Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 70 / No. 34
August 27, 2021

Progress Toward Polio Eradication — Worldwide, January 2019–June 2021

John Paul Bigouette, PhD[1,2]; Amanda L. Wilkinson, PhD[2]; Graham Tallis, MPH[3]; Cara C. Burns, PhD[4]; Steven G. F. Wassilak, MD[2]; John F. Vertefeuille, PhD[2]

In 1988, when the Global Polio Eradication Initiative (GPEI) began, polio paralyzed >350,000 children across 125 countries. Today, only one of three wild poliovirus serotypes, type 1 (WPV1), remains in circulation in only two countries, Afghanistan and Pakistan. This report summarizes progress toward global polio eradication during January 1, 2019–June 30, 2021 and updates previous reports (*1*,*2*). In 2020, 140 cases of WPV1 were reported, including 56 in Afghanistan (a 93% increase from 29 cases in 2019) and 84 in Pakistan (a 43% decrease from 147 cases in 2019). As GPEI focuses on the last endemic WPV reservoirs, poliomyelitis outbreaks caused by circulating vaccine-derived poliovirus (cVDPV) have emerged as a result of attenuated oral poliovirus vaccine (OPV) virus regaining neurovirulence after prolonged circulation in underimmunized populations (*3*). In 2020, 32 countries reported cVDPV outbreaks (four type 1 [cVDPV1], 26 type 2 [cVDPV2] and two with outbreaks of both); 13 of these countries reported new outbreaks. The updated GPEI Polio Eradication Strategy 2022–2026 (*4*) includes expanded use of the type 2 novel oral poliovirus vaccine (nOPV2) to avoid new emergences of cVDPV2 during outbreak responses (*3*). The new strategy deploys other tactics, such as increased national accountability, and focused investments for overcoming the remaining barriers to eradication, including program disruptions and setbacks caused by the COVID-19 pandemic.

Polio Vaccination

In worldwide immunization programs, OPV and at least 1 dose of injectable, inactivated poliovirus vaccine (IPV) are routinely used. Because IPV contains all three poliovirus serotypes, it protects against disease in children who seroconvert after vaccination; however, it does not prevent poliovirus transmission. In 2016, a global coordinated switch occurred from trivalent OPV (tOPV), which contains Sabin strain types 1, 2, and 3 to bivalent OPV (bOPV), which contains Sabin strain

INSIDE

Continuing Education examination available at https://www.cdc.gov/mmwr/mmwr_continuingEducation.html

U.S. Department of Health and Human Services
Centers for Disease Control and Prevention

types 1 and 3. WPV2 was declared eradicated in 2015, and cVDPV2 was the predominant cause of cVDPV outbreaks after the last WPV2 case was detected in 1999. The use of monovalent OPV Sabin strain type 2 (mOPV2) is reserved for cVDPV2 outbreak responses. In November 2020, the World Health Organization (WHO) granted Emergency Use Listing (EUL) for genetically stabilized nOPV2 to be used in a limited number of countries that have met readiness criteria for initial use* of nOPV2 (*5*) in response to outbreaks.

In 2020, the estimated global infant coverage with 3 doses of poliovirus vaccine (Pol3) by age 1 year was 83% (*6*). However, substantial variation in coverage exists by WHO region, nationally, and subnationally. In the two countries with endemic WPV (Afghanistan and Pakistan), 2020 POL3 coverage was 75% and 83%, respectively (*6*); estimated coverage in subnational areas with transmission is much lower.

In 2019, GPEI supported 199 supplementary immunization activities (SIAs)† in 42 countries with approximately 1 billion bOPV, 20 million IPV, 32 million monovalent OPV type 1 (mOPV1), and 142 million mOPV2 doses administered. In 2020, 149 SIAs were conducted in 30 countries with approximately 696 million bOPV, 6 million IPV, 4 million mOPV1, 228 million mOPV2, and 51 million tOPV doses administered; tOPV was used during four SIAs in Afghanistan and Pakistan, where cocirculation of WPV1 and cVDPV2 requires tOPV for efficiency in scheduling and implementing SIAs; GPEI authorized restarting filling of tOPV stocks for this purpose. In 2021, approximately 136 million nOPV2 doses have been released in eight countries approved for initial use (Benin, Chad, Congo, Liberia, Niger, Nigeria, Sierra Leone, and Tajikistan). SIAs continue to be affected by the COVID-19 pandemic§ in 2021.

Poliovirus Surveillance

WPV and cVDPV transmission are detected primarily through surveillance for acute flaccid paralysis (AFP) among children aged <15 years with testing of stool specimens at one of 145 WHO-accredited laboratories of the Global Polio Laboratory Network (*7*). During January–September 2020, the number of reported AFP cases declined 33% compared with the same period in 2019 (*8*). Environmental surveillance (testing of sewage for poliovirus) can supplement AFP surveillance; however, environmental sampling also declined somewhat during this period. Current data indicate that the COVID-19 pandemic has continued to limit AFP surveillance sensitivity.

*Authorization for wider use under EUL is pending review of safety and effectiveness data from the initial use.

†Mass immunization campaigns intended to interrupt poliovirus circulation by immunizing every child aged <5 years with 2 OPV doses, regardless of previous immunization status.

§GPEI implemented a pause on SIAs from mid-March through July 2020.

The *MMWR* series of publications is published by the Center for Surveillance, Epidemiology, and Laboratory Services, Centers for Disease Control and Prevention (CDC), U.S. Department of Health and Human Services, Atlanta, GA 30329-4027.

Suggested citation: [Author names; first three, then et al., if more than six.] [Report title]. MMWR Morb Mortal Wkly Rep 2021;70:[inclusive page numbers].

The continued strengthening of both surveillance systems, particularly in priority countries,[¶] is critical to tracking progress and documenting the absence of poliovirus transmission.

Reported Poliovirus Cases and Isolations

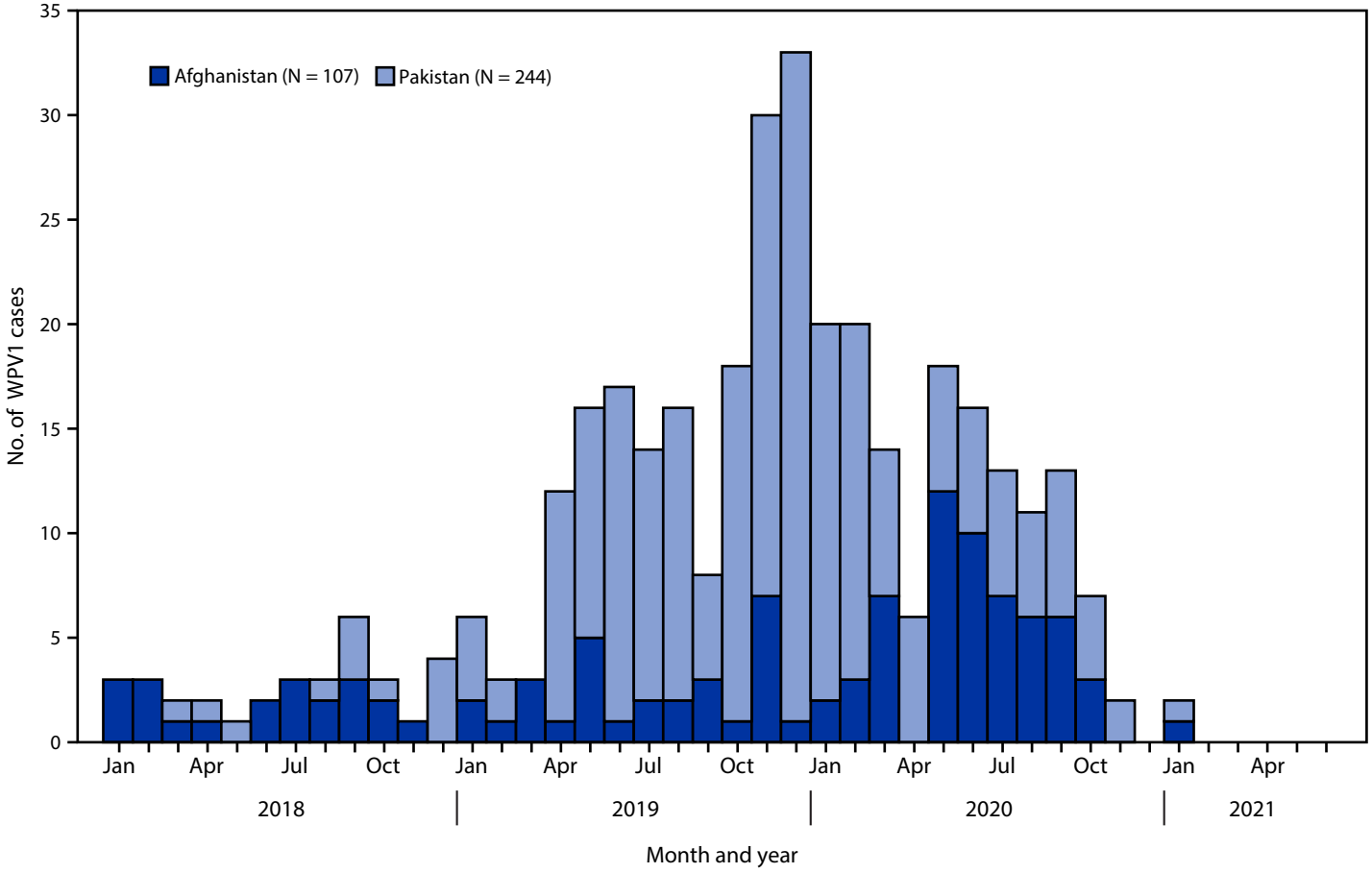
Countries reporting WPV cases and isolations. Since 2016, no WPV cases have been identified outside of Afghanistan and Pakistan. Of the 176 WPV1 cases reported in 2019, 29 (16%) occurred in Afghanistan and 147 (84%) in Pakistan (Figure) (Table 1).

