrounding the patients' residences plotted on a point density heat map generated using ArcGIS Pro (version 3.0; Esri).

TABLE 2. Potential *Legionella* sources within and outside the high-risk zone* with respect to the type of device, culture or polymerase chain reaction test results, and sequence types identified — Napa County, California, 2022

Facility	Type of device	Within high-risk zone	Sampled by public health authorities	Detection by culture or PCR	Sequence-based typing result
A	Cooling tower	Yes	Yes	*L. pneumophila*	ST35
A	Decorative fountain	Yes	Yes	*L. pneumophila*	ST1
B	Cooling tower	Yes	Yes	*L. pneumophila*	ST1
C	Cooling tower	Yes	Yes	*L. pneumophila* and *L. anisa*†	NA
D	Produce mister	Yes	Yes	No *Legionella* detected	NA
E	Cooling tower	Yes	Yes	No *Legionella* detected	NA
F	Cooling tower 1	Yes	Yes	*L. pneumophila*	ST296
F	Cooling tower 2	Yes	Yes	*L. pneumophila*	ST296
G	Cooling tower	Yes	Yes	*L. pneumophila*	ST10
H	Hot tub	No	Yes	No *Legionella* detected	NA
H	Decorative fountain	No	Yes	No *Legionella* detected	NA
I	Multiple cooling towers	No	No	No *Legionella* detected§	NA
J	Cooling tower	No	No	NA	NA
K	Cooling tower	No	No	NA	NA
L	Multiple cooling towers	No	No	No *Legionella* detected§	NA
M–S	Cooling towers	No	No	NA	NA

Abbreviations: NA = not applicable; PCR = polymerase chain reaction; ST = sequence type.
* The area within a 1.0-mile (1.6-km) radius radius from the center of a circle surrounding the patients' residences plotted on a point density heat map generated using ArcGIS Pro (version 3.0; Esri).
† CDC's Pneumonia Response and Surveillance Laboratory detected *Legionella anisa*, whereas testing at an independent private laboratory arranged by the facility shortly after sampling by public health authorities detected *L. pneumophila*.
§ Self-tested: facility voluntarily collected environmental samples and arranged testing for *Legionella* at a commercial laboratory.

Discussion

Similarities between symptoms of COVID-19 and Legionnaires disease pose challenges to investigating community clusters of Legionnaires disease, including a risk for delayed care, resulting in worse outcomes if symptoms are presumed to be caused by COVID-19. In this investigation, patient interviews and risk score analysis narrowed the environmental investigation to a few devices in downtown Napa as potential sources of the outbreak. The period between identification of the clog that impeded adequate biocide delivery at facility A's cooling tower and its remediation approximately coincided with the onset of Legionnaires disease cases. Identification of ST35 in two patient specimens and identical SNP results between the clinical and cooling tower isolates further support a potential causal link between facility A and the outbreak. This report is the first to identify ST35 in a California Legionnaires disease outbreak; previous ST35 outbreaks were identified in Mississippi, Nevada, and the U.S. Virgin Islands. ST35 strains might possess enhanced ability to cause disease and might be resistant to standard remediation efforts, resulting in reappearance after disinfection (*3*).

Despite robust surveillance, no cases were detected among occupants of facility A. Studies show that cooling towers can spread *Legionella* over a wide geographic area, with highest attack rates among persons living within 0.6 miles (1.0 km) of the tower (*4*,*5*). This investigation further highlights the risks cooling towers can pose for susceptible persons in surrounding neighborhoods. Cooling towers without a comprehensive water management program or lacking routine maintenance are associated with an increased risk for *Legionella* colonization (*6*,*7*). Even after an outbreak, building owners and managers might not always follow best water management practices (*8*). A close relationship between public health sectors and local businesses, along with guidance on recommended operation and maintenance of water systems, can help prevent further outbreaks.

Public Health Practice

A coordinated public health response was critical to the investigation of and response to this outbreak. Support from CDC and state health departments during Legionnaires disease outbreak investigations provide *Legionella*-specific subject matter expertise and laboratory capacity for environmental testing for local health jurisdictions lacking these resources. Furthermore, restricting the search area and maintaining active communication with local businesses facilitate investigation and response activities. Finally, molecular analyses of clinical specimens and environmental samples, including culture-independent techniques such as nested sequence-based typing, are powerful resources in the investigation of Legionnaires disease outbreaks. Timely identification of possible sources, sampling, and remediation of any facility testing positive for *Legionella* are crucial to interrupting further transmission. Facilities should comply with best practices for cooling tower maintenance such as having a water management program that includes routine maintenance and water quality parameters surveillance (*7*).

Summary

What is already known about this topic?

Legionnaires disease is a serious pneumonia caused by *Legionella* bacteria. Molecular analysis that compares clinical and environmental *L. pneumophila* isolates allows for identification of associations among possible sources of disease.

What is added by this report?

In a large Legionnaires disease outbreak in California in July 2022, sequence-based typing, in tandem with nucleotide polymorphism analysis linked one *Legionella* sequence type to a cooling tower and two cases. Mapping facilitated targeted sampling and remediation.

What are the implications for public health practice?

Timely source identification and remediation effectively halt disease spread. Prompt collection of respiratory specimens, paired with targeted environmental sampling, facilitates comparison with environmental samples for source attribution; culture-independent typing methods are useful when isolates are not recovered from clinical specimens.

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Progress in Immunization Safety Monitoring — Worldwide, 2020–2022

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Abstract

Effective surveillance of adverse events following immunization (AEFIs) primarily relies on the collaboration of two partners: national regulatory authorities (NRAs) and national expanded programs on immunization (EPIs). In December 2020, the World Health Organization (WHO) Global Advisory Committee for Vaccine Safety recommended a new case-based indicator of national capacity to monitor immunization safety: at least one serious AEFI reported per 1 million total population per year. To achieve this indicator, WHO-affiliated countries and territories (WHO countries) rely upon data generated from functional AEFI surveillance systems. This report describes 2020–2022 global, regional, and national progress in use of the newly introduced immunization safety monitoring indicator and progress on joint AEFI reporting from national EPIs and NRAs. Among WHO countries, 51 (24%) of 214 implemented the new indicator in 2020, 111 (52%) of 214 implemented it in 2021, and 92 (43%) of 215 in 2022. In 2020, 41 (19%) WHO countries reported AEFI data jointly from EPIs and NRAs; this increased to 55 (26%) in 2021 and 57 (27%) in 2022. These findings, resulting in part from the intensified support for COVID-19 vaccination, demonstrate that national AEFI surveillance systems increasingly support the timely use and sharing of case-based immunization safety data, but work is still needed to strengthen global vaccine safety monitoring.

