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Translocation of an Anteater (*Tamandua tetradactyla*) Infected with Rabies from Virginia to Tennessee Resulting in Multiple Human Exposures, 2021

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On August 16, 2021, the Tennessee Department of Health (TDH) was notified of a positive rabies test result from a South American collared anteater (*Tamandua tetradactyla*) in Washington County, Tennessee. Tamanduas, or lesser anteaters, are a species of anteater in which rabies has not previously been reported. The animal was living at a Tennessee zoo and had been recently translocated from a zoo in Virginia. TDH conducted an investigation to confirm the rabies result, characterize the rabies variant, and ascertain an exposure risk assessment among persons who came into contact with the tamandua. Risk assessments for 22 persons were completed to determine the need for rabies postexposure prophylaxis (rPEP); rPEP was recommended for 13 persons, all of whom agreed to receive it. Using phylogenetic results of the virus isolated from the tamandua and knowledge of rabies epidemiology, public health officials determined that the animal was likely exposed to wild raccoons present at the Virginia zoo. This report describes expansion of the wide mammalian species diversity susceptible to rabies virus infection and summarizes the investigation, highlighting coordination among veterinary and human public health partners and the importance of preexposure rabies vaccination for animal handlers and exotic zoo animals.

Case Report

In early May 2021, a tamandua was translocated from a drive-through zoo in Virginia (where animals can be viewed from visitors' vehicles) to a zoo in Washington County, Tennessee (Figure 1), where it was kept in an indoor habitat with one other tamandua and isolated from zoo visitors and wildlife. The tamanduas were not permitted out of the enclosure, and no known exposures to other animals occurred.

On June 29, the tamandua began exhibiting signs of illness including lethargy, anorexia, and diarrhea. A local veterinarian and veterinary technician at veterinary clinic A examined the tamandua on July 1. The animal was treated empirically with an antibiotic for presumed infection and vitamin K injections and returned to the zoo. After progression of clinical signs, including copious salivation, the animal was transported on July 6 to clinic B at a nearby veterinary medical college, where it was examined by a veterinarian, veterinary residents, interns, students, and a visiting veterinary consultant. Rabies was not considered in the differential diagnosis at this time because 1) there was no known bite exposure, 2) rabies had never been reported in a tamandua, and 3) the low basal body temperature of tamanduas (91°F [32.8°C]) was believed to contribute to decreased susceptibility to rabies virus infection. Routine

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diagnostics failed to reveal a primary cause, and supportive care was unsuccessful in improving the animal's condition, necessitating euthanasia on July 6.

Necropsy, including removal of brain tissue using an electric oscillating saw, was completed at the veterinary medical college. Laboratory gowns and latex gloves were used in the necropsy suite; no additional personal protective equipment, such as eye and respiratory protection, was used. Brain tissue was submitted to an academic laboratory for histopathology. The head was not submitted to the state public health laboratory; therefore, no fresh brain material was available for rabies testing. The academic laboratory reported a preliminary positive rabies result by immunohistochemistry test on August 16, approximately 6 weeks after euthanasia. The process was not expedited because rabies was not in the differential diagnosis at time of death. TDH was notified of the positive test result, fixed brain tissue was requested, and it was submitted to CDC for confirmatory rabies testing. On August 21, rabies virus antigen was confirmed in the brain of the tamandua by immunohistochemistry and by reverse transcription–polymerase chain reaction assay (*1*). On August 26, molecular characterization determined that the rabies virus was most similar to the rabies virus variant (RVV) observed in raccoons in the eastern United States and reference sequences from Virginia. RVV was divergent from all available sequences from Tennessee, suggesting that rabies infection occurred while the animal was at the Virginia zoo (Figure 2).

Public Health Investigation

TDH developed an assessment tool to identify persons potentially exposed to the tamandua during the rabies viral shedding period, defined as 14 days before onset of clinical signs (June 16) through the date of death (July 6) (*2*) or involvement in necropsy after death. All 22 persons identified with potential exposure completed the risk assessment. rPEP was recommended to 13 persons for nonbite exposures to the animal's tongue and saliva (tamanduas do not have teeth). Seven persons received this recommendation either because of known or presumed exposure to saliva or because of the inability to determine if saliva was introduced to a scratch or open skin wound. Six persons received this recommendation because of potential exposure attributable to aerosolization of brain tissue, because barrier protection was limited to latex gloves and laboratory gowns during removal of brain tissue using an oscillating saw; rPEP was recommended to persons who operated the saw, other persons <10 feet from the saw, and anyone not confident of where they were in the room when the calvarium was breached. Among the 13 persons for whom rPEP was recommended, all agreed to receive it. No human rabies cases have been reported to date. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.*

The other tamandua at the Tennessee zoo enclosure was presumed to be unvaccinated because rabies vaccination

* 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.

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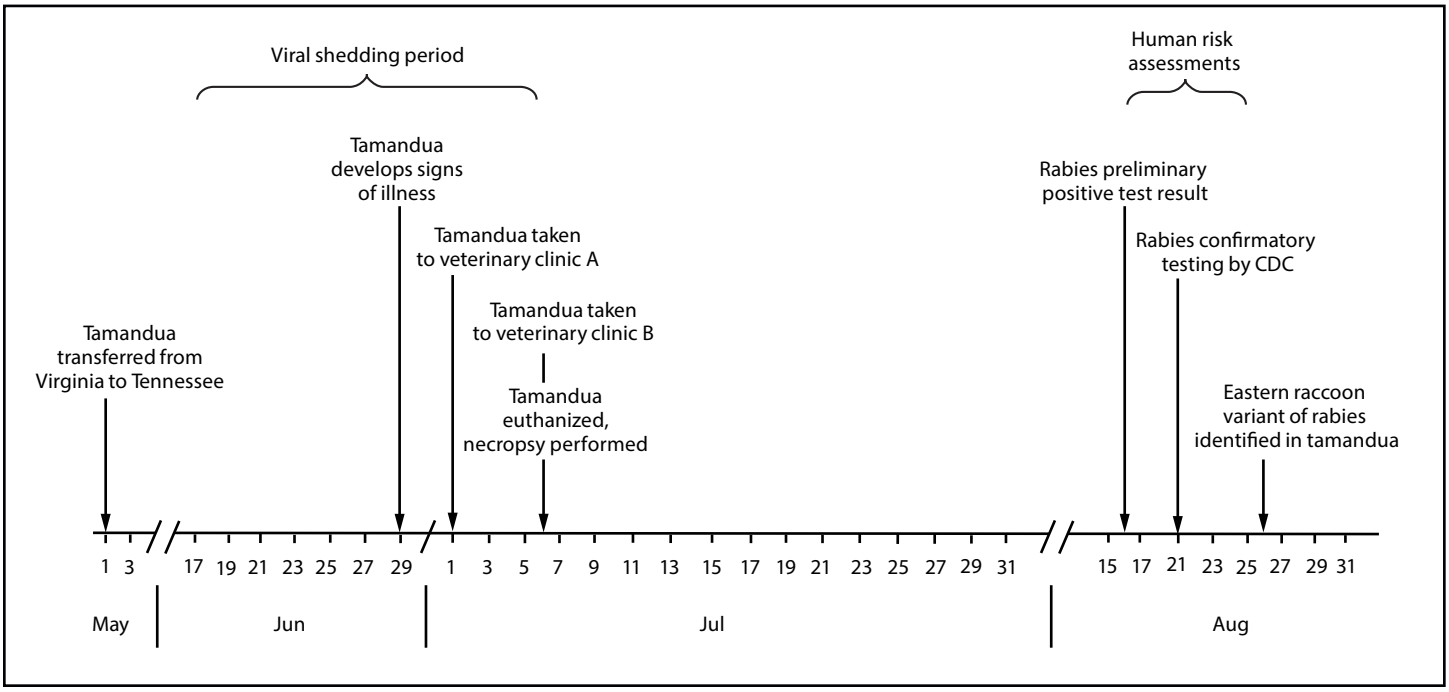
FIGURE 1. Timeline for public health investigation of a rabid tamandua (anteater) translocated from Virginia to Tennessee, May–August 2021



records could not be located. This animal received rabies vaccine, and the zoo owner was advised to strictly quarantine it for 6 months, in concordance with the 2016 Compendium of Animal Rabies Prevention and Control (*2*). The Virginia zoo was notified regarding concerns about rabid raccoons on the property. The owner of this zoo confirmed that native wildlife was present inside the fencing perimeter. As of April 1, 2022, no additional cases of rabies related to this tamandua were identified in Virginia or in Tennessee.

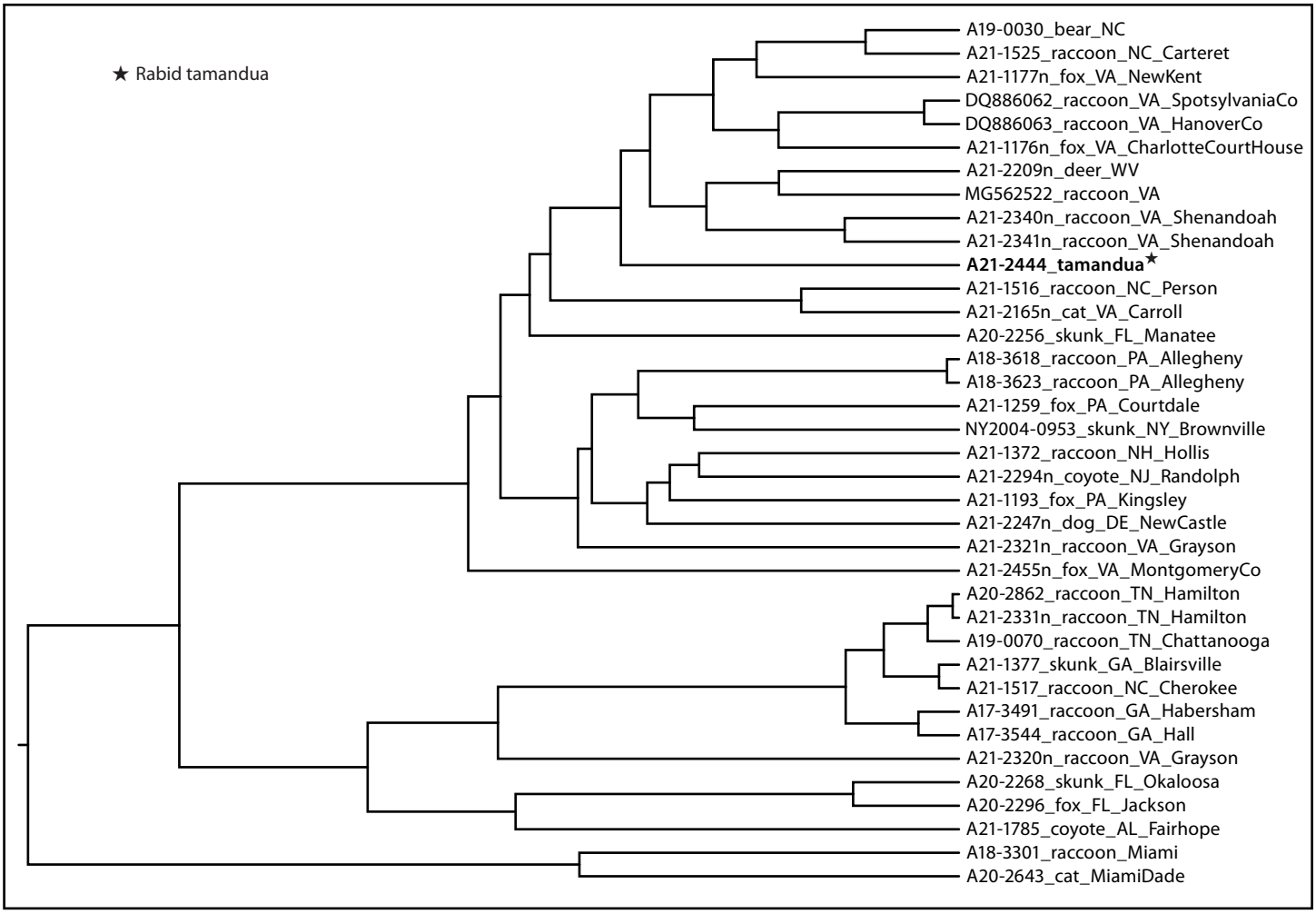
Discussion

This case demonstrates the possibility of rabies translocation by human movement of captive mammals, including species in which rabies has not been previously reported. In the United States, multiple RVVs exist in wild mammalian reservoir populations. Except for bat RVVs, distinct variants associated with major animal reservoir species occur in geographically distinct regions where transmission is mainly among members of the same species (*3*,*4*). The complete genome sequence of rabies virus isolated from this tamandua was similar to that of the eastern raccoon RVV reference sequences from Virginia, which is consistent with the presence of native wildlife (including raccoons) inside the fencing perimeter at the Virginia zoo. The eastern raccoon RVV is enzootic in 18 states and the District of Columbia (*3*). Washington County, Tennessee, has enzootic north-central skunk RVV, but this raccoon RVV is not considered enzootic in the county; no cases of the raccoon RVV have been reported in the county during the previous 5 years (*5*). Phylogenetic data and epidemiologic evidence were used to rule out local transmission and expansion of raccoon RVV into this Tennessee county, which confirmed that extensive mitigation actions were not required (*6*). Although the National Association of State Public Health Veterinarians recommends that dogs, cats, ferrets, and horses be vaccinated against rabies before interstate movement (*2*), no similar recommendations for vaccination of other captive animals are in effect. Expansion of rabies zones in the United States through translocation has substantial adverse public health implications (*7*), including threatening the health of humans, domestic animals, and other wildlife; and potentially requiring changes in wildlife rabies control measures.