In 2020, Afghanistan reported 56 WPV1 cases representing a 93% increase from cases reported in the previous year; cases were found across 38 districts compared with 20 districts in 2019. As of August 3, 2021, one WPV1 case was reported in Afghanistan in 2021, a 97% decrease compared with the first 6 months of 2020. Pakistan reported 84 WPV1 cases from 39 districts in 2020, representing a 43% decrease from the 147 cases reported in 43 districts during 2019. One WPV1 case has been reported during January–June 2021, from Balochistan province, a 98% decrease from the 60 WPV1 cases from five provinces during the same 2020 period. This period accounted for 71% of all Pakistan WPV1 cases in 2020. In both countries, the number of orphan WPV1 isolates (those with ≤98.5% genetic identity with other isolates) from AFP cases increased from five of 176 (3%) in 2019 to 18 of 140 (13%) in 2020, signifying an increase in AFP surveillance gaps in 2020 (*7*).

Environmental surveillance in Afghanistan detected WPV1 in 35 (8%) of 418 sewage samples collected during 2020 and in 57 (22%) of 264 samples in 2019 (Table 2). In Pakistan, WPV1 was detected in 434 (52%) of 830 sewage samples

[¶] 2020 priority countries: *African Region:* Angola, Benin, Burkina Faso, Cameroon, Central African Republic, Chad, Congo, Côte d'Ivoire, Democratic Republic of the Congo, Eritrea, Ethiopia, Ghana, Guinea, Kenya, Liberia, Madagascar, Mali, Mauritania, Mozambique, Niger, Nigeria, Senegal, Sierra Leone, South Sudan, Togo, and Zambia; *Eastern Mediterranean Region:* Afghanistan, Egypt, Iran, Iraq, Libya, Pakistan, Somalia, Sudan, Syria, and Yemen; *European Region:* Tajikistan and Uzbekistan; *South-East Asia Region:* Burma (Myanmar); *Western Pacific Region:* Malaysia and Philippines.

FIGURE. Number of wild poliovirus type 1 cases, by country and month of paralysis onset — worldwide, January 2019–June 2021*



Abbreviation: WPV1 = wild poliovirus type 1.
* Data are current as of August 3, 2021.

TABLE 1. Number of poliovirus cases, by country — worldwide, January 1, 2019–June 30, 2021*

	Reporting period							
	2019		2020		Jan–Jun 2020		Jan–Jun 2021	
Country (cVDPV type)	WPV1	cVDPV	WPV1	cVDPV	WPV1	cVDPV	WPV1	cVDPV
Countries with endemic WPV1 transmission								
Afghanistan (2)†	29	0	56	308	34	54	1	43
Pakistan (2)	147	22	84	135	60	52	1	8
Countries with reported cVDPV cases								
Angola (2)	0	138	0	3	0	3	0	0
Benin (2)	0	8	0	3	0	2	0	2
Burkina Faso (2)	0	1	0	65	0	26	0	1
Burma (Myanmar)(2)§	0	6	0	0	0	0	0	0
Cameroon (2)†	0	0	0	7	0	4	0	0
Central African Republic (2)	0	21	0	4	0	1	0	0
Chad (2)	0	11	0	99	0	57	0	0
China (2)	0	1	0	0	0	0	0	0
Republic of the Congo (2)†	0	0	0	2	0	0	0	2
Côte d'Ivoire (2)†	0	0	0	61	0	39	0	0
Democratic Republic of the Congo (2)	0	88	0	81	0	54	0	10
Ethiopia (2)	0	14	0	36	0	17	0	6
Ghana (2)	0	18	0	12	0	12	0	0
Guinea (2)†	0	0	0	44	0	23	0	6
Liberia (2)†	0	0	0	0	0	0	0	3
Madagascar (1)†	0	0	0	2	0	0	0	6
Malaysia (1)	0	3	0	1	0	1	0	0
Mali (2)†	0	0	0	48	0	6	0	0
Niger (2)	0	1	0	10	0	6	0	0
Nigeria (2)	0	18	0	8	0	2	0	65
Philippines (1,2)¶	0	14	0	1	0	1	0	0
Senegal (2)†	0	0	0	0	0	0	0	13
Sierra Leone (2)†	0	0	0	10	0	0	0	4
Somalia (2)	0	3	0	14	0	2	0	0
South Sudan (2)†	0	0	0	50	0	2	0	9
Sudan (2)†	0	0	0	58	0	10	0	0
Tajikistan (2)†	0	0	0	1	0	0	0	23
Togo (2)	0	8	0	9	0	9	0	0
Yemen (1)	0	1	0	31	0	22	0	3
Zambia (2)	0	2	0	0	0	0	0	0

Abbreviations: cVDPV = circulating vaccine-derived poliovirus; WPV1 = Wild poliovirus type 1.
* Data are current as of August 3, 2021.
† New cVDPV cases reported after December 31, 2019.
§ For this country, *MMWR* uses the U.S. State Department short-form name "Burma"; the World Health Organization uses "Myanmar."
¶ Reported two cVDPV type 1 cases and 12 cVDPV type 2 cases in 2019, one cVDPV type 2 case in 2020.

collected in 2020, and 44% (379/854) of sewage samples were WPV1-positive in 2019. In 2019, three (4%) of the 71 sewage samples collected in Iran contained WPV1 isolates; no positive environmental samples or cases have been reported since then.

Countries reporting cVDPV cases and isolations. During January 2019–June 2021, cVDPV transmission was identified in 32 countries; 13 countries were affected by new cVDPV outbreaks in 2020. Afghanistan reported 308 cVDPV2 cases in 2020 compared with no cases in 2019. Pakistan reported 135 cVDPV2 cases in 2020, more than a fivefold increase from the 22 reported in 2019. To date in 2021, 195 cVDPV2 cases have been identified globally, including 43 in Afghanistan and eight in Pakistan.

Discussion

With the August 2020 certification of the African Region as WPV-free,** five of the six WHO regions, representing over 90% of the world's population, are now free of wild polioviruses. Given this achievement, GPEI is focusing efforts on two goals: interrupting persistent WPV1 transmission in Pakistan and Afghanistan and stopping all current outbreaks of cVDPV2. To reach these goals, in June 2021, GPEI released a revised 5-year strategy for polio eradication that aims to address persistent challenges and recover from setbacks exacerbated by the COVID-19 pandemic (*4*).

Guided by the Polio Eradication Strategy 2022–2026, GPEI partners and in-country stakeholders are to adopt a full emergency posture and assume more accountability for eradication

** https://www.africakicksoutwildpolio.com

TABLE 2. Number of circulating wild polioviruses and circulating vaccine-derived polioviruses detected through environmental surveillance — worldwide, January 1, 2019–June 30, 2021*

Country	Jan 1–Dec 31, 2019		Jan 1–Dec 31, 2020		Jan 1–Jun 30, 2020		Jan 1–Jun 30, 2021	
	No. of samples	No. (%) with isolates	No. of samples	No. (%) with isolates	No. of samples	No. (%) with isolates	No. of samples	No. (%) with isolates
Countries with reported WPV1-positive samples (no. and percentage of isolates refer to WPV1)								
Afghanistan	264	57 (22)	418	35 (8)	172	22 (13)	213	1 (1)
Iran	71	3 (4)	43	0 (—)	0	0 (—)	0	0 (—)
Pakistan	854	379 (44)	830	434 (52)	414	238 (57)	444	59 (13)
Countries with reported cVDPV-positive samples (cVDPV type) (no. and percentage of isolates refer to cVDPVs)								
Afghanistan (2)	264	0 (—)	418	175 (42)	172	46 (27)	213	40 (19)
Angola (2)	106	17 (16)	98	0 (—)	47	0 (—)	15	0 (—)
Benin (2)	37	0 (—)	70	5 (7)	31	0 (—)	52	1 (2)
Cameroon (2)	602	4 (1)	273	9 (3)	134	4 (3)	187	0 (—)
Central African Republic (2)	149	10 (7)	97	2 (2)	43	2 (5)	48	0 (—)
Chad (2)	198	10 (5)	77	3 (4)	55	3 (5)	26	0 (—)
China (3)	0	0 (—)	0	0 (—)	0	0 (—)	1	1 (100)
Republic of the Congo (2)	0	0 (—)	12	1 (8)	0	0 (—)	213	1 (1)
Cote d'Ivoire (2)	154	7 (5)	130	91 (70)	88	62 (70)	42	0 (—)
Democratic Republic of the Congo (2)	294	0 (—)	170	1 (1)	78	1 (1)	145	0 (—)
Egypt (2)	703	0 (—)	550	1 (0)	267	0 (—)	313	10 (3)
Ethiopia (2)	159	3 (2)	51	2 (4)	33	0 (—)	15	0 (—)
Gambia (2)	0	0 (—)	0	0 (—)	0	0 (—)	9	2 (22)
Ghana (2)	202	17 (8)	184	20 (11)	100	19 (19)	99	0 (—)
Guinea (2)	103	0 (—)	67	1 (1)	38	0 (—)	61	0 (—)
Iran (2)	74	0 (—)	43	3 (7)	12	0 (—)	25	1 (4)
Kenya (2)	317	0 (—)	193	1 (1)	92	0 (—)	101	1 (1)
Liberia (2)	0	0 (—)	34	6 (18)	15	0 (—)	47	12 (26)
Madagascar (1)	520	0 (—)	351	0 (—)	232	0 (—)	134	12(9)
Malaysia (1, 2)	13	12 (92)	76	12 (16)	50	12 (24)	22	0 (—)
Mali (2)	48	0 (—)	44	4 (9)	22	2 (9)	27	0 (—)
Niger (2)	293	0 (—)	157	7 (4)	93	1 (1)	73	0 (—)
Nigeria (2)	2071	60 (3)	1294	5 (0)	625	0 (—)	868	34 (4)
Pakistan (2)	855	36 (4)	830	135 (16)	414	35 (8)	444	32 (7)
Philippines (1, 2)	67	32 (48)	80	4 (5)	50	4 (8)	18	0 (—)
Senegal (2)	56	0 (—)	27	1 (4)	14	0 (—)	10	4 (40)
Somalia (2)	92	5 (5)	88	26 (30)	52	18 (35)	52	1 (2)
South Sudan (2)	111	0 (—)	85	6 (7)	57	0 (—)	24	0 (—)
Sudan (2)	65	0 (—)	50	14 (28)	20	3 (15)	30	0 (—)
Tajikistan (2)	0	0 (—)	0	0 (—)	0	0 (—)	14	13 (93)
Uganda (2)	56	0 (—)	58	0 (—)	24	0 (—)	36	2 (6)

Abbreviations: cVDPV = circulating vaccine-derived poliovirus; WPV1 = Wild poliovirus type 1.
* Data are current as of August 3, 2021.

at every level of the program (*4*). The strategy elevates efforts in the highest-risk countries and promotes health service integration, surveillance improvement, and community engagement to enhance campaign quality through increased political advocacy to ensure timely and effective emergency outbreak SIA responses through improved government support of implementation.