Introduction

Robust postauthorization and postlicensure immunization safety monitoring systems help ensure that the benefits of vaccination continue to outweigh the risks. During the previous decade, global progress was made in achieving at least minimum functionality of immunization safety monitoring through the establishment of national immunization safety surveillance systems. In December 2014, the World Health Organization (WHO) established the first indicator of minimal national vaccine safety surveillance as aggregate reporting of more than 10 adverse events following immunization (AEFIs) per 100,000 surviving infants (*1*). In 2019, this indicator was achieved by 121 (57%) of 214 WHO-affiliated countries and territories (WHO countries).* The WHO Vaccine Safety Blueprint 2.0 highlighted the need for more comprehensive indicators for national, regional, and global safety surveillance systems (*2*,*3*). Subsequently, in December 2020, WHO's Global Advisory Committee for Vaccine Safety recommended the adoption of a new case-based indicator for monitoring progress in AEFI surveillance for all age groups: the number of serious† AEFIs reported per 1 million total national or subnational population in a year (*4*,*5*). This case-based reporting indicator was proposed to facilitate accurate AEFI reporting and increase national system sensitivity in detecting vaccine safety signals.§

In many WHO countries, effective AEFI surveillance relies on the collaboration of two national partners: 1) national regulatory authorities (NRAs), which are national organizations responsible for ensuring that pharmaceuticals and biologics are properly evaluated and that they meet international standards of quality, safety, and efficiency,¶ and 2) national expanded programs on immunization (EPIs). EPIs typically oversee national procurement, storage, and delivery of vaccines, including the staffing and training of health care workers responsible for administering vaccines and caring for patients reporting AEFIs. As a result, EPIs play an important role in identifying and reporting AEFIs. NRAs are mandated to perform postauthorization and postlicensure AEFI surveillance and must work in tandem with EPIs to support health care–worker training and management of AEFI reports and investigations, including support for independent assessments of causality for serious AEFIs. Coordination of AEFI reporting among EPIs and NRAs improves data quality, completeness, and usability, so that safety signals can be detected and identified quickly (*6*,*7*). This article updates a previous report (*6*), introduces WHO's new indicator for vaccine safety monitoring, and describes progress with national-level coordination and cooperation among two national partners in AEFI reporting.

* WHO-affiliated countries (194) and states and territories (21).

† Seriousness is based on patient or event outcome or action criteria and defines regulatory reporting obligations. An AEFI is considered serious if it results in death, is life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or substantial disability or incapacity, or is a congenital anomaly or birth defect. Other situations could also be considered serious after the application of medical and scientific judgment. The application of the criteria is dependent on its interpretation and health practices in a particular setting.

§ A vaccine safety signal is information that indicates a potential link between a vaccine and an event previously unknown or incompletely documented that might affect health.

¶ https://www.who.int/southeastasia/activities/national-regulatory-agencies#:~:text

Methods

WHO countries meeting the newly recommended global immunization safety monitoring indicator were identified using national AEFI data reported to VigiBase, WHO's global pharmacovigilance database for individual case reports of suspected adverse reactions to medicinal products, including vaccines (*8*). AEFI reports in VigiBase were classified as serious based on information with AEFI reporting forms and associated case investigation forms used by WHO countries.

Coordination of AEFI reporting among national EPI and NRA programs was measured annually based on response to the following question in the WHO and UNICEF electronic Joint Reporting Form, a questionnaire for the passive joint collection of aggregate AEFI data: "What is the source of data for the total number of serious adverse events reported?" Possible responses included "EPI only," "NRA only," "both EPI and NRA," or "other" (*9*,*10*).

National reporting to VigiBase and the Joint Reporting Form is voluntary and varies by year. WHO countries not reporting to these systems during the reporting period (2020–2022) were considered as not meeting the requirements for either the newly recommended indicator or coordination of EPI and NRA AEFI reporting; however, these countries were included in the denominator when calculating percentages. Geographic areas are reported by WHO country (214 in 2020 and 2021; 215 in 2022)** and WHO region: African Region (AFR),†† Region of the Americas (AMR),§§ Eastern Mediterranean Region (EMR),¶¶ European Region (EUR),*** South-East Asia Region (SEAR),††† and Western Pacific Region (WPR).§§§ This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.¶¶¶

Results

Indicator Data Reporting

During 2020, 2021, and 2022, a total of 51 (24%) of 214, 111 (52%) of 214, and 92 (43%) of 215 WHO countries, respectively, achieved the new safety monitoring indicator (i.e., number of serious AEFIs reported per 1 million total national or subnational population in a year). During these same years, 79 (37%), 135 (63%), and 118 (55%) WHO countries, respectively, reported any serious AEFI data to VigiBase (Figure 1) (Supplementary Figure 1, https://stacks.cdc.gov/view/cdc/135986). In 2022, the region with the highest proportion of WHO countries meeting the new indicator was EUR (76%), followed by AFR (47%), AMR (32%), EMR (27%), and WPR (22%); the region with the lowest proportion was SEAR (9%). The largest increase in the number and percentage of WHO countries meeting the new indicator occurred in AFR, where the number of WHO countries meeting the indicator increased more than eightfold, from three (6%) in 2020, to 28 (60%) in 2021, but subsequently declined 21%, to 22 (47%) in 2022. Whereas all WHO regions except SEAR observed an overall increase in the number and percentage of WHO countries achieving the new indicator from 2020 to 2022, a decrease was observed in every region from 2021 to 2022 (Table).

Sources of Indicator Data

In 2022, 169 (79%) of 215 WHO countries reported the source of national AEFI data; the primary data source was EPI for 63 (29%) countries, NRA for 33 (15%), and both EPI and NRA for 57 (27%) (Figure 2) (Supplementary Figure 2, https://stacks.cdc.gov/view/cdc/135987). Seventeen (8%) WHO countries **** reported other independent sources for national AEFI data (e.g., the Vaccine Adverse Event Reporting

** In 2022, Pitcairn Islands was added as a WHO territory in WPR, increasing the total number of WHO countries from 214 to 215, and in WPR from 36 to 37.

†† WHO countries in AFR (47): Algeria, Angola, Benin, Botswana, Burkina Faso, Burundi, Cabo Verde, Cameroon, Central African Republic, Chad, Comoros, Côte d'Ivoire, Democratic Republic of the Congo, Equatorial Guinea, Eritrea, Eswatini, Ethiopia, Gabon, The Gambia, Ghana, Guinea, Guinea-Bissau, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mauritania, Mauritius, Mozambique, Namibia, Niger, Nigeria, Republic of the Congo, Rwanda, Sao Tome and Principe, Senegal, Seychelles, Sierra Leone, South Africa, South Sudan, Togo, Uganda, Tanzania, Zambia, and Zimbabwe.

§§ WHO countries in AMR (35): Antigua and Barbuda, Argentina, Bahamas, Barbados, Belize, Bolivia, Brazil, Canada, Chile, Colombia, Costa Rica, Cuba, Dominica, Dominican Republic, Ecuador, El Salvador, Grenada, Guatemala, Guyana, Haiti, Honduras, Jamaica, Mexico, Nicaragua, Panama, Paraguay, Peru, Saint Kitts and Nevis, Saint Lucia, Saint Vincent and the Grenadines, Suriname, Trinidad and Tobago, United States, Uruguay, and Venezuela. WHO territories in AMR (nine): Anguilla, Aruba, Bermuda, British Virgin Islands, Cayman Islands, Curaçao, Montserrat, Sint Maarten, and Turks and Caicos Islands.

¶¶ WHO countries in EMR (21): Afghanistan, Bahrain, Djibouti, Egypt, Iran, Iraq, Jordan, Kuwait, Lebanon, Libya, Morocco, Oman, Pakistan, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, United Arab Emirates, and Yemen. WHO territories in EMR (one): occupied Palestinian territory, including east Jerusalem.

*** WHO countries in EUR (53): Albania, Andorra, Armenia, Austria, Azerbaijan, Belarus, Belgium, Bosnia and Herzegovina, Bulgaria, Croatia, Cyprus, Czechia, Denmark, Estonia, Finland, France, Georgia, Germany, Greece, Hungary, Iceland, Ireland, Israel, Italy, Kazakhstan, Kyrgyzstan, Latvia, Lithuania, Luxembourg, Malta, Monaco, Montenegro, Netherlands, North Macedonia, Norway, Poland, Portugal, Moldova, Romania, Russia, San Marino, Serbia, Slovakia, Slovenia, Spain, Sweden, Switzerland, Tajikistan, Turkey, Turkmenistan, Ukraine, United Kingdom, and Uzbekistan. WHO territories in EUR (one): Kosovo.