Rabies detection in animals in the United States is dependent on the public health and veterinary laboratories that routinely perform rabies testing with standardized methods. The national case definition for animal rabies requires laboratory confirmation with either a positive result for the direct fluorescent antibody test or isolation of rabies virus (*8*). Timely action is required when rabies is suspected and an animal or human rabies exposure has occurred. In this situation, >1 month had lapsed between the necropsy and confirmatory diagnosis performed by CDC. Delays in appropriate diagnostic testing for rabies after necropsy caused delays in administering rPEP and inadvertently placed persons at increased risk for rabies.

Captive mammals maintained in exhibits or zoological parks typically are not completely excluded from rabies host species and can become infected. All employees who work with animals

FIGURE 2. Phylogenetic analysis of rabies virus nucleoprotein gene from the rabid tamandua* identified in Tennessee with raccoon rabies virus variant sequences† from Tennessee, Virginia, and other nearby states, 2021



* Specimen labeled A21-2444 was collected from the rabid tamandua. This specimen clustered with rabies virus sequences from the northeast and mid-Atlantic regions and is separate from specimens from the southeast.
† Branch length is related to the number of nucleotide substitutions. The more substitutions, the longer the branch.

in areas where rabies is endemic should receive preexposure rabies vaccination in accordance with recommendations of the Advisory Committee on Immunization Practices (*2*,*9*). Three employees at the Tennessee zoo and veterinary staff members in this case had not received rabies preexposure vaccination, despite living in a skunk rabies reservoir area and routinely working with animals. These persons were recommended to receive rabies immune globulin and the 4-dose rPEP vaccination series after risk assessment (*10*). This case also highlights the importance of continued public health efforts to expand awareness and education about rabies prevention and control, responsible animal ownership, routine rabies vaccination, appropriate personal protective equipment for barrier protection when performing laboratory procedures with potentially infected animals, and consistent interdisciplinary communication.

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Summary

What is already known about this topic?

Captive mammals in zoological parks that are not completely excluded from rabies host species can become infected. Translocation of captive animals infected with rabies is responsible for spread of rabies in the United States.

What is added by this report?

Rabies virus has not previously been reported in tamanduas (anteaters). A rabies-infected tamandua was translocated from Virginia to Tennessee, exposing multiple persons. Postexposure vaccination was received by 13 persons. No human cases occurred.

What are the implications for public health practice?

Persons who routinely work with animals in areas where rabies is endemic should consider rabies preexposure vaccination. Efforts to expand rabies prevention and control awareness, responsible animal ownership, routine rabies vaccination, and interdisciplinary communication are important.

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Surveillance to Track Progress Toward Polio Eradication — Worldwide, 2020–2021

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Since the Global Polio Eradication Initiative (GPEI) was established in 1988, the number of reported poliomyelitis cases worldwide has declined by approximately 99.99%. By the end of 2021, wild poliovirus (WPV) remained endemic in only two countries (Pakistan and Afghanistan). However, a WPV type 1 (WPV1) case with paralysis onset in 2021, was reported by Malawi a year after the World Health Organization (WHO) African Region (AFR) was certified as WPV-free and circulating vaccine-derived poliovirus (cVDPV) cases were reported from 31 countries during 2020–2021 (*1*,*2*). cVDPVs are oral poliovirus vaccine-derived viruses that can emerge after prolonged circulation in populations with low immunity and cause paralysis. The primary means of detecting poliovirus transmission is through surveillance for acute flaccid paralysis (AFP) among persons aged <15 years, with confirmation through stool specimen testing by WHO-accredited laboratories, supplemented by systematic sampling of sewage and testing for the presence of poliovirus (environmental surveillance). The COVID-19 pandemic caused disruptions in polio vaccination and surveillance activities across WHO regions in 2020; during January–September 2020, the number of reported cases of AFP declined and the interval between stool collection and receipt by laboratories increased compared with the same period in 2019 (*3*). This report summarizes surveillance performance indicators for 2020 and 2021 in 43 priority countries* and updates previous reports (*4*). In 2021, a total of 32 (74%) priority countries† met two key surveillance performance indicator targets nationally, an improvement from 2020 when only 23 (53%) met both targets; however, substantial national and subnational gaps persist. High-performing poliovirus surveillance is critical to tracking poliovirus transmission. Frequent monitoring of surveillance indicators could help identify gaps, guide improvements, and enhance the overall sensitivity and timelines of poliovirus detection to successfully achieve polio eradication.

Acute Flaccid Paralysis Surveillance

Two key performance indicators used to assess AFP surveillance quality are 1) the nonpolio AFP (NPAFP) rate,§ with a NPAFP rate of ≥2 per 100,000 persons aged <15 years considered sufficiently sensitive to detect circulating poliovirus, and 2) the collection of adequate stool specimens¶ from AFP patients, with a target of ≥80% stool specimen adequacy, which indicates that surveillance can effectively identify poliovirus among AFP patients. Surveillance indicators for 43 priority countries experiencing or at high risk for poliovirus transmission were reviewed (Table 1).

African Region. Among 28 priority countries in AFR, 50% met both national surveillance indicator targets in 2020 and 79% met the targets in 2021 (as of March 25, 2022). Subnational surveillance performance also improved in AFR; both surveillance indicator targets were met in 52% of first subnational administrative level areas in 2020 and 75% in 2021 (Figure). In AFR, cVDPV type 2 (cVDPV2) cases were reported from 22 countries during 2020–2021; among 525 cVDPV2 cases reported in 2021, a total of 415 (79%) were from Nigeria. One WPV1 case was detected in a child in Malawi with paralysis onset in 2021 (*5*), approximately 1 year after AFR was certified as WPV-free; this is the first WPV1 case reported in AFR since 2016 and the isolate is genetically linked to a WPV1 lineage last detected in Pakistan in 2019.

Eastern Mediterranean Region. Among 10 priority countries in the WHO Eastern Mediterranean Region (EMR), eight met both national surveillance indicator targets in 2020 and all but one (Djibouti with stool adequacy of 75%) met both targets in 2021. Most EMR countries performed well at the

* Countries selected for this 2020–2021 report were identified as priority countries in the WHO Global Polio Surveillance Action Plan (GPSAP), 2022–2024 because of persistent surveillance gaps and susceptibility to poliovirus transmission or had ≥1 WPV1 or cVDPV isolates detected from AFP or environmental surveillance in 2021 (https://polioeradication.org/wp-content/uploads/2022/03/GPSAP_2022-2024.pdf). Note: In 2022, VDPV3 was isolated from an AFP case and genetically linked to VDPV3 strains isolated from environmental samples collected in Israel and the Palestinian Territories in 2021–2022 (https://www.euro.who.int/en/countries/israel/news/news/2022/3/circulating-vaccine-derived-poliovirus-confirmed-in-israel); the emergence was confirmed as cVDPV3 in March 2022; surveillance performance in these geographies are not included in this report.

† 2021 priority countries (30 GPSAP priority countries indicated by [G]): *African Region:* Angola (G), Benin (G), Burkina Faso (G), Cameroon (G), Central African Republic (G), Chad (G), Congo, Côte d'Ivoire (G), Democratic Republic of the Congo (G), Equatorial Guinea (G), Ethiopia (G), Gambia, Guinea (G), Guinea-Bissau (G), Kenya (G), Liberia, Madagascar (G), Malawi, Mali (G), Mauritania, Mozambique (G), Niger (G), Nigeria (G), Senegal, Sierra Leone, South Sudan (G), Togo (G), and Uganda; *Eastern Mediterranean Region:* Afghanistan (G), Djibouti, Egypt, Iran, Iraq (G), Pakistan (G), Somalia (G), Sudan (G), Syria (G), and Yemen (G); *European Region:* Tajikistan and Ukraine; *South-East Asia Region:* Burma (Myanmar) (G); *Western Pacific Region:* Papua New Guinea (G) and the Philippines (G).

§ The number of NPAFP cases per 100,000 persons aged <15 years per year.

¶ Two stool specimens collected ≥24 hours apart and within 14 days of paralysis onset, and arrival at a WHO-accredited laboratory by reverse cold chain (storing and transporting samples at recommended temperatures from the point of collection to the laboratory) and in good condition (i.e., without leakage or desiccation).

TABLE 1. National and subnational acute flaccid paralysis surveillance performance indicators, number of confirmed wild poliovirus, and circulating vaccine-derived poliovirus cases, by country — 43 priority countries, World Health Organization African, Eastern Mediterranean, European, South-East Asia, and Western Pacific regions, 2020–2021*

Year/WHO region/Country	No. of AFP cases (all ages)	Regional or national NPAFP rate†	Percentage				No. of confirmed cases	
			Subnational areas with NPAFP rate ≥2§	Regional or national AFP cases with adequate specimens¶	Subnational areas with adequate specimens	Population living in areas meeting both indicators**	WPV	cVDPV††
2020								
African Region	**19,643**	**5.1**	**NA**	**85.6**	**NA**	**NA**	—§§	**551**
Angola	383	2.4	77.8	82.2	61.1	37.3	—	3
Benin	278	5.4	100	88.1	91.7	94.5	—	3
Burkina Faso	1,181	11.8	100	86.0	92.3	95.2	—	65
Cameroon	605	5.4	100	77.9	50.0	40.3	—	7
Central African Republic	222	9.8	100	65.3	28.6	28.2	—	4
Chad	993	11.7	95.7	81.8	65.2	69.0	—	101
Congo	93	3.7	75.0	83.9	75.0	53.7	—	2
Côte d'Ivoire	742	6.0	100	85.0	36.4	30.9	—	64
Democratic Republic of the Congo	3,304	7.6	100	80.4	53.8	55.9	—	81
Equatorial Guinea	26	5.0	71.4	80.8	57.1	58.5	—	—§§
Ethiopia	1,343	2.9	90.9	86.8	90.9	93.3	—	36
Guinea	321	4.5	100	69.2	25.0	16.4	—	44
Guinea-Bissau	20	2.4	45.5	50.0	9.1	6.3	—	—
Kenya	336	1.6	29.8	86.3	68.1	17.4	—	—
Liberia	48	2.3	73.3	95.8	100	64.8	—	—
Madagascar	635	5.7	100	90.6	95.5	96.4	—	2
Malawi	134	1.4	25.0	88.8	75.0	12.5	—	—
Mali	376	3.4	90.9	76.1	45.5	59.9	—	52
Mauritania	17	0.9	26.7	64.7	13.3	0	—	—
Mozambique	375	2.6	72.7	78.7	63.6	38.1	—	—
Niger	585	4.7	100	71.8	25.0	24.1	—	10
Nigeria	6,324	7.0	100	94.6	100	100	—	8
Senegal	135	1.7	50.0	77.0	28.6	12.2	—	—
Sierra Leone	89	2.4	60.0	100	100	62.3	—	10
South Sudan	434	6.4	100	80.4	70.0	64.3	—	50
The Gambia	23	2.3	42.9	78.3	42.9	3.7	—	—
Togo	161	4.0	100	62.1	0	0	—	9
Uganda	460	2.1	46.7	90.2	86.7	46.6	—	—
Eastern Mediterranean Region	**20,336**	**9.8**	**NA**	**87.8**	**NA**	**NA**	**140**	**547**
Afghanistan	3,979	22.9	100	92.4	97.1	98.4	56	308
Djibouti	5	1.7	16.7	100	33.3	4.6	—	—
Egypt	1,009	3.0	85.2	94.5	92.6	93.8	—	—
Iran	618	3.2	87.1	98.5	100	85.6	—	—
Iraq	476	2.9	84.2	93.3	94.7	89.0	—	—
Pakistan	11,972	16.4	100	85.3	100	100	84	135
Somalia	376	4.8	90.5	94.7	95.2	96.6	—	14
Sudan	733	3.9	100	92.8	94.4	93.6	—	59
Syria	343	5.3	92.9	84.5	78.6	63.6	—	—
Yemen	825	6.8	95.7	77.1	52.2	43.6	—	31
European Region	**158**	**1.5**	**NA**	**92.4**	**NA**	**NA**	**—**	**1**
Tajikistan	83	2.4	60.0	92.8	100	18.1	—	1
Ukraine	75	1.0	24.0	94.5	76.0	19.1	—	—
South-East Asia Region	**186**	**1.3**	**NA**	**86.0**	**NA**	**NA**	**—**	**—**
Burma (Myanmar)¶¶	186	1.3	22.2	86.0	72.2	9.0	—	—
Western Pacific Region	**965**	**2.6**	**NA**	**62.9**	**NA**	**NA**	**—**	**1**
Papua New Guinea	65	1.9	31.8	53.8	27.3	0	—	—
Philippines	900	2.7	58.8	63.6	35.3	15.7	—	1
2021								
African Region	**24,250**	**6.2**	**NA**	**88.8**	**NA**	**NA**	**1**	**538**
Angola	470	3.0	88.9	82.3	66.7	46.7	—	—
Benin	259	4.9	100	88.4	91.7	97.0	—	3
Burkina Faso	1,400	14.5	100	90.2	100	100	—	2
Cameroon	755	6.7	100	82.9	50.0	43.7	—	3
Central African Republic	202	8.9	100	76.7	28.6	35.1	—	—

See table footnotes on the next page.