Although Pakistan and Afghanistan face distinct challenges, they are linked epidemiologically because of high rates of cross-border population movement. Transit-point vaccination must be maintained as emigration from Afghanistan potentially increases in 2021. The beginning of each year is typically the low season for WPV1 transmission in both countries, and AFP surveillance sensitivity has decreased. During 2019, the Pakistan polio program suffered from increased vaccine resistance fed by social media misinformation and faced continued operational problems in some localities. The program changed its management oversight and enhanced efforts to overcome community mistrust to decrease vaccine hesitancy (*9*). Inroads to improving the effectiveness of the SIAs have also been made in 2020 (*4*). Although the proportion of Pakistan environmental samples that are WPV-positive remains high in 2021 to date, the decrease from the same period in 2020 is worth noting.

In Afghanistan, the main challenges to ending poliovirus transmission are the inability to reach all children in critical areas near reservoirs in Pakistan and increasing political instability. The polio program in Afghanistan has continued to operate for many years, even during periods of insecurity and escalating conflict. Although negotiations with local leaders in Afghanistan facilitated vaccination efforts at one time, restrictions on vaccinations have persisted in areas controlled by insurgent groups since the October 2018 ban on house-to-house campaigns, which has

Summary

What is already known about this topic?

Wild poliovirus type 1 (WPV1) remains endemic in Afghanistan and Pakistan. Circulating vaccine-derived poliovirus type 2 (cVDPV2) outbreaks have increased since 2017.

What is added by this report?

From 2019 to 2020, the number of WPV1 cases increased in Afghanistan and decreased in Pakistan and the number of cVDPV2 cases increased and cVDPV2 outbreak countries increased to 32. In Afghanistan, the polio program faces challenges including an inability to reach children in critical areas and increasing political instability. The COVID-19 pandemic continues to limit the quality of immunization activities and poliovirus surveillance.

What are the implications for public health practice?

The Polio Eradication Strategy for 2022–2026 outlines measures including increased government accountability and wider use of novel, oral poliovirus vaccine type 2 that are needed to eradicate polio.

since expanded geographically (*10*). WHO is anticipating that some negotiated access will again be possible. Other challenges include current mass population movements, clusters of vaccine refusals, and suboptimal SIA quality in some areas previously under government control (*10*).

Globally, cVDPV2 outbreaks increased in number and geographic extent during 2019–2020 because of delays in mOPV2 response SIAs, which were frequently of low quality. Since the switch in 2016 from tOPV to bOPV, 1,755 cases of paralytic polio have been reported from 64 cVDPV2 outbreaks in 30 countries across four WHO regions (*4*).†† GPEI has outlined a strategy for stopping cVDPV transmission and reducing the risk of seeding new outbreaks by expanding use of nOPV2 (*4*). Continued monitoring will be needed to ensure safety and effectiveness while nOPV2 is brought into wider use and to ascertain whether it can replace mOPV2 (*5*).

The findings in this report are subject to at least one limitation. SIAs, field surveillance, and investigation activities were curtailed in 2020 because of COVID-19 pandemic mitigation measures, and laboratory testing suffered delays (*8*); limitations on SIA quality and surveillance sensitivity continue in 2021. On the other hand, the COVID-19 pandemic has presented opportunities to jointly increase the effectiveness of polio eradication activities and promote health services integration. For example, the global rollout of COVID-19 vaccines presents an opportunity to strengthen demand for vaccination against both COVID-19 and polio.

†† https://polioeradication.org/polio-today/polio-now/this-week/circulating-vaccine-derived-poliovirus/

Thousands of polio eradication workers worldwide continue to play a critical role in implementing countries' COVID-19 responses. Maintaining these partnerships will be important in eradicating WPV and stopping cVDPV transmission while simultaneously addressing other health priorities.

Acknowledgments

Ministries of Health of all countries; World Health Organization (WHO) Regional Office for the Eastern Mediterranean Region, Cairo, Egypt and its Polio Eradication Department, Amman, Jordan; WHO Regional Office for Africa, Brazzaville, Congo; WHO Regional Office for Europe, Copenhagen, Denmark; WHO Regional Office for the Western Pacific, Manila, Philippines; WHO Regional Office for South-East Asia, New Delhi, India; Global Polio Laboratory Network, Geneva, Switzerland and Regional Offices; Jane Iber, Mark Pallansch, Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, CDC.

Corresponding author: John Paul Bigouette; JBigouette@cdc.gov; 404-834-0427.

[1]Epidemic Intelligence Service, CDC; [2]Global Immunization Division, Center for Global Health, CDC; [3]Polio Eradication Department, World Health Organization, Geneva, Switzerland; [4]Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, CDC.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

References:

1. Chard AN, Datta SD, Tallis G, et al. Progress toward polio eradication—worldwide, January 2018–March 2020. MMWR Morb Mortal Wkly Rep 2020;69:784–9. PMID:32584798 https://doi.org/10.15585/mmwr.mm6925a4
2. Greene SA, Ahmed J, Datta SD, et al. Progress toward polio eradication—worldwide, January 2017–March 2019. MMWR Morb Mortal Wkly Rep 2019;68:458–62. PMID:31120868 https://doi.org/10.15585/mmwr.mm6820a3
3. Alleman MM, Jorba J, Greene SA, et al. Update on vaccine-derived poliovirus outbreaks—worldwide, July 2019–February 2020. MMWR Morb Mortal Wkly Rep 2020;69:489–95. PMID:32324719 https://doi.org/10.15585/mmwr.mm6916a1
4. Global Polio Eradication Initiative. Delivering on a promise: GPEI strategy 2022–2026. Geneva, Switzerland: World Health Organization; 2021. https://polioeradication.org/gpei-strategy-2022-2026/
5. World Health Organization. Implementation of novel oral polio vaccine type 2 (nOPV2) for circulating vaccine-derived poliovirus type 2 (cVDPV2) outbreak response: technical guidance for countries. World Health Organization; 2020. https://apps.who.int/iris/handle/10665/333520
6. World Health Organization. WHO/UNICEF estimates of national immunization coverage. Geneva, Switzerland: World Health Organization; 2021. https://immunizationdata.who.int/
7. Tuma JN, Wilkinson AL, Diop OM, et al. Surveillance to track progress toward polio eradication—Worldwide, 2019–2020. MMWR Morb Mortal Wkly Rep 2021;70:667–73. PMID:33956779 https://doi.org/10.15585/mmwr.mm7018a2

8. Zomahoun DJ, Burman AL, Snider CJ, et al. Impact of COVID-19 pandemic on global poliovirus surveillance. MMWR Morb Mortal Wkly Rep 2021;69:1648–52. PMID:33382673 https://doi.org/10.15585/mmwr.mm695152a4
9. Hsu CH, Rehman MS, Bullard K, et al. Progress toward poliomyelitis eradication—Pakistan, January 2019–September 2020. MMWR Morb Mortal Wkly Rep 2020;69:1748–52. PMID:33211676 https://doi.org/10.15585/mmwr.mm6946a5
10. Global Polio Eradication Initiative. Afghanistan National Emergency Action Plan: Polio Eradication. Geneva, Switzerland: World Health Organization; 2021. https://polioeradication.org/wp-content/uploads/2021/05/Afghanistan_NEAP_2021.pdf

Trends in Nonfatal and Fatal Overdoses Involving Benzodiazepines — 38 States and the District of Columbia, 2019–2020

Stephen Liu, PhD[1]; Julie O'Donnell, PhD[1]; R. Matt Gladden, PhD[1]; Londell McGlone, MPH[1]; Farnaz Chowdhury[2]

Nonfatal and fatal drug overdoses increased overall from 2019 to 2020 (*1*).* Illicit benzodiazepines (e.g., etizolam, flualprazolam, and flubromazolam)† were increasingly detected among postmortem and clinical samples in 2020, often with opioids,§ and might have contributed to overall increases in drug overdoses. Availability of recent multistate trend data on nonfatal benzodiazepine-involved overdoses and involvement of illicit benzodiazepines in overdoses is limited. This data gap was addressed by analyzing annual and quarterly trends in suspected benzodiazepine-involved nonfatal overdoses¶ treated in emergency departments (EDs) (benzodiazepine overdose ED visits) during January 2019–December 2020 (32 states and the District of Columbia [DC]) and benzodiazepine-involved overdose deaths (benzodiazepine deaths), which include both illicit and prescription benzodiazepines, during January 2019–June 2020 (23 states) from CDC's Overdose Data to Action (OD2A) program. From 2019 to 2020, benzodiazepine overdose ED visits per 100,000 ED visits increased (23.7%), both with opioid involvement (34.4%) and without (21.0%). From April–June 2019 to April–June 2020, overall benzodiazepine deaths increased 42.9% (from 1,004 to 1,435), prescription benzodiazepine deaths increased 21.8% (from 921 to 1,122), and illicit benzodiazepine deaths increased 519.6% (from 51 to 316). During January–June 2020, most (92.7%) benzodiazepine deaths also involved opioids, mainly illicitly manufactured fentanyls (IMFs) (66.7%). Improving naloxone availability and enhancing treatment access for persons using benzodiazepines and opioids and calling emergency services for overdoses involving benzodiazepines and opioids, coupled with primary prevention of drug use and misuse, could reduce morbidity and mortality.