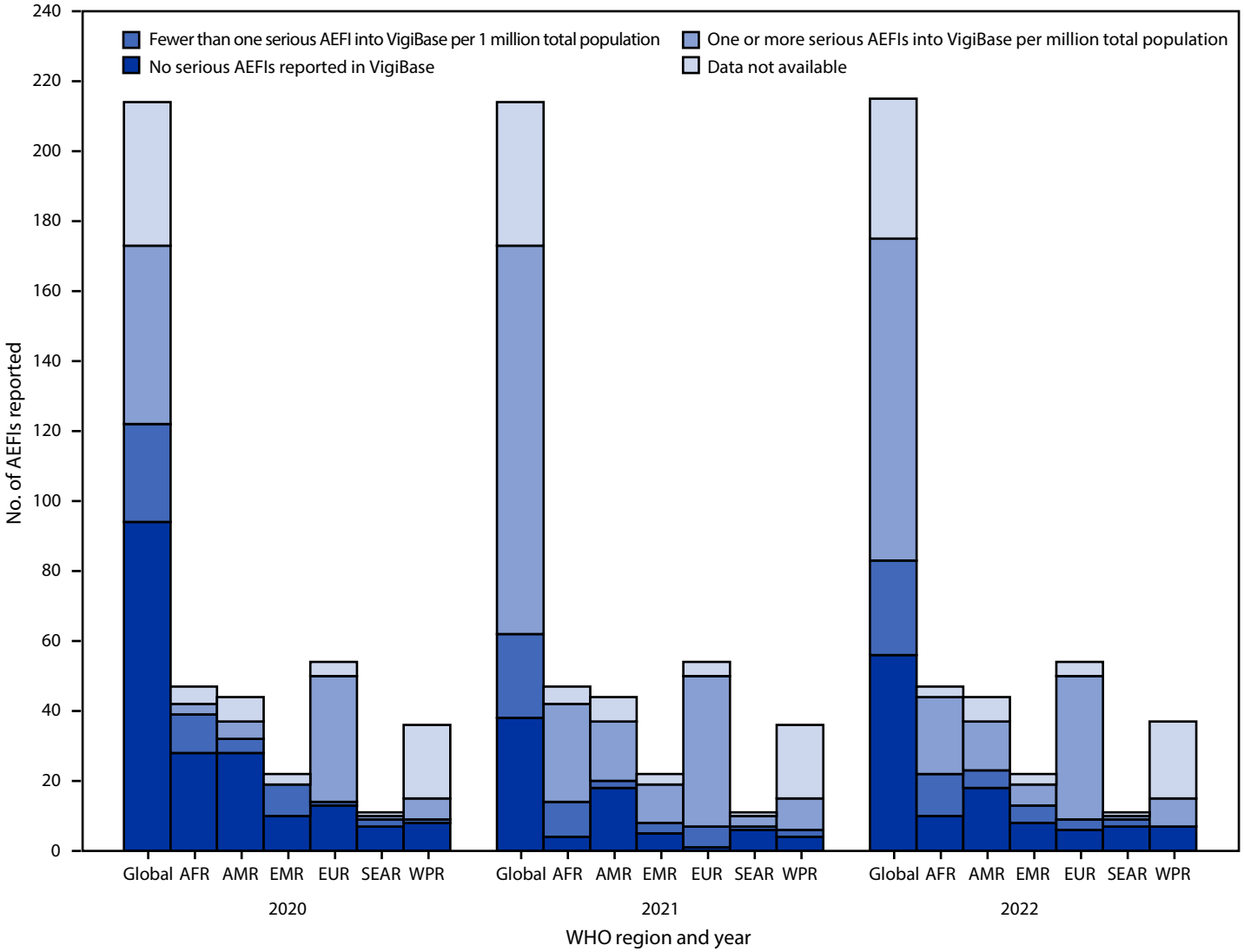
††† WHO countries in SEAR (11): Bangladesh, Bhutan, Burma, India, Indonesia, Maldives, Nepal, North Korea, Sri Lanka, Thailand, and Timor-Leste.

§§§ WHO countries in WPR (27): Australia, Brunei, Cambodia, China, Cook Islands, Federated States of Micronesia, Fiji, Japan, Kiribati, Laos, Malaysia, Marshall Islands, Mongolia, Nauru, New Zealand, Niue, Palau, Papua New Guinea, Philippines, South Korea, Samoa, Singapore, Solomon Islands, Tonga, Tuvalu, Vanuatu, and Vietnam. WHO territories in WPR (10): American Samoa, Hong Kong, Macau, French Polynesia, Guam, New Caledonia, Northern Mariana Islands, Pitcairn Islands, Tokelau, and Wallis and Futuna.

¶¶¶ 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.

**** Belarus, Canada, Democratic Republic of the Congo, Guatemala, Haiti, Indonesia, Japan, Monaco, Morocco, Peru, Philippines, Russia, San Marino, Slovakia, Somalia, Timor-Leste, and the United States.

FIGURE 1. World Health Organization–affiliated countries and territories reporting serious adverse events following immunization into VigiBase,* by World Health Organization region — worldwide, 2020–2022



Abbreviations: AEFIs = adverse events following immunization; AFR = African Region; AMR = Region of the Americas; EMR = Eastern Mediterranean Region; EUR = European Region; SEAR = South-East Asia Region; WHO = World Health Organization; WPR = Western Pacific Region.

* VigiBase is WHO's global pharmacovigilance database for individual case reports of suspected adverse reactions to medicinal products, including vaccines. https://www.who-umc.org/vigibase/

System in the United States) in 2022. During the reporting period, among six WHO regions, the percentage of countries reporting both EPI and NRA as the primary source of national AEFI data increased in four (AFR, EMR, EUR, and SEAR), decreased in AMR, and remained unchanged in WPR.

Discussion

Compared with 2020, most WHO regions made progress toward achieving the two immunization safety monitoring measures in 2021 and 2022, by attaining the Global Advisory Committee for Vaccine Safety's indicator of reporting at least one serious AEFI per 1 million total population per year, and by jointly reporting AEFI data from EPIs and NRAs. Progress has been particularly notable in AFR and EMR, where WHO has continued to support vaccine safety training and the development of standardized data collection tools and national AEFI surveillance system guidelines. Despite this progress, however, all WHO regions continue to report low percentages of countries jointly reporting EPI and NRA AEFI data; although EMR achieved the highest regional percentage of WHO countries jointly reporting EPI and NRA AEFI data, only 50% of countries in the EMR reported both. Fewer than one half, 92 (43%) of 215 WHO countries are currently meeting the target for the new safety monitoring indicator, and only in EUR are more than one half of countries reporting, demonstrating that additional work is needed to strengthen global vaccine safety monitoring.