TABLE 1. (*Continued*) National and subnational acute flaccid paralysis surveillance performance indicators and number of confirmed wild poliovirus and circulating vaccine-derived poliovirus cases, by country — 43 priority countries, World Health Organization African, Eastern Mediterranean, European, South-East Asia, and Western Pacific regions, 2020–2021*

Year/WHO region/Country	No. of AFP cases (all ages)	Regional or national NPAFP rate†	Percentage				No. of confirmed cases	
			Subnational areas with NPAFP rate ≥2§	Regional or national AFP cases with adequate specimens¶	Subnational areas with adequate specimens	Population living in areas meeting both indicators**	WPV	cVDPV††
Chad	1,055	13.6	100	84.6	69.6	70.3	—	—
Congo	178	6.9	100	79.2	58.3	31.9	—	2
Côte d'Ivoire	738	6.6	100	85.0	75.8	81.9	—	—
Democratic Republic of the Congo	3,439	7.9	100	85.3	84.6	91.0	—	28
Equatorial Guinea	15	2.8	42.9	93.3	71.4	38.8	—	—
Ethiopia	1,694	3.7	90.9	91.5	100	94.5	—	10
Guinea	370	6.2	100	79.5	50.0	49.6	—	6
Guinea-Bissau	20	1.9	36.4	65.0	27.3	28.3	—	3
Kenya	657	3.0	78.7	86.3	66.0	52.1	—	—
Liberia	131	6.0	100	99.2	100	100	—	3
Madagascar	602	5.2	100	94.7	100	100	—	13
Malawi	177	1.9	50.0	75.1	50.0	54.8	1	—
Mali	448	4.6	100	84.6	81.8	80.7	—	—
Mauritania	122	6.4	100	86.1	73.3	81.2	—	—
Mozambique	467	3.1	100	73.9	27.3	19.2	—	2
Niger	627	4.9	100	83.6	75.0	75.0	—	17
Nigeria	7,790	8.0	100	93.9	100	100	—	415
Senegal	359	4.5	100	83.6	71.4	77.5	—	17
Sierra Leone	173	5.0	100	85.0	60.0	59.4	—	5
South Sudan	543	8.8	100	89.0	90.0	84.0	—	9
The Gambia	32	3.1	57.1	90.6	57.1	56.2	—	—
Togo	298	8.6	100	91.6	100	100	—	—
Uganda	1,229	5.4	100	90.6	100	100	—	—
Eastern Mediterranean Region	**22,166**	**10.9**	**NA**	**87.8**	**NA**	**NA**	**5**	**71**
Afghanistan	4,095	25.5	100	93.4	100	100	4	43
Djibouti	8	2.7	16.7	75.0	0	0	—	—
Egypt	1,251	3.6	100	90.9	88.9	89.4	—	—
Iran	681	3.5	100	97.5	100	100	—	—
Iraq	709	4.2	94.7	91.1	94.7	85.5	—	—
Pakistan	13,084	18.0	100	85.0	100	100	1	8
Somalia	349	4.6	85.7	96.0	95.2	83.0	—	1
Sudan	637	3.6	100	94.0	100	100	—	—
Syria	431	6.7	92.9	85.4	78.6	61.9	—	—
Yemen	921	7.5	100	81.7	78.3	67.0	—	19
European Region	**294**	**2.4**	**NA**	**91.8**	**NA**	**NA**	**—**	**34**
Tajikistan	178	4.1	100	87.1	80.0	99.7	—	32
Ukraine	116	1.5	32.0	99.1	80.0	35.8	—	2
South-East Asia Region	**33**	**0.2**	**NA**	**84.8**	**NA**	**NA**	**—**	**—**
Burma (Myanmar)¶¶	33	0.2	0	84.8	33.3	0	—	—
Western Pacific Region	**975**	**2.6**	**NA**	**74.6**	**NA**	**NA**	**—**	**—**
Papua New Guinea	52	1.3	27.3	50.0	18.2	0	—	—
Philippines	923	2.7	11.8	76.6	47.1	20.5	—	—

Abbreviations: AFP = acute flaccid paralysis; cVDPV = circulating vaccine-derived poliovirus; NA = not applicable; NPAFP = nonpolio acute flaccid paralysis; WHO = World Health Organization; WPV = wild poliovirus.

* Data as of March 25, 2022.

† Per 100,000 persons aged <15 years per year.

§ For all subnational areas regardless of population size.

¶ Standard WHO target is adequate stool specimen collection from ≥80% of AFP cases, assessed by timeliness and condition. For this analysis, timeliness was defined as two specimens collected ≥24 hours apart (≥1 calendar day in this data set), both within 14 days of paralysis onset. Good condition was defined as arrival of specimens in a WHO-accredited laboratory with reverse cold chain maintained and without leakage or desiccation.

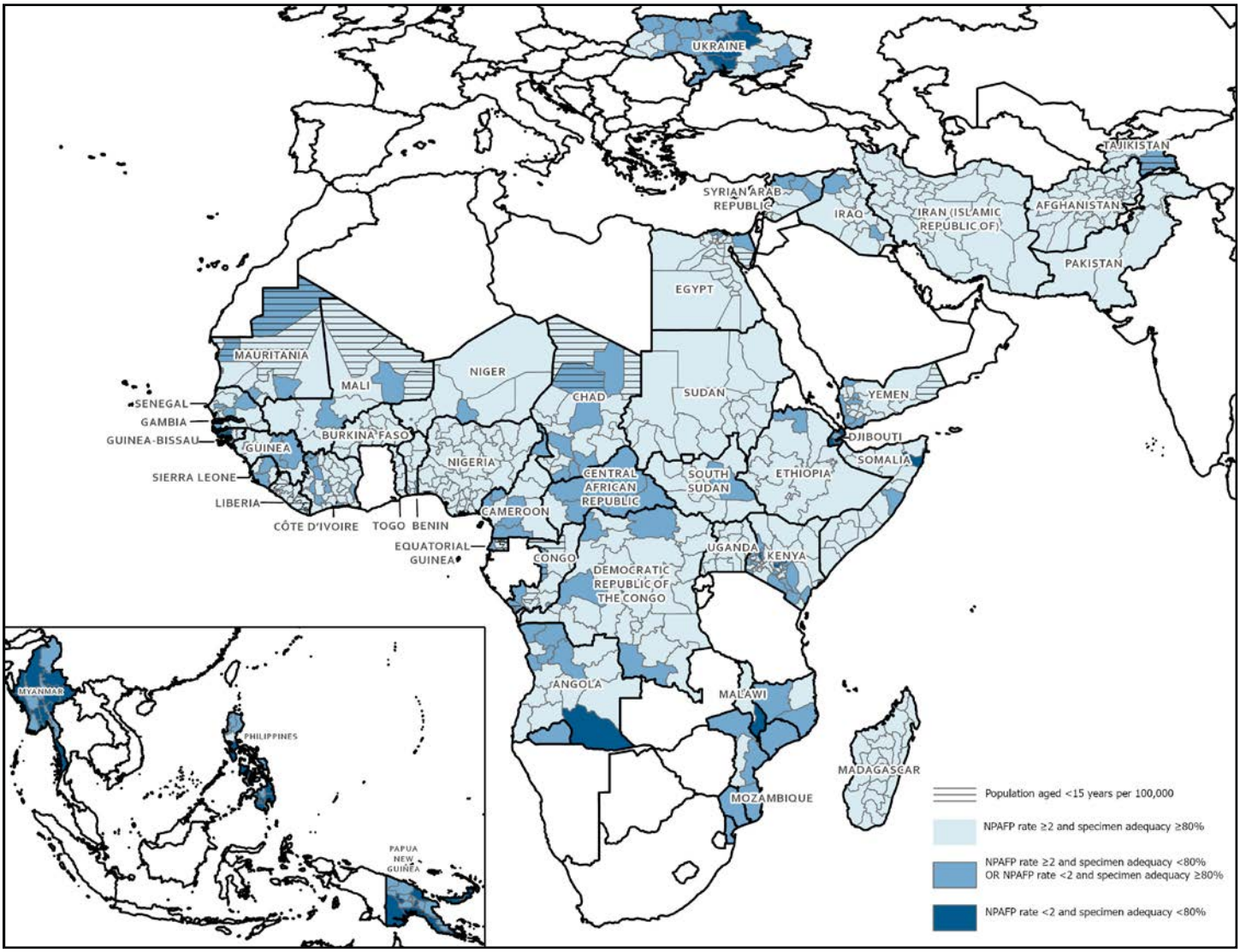
** Percentage of the country's population living in subnational areas that met both surveillance indicators (NPAFP rates ≥2 per 100,000 persons aged <15 years per year and ≥80% of AFP cases with adequate specimens).

†† Includes both cVDPV1 and cVDPV2; cVDPV was associated with ≥1 case of AFP with evidence of community transmission and genetically linked. https://polioeradication.org/wp-content/uploads/2016/09/Reporting-and-Classification-of-VDPVs_Aug2016_EN.pdf

§§ Dashes indicate that no confirmed cases were found.

¶¶ *MMWR* uses the U.S. Department of State's short-form name "Burma"; WHO uses "Myanmar."

FIGURE. Combined performance indicators for the quality of acute flaccid paralysis surveillance* in subnational areas of 43 priority countries — World Health Organization African, Eastern Mediterranean, South-East Asia, and Western Pacific regions, 2021



Abbreviations: AFP = acute flaccid paralysis; NPAFP = nonpolio acute flaccid paralysis; WHO = World Health Organization.

* Targets: ≥2 NPAFP cases per 100,000 persons aged <15 years per year and ≥80% of persons with AFP having two stool specimens collected ≥24 hours apart and within 14 days of paralysis onset, and arrival at a WHO-accredited laboratory by reverse cold chain (storing and transporting samples at recommended temperatures from the point of collection to the laboratory) and in good condition (i.e., without leakage or desiccation).

subnational level, but gaps were apparent in Djibouti. In 2020, a total of 140 WPV1 cases were detected in EMR countries (56 in Afghanistan and 84 in Pakistan), compared with five in 2021 (four in Afghanistan and one in Pakistan). Cases of cVDPV2 in EMR countries declined from 516 in 2020 to 68 in 2021, and cVDPV1 cases declined from 31 in 2020 to three in 2021 (all from Yemen).

European Region. In the WHO European Region (EUR), surveillance performance was assessed in Tajikistan and Ukraine. In 2020 and 2021, Tajikistan met both national indicators, whereas Ukraine met only the stool adequacy target. In Tajikistan, the proportion of the population living in areas that met both indicators increased significantly from 2020 to 2021.

South-East Asia Region. Surveillance performance was assessed in the WHO South-East Asia Region (SEAR), country of Burma (Myanmar),** which met the national stool adequacy target (86.0% and 84.8%, respectively) in both 2020 and

** *MMWR* uses the U.S. Department of State's short-form name "Burma"; WHO uses "Myanmar."

2021, but not the NPAFP rate target (1.3 and 0.2 per 100,000 persons aged <15 years, respectively). Subnational surveillance performance was poor in both years and none of the subnational areas met both surveillance indicator targets in 2021.

Western Pacific Region. In the WHO Western Pacific Region (WPR), surveillance performance was assessed in Papua New Guinea and the Philippines. In 2020 and 2021, the Philippines met the NPAFP rate indicator, and Papua New Guinea did not meet either of the surveillance indicators. None of the subnational areas in Papua New Guinea met the indicator targets in either year; in the Philippines, 20.5% of the population lived in subnational areas in which both surveillance indicators were met in 2021 (Figure). One cVDPV2 case was reported from the Philippines in 2020, but none in 2021.

Genomic sequence analysis identified 43 cVDPV emergence groups globally in active transmission from AFP cases during 2020–2021. These included 30 cVDPV2 and four cVDPV1 emergences in 27 countries in 2020 and 24 cVDPV emergence groups (20 cVDPV2 and 4 cVDPV1) in 22 countries in 2021.

Summary

What is already known about this topic

Acute flaccid paralysis (AFP) surveillance, the primary means of tracking poliovirus transmission, is supplemented by environmental surveillance of sewage samples. The COVID-19 pandemic negatively affected polio surveillance.

What is added by this report?

Analysis of 2020–2021 AFP surveillance data from 43 priority countries experiencing or at high risk for poliovirus transmission found that national AFP surveillance performance improved from 2020 to 2021 in many priority countries, particularly in the World Health Organization's African Region; however, substantial national and subnational gaps persist.

What are the implications for public health practice?

Surveillance gaps need to be identified and addressed to ensure timely detection of poliovirus circulation and achieve eventual eradication.

Environmental Surveillance

Poliovirus environmental surveillance is the systematic collection and testing of sewage specimens to identify poliovirus circulation. Because paralysis occurs in <1% of poliovirus infections, environmental surveillance can detect poliovirus circulation even in the absence of confirmed paralytic polio cases (*6*). During 2020–2021, cVDPV2 was detected by environmental surveillance before identification of a confirmed AFP case in Afghanistan, Liberia, and Senegal, and by environmental surveillance only in Djibouti, Egypt, Gambia, Iran, Mauritania, and Uganda.

In Nigeria, the number of cVDPV2-positive environmental surveillance samples increased from five samples collected from two sites in 2020 to 299 samples collected from 77 sites in 2021. In Afghanistan and Pakistan, the number of cVDPV2-positive samples declined from 310 across 65 sites in 2020 (56% from Afghanistan) to 75 across 30 sites in 2021 (53% from Afghanistan). During 2020–2021, 27 cVDPV emergence groups (24 cVDPV2 and three cVDPV1) were detected in sewage samples collected in 32 countries, including 22 (69%) from AFR, seven (22%) from EMR, two (6%) from WPR, and one (3%) from EUR.