CDC's OD2A program collects data on unintentional and undetermined intent drug overdoses: 1) nonfatal overdoses treated in EDs from the Drug Overdose Surveillance and Epidemiology (DOSE) system, and 2) overdose deaths from the State Unintentional Drug Overdose Reporting System (SUDORS).** Benzodiazepine overdose ED visits during January 2019–December 2020 were identified from 33 DOSE jurisdictions (32 states and DC)†† submitting data to the National Syndromic Surveillance Program. Benzodiazepine and opioid overdose ED visits were identified using diagnosis codes and chief complaint text fields.§§ Only EDs consistently reporting informative data¶¶ during January 2019–December 2020 were included to ensure valid trend analyses. Relative rate percentage changes for benzodiazepine overdose ED visits per 100,000 ED visits were calculated by quarter (Q1: January–March, Q2: April–June, Q3: July–September, and Q4: October–December) and stratified by opioid involvement.***

Benzodiazepine deaths were identified from 23 states††† participating in SUDORS. States obtained data from death certificates and medical examiner and coroner reports, including complete postmortem toxicology testing results. Benzodiazepine deaths during January 2019–June 2020,

* https://www.cdc.gov/nchs/nvss/vsrr/drug-overdose-data.htm

† "Illicit benzodiazepines" refers to benzodiazepines that are not marketed in the United States for medical purposes; "prescription benzodiazepines" refers to those that are marketed as prescription drugs in the United States (but does not imply that the decedent had a prescription for that benzodiazepine; prescription benzodiazepines might be diverted). https://www.who.int/medicines/access/controlled-substances/Final_Etizolam.pdf; https://www.npsdiscovery.org/wp-content/uploads/2019/12/Public-Alert_Flualprazolam_NPS-Discovery_120519.pdf; https://www.who.int/docs/default-source/controlled-substances/43rd-ecdd/final-flubromazolam-a.pdf?sfvrsn

§ https://www.npsdiscovery.org/reports/trend-reports/

¶ Analyses were intended to include nonfatal overdose visits with unintentional and undetermined intents. ED visits resulting in death were not excluded but accounted for < 0.5% of total benzodiazepine overdose ED visits in ESSENCE during the study period.

** https://www.cdc.gov/drugoverdose/od2a/index.html; https://www.cdc.gov/drugoverdose/data/nonfatal/

†† Alabama, Arizona, Arkansas, Connecticut, Delaware, District of Columbia, Florida, Georgia, Illinois, Kansas, Kentucky, Louisiana, Maine, Maryland, Mississippi, Missouri, Montana, Nevada, New Jersey, New Mexico, New York, North Carolina, Ohio, Oregon, Pennsylvania, Rhode Island, South Carolina, Tennessee, Utah, Virginia, Washington, West Virginia, and Wisconsin.

§§ https://www.cdc.gov/drugoverdose/data/nonfatal/case.html; https://knowledgerepository.syndromicsurveillance.org/cdc-benzodiazepine-v1

¶¶ Some ED facilities might have started reporting to National Syndromic Surveillance Program during the study period, and others experienced reporting disruptions. Analyses were performed among approximately 62% of EDs submitting data to National Syndromic Surveillance Program that had relatively stable trends based on a coefficient of variation ≤45 and average weekly discharge diagnosis informative ≥75%.

*** Both nonfatal and fatal overdoses often involve multiple drugs; therefore, estimates for drugs are not mutually exclusive. For example, an overdose co-involving opioid and benzodiazepine would be counted as both an opioid and benzodiazepine overdose.

††† Alaska, Connecticut, Delaware, Georgia, Illinois, Maine, Massachusetts, Minnesota, Missouri, Nevada, New Hampshire, New Mexico, North Carolina, Oklahoma, Pennsylvania, Rhode Island, Tennessee, Utah, Vermont, Virginia, Washington, West Virginia, and Wisconsin.

percentages involving any opioids and opioid type (heroin, IMFs, or prescription opioids),[§§§] and percentage change in deaths, were calculated by quarter.

Demographic characteristics of persons experiencing nonfatal and fatal benzodiazepine overdoses, and specific drug co-involvement for benzodiazepine deaths, were described using the most recent period of available data (benzodiazepine overdose ED visits: January–December 2020, benzodiazepine deaths: January–June 2020). Benzodiazepine deaths were stratified by benzodiazepine type (prescription or illicit). Chi-square tests were used for pairwise comparisons; p-values <0.05 were considered statistically significant. Analyses were conducted using SAS (version 9.4; SAS Institute). This activity was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.[¶¶¶]

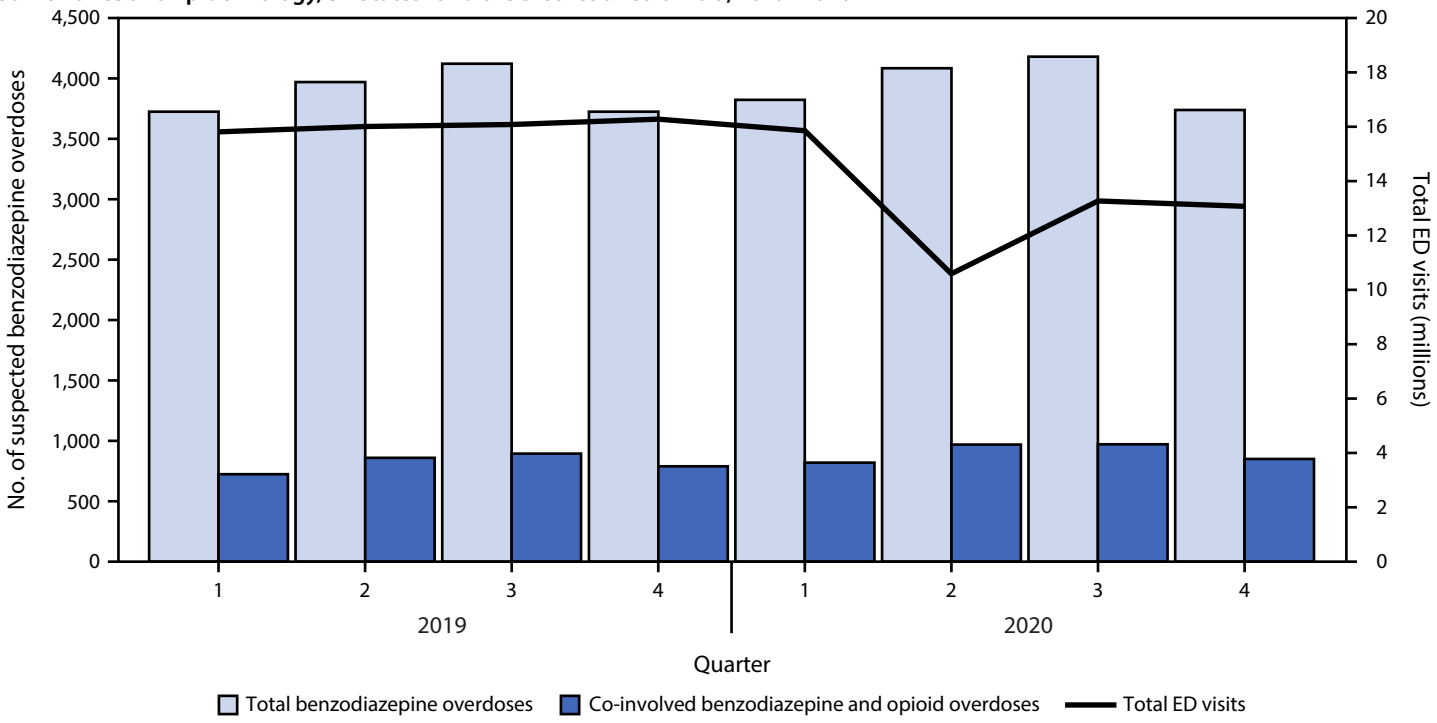
During January 2019–December 2020, 117 million ED visits reported in the 33 jurisdictions (72% of total ED visits) qualified for inclusion in analyses. Among these, 31,377 benzodiazepine overdose ED visits were identified, including 15,547 in 2019 and 15,830 in 2020; 6,883 (21.9%) also involved opioids. The highest number of benzodiazepine overdose ED visits occurred in Q3 2020 (4,181) (Figure 1).

In 2020, benzodiazepine overdose ED visits more often involved females (51.5%) and persons aged 25–34 years

[§§§] Drugs coded as prescription opioids were alfentanil, buprenorphine, codeine, hydrocodone, hydromorphone, levorphanol, loperamide, meperidine, methadone, morphine, noscapine, oxycodone, oxymorphone, pentazocine, prescription fentanyl, propoxyphene, remifentanil, sufentanil, tapentadol, and tramadol. IMFs include illicitly manufactured fentanyl and illicit fentanyl analogs. Fentanyl was classified as likely illicitly manufactured or likely prescription using toxicology, scene, and witness evidence. In the absence of sufficient evidence to classify fentanyl as illicit or prescription (<7% of deaths involving fentanyl), it was classified as illicit because most fentanyl overdose deaths involve illicit fentanyl.

[¶¶¶] 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.

FIGURE 1. Number of benzodiazepine overdose and co-involved opioid overdose emergency department visits, by quarter — Drug Overdose Surveillance and Epidemiology, 32 States* and the District of Columbia, 2019–2020[†, §, ¶]



Abbreviations: ED = emergency department; Q = quarter.

* Alabama, Arizona, Arkansas, Connecticut, Delaware, Florida, Georgia, Illinois, Kansas, Kentucky, Louisiana, Maine, Maryland, Mississippi, Missouri, Montana, Nevada, New Jersey, New Mexico, New York, North Carolina, Ohio, Oregon, Pennsylvania, Rhode Island, South Carolina, Tennessee, Utah, Virginia, Washington, West Virginia, and Wisconsin.

† All analyses were restricted to facilities with a coefficient of variation ≤45 and average weekly discharge diagnosis informative ≥75% during the study period, to include consistently reporting facilities with consistent data quality.