TABLE. World Health Organization–affiliated countries and territories* reporting at least one serious adverse event following immunization per 1 million total population into VigiBase,† by World Health Organization region — worldwide, 2020–2022

WHO region	No. of WHO-affiliated countries	Yr, no. (%)		
		2020	2021	2022
AFR	47	3 (6.4)	28 (59.6)	22 (46.8)
AMR	44	5 (11.4)	17 (38.6)	14 (31.8)
EMR	22	0 (—)	11 (50.0)	6 (27.3)
EUR	54	36 (66.7)	43 (79.6)	41 (75.9)
SEAR	11	1 (9.1)	3 (27.3)	1 (9.1)
WPR	36 (2020–2021) 37 (2022)§	6 (16.7)	9 (25.0)	8 (22.2)
All regions	**214 (2020–2021) 215 (2022)**	**51 (23.8)**	**111 (51.9)**	**92 (42.8)**

Abbreviations: AFR = African Region; AMR = Region of the Americas; EMR = Eastern Mediterranean Region; EUR = European Region; SEAR = South-East Asia Region; WHO = World Health Organization; WPR = Western Pacific Region.

* Members of WHO are grouped according to regional distribution (194 countries and 21 territories). All countries that are members of the United Nations can become members of WHO by accepting its constitution. Other countries can be admitted as members when their application has been approved by a simple majority vote of the World Health Assembly. Territories that are not responsible for the conduct of their international relations can be admitted as associate members upon application made on their behalf by the WHO member or other authority responsible for their international relations.

† VigiBase is WHO's global pharmacovigilance database for individual case reports of suspected adverse reactions to medicinal products, including vaccines. https://www.who-umc.org/vigibase/

§ In 2022, Pitcairn Islands was added as a WHO territory in WPR, increasing the total number of WHO countries and territories from 214 to 215, and in WPR from 36 to 37.

The recent COVID-19 pandemic response and subsequent national immunization activities likely contributed substantially to the progress in global immunization safety monitoring, in large part because of increased funding and provision of intensified technical support from global partners. With nationally focused activities to increase COVID-19 vaccine distribution and vaccination coverage paired with innovative vaccine safety monitoring approaches (e.g., smartphone applications), the highest proportion of WHO countries meeting the new indicator was observed in 2021. Most AEFI cases reported in 2021 were associated with COVID-19 vaccines, reinforcing that case-based data from national AEFI surveillance systems can be shared globally (i.e., to VigiBase). Despite these gains, a slight decrease was observed in the proportion of WHO countries meeting the new reporting indicator in many WHO regions during 2022, likely because of a decline in national COVID-19 vaccination campaigns and less intensive AEFI surveillance. The current findings indicate that further measures are needed to strengthen global vaccine safety monitoring though technical support, standardized tools, and guidelines, and that better approaches to promote nationally coordinated AEFI reporting among EPIs and NRAs are needed.

Summary

What is already known about this topic?

In 2020, the World Health Organization (WHO) recommended a new case-based vaccine safety monitoring indicator: one or more serious adverse events following immunization (AEFIs) per 1 million total population per year.

What is added by this report?

In 2022, 92 (43%) of 215 WHO-affiliated countries and territories achieved the new case-based indicator. During 2020–2022, four of six WHO regions reported an increase in joint reporting of national AEFI data from national regulatory authorities (NRAs) and national expanded programs on immunization (EPIs).

What are the implications for public health practice?

Case-based reporting promotes timely AEFI detection, reporting, investigation, and response by NRAs and EPIs. Improving case-based data sharing globally can provide valuable insights into trends and regional characteristics of serious AEFI.

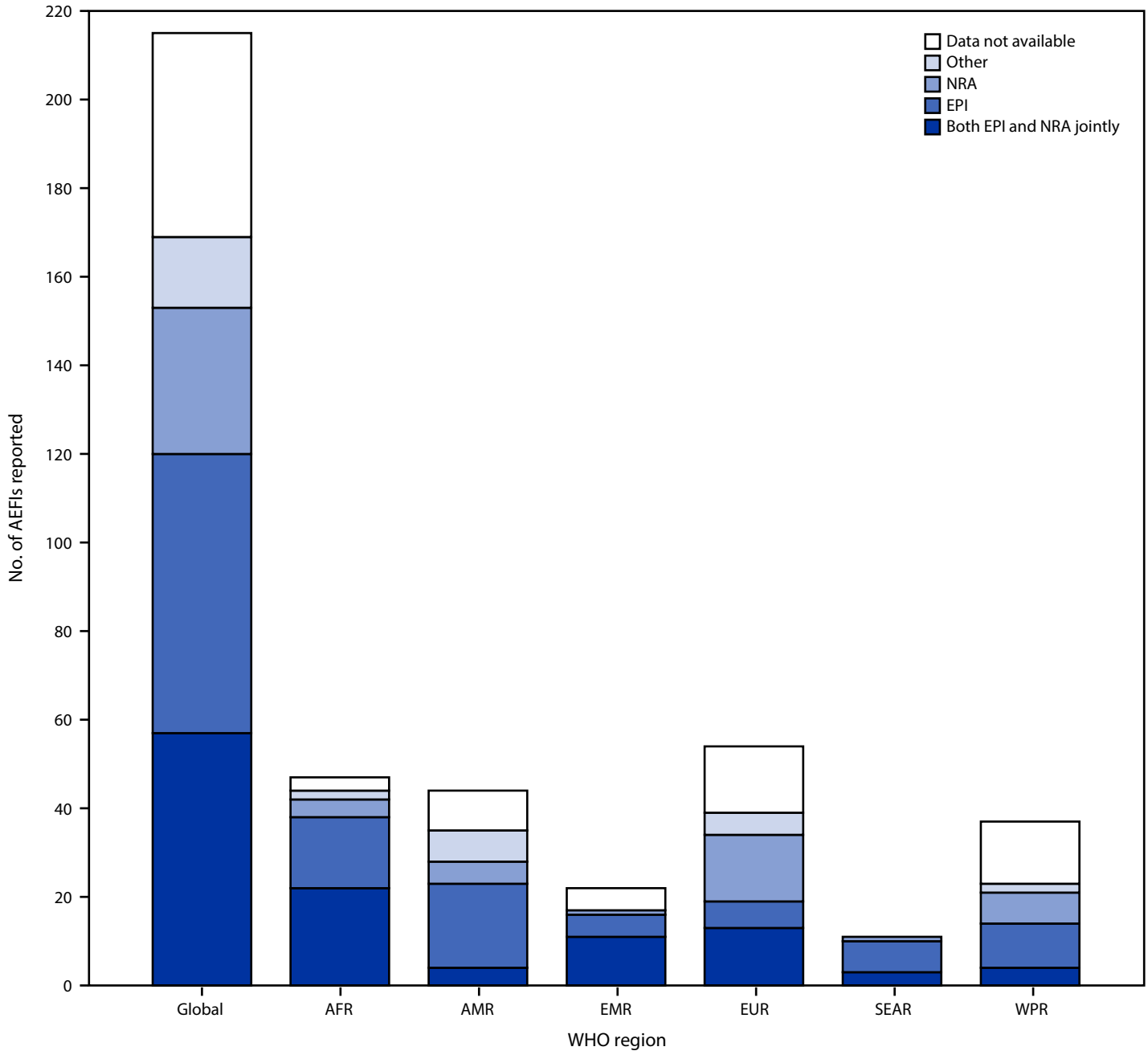
Limitations

The findings in this report are subject to at least three limitations. First, this report relied only on data submitted to VigiBase to determine progress toward meeting the new AEFI surveillance indicator. Reporting to VigiBase is voluntary and varies by year. Some WHO countries might not consistently submit data to VigiBase and thus are not identified as meeting the AEFI surveillance indicator during the reporting period. Second, because of the distinct roles of reporting to VigiBase by NRAs and to the Joint Reporting Form by EPIs, assessment of the role the relationship among NRAs and EPIs plays in meeting the new immunization safety monitoring indicator was not possible. Finally, whereas other factors contribute to national capacity to develop and maintain an immunization safety system, this report focused on only two immunization safety measures: the new case-based indicator and the reporting source of AEFI data, which might not reflect the actual functionality of a national immunization safety surveillance system.