In Afghanistan, WPV1 was isolated from only one environmental surveillance sample in 2021 compared with 35 samples from 15 sites in 2020 (*7*). In Pakistan, WPV1-positive samples also declined from 434 across 67 sites in 2020 to 65 across 34 sites in 2021 (*8*).

Global Polio Laboratory Network

The WHO Global Polio Laboratory Network (GPLN) comprises 145 quality-assured poliovirus laboratories in the six WHO regions. GPLN laboratories implement standardized protocols to 1) isolate polioviruses (all laboratories); 2) conduct intratypic differentiation (ITD) to distinguish between WPV, Sabin (oral poliovirus vaccine) virus, and VDPV (134 laboratories); and 3) conduct genomic sequencing (28 laboratories). Poliovirus transmission pathways are monitored through sequence analysis of the viral protein 1 (VP1) capsid protein from virus isolates. The accuracy and quality of testing at GPLN laboratories are monitored through a comprehensive standardized quality assurance program of onsite reviews and proficiency testing (*9*). A different accreditation checklist with separate timeliness indicators is used for laboratories that conduct environmental surveillance.

GPLN tested 147,582 stool specimens in 2020 and 170,881 in 2021 (Table 2); cVDPVs were isolated from 1,067 AFP cases in 2020 and from 659 in 2021. From 2020 to 2021, the number of cVDPV isolates decreased from 530 to 521 in AFR, from 533 to 70 in EMR, and from two to zero in WPR; the number increased from two to 68 in EUR and was zero for both years in SEAR. During both 2020 and 2021, GPLN laboratories in all regions met the overall timeliness for onset to ITD results (80% of specimens within 60 days), and all but EUR in 2021 met the timeliness indicators for poliovirus isolation (80% of specimens within 14 days), 79% on time.

Since 2017, the WPV1 South Asia genotype is the only WPV1 genotype that has been detected globally. Orphan isolates (isolates with ≤98.5% genetic identity in the VP1 capsid region, compared with other isolates) accounted for 18 of 140 (13%) WPV1 isolates from AFP patients in 2020 and two of six (33%) in 2021.

TABLE 2. Number of poliovirus isolates from stool specimens of persons with acute flaccid paralysis and timing of results, by World Health Organization region — worldwide, 2020 and 2021*

WHO region/Year	No. of specimens	No. of poliovirus isolates			% Poliovirus isolation results on time**	% ITD results within 7 days of receipt at laboratory††	% ITD results within 60 days of paralysis onset
		Wild†	Sabin§	cVDPV¶			
African Region							
2020	47,914	0	3,314	530	91	91	80
2021	58,004	1	3,396	521	89	79	85
American Region							
2020	1,066	0	12	0	81	82	82
2021	1,152	0	6	0	83	100	100
Eastern Mediterranean Region							
2020	40,179	245§§	1,311	533	96	61	95
2021	43,370	5	1,050	70	97	97	94
European Region							
2020	2,016	0	24	2	89	73	82
2021	2,350	0	53	68	79	96	95
South-East Asia Region							
2020	44,799	0	1,315	0	94	95	90
2021	53,649	0	1,030	0	93	89	90
Western Pacific Region							
2020	11,608	0	124	2	96	100	84
2021	12,356	0	58	0	97	100	99
Total¶¶							
2020	**147,582**	**245**	**6,100**	**1,067**	**94**	**84**	**92**
2021	**170,881**	**6**	**5,593**	**659**	**93**	**84**	**88**

Abbreviations: AFP = acute flaccid paralysis; cVDPV = circulating vaccine-derived poliovirus; ITD = intratypic differentiation; VDPV = vaccine-derived poliovirus; WHO = World Health Organization; VP1 = viral protein 1; WPV = wild poliovirus.

* Data as of March 31, 2022.

† Number of AFP cases with WPV isolates.

§ Either 1) concordant Sabin-like results in ITD test and VDPV screening, or 2) ≤1% VP1 nucleotide sequence difference compared with Sabin vaccine virus (≤0.6% for type 2).

¶ Includes both cVDPV1 and cVDPV2. For cVDPV types 1 and 3, ≥10 VP1 nucleotide differences from the respective poliovirus; for cVDPV2, ≥6 VP1 nucleotide differences from Sabin type 2 poliovirus.

** Results reported within 14 days of receipt of specimen.

†† Results of ITD reported within 7 days of receipt of specimen.

§§ Number of specimens with WPV isolates.

¶¶ For the last three indicators, total represents weighted mean percentage of regional performance.

Discussion

All priority countries faced setbacks in surveillance performance in 2020 because of the COVID-19 pandemic and associated risk mitigation measures (*3*); in 2021, AFP surveillance performance indicators rebounded in many countries. Several AFR countries' subnational performance on surveillance indicators in 2021 improved compared with their prepandemic performance in 2019, including Burkina Faso, Côte d'Ivoire, Democratic Republic of the Congo, and Niger (*4*). Subnational surveillance gaps were apparent among one or more priority countries in each WHO region that included a priority country. Although WPV1 cases significantly declined in 2021, the recent detection of a WPV1 case in Malawi demonstrates that all countries remain at risk for WPV1 until global transmission is interrupted and underscores the critical importance of maintaining sensitive poliovirus surveillance in all countries, even those considered to be at low risk. An updated Global Polio Surveillance Action Plan for 2022–2024 was developed to guide and monitor surveillance system improvements at all levels of the GPEI (*10*); the plan is applicable globally but focuses on 30 priority countries.

The findings in this report are subject to at least three limitations. First, issues related to security and hard-to-access populations could affect AFP surveillance and limit interpretation of surveillance indicators. Second, high NPAFP rates do not necessarily indicate highly sensitive surveillance because not all reported AFP cases might meet the case definition, some actual AFP cases might go undetected, and background NPAFP rates might vary. Finally, the accuracy of stool specimen adequacy depends on whether the field investigator can elicit an accurate paralysis onset date.

High-quality surveillance is critical to reaching the milestone of global polio eradication and includes timely and effective AFP case detection, notification, and investigation; specimen transport; and laboratory testing. Frequent monitoring of surveillance indicators could help identify gaps, guide improvements, and

enhance the overall sensitivity and timelines of poliovirus detection to successfully achieve polio eradication.

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COVID-19 Mortality and Vaccine Coverage — Hong Kong Special Administrative Region, China, January 6, 2022–March 21, 2022

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On January 6, 2022, a cluster of COVID-19 cases* caused by the Omicron variant of SARS-CoV-2, the virus that causes COVID-19, was detected in Hong Kong Special Administrative Region, China (Hong Kong), resulting in the territory's fifth wave of COVID-19 cases (*1*). This wave peaked on March 4, 2022, with 8,764 COVID-19 cases per million population (*2*), resulting in a total of 1,049,959 cases and 5,906 COVID-19–associated deaths reported to the Hong Kong Department of Health during January 6–March 21, 2022.† Throughout this period, the COVID-19 mortality rate in Hong Kong (37.7 per million population) was among the highest reported worldwide since the COVID-19 pandemic began (*3*). Publicly available data on age-specific vaccination coverage in Hong Kong with a 2-dose primary vaccination series (with either Sinovac-CoronaVac [Sinovac], an inactivated COVID-19 viral vaccine, recommended for persons aged ≥3 years or BNT162b2 [Pfizer-BioNTech], an mRNA vaccine, for persons aged ≥5 years), as of December 23, 2021,§,¶ and COVID-19 mortality during January 6–March 21, 2022, were analyzed. By December 23, 2021, 67% of vaccine-eligible persons in Hong Kong had received ≥1 dose of a COVID-19 vaccine, 64% had received ≥2 doses, and 5% had received a booster dose. Among persons aged ≥60 years, these proportions were 52%, 49%, and 7%, respectively. Among those aged ≥60 years, vaccination coverage declined with age: 48% of persons aged 70–79 years had received ≥1 dose, 45% received ≥2 doses, and 7% had received a booster, and among those aged ≥80 years, 20%, 18%, and 2% had received ≥1 dose, ≥2 doses, and a booster dose, respectively. Among 5,906 COVID-19 deaths reported, 5,655 (96%) occurred in persons aged ≥60 years**; among these decedents, 3,970 (70%) were unvaccinated, 18% (1,023) had received 1 vaccine dose, and 12% (662) had received ≥2 doses. The overall rates of COVID-19–associated mortality among persons aged ≥60 years who were unvaccinated, who had received 1 COVID-19 vaccine dose, and who had received ≥2 vaccine doses were 10,076, 1,099, and 473 per million population, respectively; the risk for COVID-19–associated death among unvaccinated persons was 21.3 times that among recipients of 2–3 doses in this age group. The high overall mortality rate during the ongoing 2022 Hong Kong Omicron COVID-19 outbreak is being driven by deaths among unvaccinated persons aged ≥60 years. Efforts to identify and address gaps in age-specific vaccination coverage can help prevent high mortality from COVID-19, especially among persons aged ≥60 years.

The Chinese Center for Disease Control and Prevention and the U.S. CDC conducted a descriptive analysis of COVID-19 incidence, mortality, age-specific vaccination coverage, and booster dose coverage after introduction of the Omicron variant in Hong Kong.†† Relative risks were calculated using mortality rates (deaths per million persons) by vaccination status and age, with the referent groups being ≥2-dose recipients; persons aged <30 years; or, within specific age groups, receipt of ≥2 vaccine doses. Data were obtained from publicly available sources, primarily the Hong Kong Department of Health (*2*) and Our World in Data (*3*). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.§§

* A hotel cluster of COVID-19 cases on January 6, 2022, is thought to have been the origin of the fifth wave of cases, based on genomic surveillance data from sequences uploaded to GISAID. Before January 6, previous Omicron cases with different sequences were detected from sporadic introduction and community transmission (https://www.ceo.gov.hk/eng/pdf/article20220128.pdf); 50 cases were detected as of December 28, 2021 (https://www.ceo.gov.hk/eng/pdf/article20211228.pdf).

† Daily new confirmed COVID-19 cases and deaths per million persons listed are 7-day rolling averages.

§ Vaccination rates and vaccine-derived immunity were calculated 14 days before the introduction of the Omicron variants leading to Hong Kong's fifth wave.

¶ Sinovac is recommended in persons aged ≥3 years. For persons aged ≥18 years, a 28-day interval between the first and second dose, a 28-day interval for immunocompromised persons, and a 90-day interval for the general population (priority for those aged ≥60 years) between the second and third dose is recommended; a fourth dose is recommended 90 days after the third dose for immunocompromised persons. Pfizer BioNTech vaccine is recommended for persons aged ≥5 years. For persons aged ≥18 years, a 56-day interval is recommended between the first and second doses, a 28-day interval for those who are immunocompromised, and a 90-day interval for the general population (priority to those aged ≥60 years) between the second and third dose; a fourth dose with an interval of 90 days after the third dose is recommended for immunocompromised persons. https://www.covidvaccine.gov.hk/en/vaccine

** Age was unknown for two unvaccinated decedents.

†† Death counts were obtained from the Hong Kong Department of Health, which provides the most up-to-date mortality data, but these data might differ slightly from other sources because of differences in completeness. The government of Hong Kong has established processes for linking case and vaccination data. COVID-19–associated death is defined as a death in a person who received a positive SARS-CoV-2 test result who died within 28 days of the collection date of the first positive specimen. The underlying cause of death might have been unrelated to COVID-19.

§§ 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.

During February 2020–December 2021, Hong Kong reported 12,649 COVID-19 cases and 213 associated deaths. On January 6, 2022, the first cluster of COVID-19 cases attributable to the Omicron variant were identified in guests in a hotel for compulsory quarantine after arrival in Hong Kong from abroad (*1*). Daily COVID-19 incidence increased sharply, from 1.7 per million population on January 6 to a peak of 8,764.2 per million on March 4, before declining to 2,716.0 by March 21, 2022. By February 14, 2022, 100% of sequenced isolates were Omicron variant, BA.2 lineage.

As of December 23, 2021, two thirds (67%) of vaccine-eligible persons overall in Hong Kong had received ≥1 COVID-19 vaccine dose, 64% had received ≥2 doses, and 5% had received a booster dose (Table 1). Vaccination coverage varied by age; among persons aged 30–59 years, 82%, 80%, and 5% had received ≥1 dose, ≥2 doses, and a booster dose, respectively. Among persons aged ≥60 years, approximately one half (52% and 49%) had received ≥1 and ≥2 vaccine doses, respectively, and 7% had received a booster dose. Coverage declined with increasing age: 48% of persons aged 70–79 years and 20% of those aged ≥80 years had received ≥1 vaccine dose, 45% and 18% had received ≥2 doses, and 7% and 2% had received a booster dose.

A total of 5,906 COVID-19–related deaths were reported in Hong Kong during January 6–March 21, 2022 (Table 2). The daily mortality rate increased from zero on January 6 to 34.8 per million on March 21 and peaked at 37.7 on March 14. Among all deaths, 4,118 (70%) occurred in unvaccinated persons and 5,655 (96%) occurred in persons aged ≥60 years. Unvaccinated decedents aged ≥60 years (3,970) accounted for 67% of total deaths, and among the 5,655 deaths in persons aged ≥60 years, 70% were in unvaccinated persons. Unvaccinated decedents aged ≥70 years (3,661) and ≥80 years (3,036) accounted for 62% and 51% of all deaths, respectively.