§ Relative rate changes from 2019 to 2020 were calculated based on total benzodiazepine overdose visits per 100,000 ED visits (15,547/64,200,344 and 15,830/52,816,815, respectively; 23.7% increase); benzodiazepine overdose visits co-involving opioids (3,271/64,200,344 and 3,612/52,816,815, respectively; 34.4% increase); and those with no opioid co-involvement (12,276/64,200,344 and 12,218/52,816,815, respectively; 21.0% increase).

¶ Relative rates increased from Q4 2019 to Q4 2020 for total benzodiazepine overdose visits by 24.9% (3,727/16,279,535 and 3,739/13,080,832, respectively), those co-involving opioids by 34.0% (791/16,279,535 and 851/13,080,832, respectively), and those without opioids by 22.5% (2,936/16,279,535 and 2,888/13,080,832, respectively).

(20.9%); nearly one quarter (22.8%) also involved opioids (Table). From 2019 to 2020, benzodiazepine overdose ED visits per 100,000 ED visits increased 23.7%, from 24.22 in 2019 to 29.97 in 2020, with larger rate increases among ED visits involving opioids (34.4% [from 5.09 to 6.84 per 100,000]) compared with those without opioids (21.0% [from 19.12 to 23.13 per 100,000]). Rates for any benzodiazepine ED visits were 24.9% higher in Q4 2020 (28.58) compared with those in Q4 2019 (22.89), as were rates for ED visits also involving opioids (34.0% increase from 4.86 in 2019 to 6.51 in 2020), and those without

TABLE. Demographics of persons experiencing nonfatal and fatal benzodiazepine overdoses and specific drug involvement in fatal benzodiazepine overdoses — 38 States and the District of Columbia, 2020*

	No. (%)			
	DOSE data: nonfatal benzodiazepine ODs, Q1–Q4 2020	SUDORS data: fatal benzodiazepine ODs, Q1–Q2 2020		
	Any benzodiazepine	Prescription	Illicit	Any benzodiazepine†
Characteristic	N = 15,830	N = 2,174	N = 532	N = 2,721
Sex				
Male	7,655 (48.4)	1,288 (59.2)	382 (71.8)	1,690 (62.1)
Female	8,144 (51.5)	886 (40.8)	150 (28.2)	1,031 (37.9)
Unknown	31 (0.2)	0 (—)	0 (—)	0 (—)
Age group, yrs				
Median (IQR), yrs	38 (26–56)	41 (32–53)	33 (26–46)	40 (31–52)
0–14	545 (3.4)	—§	0 (—)	—§
15–24	2,928 (18.5)	155 (7.1)	111 (20.9)	261 (9.6)
25–34	3,302 (20.9)	513 (23.6)	175 (32.9)	687 (25.2)
35–44	2,666 (16.8)	606 (27.9)	108 (20.3)	707 (26.0)
45–54	2,128 (13.4)	440 (20.2)	75 (14.1)	526 (19.3)
55–64	2,255 (14.2)	372 (17.1)	53 (10.0)	437 (16.1)
≥65	1,961 (12.4)	86 (4.0)	10 (1.9)	101 (3.7)
Unknown/Missing	45 (0.3)	—§	0 (—)	—§
Race/Ethnicity				
White, non-Hispanic	N/A	1,762 (81.0)	349 (65.6)	2,116 (77.8)
Black, non-Hispanic	N/A	202 (9.3)	110 (20.7)	319 (11.7)
Other, non-Hispanic	N/A	43 (2.0)	—§	58 (2.1)
Hispanic	N/A	148 (6.8)	52 (9.8)	204 (7.5)
Unknown/Missing	N/A	19 (0.9)	—§	24 (0.9)
Drug involvement				
Any opioid¶	3,612 (22.8)	2,025 (93.1)	493 (92.7)	2,523 (92.7)
Heroin	675 (4.3)	460 (21.2)	145 (27.3)	596 (21.9)
IMFs**	N/A	1,421 (65.4)	417 (78.4)	1,815 (66.7)
Illicit opioids††	N/A	1,542 (70.9)	459 (86.3)	1,973 (72.5)
Prescription opioids§§	N/A	922 (42.4)	117 (22.0)	1,026 (37.7)
Prescription and illicit opioids	N/A	452 (20.8)	83 (15.6)	518 (19.0)
Prescription benzodiazepines	N/A	2,174 (100)	79 (14.8)	2,174 (79.9)
Alprazolam	N/A	1,224 (56.3)	52 (9.8)	1,224 (45.0)
Other	N/A	1,166 (53.6)	32 (6.0)	1,166 (42.9)
Illicit benzodiazepines	N/A	79 (3.6)	532 (100)	532 (19.6)
Etizolam	N/A	35 (1.6)	151 (28.4)	151 (5.5)
Flualprazolam	N/A	41 (1.9)	376 (70.7)	376 (13.8)
Other	N/A	—§	20 (3.8)	20 (0.7)

Abbreviations: DOSE = Drug Overdose Surveillance and Epidemiology; IMFs = illicitly manufactured fentanyls; IQR = interquartile range; N/A = data not available; OD = overdose; Q = quarter; SUDORS = State Unintentional Drug Overdose Reporting System.

* Nonfatal benzodiazepine overdose data were from 32 states and the District of Columbia for overdose emergency department visits during January 1, 2020–December 31, 2020. Fatal benzodiazepine overdose data were from 23 states for deaths during January 1, 2020–June 30, 2020.

† Numbers of any benzodiazepines fatal ODs will not reflect the sum of prescription plus illicit benzodiazepine fatal ODs because some deaths involved both, and some deaths had a generic listing of benzodiazepine involvement; therefore, the prescription or illicit status could not be classified.

§ Dashes indicate cell data suppressed because cell contains one to nine cases or to prevent calculation of other suppressed cells.

¶ Comparing prescription benzodiazepine overdose deaths to illicit benzodiazepine overdose deaths, the percent co-involvement of any opioids was not statistically significantly different at $p<0.05$; all other comparisons were statistically significantly different (sex, age, race/ethnicity, co-involvement of heroin, IMFs, illicit opioids, prescriptions opioids, prescription and illicit opioids, and benzodiazepine type). Because prescription/illicit benzodiazepine deaths were not mutually exclusive, chi-square testing was performed after excluding 79 deaths with both prescription and illicit benzodiazepine involvement; however, percentages of each demographic category and with each substance co-involvement were similar to the nonmutually exclusive categorizations.

** IMFs include fentanyl and illicit fentanyl analogs.

†† Illicit opioids include heroin, IMFs, and other non-fentanyl illicit synthetic opioids (e.g., isotonitazene).

§§ Prescription opioids include alfentanil, buprenorphine, codeine, hydrocodone, hydromorphone, levorphanol, loperamide, meperidine, methadone, morphine, noscapine, oxycodone, oxymorphone, pentazocine, prescription fentanyl, propoxyphene, remifentanil, sufentanil, tapentadol, and tramadol.

opioids (22.5% increase from 18.03 in 2019 to 22.08 in 2020) (Figure 1). All relative rate changes were statistically significant.

Benzodiazepines were involved in 6,982 (16.8%) of 41,496 overdose deaths during January 2019–June 2020 reported by 23 states, with opioids involved in 6,384 (91.4%) benzodiazepine deaths. During the first 6 months of 2020, a total of 2,721 overdose deaths involved any benzodiazepine, 2,174 involved prescription benzodiazepines, and 532 involved illicit benzodiazepines (Table). Compared with prescription benzodiazepine overdose decedents, higher percentages of illicit benzodiazepine overdose decedents were male (71.8% versus 59.2%); Black, non-Hispanic (20.7% versus 9.3%); and younger (53.8% versus 30.7% aged 15–34 years); and a lower percentage was non-Hispanic White (65.6% versus 81.0%). Almost all benzodiazepine deaths during January–June 2020 also involved opioids (92.7%) and often involved IMFs (66.7%). Illicit benzodiazepine deaths more often involved IMFs than did prescription benzodiazepine deaths (78.4% versus 65.4%), and less often involved prescription opioids (22.0% versus 42.4%).