Implications for Public Health Practice

A shift to case-based reporting enables and promotes the use of AEFI data for action, including timely detection, reporting, investigation, and causality assessment by national AEFI committees, and response to reported serious AEFIs or clusters by national EPIs and NRAs. In addition, when shared globally, individual case safety reports can collectively contribute to the description of trends and regional characteristics of rare, but serious, AEFIs that might be difficult to detect through national

FIGURE 2. Number of adverse events following immunization reported on the World Health Organization/UNICEF Joint Reporting Form, by data source and World Health Organization region — worldwide, 2022



Abbreviations: AEFIs = adverse events following immunization; AFR = African Region; AMR = Region of the Americas; EMR = Eastern Mediterranean Region; EPI = expanded program on immunization; EUR = European Region; NRA = national regulatory authority; SEAR = South-East Asia Region; WHO = World Health Organization; WPR = Western Pacific Region.

aggregate data. Continued efforts in capacity building of immunization safety monitoring systems are needed to ensure and promote public confidence in national vaccination programs.

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Use of Inactivated Polio Vaccine Among U.S. Adults: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, 2023

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Abstract

Poliovirus can cause poliomyelitis and lifelong paralysis. Although wild poliovirus types 2 and 3 have been eradicated, wild poliovirus type 1 and vaccine-derived polioviruses are still circulating in multiple countries worldwide. In 2022, a case of paralytic polio caused by vaccine-derived poliovirus type 2 was identified in an unvaccinated young adult in New York. This case and subsequent detection of community transmission underscored the ongoing risk for importation of poliovirus into the United States and risk for poliomyelitis among unvaccinated persons. However, previous Advisory Committee on Immunization Practices (ACIP) recommendations for adult polio vaccination were limited to adults known to be at increased risk for exposure. During October 2022–June 2023, the ACIP Polio Vaccine Work Group reviewed data on poliovirus surveillance and epidemiology, safety and effectiveness of inactivated poliovirus vaccine (IPV), and other considerations outlined in the ACIP Evidence to Recommendations Framework. On June 21, 2023, ACIP voted to recommend that all U.S. adults aged ≥18 years who are known or suspected to be unvaccinated or incompletely vaccinated against polio complete a primary polio vaccination series with IPV. This report summarizes evidence considered for this recommendation and provides clinical guidance for the use of IPV in adults.

Introduction

Poliovirus infection can cause poliomyelitis and permanent paralysis. The incidence of paralytic polio in the United States decreased rapidly after introduction of the Salk inactivated poliovirus vaccine (IPV) in 1955 followed by the Sabin oral poliovirus vaccine (OPV) in 1961 (*1*). Trivalent OPV (tOPV), containing poliovirus vaccine serotypes 1, 2, and 3, was administered as part of the routine childhood immunization schedule starting in the 1960s and led to the elimination of wild poliovirus and community poliovirus transmission in the United States in 1979. In 1996, the current enhanced-potency formulation of IPV was introduced as part of a sequential vaccination schedule with tOPV. In 1999, the United States adopted an IPV-only schedule, removing tOPV. Since then, IPV has been the only polio vaccine recommended for routine immunization in the United States.

Historically, the Advisory Committee on Immunization Practices (ACIP) has not recommended polio vaccination for persons aged ≥18 years unless they are known to be at increased risk for poliovirus exposure* (*2*). In 2022, a case of paralytic polio caused by circulating vaccine-derived poliovirus type 2 (cVDPV2) was identified in an unvaccinated young adult in New York (*3*,*4*). Shortly thereafter, retrospective and prospective wastewater testing detected poliovirus type 2 genetically linked to the case in six New York counties during April–October 2022 (*5*), indicating community circulation. Genetic sequencing subsequently demonstrated linkages between the New York virus and polioviruses collected from wastewater in Canada, Israel, and the United Kingdom. Rockland County, New York has reported low rates of childhood vaccination for >20 years; in the summer of 2022, 60% of Rockland County children aged <2 years had received the recommended 3 doses of IPV, and coverage in some county zip codes was as low as 37%. In comparison, national 3-dose IPV coverage by age 2 years was 93.4% among children born during 2018–2019 (*6*).

These events represent only the second known instance of community transmission of poliovirus in the United States since 1979. The occurrence of this paralytic polio case, along with ongoing global poliovirus circulation and risk for future poliovirus importations into the United States, prompted a reexamination of polio vaccination recommendations and guidance for U.S. adults, particularly those who are known to be unvaccinated or incompletely vaccinated.

Methods

The ACIP Polio Vaccination Work Group includes clinicians and experts in infectious diseases, vaccinology, and public health. During October 2022–June 2023, the Work Group met at least monthly to discuss adult IPV recommendations using the ACIP Evidence to Recommendations Framework†

* In the 2000 ACIP statement on polio vaccination, persons who were at higher risk for poliovirus exposure than the general population included travelers to areas or countries where polio is epidemic or endemic, members of communities or specific population groups with disease caused by wild polioviruses, laboratory workers who handle specimens that might contain polioviruses, health care workers who have close contact with patients who might be excreting wild polioviruses, and unvaccinated adults whose children will be receiving oral poliovirus vaccine.

† Evidence to Recommendation documents are available for adult primary vaccination with IPV (https://www.cdc.gov/vaccines/acip/recs/grade/primary-IPV-polio-vax-adults-etr.html) and for the adult IPV booster dose (https://www.cdc.gov/vaccines/acip/recs/grade/booster-IPV-polio-vax-adults-etr.html).

to guide deliberations. The framework considerations included polio as a public health problem, resource use, benefits and harms of vaccination, patient values and preferences, acceptability, feasibility, and equity. Deliberations included review of poliovirus surveillance and epidemiologic information, as well as published data on IPV safety and effectiveness identified through literature searches. A summary of the Work Group's deliberations and conclusions was presented to ACIP at a public meeting on June 21, 2023.

Rationale and Evidence: Unvaccinated and Incompletely Vaccinated Adults

The immunogenicity and effectiveness of enhanced-potency IPV has been established; the presence of neutralizing antibodies correlates with protection against paralytic disease (*7*). Seroconversion rates and antibody titers after vaccination vary depending on age at receipt of the first dose and vaccination schedule, but administration of 3 IPV doses ≥2 months apart to children aged ≥2 months results in ≥95% seroconversion 1 month after receipt of the third dose (*8*,*9*). In contrast to OPV, IPV does not prevent gastrointestinal infection or shedding in exposed persons (*10*); however, IPV does appear to reduce the odds of nasopharyngeal shedding in infected persons (*11*,*12*).

During >20 years of use in routine immunization, the current formulation of enhanced-potency IPV has been demonstrated to have a highly favorable safety profile. Local reactions at the injection site are the most commonly reported adverse events, with 14%–29% of clinical trial recipients reporting tenderness at the injection site (*13*). Concurrent administration of IPV with other vaccines was not associated with increased frequency of adverse events or severity of adverse events compared with administering the other vaccines alone (*8*,*14*,*15*), and no serious adverse events have been causally associated with the current IPV formulation (*15*–*17*).