Overall, the relative risk of dying from COVID-19 among unvaccinated persons in Hong Kong was 33.2 times the risk among persons who received ≥2 doses (Table 3). Compared with persons aged <30 years, mortality risk among those aged ≥60 years was 252.7 times as high, and among persons aged ≥80 years was 946.2 times as high. Among persons aged ≥60 years, the relative risks for death among those who were unvaccinated were 21.3 times the risk among persons who had received ≥2 doses and 2.3 times the risk among those who had received 1 vaccine dose.

Discussion

After the emergence of the Omicron variant in Hong Kong in early January 2022, COVID-19 cases increased rapidly, resulting in 5,906 deaths as of March 21, 2022. At the start of this outbreak, immunity in Hong Kong was presumed to be predominantly vaccine-derived as a result of a dynamic COVID-Zero strategy, whereby after successful containment, every case is investigated, and measures are implemented to interrupt onward transmission (*4*). Although overall 2-dose vaccination coverage was 64%, rates varied between age groups and were lower among older adults: 2-dose vaccination coverage was 63% among persons aged 60–69 years, 45% among those aged 70–79 years, and 18% among those aged ≥80 years. New Zealand, a country with a much lower population density than Hong Kong, also had largely vaccine-derived immunity. Although New Zealand's 2-dose COVID-19 vaccination coverage was 95% among persons aged ≥60 years, the country experienced a similar increase in incidence after introduction of Omicron; however, mortality in New Zealand peaked at 2.1 per million population per day compared with 38.0 in Hong Kong (*5*). These findings align with data from existing studies indicating that the risk for death from

TABLE 1. COVID-19 vaccination coverage, by age group — Hong Kong Special Administrative Region, China, December 23, 2021

	No. of doses received/vaccination coverage*		
Age group, yrs	≥1 dose no./total no. (%)	≥2 doses no./total no. (%)	Booster† no./total no. (%)
3–29	980,945/1,784,800 (55)	869,096/1,784,800 (49)	14,471/1,784,800 (0.8)
3–19	345,393/976,100 (35)	255,510/976,100 (26)	730/976,100 (0.1)
20–29	635,552/808,700 (79)	613,586/808,700 (76)	13,741/808,700 (2.0)
30–59	2,817,846/3,443,000 (82)	2,751,916/3,443,000 (80)	171,899/3,443,000 (5.0)
30–39	889,354/1,126,300 (79)	864,294/1,126,300 (77)	32,943/1,126,300 (3.0)
40–49	983,239/1,142,500 (86)	963,035/1,142,500 (84)	63,356/1,142,500 (6.0)
50–59	945,253/1,174,200 (81)	924,587/1,174,200 (79)	75,600/1,174,200 (6.0)
≥60	1,049,110/2,034,100 (52)	1,004,606/2,034,100 (49)	145,989/2,034,100 (7.0)
60–69	701,148/1,071,800 (65)	679,592/1,071,800 (63)	96,451/1,071,800 (9.0)
70–79	266,706/560,500 (48)	253,378/560,500 (45)	39,761/560,500 (7.0)
≥80	81,256/401,800 (20)	71,635/401,800 (18)	9,777/401,800 (2.0)
Total	**4,847,901/7,261,900 (67)**	**4,625,618/7,261,900 (64)**	**332,359/7,261,900 (5.0)**

Source: COVID-19 Vaccination Programme. https://www.covidvaccine.gov.hk
* Total persons vaccinated divided by total population in the age group.
† In Hong Kong, booster doses are considered third and fourth doses after the 2-dose primary COVID-19 vaccination series vaccines.

COVID-19 increases with age and reinforce the effectiveness of vaccination in preventing death from the Omicron variant in older adults (*6*,*7*).

COVID-19 vaccine-induced immunity wanes over time, but booster vaccinations can elicit a strong immune response and restore vaccine effectiveness (*7*). At the beginning of the Omicron wave in Hong Kong, only 7% of persons aged ≥60 years had received a booster dose, including just 2% of those aged ≥80 years. The primary series of COVID-19 vaccines plus a booster dose is more effective at preventing severe outcomes caused by the Omicron variant than a primary series alone (*8*). In addition to the low vaccination coverage among persons aged ≥60 years, waning immunity since the last vaccine dose could have contributed to COVID-19–associated mortality in Hong Kong.

The reasons for low COVID-19 vaccination coverage among older persons in Hong Kong are not clear. Low vaccine confidence has presented major hurdles for governments aiming to reduce COVID-19 transmission and mortality. A June 2021 survey in Hong Kong found that 56.8% of participants were hesitant about or resistant to receiving a COVID-19 vaccine (*9*). The dynamic COVID-Zero strategy, successful until the emergence of the Omicron variant, might have resulted in further complacency, particularly among older persons. A survey conducted during November 2020–January 2021 in China found that older adults were more likely to accept a COVID-19 vaccine if they perceived themselves to be at high risk for infection or had trust in the government (*10*). Experience with the COVID-19 pandemic can motivate public health officials to increase vaccine distribution and coverage. Hong Kong targeted older persons for vaccination during the outbreak. As of March 21, 2022, 2-dose COVID-19 vaccination coverage in Hong Kong has increased substantially, to 81% among persons aged 60–69 years, 69% among persons aged 70–79 years, and 39% among persons aged ≥80 years (*3*).

Summary

What is already known about this topic?

COVID-19 vaccines are important tools to protect populations from severe disease and death.

What is added by this report?

Among persons aged ≥60 years in Hong Kong, 49% had received ≥2 doses of a COVID-19 vaccine, and vaccination coverage declined with age. During January–March 2022, reported COVID-19–associated deaths rose rapidly in Hong Kong. Among these deaths, 96% occurred in persons aged ≥60 years; within this age group, the risk for death was 20 times lower among those who were fully vaccinated compared with those who were unvaccinated.

What are the implications for public health practice?

Efforts to identify and address gaps in age-specific vaccination coverage can help prevent high mortality from COVID-19, especially in older adults.

The findings in this report are subject to at least four limitations. First, summary-level data were analyzed, and other risk factors for death, including comorbidities, could not be examined. Second, completeness of reporting of COVID-19–attributed deaths is unknown. Third, immunity due to previous infection could not be assessed; however, such immunity was likely low given that few cases had been reported during previous waves (*4*). Finally, vaccine effectiveness can vary by type and timing of vaccination, which were not accounted for in this analysis.

TABLE 2. COVID-19–associated mortality,* by age group and vaccination status — Hong Kong Special Administrative Region, China, January 6–March 21, 2022

Age group, yrs	Total no. of deaths† (% of total)	Age-specific mortality*	No. of deaths, by no. of vaccine doses			Mortality,* by no. of vaccine doses		
			None	1	≥2	None	1	≥2
Total	**5,906 (100)**	**799**	**4,118**	**1,068**	**720**	**4,277**	**317**	**129**
<30	21 (0.4)	11	13	4	4	29	6	4
<3	1 (0.0)	8	1	0	0	8	0	0
3–11	5 (0.1)	9	3	2	0	13	8	0
12–19	5 (0.1)	11	3	1	1	158	7	3
20–29	10 (0.2)	12	6	1	3	92	4	4
30–59	228 (4.0)	66	133	41	54	1,039	23	17
30–39	15 (0.3)	13	8	3	4	140	6	4
40–49	43 (0.7)	38	30	4	9	1,000	6	8
50–59	170 (2.9)	145	95	34	41	2,317	52	39
≥60	5,655 (95.9)	2,780	3,970	1,023	662	10,076	1,099	473
60–69	496 (8.4)	463	309	94	93	2,784	168	108
70–79	977 (16.5)	1,743	625	201	151	5,841	786	396
≥70	5,159 (87.4)	5,363	3,661	929	569	12,936	2,490	1,061
≥80	4,182 (70.8)	10,408	3,036	728	418	17,250	6,207	2,696

* Deaths per million population.
† Age was unknown for two unvaccinated decedents.

TABLE 3. COVID-19 mortality* and relative mortality risk† among persons aged <30 years, 30–59 years, and ≥60 years, overall and by age and vaccination status — Hong Kong Special Administrative Region, China, January 6–March 21, 2022

Characteristic	Mortality rate*	Relative mortality risk†
Overall no. of COVID-19 vaccine doses received		
≥2	129	Ref
1	317	2.5
0	4,277	33.2
All vaccination groups, by age group, yrs		
<30	11	Ref
30–59	66	6
≥60	2,780	252.7
60–69	463	42.1
70–79	1,743	158.5
≥80	10,408	946.2
No. of doses received, by age group, yrs		
<30		
≥2	4	Ref
1	6	1.5
0	29	7.3
30–59		
≥2	17	Ref
1	23	1.4
0	1,039	61.1
≥60		
≥2	473	Ref
1	1,099	2.3
0	10,076	21.3
60–69		
≥2	108	Ref
1	168	1.6
0	2,784	25.8
70–79		
≥2	396	Ref
1	786	2.0
0	5,841	14.7
≥80		
≥2	2,696	Ref
1	6,207	2.3
0	17,250	6.4

Abbreviation: Ref = referent group.
* Deaths per million population.
† Compared with referent group of ≥2 doses.

During January–March 2022, data from Hong Kong suggested that higher mortality rates were driven by low vaccination coverage among older adults. These data underscore the importance of monitoring age-specific vaccination coverage and implementing strategies that increase COVID-19 vaccination coverage among all population groups, especially those most at risk for severe illness. Efforts to identify disparities in age-specific vaccination rates and address gaps in vaccination coverage among groups at high risk can help prevent high mortality from COVID-19, especially in older adults.

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Effectiveness of COVID-19 mRNA Vaccination in Preventing COVID-19–Associated Hospitalization Among Adults with Previous SARS-CoV-2 Infection — United States, June 2021–February 2022

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Previous infection with SARS-CoV-2, the virus that causes COVID-19, has been estimated to confer up to 90% protection against reinfection, although this protection was lower against the Omicron variant compared with that against other SARS-CoV-2 variants (*1*–*3*). A test-negative design was used to estimate effectiveness of COVID-19 mRNA vaccines in preventing subsequent COVID-19–associated hospitalization among adults aged ≥18 years with a previous positive nucleic acid amplification test (NAAT) or diagnosis of COVID-19.† The analysis used data from Cosmos, an electronic health record (EHR)–aggregated data set (*4*), and compared vaccination status of 3,761 case-patients (positive NAAT result associated with hospitalization) with 7,522 matched control-patients (negative NAAT result). After previous SARS-CoV-2 infection, estimated vaccine effectiveness (VE) against COVID-19–associated hospitalization was 47.5% (95% CI = 38.8%–54.9%) after 2 vaccine doses and 57.8% (95% CI = 32.1%–73.8%) after a booster dose during the Delta-predominant period (June 20–December 18, 2021), and 34.6% (95% CI = 25.5%–42.5%) after 2 doses and 67.6% (95% CI = 61.4%–72.8%) after a booster dose during the Omicron-predominant period (December 19, 2021–February 24, 2022). Vaccination provides protection against COVID-19–associated hospitalization among adults with previous SARS-CoV-2 infection, with the highest level of protection conferred by a booster dose. All eligible persons, including those with previous SARS-CoV-2 infection, should stay up to date with vaccination to prevent COVID-19–associated hospitalization.

Data were obtained from Cosmos (*4*), an EHR data set that includes information from more than 135 million patients and 154 health care organizations in the United States.§ Patients eligible for inclusion in the analysis met the following four criteria: 1) age ≥18 years, 2) residence in the United States, 3) at least one hospital admission for a COVID-19–like illness,¶ with a hospitalization-associated NAAT performed from 10 days before through 3 days after admission during June 20, 2021–February 24, 2022, and 4) a previous positive NAAT result or diagnostic code of COVID-19 (with or without hospitalization) >90 days before the date of the NAAT associated with the subsequent hospitalization.** Patients under the billing category of "observation" and patients who were admitted and discharged on the same day were excluded. Vaccination status was categorized on the day of the NAAT associated with the hospitalization as 1) unvaccinated, 2) after dose 1, 3) after dose 2, or 4) after a booster dose††; patients were excluded if

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† A test-negative design is a type of vaccine effectiveness study that compares the vaccination status of persons who seek testing in the same way (in this study, with COVID-19–like illness) and received either positive results (case-patients) or negative results (control-patients). Potential selection bias is limited by including patients who receive positive or negative test results but are otherwise similar. Vaccine effectiveness is estimated as the percentage of protection by being in a specified vaccination group compared with a referent group.

§ Cosmos is an aggregated EHR data platform of participating health systems that use software provided by Epic Systems Corporation that includes more than 135 million patients with similar demographics to U.S. Census data. Of 154 health systems included in the Cosmos dataset, 130 health systems that had data available since 2019 were included in the current analysis. https://epicresearch.org/about-cosmos

¶ COVID-19–like illness diagnoses included acute respiratory illness (e.g., COVID-19, respiratory failure, or pneumonia) or related signs or symptoms (cough, fever, dyspnea, vomiting, or diarrhea) using diagnosis codes from the *International Classification of Diseases, Tenth Revision*.

** COVID-19 was defined as a clinical encounter with any of the following *International Classification of Diseases, Tenth Revision* diagnostic codes: U07.1, J12.81, and J12.82. A difference of >90 days was used consistent with the Council of State and Territorial Epidemiologists case definition of COVID-19: https://ndc.services.cdc.gov/case-definitions/coronavirus-disease-2019-2021/.