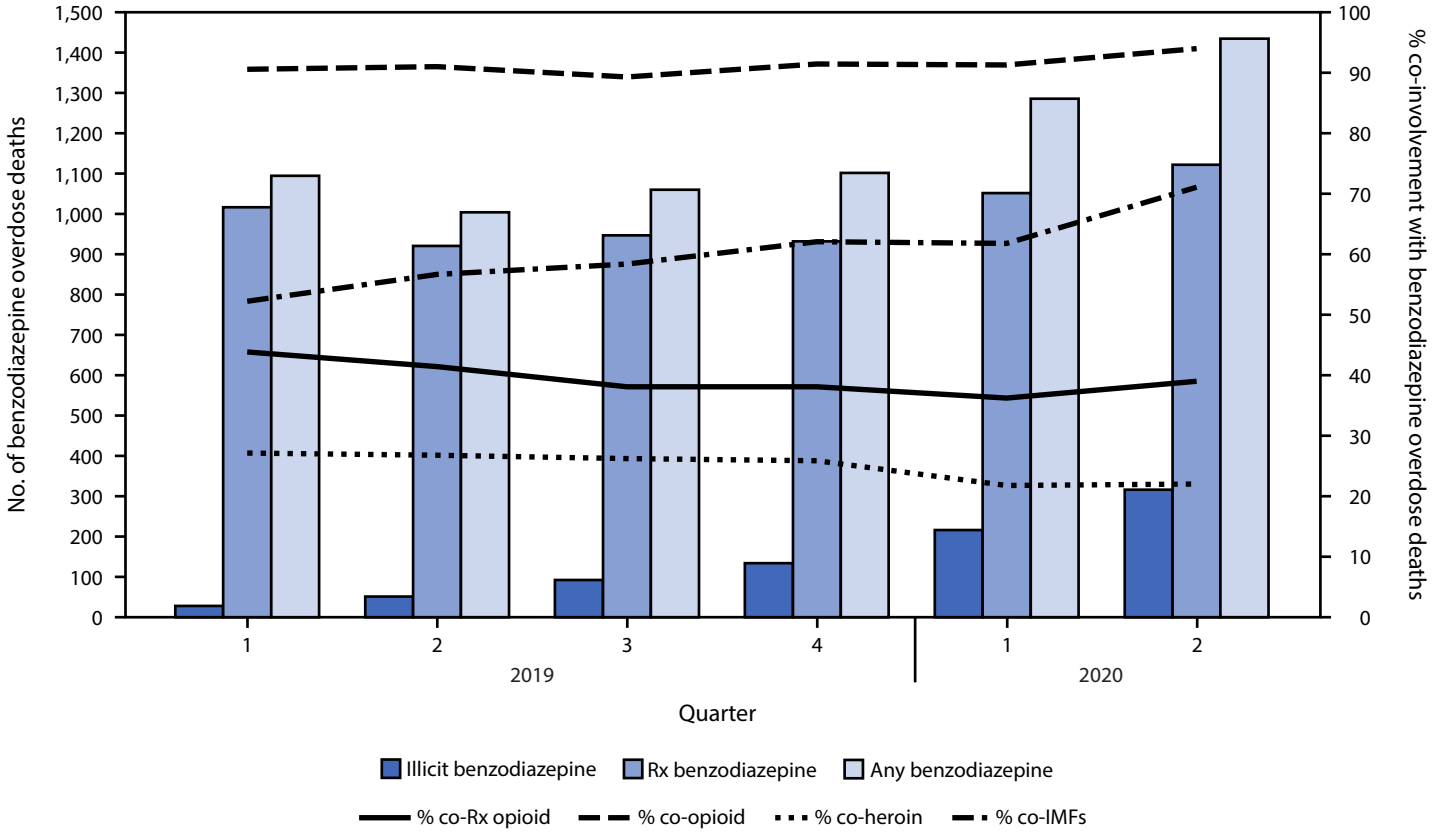
The number of benzodiazepine deaths increased 42.9% from Q2 2019 (1,004) through Q2 2020 (1,435), with increases in both prescription (from 921 to 1,122; 21.8% increase) and illicit (from 51 to 316; 519.6% increase) benzodiazepine deaths (Figure 2). During this time, co-involvement of IMFs in benzodiazepine deaths increased 25.4%, from 56.7% to 71.1%.

Discussion

This is the first multistate report to examine recent trends in both nonfatal and fatal benzodiazepine overdoses. Three concerning trends during 2019–2020 were identified: 1) increases in both nonfatal and fatal overdoses involving benzodiazepines and opioids; 2) marked increases in illicit benzodiazepine deaths, although overdose deaths involving prescription benzodiazepines still far outnumber those involving illicit benzodiazepines; and 3) increases in nonfatal benzodiazepine overdoses not involving opioids. In 2016, the CDC Opioid Prescribing Guideline discouraged co-prescribing opioids and benzodiazepines,**** and

**** https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm?CDC_AA_refVal

FIGURE 2. Benzodiazepine overdose deaths with opioid co-involvement — State Unintentional Drug Overdose Reporting System, 23 states,* January 2019–June 2020†



Abbreviations: co- = co-involved; IMFs = illicitly manufactured fentanyls; Rx = prescription.

* Alaska, Connecticut, Delaware, Georgia, Illinois, Maine, Massachusetts, Minnesota, Missouri, Nevada, New Hampshire, New Mexico, North Carolina, Oklahoma, Pennsylvania, Rhode Island, Tennessee, Utah, Vermont, Virginia, Washington, West Virginia, and Wisconsin.

† IMFs include fentanyl and illicit fentanyl analogs.

the Food and Drug Administration imposed its most prominent warning on all benzodiazepine medications,[††††] describing the risks of use with opioids. Despite progress in reducing co-prescribing before 2019 (*2*), this study suggests a reversal in the decline in benzodiazepine deaths from 2017 to 2019,[§§§§] driven in part by increasing involvement of IMFs in benzodiazepine deaths and influxes of illicit benzodiazepines, likely indicating simultaneous use of nonprescribed opioids and benzodiazepines.

During 2019–2020, benzodiazepine deaths (both prescription and illicit) were characterized by high and increasing co-involvement of IMFs, a trend documented as early as during 2017–2018 (*3*). Substantial increases in the supply of IMFs during January 2013–June 2020,[¶¶¶¶] coupled with the high potency and rapid absorption of IMFs (*4*), which increase overdose risk above that of heroin and prescription opioids, is likely a principal driver of fatal benzodiazepine and IMF overdose. The largest increase in IMF involvement among benzodiazepine deaths occurred in 2020 between Q1 and Q2, possibly reflecting altered drug use patterns that increased overdose risk (e.g., decreased naloxone access); and possible drug supply disruptions; during the COVID-19 pandemic (*5*). Although the much greater involvement of opioids in benzodiazepine deaths (91.4%) compared with benzodiazepine overdose ED visits (21.9%) underscores the dangers of co-use, increases in opioid involvement among benzodiazepine ED visits (34.4% increase) throughout 2020 might be an early indicator of continued and amplified increases in morbidity and mortality related to benzodiazepine and opioid co-use.

Other factors accelerating increases in benzodiazepine deaths involving opioids are rapid increases in supply and co-use of illicit benzodiazepines among persons using illicit opioids, especially IMFs. Whereas law enforcement reports of diverted prescription benzodiazepines declined from 2015 through June 2020, reports of illicit benzodiazepines (particularly etizolam and flualprazolam) surged during that period, indicating increased availability (*6*).[*****] Reductions in benzodiazepine and opioid co-prescribing must be coupled with efforts to disrupt and reduce the availability of and harms associated with concurrent use of illicit benzodiazepines and IMFs.

Although rates of ED visits for mental health conditions increased during 2019–2020 (*1*), benzodiazepine prescriptions remained relatively stable during January 2019–May 2020, with a transient spike in March 2020 indicating, per recommendations, increases in the availability of medications on hand because of stay-at-home orders to slow the spread of COVID-19 (*7*). However, the increases in benzodiazepine overdose ED visit rates, including those without opioids, raise concerns about increased misuse and warrant further investigation. Because benzodiazepine use is less likely to result in fatal overdose without use of opioids or other depressants (*6*), tracking nonfatal benzodiazepine overdoses is critical to tracking benzodiazepine misuse trends.

The findings in this report are subject to at least five limitations. First, jurisdictions included in nonfatal and fatal overdose analyses are not nationally representative and differ from each other, limiting the extent to which trends can be compared. Second, full toxicology results for nonfatal overdoses were not available, and opioid and benzodiazepine involvement in nonfatal overdoses is likely underestimated because comprehensive toxicology testing of persons treated for overdoses varies within and across EDs, and hospital discharge codes with drug specific information might be unavailable (*8*). Third, despite only including consistently reporting facilities, ED visits decreased sharply after implementation of COVID-19 mitigation measures in March 2020, which might inflate rate increases (*9*). Fourth, four states (Illinois, Missouri, Pennsylvania, and Wisconsin) reported overdose deaths from varying subsets of counties. Results were similar with and without these states. Finally, postmortem toxicology testing and drug involvement determination vary over time and across states, potentially affecting detection of specific drugs involved in deaths.

Increases in benzodiazepine overdose ED visits throughout 2020, coupled with increases in illicit benzodiazepine deaths since 2019, highlight the need to enhance efforts to mitigate harm from simultaneously using benzodiazepines and opioids and monitor the magnitude and persistence of increases in illicit benzodiazepine deaths. Persons who co-use opioids and benzodiazepines might be less likely to receive medications for opioid use disorder than persons using opioids only (*10*); therefore, efforts to increase treatment access should be enhanced. Expansion of naloxone availability and rapid naloxone administration should be encouraged for overdoses involving benzodiazepines and opioids because naloxone reverses opioid overdoses irrespective of benzodiazepine presence. However, educational efforts should emphasize the dangers of using illicit benzodiazepines, especially in combination with opioids, and the importance of calling 9-1-1 even after naloxone administration, because benzodiazepine overdose symptoms are unaffected by naloxone and might require additional medical treatment. These efforts, complemented by broader primary prevention of drug use and misuse, could prevent drug overdose morbidity and mortality.

[††††] https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-warns-about-serious-risks-and-death-when-combining-opioid-pain-or; https://www.fda.gov/drugs/drug-safety-and-availability/fda-requiring-boxed-warning-updated-improve-safe-use-benzodiazepine-drug-class

[§§§§] https://www.drugabuse.gov/drug-topics/trends-statistics/overdose-death-rates; https://wonder.cdc.gov/

[¶¶¶¶] https://www.nflis.deadiversion.usdoj.gov/nflisdata/docs/13915NFLISdrugMidYear2020.pdf

[*****] https://www.nflis.deadiversion.usdoj.gov/nflisdata/docs/13915NFLISdrugMidYear2020.pdf

Summary

What is already known about this topic?

Benzodiazepine-involved overdose deaths decreased during 2017–2019; however, since 2019, the illicit benzodiazepine supply increased.

What is added by this report?

From 2019 to 2020, benzodiazepine overdose visits per 100,000 emergency department visits increased (23.7%), both with (34.4%) and without (21.0%) opioid co-involvement. From April–June 2019 to April–June 2020, prescription and illicit benzodiazepine-involved overdose deaths increased 21.8% and 519.6%, respectively. During January–June 2020, 92.7% of benzodiazepine-involved deaths also involved opioids, and 66.7% involved illicitly manufactured fentanyls.

What are the implications for public health practice?

Improving naloxone availability and enhancing treatment access for persons using benzodiazepines and opioids and calling emergency services for overdoses involving benzodiazepines and opioids, coupled with primary prevention of drug use and misuse, could reduce morbidity and mortality.

Acknowledgments

Jurisdictions participating in CDC's Overdose Data to Action (OD2A) program and providing data in the Drug Overdose Surveillance and Epidemiology system and the State Unintentional Drug Overdose Reporting System, including state and jurisdictional health departments, vital registrar offices, and coroner and medical examiner offices; CDC OD2A team, and the National Syndromic Surveillance Program, CDC.