The most recent ACIP statement on adult polio vaccination was published in 2000 and recommended IPV for unvaccinated and incompletely vaccinated adults who were at increased risk for exposure to poliovirus (*2*). However, this recommendation did not directly address other unvaccinated and incompletely vaccinated adults. The detection of a paralytic polio case caused by cVDPV2 in Rockland County, New York in July 2022 (*3*,*4*) demonstrated that adults are living in the United States who are known to be unvaccinated or incompletely vaccinated and that they are frequently clustered together in communities that also have low childhood vaccination rates. The events in New York also served as a reminder of the risk for importation of poliovirus into the United States as long as any polioviruses are circulating globally. A uniform recommendation for all adults who are known or suspected to be unvaccinated or incompletely vaccinated would allow these adults to benefit from opportunities to receive IPV vaccination and be protected from paralytic polio before they are at risk for exposure.

Rationale and Evidence: Booster Doses for Previously Vaccinated Adults

A national serosurvey conducted during 2009–2010 determined that ≥79% of adults aged 20–49 years have antibodies to poliovirus types 1, 2, and 3 (*18*), indicating the persistence of antibodies for at least several decades. No data on comparative vaccine effectiveness of a primary series alone versus a primary series plus booster IPV dose exist; however, studies in groups of adults with varying vaccination histories and a range of prebooster seroprevalences have demonstrated that administering an IPV booster dose increases the percentage of adults who are seropositive to 98%–100% (*19*–*24*). Although the need for an IPV booster after primary polio vaccination is uncertain, some adults might benefit from the increased immunity provided by an additional IPV dose when exposure to poliovirus can reasonably be expected. Therefore, adults who have completed a primary series of tOPV or IPV and who are at increased risk for exposure to poliovirus may receive another dose of IPV. This recommendation is unchanged from the previous booster recommendation (*2*).

Recommendations

Unvaccinated or Incompletely Vaccinated Adults

Adults aged ≥18 years who are known or suspected to be unvaccinated or incompletely vaccinated against polio should complete a primary vaccination series with IPV.

Vaccinated Adults Who are at Risk for Exposure to Poliovirus

Adults who have received a primary series of tOPV or IPV in any combination and who are at increased risk for exposure to poliovirus may receive another dose of IPV. Available data do not indicate the need for more than a single lifetime booster dose with IPV for adults.

Clinical Considerations

Polio vaccination has been part of routine childhood immunization since the late 1950s. Adults who received any childhood vaccines almost certainly were vaccinated against polio. Thus, most adults who were born and raised in the United States can assume they were vaccinated against polio as children, even if they do not have written documentation of vaccination, unless they have specific reasons to believe they were not vaccinated. The current definition of a complete primary polio vaccination series is receipt of ≥3 appropriately spaced doses of tOPV or IPV in any combination, with the final dose in the series administered on or after the fourth birthday.[§]

[§] The recommendation for a dose on or after the fourth birthday was made in August 2009. Therefore, persons who received ≥4 doses of tOPV or IPV before August 2009 may be considered fully vaccinated, regardless of the age of the final dose.

Summary

What is already known about this topic?

Previously, inactivated polio vaccine (IPV) recommendations for U.S. adults addressed adults known to be at increased risk for poliovirus exposure.

What is added by this report?

On June 21, 2023, the Advisory Committee on Immunization Practices issued an IPV recommendation for all adults known or suspected to be unvaccinated or incompletely vaccinated against polio. Risk-based recommendations for IPV boosters have not changed.

What are the implications for public health practice?

Adults aged ≥18 years who are known or suspected to be unvaccinated or incompletely vaccinated against polio should complete a primary polio vaccination series with IPV. Fully vaccinated adults at increased risk for poliovirus exposure may receive a single lifetime booster dose of IPV.

Persons at Increased Risk for Poliovirus Exposure

Adults who might be at increased risk for exposure to poliovirus include travelers to countries where polio is epidemic or endemic, laboratory and health care workers who handle specimens that might contain polioviruses, health care workers or other caregivers who have close contact with patients in a community with a polio outbreak, and other adults who are identified by public health authorities as being part of a group or population at increased risk for exposure to poliovirus because of an outbreak.

Dosing Schedule

Adults requiring a primary polio vaccination series should receive 2 doses of IPV administered at an interval of 4–8 weeks; a third dose should be administered 6–12 months after the second dose. There is no need to restart the series if the interval between doses exceeds the recommended interval. If 3 doses of IPV cannot be administered within the recommended interval before protection is needed (e.g., before travel to a country with endemic polio), an accelerated schedule is recommended based on the amount of time available.¶

Considerations for Persons with Altered Immunocompetence

IPV is an inactivated vaccine and is safe to administer to persons who are immunocompromised or who have close contact with other persons who are immunocompromised. However, IPV might be less effective when administered during periods of altered immunocompetence. For this reason, when feasible, IPV should be administered before initiation of immunosuppressive therapy or anticipated period of altered immunocompetence. Specifically, for persons anticipated to be eligible for an IPV booster in the future (e.g., before travel to a country with endemic polio), administration of the booster dose before the period of altered immunocompetence should be considered. Additional guidance regarding immunization in persons with specific conditions is available at https://www.cdc.gov/vaccines/hcp/acip-recs/general-recs/immunocompetence.html.

Contraindications and Precautions

Contraindications and precautions are unchanged from previous recommendations. Severe allergic reaction (e.g., anaphylaxis) to IPV or to antibiotics contained in trace amounts in IPV (streptomycin, polymyxin B, or neomycin) is the only contraindication to administration of IPV. Pregnancy is a precaution to administration of IPV. Although there is no evidence that IPV vaccine causes harm to pregnant persons or their fetuses, out of an abundance of caution IPV should not be given during pregnancy if there is not an increased risk for exposure. However, if a pregnant person is at increased risk for exposure and requires immediate protection against polio, IPV can be administered in accordance with the recommended schedule for adults (*2*).

Reporting of Vaccine Adverse Reactions

Adverse events occurring after administration of any vaccine should be reported to the Vaccine Adverse Event Reporting System (VAERS). Reports can be submitted to VAERS online, by fax, or by mail. Additional information about VAERS is available by telephone (1-800-822-7967) or online at vaers.hhs.gov.

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¶ If >8 weeks are available before protection is needed, 3 doses of IPV should be administered ≥4 weeks apart. If <8 weeks but >4 weeks are available before protection is needed, 2 doses of IPV should be administered ≥4 weeks apart. If <4 weeks are available before protection is needed, a single dose of IPV is recommended. The remaining doses of vaccine should be administered later, at the recommended intervals.

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Notes from the Field

Undiagnosed Tuberculosis During Pregnancy Resulting in a Neonatal Death — United States, 2021

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In 2022, the World Health Organization reported 10.6 million new cases of tuberculosis (TB) globally. One third of these new cases were reported in women; however, pregnancy status was not included in these data.* CDC recently added pregnancy status to national TB reporting in the United States; however, because the number of U.S. TB cases during pregnancy is presumed to be low, adverse effects of TB on pregnancy and postpartum outcomes are likely not well characterized.† A 2017 meta-analysis of 13 studies that included approximately 123,000 pregnancies from several countries found that TB disease during pregnancy was associated with increased odds of maternal morbidity and mortality, including hospital admission, anemia of pregnancy, cesarean birth, miscarriage, preterm birth, low birthweight, and neonatal TB (*1*). TB diagnosis during pregnancy might be delayed because of overlap in symptoms of TB with those of pregnancy, as well as clinician reluctance to use chest radiography during pregnancy.§ Perinatal TB is a life-threatening illness, with a congenital and neonatal TB mortality rate of approximately 50% (*2*), highlighting the importance of diagnosing and treating TB before and during pregnancy. This report describes a case of fatal neonatal TB after successful in vitro fertilization in 2021.