†† Patients were categorized on the date of NAAT associated with hospitalization as unvaccinated if no COVID-19 vaccine had been received; after dose 1 if ≥14 days had elapsed since receipt of the first dose of an mRNA COVID-19 vaccine and before any second dose; and after dose 2 if ≥14 days had elapsed since completion of a second mRNA vaccine dose, and no subsequent dose was received. To limit early additional doses (for example, among immunocompromised persons), patients were categorized as after booster if ≥14 days had elapsed since receipt of an mRNA booster dose administered ≥5 months after a second dose, and if no further doses had been received. Patients were excluded from the analysis if they received a non-mRNA COVID-19 vaccine; the day of the NAAT-associated hospitalization was <14 days after dose 1, dose 2 or a booster dose; dose 2 was received <14 days after dose 1; any booster dose was <5 months after dose 2; they received >3 doses of vaccine; or their previous positive NAAT or COVID-19 diagnosis was after the most recent vaccine dose. In addition, if patients had more than one hospitalization-associated NAAT, they were considered a case-patient if their NAAT was positive at any point and were excluded from being a control-patient, (i.e., cases-patients could not also serve as control-patients).

they did not meet one of these definitions or if the previous positive NAAT result or COVID-19 diagnosis was after the date of the most recent vaccine dose. Vaccination information was collected during the 14 days after hospitalization or other health care visit from a patient's health system, other health systems via clinical record exchanges, state registries, and patient-reported history.[§§]

VE was estimated using conditional logistic regression, comparing the vaccination status among case-patients and control-patients. VE after each vaccine dose was estimated using the unvaccinated group as a referent. For estimation of relative VE after a booster dose, the referent group had received dose 2 (but not a booster dose) ≥5 months previously. Eligible case-patients were matched with control-patients using a 1:2 ratio by 2-week period of the hospitalization-associated NAAT, 10-year age group, and state of residence. After matching, estimates were adjusted for sex, race/ethnicity, number of clinical encounters during 2019, number of underlying health conditions, and days since the previous infection.[¶¶] The period June 20–December 18, 2021, was categorized as Delta-predominant, and the period December 19, 2021–February 24, 2022, as Omicron-predominant; periods were defined as range of dates when estimated national prevalence of a SARS-CoV-2 variant exceeded 50%.[***] In a sensitivity analysis, VE was also estimated defining previous infection as a positive NAAT result. Wilcoxon rank-sum tests and chi-square tests were used to compare group medians and proportions, respectively; p-values <0.05 were considered statistically significant. Data were analyzed using R software (version 4.1.2; R Foundation). This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[†††]

Among 5,116,024 adults aged ≥18 years with an initial positive NAAT result or diagnosis of COVID-19, 51,609 patients were hospitalized with COVID-19–like illness associated with a NAAT result >90 days after the previous infection,[§§§] including 5,048 (9.8%) with a positive NAAT result. Among these 5,048 case-patients, 2,436 (48.3%; median = 67 reinfections per week) were admitted during the Delta-predominant period, and 2,612 (51.7%; median = 343 reinfections per week) during the Omicron-predominant period (Supplementary Figure, https://stacks.cdc.gov/view/cdc/116026).

After 7,569 patients were excluded, 11,283 of 44,040 eligible patients were matched and included in the analysis, 3,761 (87.1%) of 4,319 eligible case-patients and 7,522 (18.9%) of 39,721 eligible control-patients. Case- and control-patients were demographically similar, with fewer underlying conditions and previous health care encounters among case-patients (Table 1). Overall, 61.2% of case-patients were unvaccinated, 4.3% had received 1 vaccine dose, 27.6% had received 2 doses, and 6.9% had received a booster dose, compared with 47.5%, 5.5%, 33.2%, and 13.9% of control-patients, respectively.

During the Delta-predominant period, estimated adjusted VE was 58.8% (95% CI = 41.3%–71.1%) after dose 1, 47.5% (95% CI = 38.8%–54.9%) after dose 2, and 57.8% (95% CI = 32.1%–73.8%) after a booster dose; during the Omicron-predominant period, adjusted VE was 33.0% (95% CI = 15.0%–47.2%) after dose 1, 34.6% (95% CI = 25.5%–42.5%) after dose 2, and 67.6% (95% CI = 61.4%–72.8%) after a booster dose (Table 2). VE estimates were similar whether hospitalizations were <90 days or ≥90 days after the most recent vaccine dose. Similar estimates were obtained in a sensitivity analysis that included 2,146 case-patients and 4,887 control-patients with previous infection confirmed by NAAT (Supplementary Table, https://stacks.cdc.gov/view/cdc/116025).

During the analysis period, among persons who had a previous positive NAAT result or COVID-19 diagnosis before the first vaccine dose, estimated VE was 43.1% (95% CI = 30.7%–53.2%) after dose 1, 41.7% (95% CI = 35.5%–47.3%) after dose 2, and 70.3% (95% CI = 64.1%–75.4%) after a booster dose (Table 3). Among persons whose initial infection occurred between dose 2 and a booster dose, VE after the booster dose was 50.0% (95% CI = 26.9%–65.8%). Estimated VE of a booster dose was similar among persons aged <65 years (67.7%; 95% CI = 57.7%–75.3%) and ≥65 years (64.5%; 95% CI 56.0%–71.4%). Relative VE of a booster dose compared with ≥5 months after dose 2 was 55.9% (95% CI = 43.6%–65.5%).

[§§] Vaccination information for each patient was collected from four sources: 1) vaccine doses administered within the health system, 2) electronic health records, 3) vaccination information obtained from other health systems using a shared data platform, and 4) vaccination information obtained directly from a state or other vaccine registry.

[¶¶] Characteristics were classified on the date of the NAAT associated with the hospital admission. Underlying conditions were extracted from EHR clinical encounter data and were based on a CDC list of conditions associated with the highest risk for COVID-19 (https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html, accessed March 23, 2022) and included the following: alcoholic liver disease, autoimmune hepatitis, bronchiectasis, bronchopulmonary dysplasia, cancer, cardiomyopathy, cerebrovascular disease, chronic kidney disease, cirrhosis, chronic obstructive pulmonary disease, coronary artery disease, current smoker, receipt of nontopical glucocorticoids within the previous 12 months, heart failure, HIV, immune deficiency, receipt of immunosuppressive medications within the previous 12 months, interstitial lung disease, nonalcoholic fatty liver disease, obesity, pulmonary arterial hypertension, pulmonary embolus, pregnancy, solid organ transplant, tuberculosis, and type 1 or 2 diabetes.

[***] https://covid.cdc.gov/covid-data-tracker/#variant-proportions

[†††] 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.

[§§§] Among 25,641 patients with a positive NAAT >90 days after an initial positive SARS-CoV-2 NAAT or diagnosis of COVID-19 during June 20–December 31, 2021, 2,378 (9.3%) were admitted to a hospital with COVID-19–like illness between 10 days after and 3 days before the subsequent positive NAAT result, indicating reinfection with COVID-19–associated hospitalization.

TABLE 1. Characteristics of hospitalized adults with previous SARS-CoV-2 infection,* by subsequent nucleic acid amplification test result†—United States, June 2021–February 2022§

Characteristic	No. (column %) Total (N = 11,283)	Case-patients (NAAT-positive)¶ (n = 3,761)	Control-patients (NAAT-negative)¶ (n = 7,522)	p-value**
Age group, yrs				
18–29	**993 (8.8)**	331 (8.8)	662 (8.8)	>0.990
30–44	**1,717 (15.2)**	573 (15.2)	1,144 (15.2)	
45–64	**3,804 (33.7)**	1,273 (33.8)	2,531 (33.6)	
≥65	**4,769 (42.3)**	1,584 (42.1)	3,185 (42.3)	
Sex				
Women	**6,391 (56.6)**	2,114 (56.2)	4,277 (56.9)	0.510
Men	**4,892 (43.4)**	1,647 (43.8)	3,245 (43.1)	
Race and ethnicity				
White, non-Hispanic	**6,963 (61.7)**	2,286 (60.8)	4,677 (62.2)	0.026
Black, non-Hispanic	**2,821 (25.0)**	924 (24.6)	1,897 (25.2)	
Hispanic	**1,131 (10.0)**	413 (11.0)	718 (9.5)	
Other, non-Hispanic††	**368 (3.3)**	138 (3.7)	230 (3.1)	
Underlying health conditions§§				
0	**536 (4.8)**	198 (5.3)	338 (4.5)	<0.001
1	**1,610 (14.3)**	641 (17.0)	969 (12.9)	
>1	**9,137 (81.0)**	2,922 (77.7)	6,215 (82.6)	
Vaccination status¶¶				
Unvaccinated	**5,874 (52.1)**	2,303 (61.2)	3,571 (47.5)	<0.001
Any mRNA vaccine, 1 dose	**574 (5.1)**	161 (4.3)	413 (5.5)	
Any mRNA vaccine, 2 doses	**3,534 (31.3)**	1,038 (27.6)	2,496 (33.2)	
Any mRNA vaccine, booster dose	**1,301 (11.5)**	259 (6.9)	1,042 (13.9)	
Clinical encounters during 2019				
0	**2,403 (21.3)**	781 (20.8)	1,622 (21.6)	<0.001
1–9	**4,199 (37.2)**	1,628 (43.3)	2,571 (34.2)	
≥10	**4,681 (41.5)**	1,352 (35.9)	3,329 (44.3)	
Month of hospital admission				
Jun 2021	**156 (1.4)**	54 (1.4)	102 (1.4)	0.930
Jul 2021	**528 (4.7)**	179 (4.8)	349 (4.6)	
Aug 2021	**982 (8.7)**	320 (8.5)	662 (8.8)	
Sep 2021	**874 (7.7)**	294 (7.8)	580 (7.7)	
Oct 2021	**621 (5.5)**	204 (5.4)	417 (5.5)	
Nov 2021	**583 (5.2)**	198 (5.3)	385 (5.1)	
Dec 2021	**1,875 (16.6)**	601 (16.0)	1,274 (16.9)	
Jan 2022	**4,555 (40.4)**	1,548 (41.2)	3,007 (40.0)	
Feb 2022	**1,109 (9.8)**	363 (9.7)	746 (9.9)	

See table footnotes on the next page.

Discussion

Among persons with previous SARS-CoV-2 infection or COVID-19 diagnosis, receipt of a COVID-19 mRNA vaccine provided protection against subsequent COVID-19 hospitalization. The highest level of protection was conferred by a booster vaccine dose, with similar VE during the Delta- and Omicron-predominant periods (approximately 60%–70%). In contrast, VE of 1 or 2 doses declined from 50%–60% during the Delta-predominant to approximately 35% during the Omicron-predominant period. Receiving a booster dose conferred protection even if the previous infection occurred after receipt of the second vaccine dose. Findings from this report indicate that SARS-CoV-2 reinfections leading to COVID-19–associated hospitalizations are preventable by COVID-19 vaccination.

Benefit of vaccination after previous SARS-CoV-2 infection was also indicated by an analysis of surveillance data from New York City that estimated approximately 50%–70% protection against hospitalization from reinfection (*5*). A case-control analysis using surveillance data from Brazil estimated 90% protection by 2 doses of Pfizer-BioNTech vaccine against hospitalization or death after reinfection (*6*); the high estimated VE might partly reflect recent vaccination in the context of potential decreased infection-induced immunity. The similar estimated benefit from 1 or 2 vaccine doses in preventing reinfection leading to hospitalization in the current study is consistent with evidence that vaccination elicits a more rapid immunologic response if preceded by a SARS-CoV-2 infection¶¶¶ (*7*). In the current analysis, a booster dose offered superior protection against reinfection leading to hospitalization.

¶¶¶ https://www.medrxiv.org/content/10.1101/2021.12.23.21268285v1

TABLE 1. (*Continued*) Characteristics of hospitalized adults with previous SARS-CoV-2 infection,* by subsequent nucleic acid amplification test result† — United States, June 2021–February 2022§

Characteristic	No. (column %) Total (N = 11,283)	Case-patients (NAAT-positive)¶ (n = 3,761)	Control-patients (NAAT-negative)¶ (n = 7,522)	p-value**
Hospitalization variant predominance period* **				
B.1.617.2 (Delta)	**4,385 (38.9)**	1,437 (38.2)	2,948 (39.2)	0.310
B.1.1.529 (Omicron)	**6,898 (61.1)**	2,324 (61.8)	4,574 (60.8)	
U.S. Census region				
Northeast	**2,340 (20.7)**	780 (20.7)	1,560 (20.7)	
Midwest	**3,300 (29.2)**	1,100 (29.2)	2,200 (29.2)	>0.990
South	**5,133 (45.5)**	1,711 (45.5)	3,422 (45.5)	
West	**510 (4.5)**	170 (4.5)	340 (4.5)	
Initial infection variant predominance period* **				
Pre-Delta*	**9,593 (85.0)**	3,226 (85.8)	6,367 (84.6)	0.110
B.1.617.2 (Delta)[5]	**1,690 (15.0)**	535 (14.2)	1,155 (15.4)	
Initial diagnosis source*				
COVID-19 diagnosis	**4,250 (37.7)**	1,615 (42.9)	2,635 (35.0)	<0.001
NAAT result	**1,013 (9.0)**	317 (8.4)	696 (9.3)	
Both	**6,020 (53.4)**	1,829 (48.6)	4,191 (55.7)	
Initial infection to NAAT associated with hospitalization, days†				
90–119	**735 (6.5)**	287 (7.6)	448 (6.0)	<0.001
120–179	**1,389 (12.3)**	479 (12.7)	910 (12.1)	
180–269	**1,787 (15.8)**	552 (14.7)	1,235 (16.4)	
270–364	**2,402 (21.3)**	711 (18.9)	1,691 (22.5)	
≥365	**4,970 (44.0)**	1,732 (46.1)	3,238 (43.0)	

Abbreviation: NAAT = nucleic acid amplification test.