Corresponding authors: Stephen Liu, ice5@cdc.gov, 404-498-5686; Julie O'Donnell, irh8@cdc.gov, 404-498-5005.

[1]Division of Overdose Prevention, National Center for Injury Prevention and Control, CDC; [2]Peers and Partners, Inc., Seattle, Washington.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

References

1. Holland KM, Jones C, Vivolo-Kantor AM, et al. Trends in US emergency department visits for mental health, overdose, and violence outcomes before and during the COVID-19 pandemic. JAMA Psychiatry 2021;78:372–9. PMID:33533876 https://doi.org/10.1001/jamapsychiatry.2020.4402
2. Jeffery MM, Hooten WM, Jena AB, Ross JS, Shah ND, Karaca-Mandic P. Rates of physician coprescribing of opioids and benzodiazepines after the release of the Centers for Disease Control and Prevention Guidelines in 2016. JAMA Netw Open 2019;2:e198325. PMID:31373650 https://doi.org/10.1001/jamanetworkopen.2019.8325
3. Gladden RM, O'Donnell J, Mattson CL, Seth P. Changes in opioid-involved overdose deaths by opioid type and presence of benzodiazepines, cocaine, and methamphetamine—25 states, July–December 2017 to January–June 2018. MMWR Morb Mortal Wkly Rep 2019;68:737–44. PMID:31465320 https://doi.org/10.15585/mmwr.mm6834a2
4. Gill H, Kelly E, Henderson G. How the complex pharmacology of the fentanyls contributes to their lethality. Addiction 2019;114:1524–5. PMID:30883941 https://doi.org/10.1111/add.14614
5. O'Donoghue AL, Biswas N, Dechen T, et al. Trends in filled naloxone prescriptions before and during the COVID-19 pandemic in the United States. JAMA Health Forum 2021;2:e210393. https://doi.org/10.1001/jamahealthforum.2021.0393
6. Bollinger K, Weimer B, Heller D, et al. Benzodiazepines reported in NFLIS-Drug, 2015 to 2018. Forensic Sci Int Synerg 2021;3:100138. PMID:33665593 https://doi.org/10.1016/j.fsisyn.2021.100138
7. Jones CM, Guy GP Jr, Board A. Comparing actual and forecasted numbers of unique patients dispensed select medications for opioid use disorder, opioid overdose reversal, and mental health, during the COVID-19 pandemic, United States, January 2019 to May 2020. Drug Alcohol Depend 2021;219:108486. PMID:33421802 https://doi.org/10.1016/j.drugalcdep.2020.108486
8. Morrow JB, Ropero-Miller JD, Catlin ML, et al. The opioid epidemic: moving toward an integrated, holistic analytical response. J Anal Toxicol 2019;43:1–9. PMID:30165647 https://doi.org/10.1093/jat/bky049
9. Adjemian J, Hartnett KP, Kite-Powell A, et al. Update: COVID-19 pandemic–associated changes in emergency department visits—United States, December 2020–January 2021. MMWR Morb Mortal Wkly Rep 2021;70:552–6. PMID:33857069 https://doi.org/10.15585/mmwr.mm7015a3
10. Ford BR, Bart G, Grahan B, Shearer RD, Winkelman TNA. Associations between polysubstance use patterns and receipt of medications for opioid use disorder among adults in treatment for opioid use disorder. J Addict Med 2021;15:159–62. PMID:32868682 https://doi.org/10.1097/ADM.0000000000000726

Mental Health and Substance Use Among Adults with Disabilities During the COVID-19 Pandemic — United States, February–March 2021

Mark É. Czeisler[1,2,3,4]; Amy Board, DrPH[5,6,7]; JoAnn M. Thierry, PhD[5]; Charles A. Czeisler, PhD, MD[1,3,4]; Shantha M.W. Rajaratnam, PhD[1,2,3,4]; Mark E. Howard, MBBS, PhD[1,2,8]; Kristie E.N. Clarke, MD[5]

Adults with disabilities, a group including >25% of U.S. adults (*1*), experience higher levels of mental health and substance use conditions and lower treatment rates than do adults without disabilities* (*2*,*3*). Survey data collected during April–September 2020 revealed elevated adverse mental health symptoms among adults with disabilities (*4*) compared with the general adult population (*5*). Despite disproportionate risk for infection with SARS-CoV-2, the virus that causes COVID-19, and COVID-19–associated hospitalization and mortality among some adults with disabilities (*6*), information about mental health and substance use in this population during the pandemic is limited. To identify factors associated with adverse mental health symptoms and substance use among adults with disabilities, the COVID-19 Outbreak Public Evaluation (COPE) Initiative† administered nonprobability–based Internet surveys to 5,256 U.S. adults during February–March 2021 (response rate = 62.1%). Among 5,119 respondents who completed a two-item disability screener, nearly one-third (1,648; 32.2%) screened as adults with disabilities. These adults more frequently experienced symptoms of anxiety or depression (56.6% versus 28.7%, respectively), new or increased substance use (38.8% versus 17.5%), and suicidal ideation (30.6% versus 8.3%) than did adults without disabilities. Among all adults who had received a diagnosis of mental health or substance use conditions, adults with disabilities more frequently (42.6% versus 35.3%; p <0.001) reported that the pandemic made it harder for them to access related care or medication. Enhanced mental health and substance use screening among adults with disabilities and improved access to medical services are critical during public health emergencies such as the COVID-19 pandemic.

During February 16–March 8, 2021, among 8,475 eligible invited respondents aged ≥18 years, 5,261 (62.1%) completed nonprobability based, English-language, Internet-based Qualtrics surveys for COPE.§ Participants provided informed consent electronically. Quota sampling and survey weighting were used to match U.S. Census Bureau's 2019 American Community Survey adult U.S. population estimates for sex, age, and race/ethnicity to enhance the representativeness of this nonrandom sample.

Among 5,256 respondents who answered questions for weighting variables, 5,119 (97.4%) completed a two-question disability screener.¶ Respondents completed clinically validated self-screening instruments for symptoms of anxiety and depression** and reported past-month new or increased substance use to cope with stress or emotions and serious suicidal ideation.†† Respondents also indicated prepandemic and past-month use of seven classes§§ of substances to cope with stress or emotions. Adults with diagnosed anxiety, depression, posttraumatic stress disorder, or substance use disorders indicated whether their ability to access care or medications for these conditions was easier, harder, or unaffected because of the pandemic. Prevalence estimates for adverse mental health symptoms and substance use were compared among adults with and without disabilities using chi-square tests. Multivariable Poisson regression models with robust standard error estimators were used to estimate adjusted prevalence ratios (aPRs) by symptom type among adults with and without disabilities. To calculate associations between disability status and adverse

* https://store.samhsa.gov/sites/default/files/d7/priv/pep19-02-00-002_508_022620.pdf

† The COVID-19 Outbreak Public Evaluation (COPE) Initiative (https://www.thecopeinitiative.org/) is designed to assess public attitudes, behaviors, and beliefs related to COVID-19 pandemic and to evaluate mental and behavioral health during the pandemic. The COPE Initiative surveys included in this analysis were administered by Qualtrics, LLC (https://www.qualtrics.com), a commercial survey company with a network of participant pools with varying recruitment methodologies that include digital advertisements and promotions, word-of-mouth and membership referrals, social networks, television and radio advertisements, and offline mail-based approaches.

§ Eligibility to complete surveys was determined after electronic contact of potential participants with inclusion criteria of age ≥18 years and residence within the United States.

¶ Disability was defined as such based on a qualifying response by an adult to either one of two questions: "Are you limited in any way in any activities because of physical, mental, or emotional condition?" and "Do you have any health conditions that require you to use special equipment, such as a cane, wheelchair, special bed, or special telephone?" https://www.cdc.gov/brfss/questionnaires/pdf-ques/2015-brfss-questionnaire-12-29-14.pdf

** Symptoms of anxiety and depression were assessed with the four-item Patient Health Questionnaire (PHQ-4). Respondents who scored ≥3 out of 6 on the Generalized Anxiety Disorder (GAD-2) and Patient Health Questionnaire (PHQ-2) subscales were considered symptomatic for the respective conditions.

†† New or increased substance use was assessed with the question, "Have you started or increased using substances to help you cope with stress or emotions during the COVID-19 pandemic? Substance use includes alcohol, legal or illegal drugs, or prescription drug use in any way not directed by a doctor." Suicidal ideation was assessed with an item from the National Survey on Drug Use and Health (https://nsduhweb.rti.org/respweb/homuepage.cfm) adapted to refer to the preceding 30 days, "At any time in the past 30 days, did you seriously think about trying to kill yourself?"