Investigation and Outcomes

The infant's mother underwent in vitro fertilization for infertility in her home country of India, which accounted for 27% of global TB incidence in 2022¶; she returned to the United States 1 month before delivery. During U.S. prenatal visits, she experienced insufficient weight gain, hyperemesis, and chronic cough, which was attributed to gastroesophageal reflux disease. Results for standard pregnancy laboratory tests were normal; no test for TB infection was performed. The mother experienced premature rupture of membranes at 33 weeks' gestation followed by an uncomplicated spontaneous vaginal delivery of a healthy-appearing newborn and a normal-appearing placenta.

The newborn had 1- and 5-minute Apgar scores of 7 of 10 and 9 of 10, respectively, and weighed 5 lbs 6.7 oz (2,460 g) (90th percentile for gestational age). After receiving inpatient care for prematurity, the newborn was discharged home on the 14th day of life. However, shortly after hospital discharge, the infant developed labored breathing, became progressively ill, and was readmitted 4 days later (the 18th day of life) in septic shock, which was managed with endotracheal intubation and admission to an intensive care unit. Chest radiography demonstrated overall ground-glass–appearing infiltrates, suggesting inflammation, and loss of lung volume. On the basis of these findings, the mother's chronic cough, and her origin from a country with high TB incidence, pulmonary TB was suspected. The infant's gastric aspirate samples contained acid-fast bacilli on smear microscopy (an indicator of pulmonary TB) and grew *Mycobacterium tuberculosis* in culture. TB treatment** was commenced on the 22nd day of life. Initially, the infant's condition improved, but 12 days after the diagnosis of TB, a pneumothorax was identified in the context of sudden respiratory deterioration. Respiratory treatments were not effective, and in alignment with the family's wishes, support was withdrawn with institution of comfort measures. The infant died on the 42nd day of life of TB-related respiratory failure.

The mother's chest radiograph demonstrated bilateral reticular nodular opacities. Acid-fast bacilli were identified on sputum smear microscopy, and a sputum sample tested positive for *M. tuberculosis* by polymerase chain reaction; a sputum culture was also positive. The mother recovered while completing a full course of treatment for drug-susceptible pulmonary TB, the same treatment that would have been recommended if a diagnosis had occurred during pregnancy. The only other household contact was determined not to have TB disease or latent TB infection after evaluation. This activity was reviewed by CDC, deemed research not involving human subjects, and was conducted consistent with applicable federal law and CDC policy.††

Preliminary Conclusions and Actions

Although TB disease typically affects the lungs, it can involve any system, including the reproductive system, which can be

* https://www.who.int/news-room/fact-sheets/detail/tuberculosis
† https://www.cdc.gov/tb/programs/rvct/instructionmanual.pdf
§ https://doi.org/10.1097/AOG.0000000000003890
¶ https://www.who.int/teams/global-tuberculosis-programme/tb-reports/global-tuberculosis-report-2023/tb-disease-burden/1-1-tb-incidence

** The infant's treatment course was complicated by necrotizing enterocolitis, which precluded the administration of standard oral isoniazid (INH). Because intravenous INH could not be located in the United States, the infant received an intravenous regimen of meropenem, levofloxacin, linezolid, and rifampin.
†† 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.

affected in the absence of pulmonary findings (*3*). TB of the female reproductive system can cause infertility, pain, a pelvic mass, or menstrual disorders (*3*). Diagnosis requires a high index of suspicion for TB when a person from a country with endemic TB experiences genitourinary symptoms, including infertility. In India, TB is considered the likely cause of infertility in nearly one quarter (24.2%) of women with infertility (*3*). The sensitivity of chest radiography in detecting disease is 10%–75% in genitourinary TB (*4*). Ascertaining a diagnosis of TB during a female infertility evaluation should include consideration of pelvic organ imaging and specimen collection via laparoscopy and endometrial biopsy for acid-fast bacilli smear microscopy, polymerase chain reaction and culture for *M. tuberculosis*, and histology (*4*).

The fatal case reported here might have been avoided by TB prevention or TB treatment during the infertility evaluation or during pregnancy. This case underscores the importance of considering TB during an evaluation of women with infertility or a history of infertility if they are from a country with endemic TB. To reduce TB-associated morbidity and mortality, including congenital and neonatal TB, all persons, including those who are pregnant, should be considered for TB evaluation by assessing risk factors for TB infection (e.g., current or previous residence in a high TB-incidence country, a homeless shelter, or correctional facility) and risk factors for progression to TB disease if TB infection is present (e.g., diabetes, HIV infection, or substance use disorder)[§§] (*5*) (Box).

[§§] https://doi.org/10.1542/9781610020886

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BOX. Selected groups with increased likelihood of infection with *Mycobacterium tuberculosis* and with increased risk for developing tuberculosis disease if infected[*,†,§]

Groups with increased likelihood of infection with *Mycobacterium tuberculosis*

- Household contacts of or persons with recent exposure to an active tuberculosis case
- Immigrants from countries with a high tuberculosis incidence (>20 cases per 100,000 population)
- Residents and employees of high-risk congregate settings (e.g., homeless shelters or correctional facilities)
- Mycobacteriology laboratory personnel

Groups with increased likelihood of developing tuberculosis disease if infected[§]

- Children aged <5 years
- Persons with clinical predisposition (e.g., diabetes, HIV infection, receipt of immunosuppressive therapy, substance use disorder, or silicosis)
- Persons with abnormal chest radiograph consistent with previous tuberculosis disease

[*] https://doi.org/10.1093/cid/ciw778
[†] https://doi.org/10.1542/9781610020886
[§] Screening for persons at low risk is not recommended. The guidance in this box does not differentiate among likelihood or levels of risk for progression.

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Notes from the Field

Responding to the Wartime Spread of Antimicrobial-Resistant Organisms — Ukraine, 2022

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Worldwide, bacterial antimicrobial resistance is estimated to cause more deaths than HIV or malaria and is recognized as a leading global public health threat (*1*). In Ukraine, the confluence of high prewar rates of antimicrobial resistance, an increase in the prevalence of traumatic wounds, and the war-related strain on health care facilities is leading to increased detection of multidrug-resistant organisms with spread into Europe (*2*,*3*). Evidence of increased rates of antimicrobial resistance in other conflict settings such as Iraq (*4*), and the long-term consequences for civilian, military, and other populations, argue that the spread of antimicrobial resistance in Ukraine is an urgent crisis that must be addressed, even during an ongoing war.

In mid-2022, a collaboration was established between CDC, the Center for Public Health of Ukraine (UPHC), local clinical and public health authorities, and international partners, including the World Health Organization regional office for Europe, ICAP at Columbia University, and the European Society for Clinical Microbiology and Infectious Diseases. The purpose of this collaboration was to improve laboratory detection, clinical treatment, and infection control response for antimicrobial resistance in the Ternopil, Khmelnytskyi, and Vinnytsia regions supported by U.S. Ukraine supplemental appropriations emergency funding.*

Investigation and Outcomes

In August 2022, UPHC and regional collaborators conducted infection prevention and control and antimicrobial resistance laboratory capacity assessments in the three regional public health facilities and the three regional hospitals in the Ternopil, Khmelnytskyi, and Vinnytsia regions. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.†

The infection prevention and control assessments identified inadequacies in surveillance of health care–associated infections, implementation of infection prevention and control measures such as recommended hand hygiene, and monitoring, evaluation, and feedback to the hospital staff members.§,¶ The laboratory assessments identified multiple challenges, especially inadequate quantities of automated microbiology equipment, and suboptimal laboratory quality and information management systems, biosafety practices, and staffing, as well as inconsistent availability of essential antibiotic susceptibility testing consumables.