* Initial diagnosis was based on a previous positive SARS-CoV-2 NAAT or clinical diagnosis of COVID-19 >90 days before the date of the NAAT associated with subsequent hospitalization. COVID-19 was defined as a clinical encounter with any of the following *International Classification of Diseases, Tenth Revision* diagnostic codes: U07.1, J12.81, or J12.82.

† Defined as NAAT performed between 10 days before and 3 days after the date of hospital admission with a diagnosis of COVID-19-like illness. COVID-19–like illness diagnoses were defined based on others' methods (https://www.nejm.org/doi/full/10.1056/nejmoa2110362, Supplement Table S2) and included acute respiratory illness (e.g., COVID-19, respiratory failure, or pneumonia) or related signs or symptoms (e.g., cough, fever, dyspnea, vomiting, or diarrhea) using diagnostic codes from the *International Classification of Diseases, Tenth Revision*.

§ Patients were eligible for inclusion if the hospitalization-associated SARS-CoV-2 NAAT was performed during June 20, 2021–February 24, 2022.

¶ Cases had a positive SARS-CoV-2 NAAT result associated with hospitalization; controls had a negative SARS-CoV-2 NAAT result associated with hospitalization.

** Wilcoxon rank-sum tests and chi-square tests were used to compare medians and proportions, respectively; p-values <0.05 were considered statistically significant.

†† Other non-Hispanic includes Asian, Native Hawaiian or other Pacific Islander, and American Indian or Alaska Native persons.

§§ Underlying conditions were extracted from electronic health record clinical encounter data and were based on a CDC list of conditions associated with the highest risk for COVID-19 (https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html, accessed March 23, 2022), and included the following: alcoholic liver disease, autoimmune hepatitis, bronchiectasis, bronchopulmonary dysplasia, cancer, cardiomyopathy, cerebrovascular disease, chronic kidney disease, cirrhosis, chronic obstructive pulmonary disease, coronary artery disease, current smoker, administration or prescription of nontopical glucocorticoids within the previous 12 months, heart failure, HIV, immune deficiency, administration or prescription of immunosuppressive medications within the previous 12 months, interstitial lung disease, nonalcoholic fatty liver disease, obesity, pulmonary arterial hypertension, pulmonary embolus, pregnancy, solid organ transplant, tuberculosis, and type 1 or 2 diabetes. Among these, diagnoses associated with immunocompromise had overall similar prevalence between cases and controls, including immunosuppressive medications other than steroids (7.9% of case-patients and 7.3% of control-patients), immune deficiencies (4.4% of case-patients and 4.5% of control-patients), solid organ transplant recipients (2.4% of case-patients and 1.8% of control-patients) and HIV (0.9% of case-patients and 0.9% of control-patients).

¶¶ Patients were categorized on the date of NAAT associated with hospitalization as unvaccinated if no COVID-19 vaccine had been received; after dose 1 if ≥14 days had elapsed since receipt of the first dose of an mRNA COVID-19 vaccine and before any second dose; after dose 2 if ≥14 days had elapsed since receipt of the second dose of an mRNA COVID-19 vaccine, and no subsequent dose was received; and after a booster dose if ≥14 days had elapsed since receipt of an mRNA booster dose administered ≥5 months after a second dose. Patients were excluded from the analysis if they received a non-mRNA COVID-19 vaccine; the day of the NAAT-associated hospitalization was <14 days after dose 1, dose 2, or a booster dose; dose 2 was received <14 days after dose 1; any booster dose was <5 months after dose 2, they received >3 doses of vaccine, or their previous positive NAAT result or COVID-19 diagnosis was after date of the most recent vaccine dose. Median time from receipt of dose 1 to dose 2 was 21 days (IQR = 21–24) for Pfizer-BioNTech and 28 days (IQR = 28–30) for Moderna vaccines. Median time from receipt of dose 2 to dose 3 was 232 days (IQR = 203–258) for Pfizer-BioNTech and 236 days (IQR = 210–261) for Moderna vaccines.

*** Periods were defined as a range of dates when estimated national prevalence of a SARS-CoV-2 variant exceeded 50% as pre-Delta (before June 20, 2021), Delta (during June 20, 2021–December 18, 2021), and Omicron (from December 19, 2021). https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Immunity from previous SARS-CoV-2 infection wanes over time (*1*,*8*) and was lower against the Omicron variant compared with immunity against other virus variants (*2*). However, protection is estimated to have remained stable against SARS-CoV-2 reinfection leading to hospitalization or death (*2*). Previous studies have indicated that, in general, protection by a hybrid of infection-induced and vaccination-induced immunity is superior to that from either alone and is less likely to wane over time (*1*,*8*). Compared with unvaccinated persons without previous infection, persons with a booster dose of mRNA vaccine have been estimated to have

TABLE 2. Estimated vaccine effectiveness against hospitalization with COVID-19 after previous SARS-CoV-2 infection* — United States, June 2021–February 2022

Variant period/Vaccination status	No. of case-patients† (N = 3,761)	No. of control-patients† (N = 7,522)	VE§ (95% CI)	
			Unadjusted	Adjusted
Overall				
Unvaccinated (Ref)	2,303	3,571	—	—
Any mRNA vaccine, 1 dose¶,**	161	413	41.6 (29.3–51.8)	41.9 (29.5–52.1)
Any mRNA vaccine, 2 doses¶,**	1,038	2,496	38.2 (32.2–43.7)	39.4 (33.3–45.0)
Pfizer-BioNTech¶	588	1,432	40.8 (33.1–47.5)	42.7 (35.0–49.4)
Moderna¶	450	1,064	37.1 (27.6–45.3)	38.7 (29.1–46.9)
Any mRNA vaccine, booster dose¶,**	259	1,042	66.4 (60.7–71.3)	67.0 (61.3–71.9)
Delta predominant				
Unvaccinated (Ref)	950	1,468	—	—
Any mRNA vaccine, 1 dose¶	45	171	61.0 (44.7–72.5)	58.8 (41.3–71.1)
Any mRNA vaccine, 2 doses¶	415	1,209	50.7 (42.9–57.5)	47.5 (38.8–54.9)
Pfizer-BioNTech¶	234	678	52.8 (42.8–61.1)	50.0 (39.0–59.0)
Moderna¶	181	531	47.9 (35.3–58.1)	44.0 (29.9–55.2)
Any mRNA vaccine, booster dose¶	27	100	60.2 (36.4–75.0)	57.8 (32.1–73.8)
Omicron predominant				
Unvaccinated (Ref)	1,353	2,103	—	—
Any mRNA vaccine, 1 dose¶	116	242	27.3 (8.14–42.5)	33.0 (15.0–47.2)
Any mRNA vaccine, 2 doses¶	623	1,287	26.9 (17.4–35.4)	34.6 (25.5–42.5)
Pfizer-BioNTech¶	354	754	29.2 (16.9–39.7)	37.3 (25.8–46.9)
Moderna¶	269	533	26.2 (10.8–39.0)	35.9 (21.7–47.4)
Any mRNA vaccine, booster dose¶	232	942	64.6 (58.1–70.2)	67.6 (61.4–72.8)
Relative VE of booster dose compared with primary series††				
Overall				
≥5 months after second dose (Ref)††	697	1,536	—	—
Any mRNA vaccine, booster dose††	259	1,042	56.5 (44.6–65.9)	55.9 (43.6–65.5))

Abbreviations: NAAT = nucleic acid amplification test; Ref = referent group; VE = vaccine effectiveness.

* Initial diagnosis was based on a previous positive SARS-CoV-2 NAAT or clinical diagnosis of COVID-19 >90 days before the date of the NAAT associated with subsequent hospitalization. COVID-19 was defined as a clinical encounter with any of the following *International Classification of Diseases, Tenth Revision* diagnostic codes: U07.1, J12.81, or J12.82.

† Case-patients had a positive NAAT performed 10 days before through 3 days after the date of hospitalization with a diagnosis of COVID-19-like illness; control-patients had a negative NAAT result. COVID-19–like illness diagnoses were defined based on other methods (https://www.nejm.org/doi/full/10.1056/nejmoa2110362, Supplement Table S2) and included acute respiratory illness (e.g., COVID-19, respiratory failure, or pneumonia) or related signs or symptoms (e.g., cough, fever, dyspnea, vomiting, or diarrhea) using diagnostic codes from the *International Classification of Diseases, Tenth Revision*. Patients were eligible for inclusion if the hospitalization-associated SARS-CoV-2 NAAT was performed during June 20, 2021–February 24, 2022.

§ VE was calculated as [1 − odds ratio] x 100, estimated using conditional logistic regression in a test-negative design after matching by 2-week calendar period of NAAT associated with hospital admission, 10-year age group, and state of residence. Adjusted estimates accounted in addition for measured differences in sex, race/ethnicity (White non-Hispanic race: yes/no and Hispanic ethnicity: yes/no), number of clinical encounters during 2019 (0, 1–9, or ≥10), number of underlying conditions (0, 1, or >1), and days since previous infection (as a continuous variable). Underlying conditions were extracted from EHR clinical encounter data and based on a CDC list of conditions associated with the highest risk for COVID-19 (https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html, accessed March 23, 2022), including the following diagnoses: alcoholic liver disease, autoimmune hepatitis, bronchiectasis, bronchopulmonary dysplasia, cancer, cardiomyopathy, cerebrovascular disease, chronic kidney disease, cirrhosis, chronic obstructive pulmonary disease, coronary artery disease, current smoker, administration or prescription of nontopical glucocorticoids within the previous 12 months, heart failure, HIV, immune deficiency, administration or prescription of immunosuppressive medications within the previous 12 months, interstitial lung disease, nonalcoholic fatty liver disease, obesity, pulmonary arterial hypertension, pulmonary embolus, pregnancy, solid organ transplant, tuberculosis, and type 1 or 2 diabetes.

¶ Patients were categorized on the date of NAAT associated with hospitalization as unvaccinated if no COVID-19 vaccine had been received; after dose 1 if ≥14 days had elapsed since receipt of the first dose of an mRNA COVID-19 vaccine and before any second dose; after dose 2 if ≥14 days had elapsed since receipt of the second dose of an mRNA COVID-19 vaccine and no subsequent dose was received; and after a booster dose if ≥14 days had elapsed since receipt of an mRNA booster dose administered ≥5 months after a second dose. Patients were excluded from the analysis if they received a non-mRNA COVID-19 vaccine; the day of the NAAT-associated hospitalization was <14 days after dose 1, dose 2, or a booster dose; dose 2 was received <14 days after dose 1; any booster dose was <5 months after dose 2, they received >3 doses of vaccine, or the previous positive NAAT result or COVID-19 diagnosis was after the date of the most recent vaccine dose.

** Among persons with a previous infection, adjusted VE <90 days after dose 1 was 42.0% (95% CI = 16.8%–59.5%) and ≥90 days after dose 1 was 42.2% (95% CI = 26.0%–54.8%); adjusted VE <90 days after dose 2 was 44.6% (95% CI = 28.6%–56.9%) and ≥90 days after dose 2 was 39.3% (95% CI = 32.4%–45.4%); and adjusted VE <90 days after dose 3 was 67.9% (95% CI = 60.3%–74.0%) and ≥90 days after dose 3 was 62.4% (95% CI = 48.6%–72.5%).

†† For estimation of relative VE after a booster dose, the referent group had received dose 2 (but not a booster dose) ≥5 months previously.

90% protection against hospitalization with COVID-19 during the Omicron period; the highest estimated protection was among vaccinated persons with previous infection.****

**** https://www.medrxiv.org/content/10.1101/2022.03.22.22272745v1

The findings in this report are subject to at least five limitations. First, underascertainment of vaccination status from available information would likely lead to an underestimation of VE, particularly if vaccinated control-patients were misclassified as unvaccinated; this might have led to lower estimated VE

TABLE 3. Estimated vaccine effectiveness against hospitalization with COVID-19 after previous SARS-CoV-2 infection* among persons with initial infection occurring before the first vaccine dose, and by age group —United States, June 2021–February 2022

Characteristic	No. of case-patients† (N = 3,761)	No. of control-patients† (N = 7,522)	VE (95% CI)§	
			Unadjusted	Adjusted
Infection before dose 1				
Unvaccinated (Ref)	2,304	3,581	—	—
Any mRNA vaccine, 1 dose¶,**	161	412	42.5 (30.2–52.7)	43.1 (30.7–53.2)
Any mRNA vaccine, 2 doses¶,**	960	2,356	39.1 (32.9–44.7)	41.7 (35.5–47.3)
Any mRNA vaccine, booster dose¶,**	183	777	67.6 (61.1–73.0)	70.3 (64.1–75.4)
Age ≥65 yrs				
Unvaccinated (Ref)	823	1,196	—	—
Any mRNA vaccine, 1 dose	72	163	35.3 (11.6–52.6)	35.7 (11.9–53.1)
Any mRNA vaccine, 2 doses	520	1,167	33.5 (23.0–42.6)	33.4 (22.4–42.9)
Any mRNA vaccine, booster dose	169	659	64.9 (56.6–71.6)	64.5 (56.0–71.4)
Age <65 yrs				
Unvaccinated (Ref)	1,480	2,375	—	—
Any mRNA vaccine, 1 dose	89	250	46.0 (29.6–58.6)	45.7 (28.9–58.5)
Any mRNA vaccine, 2 doses	518	1,329	40.3 (32.0–47.6)	41.9 (33.5–49.2)
Any mRNA vaccine, booster dose	90	383	66.1 (55.9–74.0)	67.7 (57.7–75.3)

Abbreviations: NAAT = nucleic acid amplification test; Ref = referent group; VE = vaccine effectiveness.