UPHC also conducted health care–associated infections and antimicrobial resistance point prevalence surveys at three regional hospitals during November–December 2022. Among 353 patients on surveyed wards, 50 (14%) had health care–associated infections.** High rates of antimicrobial resistance were identified among isolates from patients with health care–associated infections, with 30 of 50 (60%) patients having an infection with a carbapenem-resistant organism. Among 20 *Klebsiella pneumoniae* isolates, all were resistant to third-generation cephalosporins, and among the 19 *Klebsiella* isolates tested, all were also carbapenem-resistant. These rates are substantially higher than those reported from a 2016–2017 European Union–wide point prevalence survey, which included more than 300,000 acute care hospital patients and 100,000 long-term care facility residents; among these respondents, the study found a health care–associated infection rate of 5.5%. Among the subset of infections caused by the Enterobacteriaceae family of bacteria (including *Klebsiella*), 6.2% of isolates were resistant to carbapenem (*5*).

Preliminary Conclusions and Actions

Urgent capacity building to prevent, detect, and respond to antimicrobial resistance is needed to save lives within Ukraine and limit international spread. UPHC and partners are collaborating to improve laboratory detection of antimicrobial resistance, antimicrobial prescribing, and infection prevention and control, starting in the Ternopil, Khmelnytskyi, and Vinnytsia regions. UPHC is prioritizing interventions to strengthen infection prevention and control and the laboratory-clinical interface via multidisciplinary hospital teams, establishing routine health care–associated infections and antimicrobial resistance surveillance, utilizing guidelines and locally collected data to inform clinical care, upgrading laboratory equipment and workflows, increasing availability and use of hand-hygiene disinfectants, and providing technical

* The U.S. State Department's Office of the Coordinator of U.S. Assistance to Europe and Eurasia transferred to CDC via an interagency agreement.

† 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/drugresistance/intl-activities/laarc.html

¶ https://www.who.int/publications/i/item/WHO-HIS-SDS-2018.9

** https://www.ecdc.europa.eu/en/publications-data/point-prevalence-survey-healthcare-associated-infections-and-antimicrobial-use-4

training for staff members. UPHC has issued clinical guidance on indications for bacteriology testing, including to military hospitals. Partners are supporting training curricula that include clinical and laboratory twinning[††] between international experts on antimicrobial resistance and Ukrainian clinicians and laboratorians. In addition, partners are conducting workshops for regional and hospital staff members to develop and use clinical and laboratory standard operating procedures to strengthen infection prevention and control practices and clinical management of infected patients. Lastly, partners are working to provide additional laboratory supplies to meet the increased wartime demands, to capacitate laboratories to test for bacterial susceptibility to newer-generation antibiotics, and to improve reliable hospital access to these antibiotics.

To address the alarming increase of antimicrobial resistance in Ukraine, UPHC with assistance from international partners, is developing locally led and implemented measures to address antimicrobial resistance and will need ongoing support to scale them nationally. In addition, development of national action plans and context-specific policies and strategies are needed to improve infection prevention and control and monitor antibiotic use and antimicrobial resistance.

[††] An approach to strengthening national public health laboratory systems by pairing laboratories from different countries and working to build bidirectional peer-mentoring relationships among them.

Acknowledgment

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Erratum

Vol. 72, No. 42

The report, "Use of Updated COVID-19 Vaccines 2023–2024 Formula for Persons Aged ≥6 Months: Recommendations of the Advisory Committee on Immunization Practices — United States, September 2023," contained several errors.

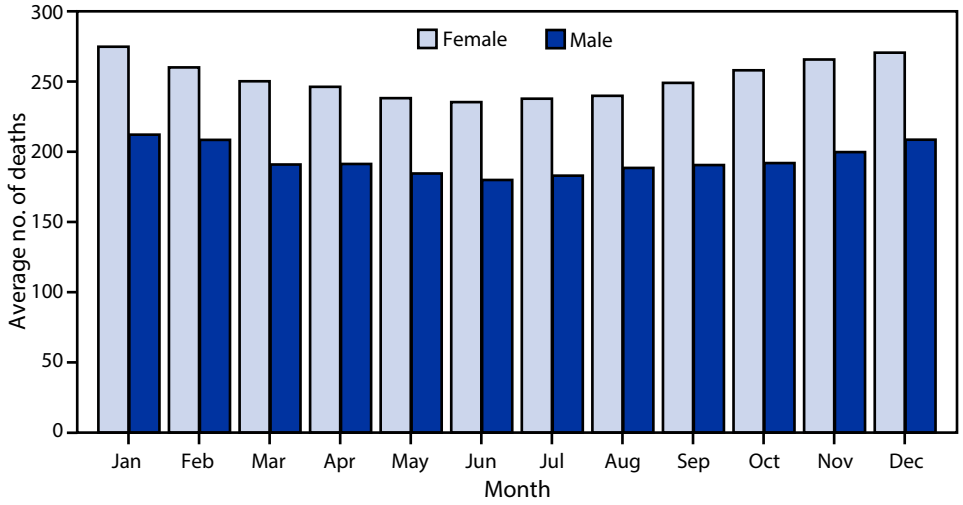
On page 1141, the last sentence of the first complete paragraph should have read, "During January 1–July 22, 2023, a total of **28,128** persons, including 26 aged <1 year, 18 aged 1–4 years, 36 aged 5–19 years, **451** aged **20**–44 years, 2,821 aged 45–64 years, and 24,776 aged ≥65 years, died from COVID-19, as evidenced by COVID-19 being listed as the underlying cause of death on the death certificate.†"

On page 1142, the second sentence of the second complete paragraph should have read, "During September 2022–August 2023, VE against hospitalization among adults aged ≥65 years without an immunocompromising condition waned from 67% (95% CI = 62%–71%) at 7–59 days postvaccination to 28% (95% CI = 18%–36%) at **120–179** days (*13*)." In addition, the fifth sentence of the second complete paragraph should have read, "VE against emergency department and urgent care visits among persons aged 5–17**, 18–64, and ≥65** years ranged from 59%–63% by age group 7–59 days after a bivalent dose, waning to 36%–47% by age group 60–119 days after a bivalent dose (*13*)."

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Average Number of Stroke* Deaths per Day, by Month and Sex — National Vital Statistics System, United States, 2021



* Deaths attributed to stroke were identified using *International Classification of Diseases, Tenth Revision* underlying cause of death codes I60–I69.

In 2021, the average number of stroke deaths per day was highest in January (275 for females and 212 for males) and then declined to a monthly low in June (235 for females and 180 for males). Beginning in July, the average number of stroke deaths per day increased for each successive month through the end of the year among both males and females, with the average number of stroke deaths higher among females than males for every month.

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

Reported by: Sally C. Curtin, MA, sac2@cdc.gov.

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

The *Morbidity and Mortality Weekly Report (MMWR)* Series is prepared by the Centers for Disease Control and Prevention (CDC) and is available free of charge in electronic format. To receive an electronic copy each week, visit *MMWR* at *https://www.cdc.gov/mmwr/index.html*.

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