* Initial diagnosis was based on a previous positive SARS-CoV-2 NAAT or clinical diagnosis of COVID-19 >90 days before the date of the NAAT associated with subsequent hospitalization. COVID-19 diagnosis was defined as a clinical encounter with any of the following *International Classification of Diseases, Tenth Revision* diagnostic codes: U07.1, J12.81, or J12.82.

† Case-patients had a positive NAAT performed between 10 days before and 3 days after the date of hospital admission with a diagnosis of COVID-19-like illness; control-patients had a negative NAAT result. COVID-19–like illness diagnoses were defined based on others' methods (https://www.nejm.org/doi/full/10.1056/nejmoa2110362, Supplement Table S2) and included acute respiratory illness (e.g., COVID-19, respiratory failure, or pneumonia) or related signs or symptoms (e.g., cough, fever, dyspnea, vomiting, or diarrhea) using diagnostic codes from the *International Classification of Diseases, Tenth Revision*. Patients were eligible for inclusion if the hospitalization-associated SARS-CoV-2 NAAT was performed during June 20, 2021 and February 24, 2022.

§ VE was calculated as [1 − odds ratio] x 100, estimated using conditional logistic regression in a test-negative design after matching by 2-week calendar period of NAAT associated with hospital admission, 10-year age group, and state of residence. Adjusted estimates accounted in addition for measured differences in sex, race/ethnicity (White non-Hispanic race: yes/no and Hispanic ethnicity: yes/no), number of clinical encounters during 2019 (0, 1–9, or ≥10), number of underlying conditions (0, 1, or >1), and days since previous infection (as a continuous variable). Underlying conditions were extracted from EHR clinical encounter data and classified based on a CDC list of conditions associated with the highest risk for COVID-19 (https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-care/underlyingconditions.html, accessed March 23, 2022), including the following diagnoses: alcoholic liver disease, autoimmune hepatitis, bronchiectasis, bronchopulmonary dysplasia, cancer, cardiomyopathy, cerebrovascular disease, chronic kidney disease, cirrhosis, chronic obstructive pulmonary disease, coronary artery disease, current smoker, administration or prescription of nontopical glucocorticoids within the previous 12 months, heart failure, HIV, immune deficiency, administration or prescription of immunosuppressive medications within the previous 12 months, interstitial lung disease, nonalcoholic fatty liver disease, obesity, pulmonary arterial hypertension, pulmonary embolus, pregnancy, solid organ transplant, tuberculosis, and type 1 or 2 diabetes.

¶ Patients were categorized on the date of NAAT associated with hospitalization as unvaccinated if no COVID-19 vaccine had been received; after dose 1 if ≥14 days had elapsed since receipt of the first dose of an mRNA COVID-19 vaccine and before any second dose; after dose 2 if ≥14 days had elapsed since receipt of the second dose of an mRNA COVID-19 vaccine, and no subsequent dose was received; and after a booster dose if ≥14 days had elapsed since receipt of an mRNA booster dose administered ≥5 months after a second dose. Patients were excluded from the analysis if they received a non-mRNA COVID-19 vaccine; the day of the NAAT-associated hospitalization was <14 days after dose 1, dose 2, or a booster dose; dose 2 was received <14 days after dose 1; any booster dose was <5 months after dose 2, they received >3 doses of vaccine, or their previous positive NAAT result or COVID-19 diagnosis was after the most recent vaccine dose. VE was calculated using the unvaccinated group as the referent.

** Among persons with a previous infection <180 days and ≥180 days before dose 1, adjusted VE after dose 1 was 43.2% (95% CI = 25.3%–56.8%) and 36.8% (95% CI = 14.0%–53.5%), respectively; adjusted VE after dose 2 was 37.6% (95% CI = 29.6%–44.6%) for persons with a previous infection <180 days before dose 1 and 38.9% (95% CI = 28.2%–48.1%) for persons with a previous infection ≥180 days before dose 1; adjusted VE after a booster dose was 72.5% (95% CI = 65.2%–78.2%) for persons with a previous infection <180 days before dose 1 and 46.7% (95% CI = 24.9%–62.2%) for persons with a previous infection ≥180 days before dose 1.

compared with similar analyses (*5*,*6*,*9*). Second, generalizability might be limited by incomplete data or by missing data from persons who do not seek health care; however, Cosmos data are broadly representative of the U.S. population (*4*). Third, several VE estimates were imprecise, with broad CIs; estimates should be interpreted with caution. Fourth, underascertainment of previous infection might have occurred because of dependence on EHR data; however, findings were similar when restricting analyses to case-patients with positive initial NAAT results, and the test-negative design for an endpoint of severe illness mitigates the risk for selection bias. Finally, there might be residual or unmeasured confounding by characteristics associated with exposure, vaccination, or hospitalization that were not recorded in the data set.

An increasing proportion of the U.S. population has had SARS-CoV-2 infection†††† and might be at risk for SARS-CoV-2 reinfection leading to hospitalization. In the current analysis, approximately 50% of these reinfections occurred during the Omicron-predominant period. Vaccination remains the safest strategy for preventing complications of SARS-CoV-2 infection. COVID-19 vaccination offers additional protection against reinfection leading to hospitalization, with a booster

†††† https://covid.cdc.gov/covid-data-tracker/#antibody-seroprevalence

Summary

What is already known about this topic?

Persons with previous SARS-CoV-2 infection have some protection against reinfection leading to hospitalization, but there is limited evidence regarding the additional benefit of vaccination among these persons.

What is added by this report?

Among persons with previous infection, COVID-19 mRNA vaccination provided protection against subsequent COVID-19–associated hospitalization. Estimated vaccine effectiveness against reinfection leading to hospitalization during the Omicron-predominant period was approximately 35% after dose 2, and 68% after a booster dose.

What are the implications for public health practice?

To prevent COVID-19–associated hospitalization, all eligible persons should stay up to date with vaccination, including those with previous SARS-CoV-2 infection.

dose offering the highest level of protection. To prevent COVID-19–associated hospitalization, all eligible persons should stay up to date with vaccination, including those with previous SARS-CoV-2 infection.

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Wound Botulism Outbreak Among a Group of Persons Who Inject Drugs — Dallas, Texas, 2020

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On December 9, 2020, Dallas County Health and Human Services (DCHHS) was notified of a hospitalized male, aged 33 years (patient A), who was experiencing homelessness and had bilateral ptosis, upper and lower extremity weakness, and respiratory failure requiring intubation. The patient reported injecting methamphetamines, and physical examination noted track marks but no overt skin wounds or abscesses. Patient A was treated with naloxone. Heroin and methamphetamines were detected in the patient's urine. Myasthenia gravis was initially suspected; however, botulism was considered when the patient did not respond to treatment with pyridostigmine and steroids and the patient's weakness continued to progress. DCHHS contacted the Texas Department of State Health Services (DSHS) and CDC's botulism clinical consultation service.* Heptavalent botulinum antitoxin (BAT) was released by CDC on December 9, 2020, and administered to the patient on December 10. Botulism testing results were not available before treatment with BAT. Botulism neurotoxin (BoNT) types A and B were detected in the patient's serum specimen using the BoNT Endopep-MS assay (*1*).

On December 18, 2020, DCHHS was notified of a female aged 39 years (patient B), admitted to a different hospital with difficulty swallowing during the past 2 weeks and respiratory failure requiring intubation. Patient B was treated with naloxone. Multiple chronic and several fresh wounds were noted during the physical examination. BAT was administered, and BoNT types A and B were detected in this patient's serum specimen. Acquaintances of patient B reported injecting black tar heroin subcutaneously (skin popping) and sharing this drug with patient A.

Interviews with acquaintances of patient B identified three additional persons (patients C, D, and E) who injected drugs and were admitted to the hospital during December 2–21, 2020, with cranial nerve impairment including diplopia (two), blurred vision (two), bilateral ptosis (one), upper extremity weakness (two), and respiratory failure requiring intubation (two). Patient D was 13 weeks pregnant at the time of hospitalization and left the hospital against medical advice 10 weeks after receiving BAT. Patient E was located and brought to the hospital by family members following health department outreach and left against medical advice immediately after receiving BAT. In January 2021, two persons (patients F and G) with diplopia, blurred vision, and shortness of breath who had injected drugs with either patient B or patient E were concerned that they might have botulism and were evaluated at area hospitals. All seven patients identified in this investigation were treated with BAT. Four (57%) patients required mechanical ventilation and prolonged intensive care.

Serum specimen collected from all seven patients before administration of BAT were tested for BoNT; patients C, D, E, F, and G received a negative test result and were classified as having probable wound botulism cases for surveillance purposes.† Three serum specimens were not maintained at proper temperature during shipping, which might have affected testing results. Stool cultures from patient D yielded positive test results for *Clostridium botulinum* type A using the BoNT Endopep-MS assay, raising the question of whether this patient was part of the wound botulism outbreak or had foodborne botulism.

This is the first wound botulism outbreak reported in Texas and the largest in the United States outside of California (*2*,*3*). During 2010–2019, a total of 206 laboratory-confirmed cases of wound botulism were reported in the United States, including 160 (78%) in California and eight (4%) in Texas.§ The rarity of reported wound botulism outbreaks might be partially related to challenges from stigma precluding identification and epidemiologic linkage of patients who injected drugs together or purchased drugs from the same source. In this outbreak, public health officials discovered additional cases by interviewing patient acquaintances who had also injected drugs and were aware of the early signs and symptoms of botulism. Case-finding efforts could be improved if clinicians ask patients with suspected wound botulism whether they have acquaintances with symptoms and whether syringe exchange service programs share wound botulism educational materials with clients. Increased awareness of wound botulism among patients with cranial nerve impairment and progressive weakness, and among persons who inject drugs outside of California, might also help to identify additional cases.

* https://www.cdc.gov/botulism/health-professional.html#:~:text=If%20you%20suspect%20your%20patient,at%20770%2D488%2D7100

† https://ndc.services.cdc.gov/case-definitions/botulism-2011/#:~:text=Botulism%2C%20wound-,Clinical%20Description,Symmetric%20paralysis%20may%20progress%20rapidly

§ https://www.cdc.gov/botulism/surveillance.html

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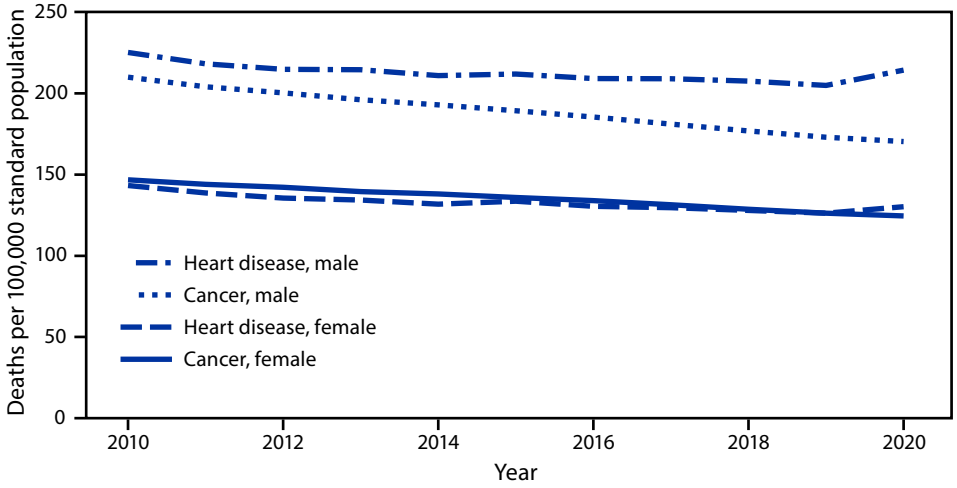
FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Age-Adjusted Death Rates* of Heart Disease and Cancer, by Sex — United States, 2010–2020



Abbreviation: ICD-10 = *International Classification of Diseases, Tenth Revision*.

* Age-adjusted rates are heart disease and cancer deaths per 100,000 standard population. Heart disease deaths were identified using ICD-10 codes I00–I09, I11, I13, and I20–I51; cancer deaths were identified using ICD-10 codes C00–C97.

Age-adjusted cancer and heart disease death rates for both males and females declined steadily from 2010 to 2019. Cancer death rates continued to decline for both males and females during 2019–2020 to 170.3 per 100,000 population (males) and 124.5 (females) in 2020. The pattern was different for deaths caused by heart disease for both males and females. Heart disease death rates increased during 2019–2020 to 214.2 (males) and 130.2 (females) in 2020. During 2010–2020, higher death rates were reported for males than females for both heart disease and cancer, with the cancer death rate for males exceeding the heart disease death rate for females.

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

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