§§ Alcohol, marijuana, cocaine, methamphetamine, prescription or illicit opioids, benzodiazepines, and prescription drugs other than opioids used in a way not directed by a doctor.

mental health symptoms or substance use over time, aPRs were estimated for symptoms among unique participants in previous COPE survey waves (June, September, and December 2020). Covariates[¶¶] included sex, age group, race/ethnicity, income, U.S. Census region, urbanicity, and parental or unpaid caregiving roles.[***] McNemar's test assessed prepandemic and past-month substance use among adults with and without disabilities. Analyses were conducted using Python software (version 3.7.8; Python Software Foundation) and R statistical software (version 4.0.2; R Foundation) using the R survey package (version 3.29; R Foundation). The Monash University Human Research Ethics Committee reviewed and approved the study. This activity was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.[†††]

Among a total of 5,119 respondents, 1,648 (32.2%) respondents reported living with disabilities (778 [47.2%] with limiting physical, mental, or emotional conditions only; 171 [10.4%] with health conditions requiring special equipment only; and 669 [42.4%] with both types of conditions) (Table). Overall, 64.1% of adults with disabilities reported adverse mental health symptoms or substance use compared with 36.0% of adults without disabilities; past-month substance use was higher among adults with disabilities (40.6%) than among adults without disabilities (24.5%). Prevalence estimates of each of the following were higher among adults with disabilities than among adults without disabilities: symptoms of anxiety or depression (56.6% versus 28.7%, respectively), new or increased substance use (38.8% versus 17.5%), and serious suicidal ideation (30.6% versus 8.3%) (Supplementary Table, https://stacks.cdc.gov/view/cdc/108999). At all timepoints, aPRs for all symptom types were significantly higher among adults with disabilities than among adults without disabilities (Figure 1). During February 16–March 8, 2021, among adults with disabilities, aPRs for symptoms of anxiety or depression and new or increased substance use were approximately 1.5 times as high, and the aPR for serious suicidal ideation was approximately 2.5 times as high as in adults without disabilities. Comparing subgroups of adults with and without disabilities, symptoms of anxiety or depression were approximately twice as prevalent among adults with disabilities who were aged ≥50 years (aPR = 2.4; 95% confidence interval [CI] = 1.7–3.2), those of non-Hispanic Asian race/ethnicity (2.4; 95% CI = 1.3–4.8), those of Hispanic or Latino (Hispanic) ethnicity (2.1; 95% CI = 1.4–3.0), and those who were not in parental or caregiver roles (2.1; 95% CI = 1.7–2.6). New or increased substance use was approximately twice as prevalent among adults with disabilities in parental roles only (2.4; 95% CI = 1.5–3.9) and among essential workers (2.3; 95% CI = 2.0–2.7). Suicidal ideation was also more prevalent among adults with disabilities aged ≥50 years (4.0; 95% CI = 2.1–7.8), those of Hispanic ethnicity (3.4; 95% CI = 1.9–6.0), adults in unpaid caregiving roles (3.4; 95% CI = 1.5–7.7), and essential (3.5; 95% CI = 2.8–4.4) or nonessential (5.3; 95% CI = 2.8–10.1) workers.

The prevalence of substance use to cope with stress or emotions among adults with disabilities was higher than that among adults without disabilities, both prepandemic (39.7% versus 25.3%, respectively) and in the past month (40.6% versus 24.5%; both p<0.001) (Figure 2). Among adults with disabilities, the past-month prevalence of methamphetamine use (8.4%), nonopioid prescription drug misuse (4.9%), and polysubstance use (16.9%) was approximately twice as high, and the prevalence of cocaine use (6.4%) and prescription or illicit opioid use (9.1%) were nearly three times as high compared with those among adults without disabilities (methamphetamine use 3.4%; nonopioid prescription drug misuse 2.0%; polysubstance use 7.9%; cocaine use 2.2%; prescription or illicit opioid use 3.2%). Past-month methamphetamine use prevalence increased significantly compared with prepandemic use prevalence among all respondents (with disabilities, 45.6% increase, p<0.001; without disabilities, 40.6% increase, p = 0.003). Among respondents who reported a diagnosed mental health or substance use condition, a higher percentage of adults with (versus without) disabilities reported that accessing care or medication was harder because of the COVID-19 pandemic (42.6% versus 35.3%, respectively, p<0.001).

Discussion

Nearly two thirds of surveyed adults with disabilities (who represented approximately 32% of the sample) reported adverse mental health symptoms or substance use in early 2021, compared with approximately one third of adults without disabilities. Serious suicidal ideation was approximately 2.5 times as high among adults with disabilities, and methamphetamine use, opioid use, nonopioid prescription drug misuse, and polysubstance use were at least twice as

[¶¶] Models to estimate aPRs for adverse mental health symptoms and substance use were run with each of the collinear variables income and education during preliminary analysis. Estimated aPRs did not differ meaningfully. In the report, the models including income were included to account for potential differences in access to health care more directly. To avoid collinearity with age, employment status was included in a separate model, and aPRs were not estimated for retired status or student employment status.

[***] Adults who were in parental or unpaid caregiving roles were self-identified. For this analysis, the definition of unpaid caregivers of adults was having provided unpaid care to a relative or friend aged ≥18 years to help them take care of themselves at any time during the three months before the survey. The definition of someone in a parental role was having provided unpaid care to a relative or friend aged <18 years. Respondents were categorized as being in a parental role only, a caregiver of adults role only, having both parental and caregiving roles, or having neither parental nor caregiving roles. Adults in parenting roles might not have been biologic or adoptive parents of the children.

[†††] 45 C.F.R. part 46, 21 C.F.R. part 56; 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a; 44 U.S.C. Sect. 3501 et seq.

TABLE. Prevalence of symptoms of anxiety or depression, substance use, and suicidal ideation among adults with disabilities, by disability status and other characteristics — United States, February 16–March 8, 2021

Characteristic	No. (%)		Adults with disabilities, No. (%)*			
	All respondents	Adults with disabilities	Symptoms of anxiety or depression†	New or increased substance use to cope§	Seriously considered suicide¶	One or more of these symptoms
Total	**5,119 (100)**	**1,648 (32.2)**	**932 (56.6)**	**640 (38.8)**	**504 (30.6)**	**1,057 (64.1)**
Disability screener**						
Limited by a physical, mental, or emotional condition	778 (15.2)	778 (47.2)	417 (53.7)	218 (28.0)	148 (19.0)	465 (59.8)
Limited by a health condition that requires special equipment	171 (3.3)	171 (10.4)	104 (60.5)	88 (51.5)	65 (38.2)	123 (71.8)
Both of above	699 (13.7)	669 (42.4)	411 (58.8)	334 (47.8)	291 (41.5)	469 (67.1)
Neither of above	3,471 (67.8)	0 (—)	N/A	N/A	N/A	N/A
Sex††						
Female	2,499 (48.8)	789 (47.9)	445 (56.5)	260 (32.9)	178 (22.6)	501 (63.5)
Male	2,583 (50.5)	838 (50.8)	469 (55.9)	369 (44.0)	314 (37.4)	537 (64.1)
Age group, yrs						
18–29	938 (18.3)	314 (19.0)	250 (79.8)	185 (59.1)	136 (43.3)	276 (87.8)
30–39	967 (18.9)	325 (19.7)	259 (79.8)	198 (60.9)	166 (51.1)	281 (86.6)
40–49	818 (16.0)	253 (15.4)	180 (70.9)	137 (54.0)	125 (49.5)	202 (79.6)
50–59	972 (19.0)	309 (18.8)	132 (42.6)	80 (25.9)	54 (17.5)	158 (51.2)
60–69	790 (15.4)	235 (14.2)	59 (25.2)	21 (8.9)	4 (1.8)	72 (30.7)
≥70	634 (12.4)	213 (12.9)	52 (24.7)	19 (8.8)	19 (8.8)	68 (31.9)
Race/Ethnicity						
White, non-Hispanic	3,103 (60.6)	975 (59.2)	522 (53.6)	327 (33.5)	266 (27.3)	585 (60.0)
Black, non-Hispanic	638 (12.5)	181 (11.0)	99 (54.6)	68 (37.9)	35 (19.3)	110 (60.9)
Asian, non-Hispanic	289 (5.6)	65 (3.9)	39 (61.1)	18 (27.8)	14 (21.0)	47 (72.1)
Multiple/other race, non-Hispanic§§	188 (3.7)	70 (4.3)	32 (45.2)	16 (23.3)	13 (18.3)	32 (45.8)
Hispanic or Latino, any race	902 (17.6)	357 (21.7)	240 (67.2)	210 (58.8)	177 (49.5)	283 (79.3)
2020 Household income, USD¶¶						
<25,000	1,182 (23.1)	544 (33.0)	286 (52.6)	151 (27.8)	107 (19.7)	327 (60.0)
25,000–49,999	1,203 (23.5)	355 (21.5)	179 (50.4)	110 (30.9)	82 (23.2)	202 (56.9)
50,000–99,999	1,306 (25.5)	350 (21.2)	191 (54.6)	134 (38.2)	103 (29.5)	218 (62.1)
≥100,000	1,204 (23.5)	341 (20.7)	253 (74.1)	232 (68.1)	205 (60.1)	286 (83.8)
Education						
High school diploma or less	1,379 (26.9)	485 (29.4)	264 (54.4)	155 (31.8)	135 (27.9)	309 (63.7)
College or some college	2,876 (56.2)	865 (52.5)	463 (53.5)	312 (36.0)	213 (24.6)	520 (60.1)
After bachelor's degree	865 (16.9)	298 (18.1)	206 (69.0)	174 (58.2)	156 (52.3)	228 (76.4)
Employment status						
Employed (essential employee)	1,797 (35.1)	605 (36.7)	475 (78.6)	448 (74.2)	371 (61.4)	542 (89.6)
Employed (nonessential employee)	941 (18.4)	151 (9.1)	87 (57.9)	53 (35.2)	38 (25.4)	103 (68.3)
Unemployed	936 (18.3)	349 (21.2)	190 (54.5)	77 (22.2)	55 (15.9)	207 (59.3)
Retired	1,263 (24.7)	493 (29.9)	142 (28.8)	45 (9.1)	24 (4.8)	167 (33.8)
Student	182 (3.6)	51 (3.1)	38 (73.7)	16 (31.9)	15 (29.8)	38 (74.5)
Parental role and unpaid caregiving status***						
Neither parent nor caregiver	2,882 (56.3)	741 (44.9)	294 (39.7)	90 (12.2)	70 (9.4)	323 (43.6)
Parent only	611 (11.9)	189 (11.5)	97 (51.3)	48 (25.1)	21 (11.3)	110 (58.0)
Caregiver role of adults only	426 (8.3)	117 (7.1)	57 (48.6)	39 (33.1)	24 (20.9)	71 (60.5)
Parental and caregiver roles	1,201 (23.5)	602 (36.5)	485 (80.5)	463 (77.0)	389 (64.6)	553 (92.0)
U.S. Census region†††						
Northeast	899 (17.6)	267 (16.2)	177 (66.0)	119 (44.7)	109 (40.6)	188 (70.5)
Midwest	1,069 (20.9)	349 (21.1)	208 (59.8)	126 (36.0)	94 (27.1)	222 (63.6)
South	2,074 (40.5)	700 (42.5)	367 (52.4)	262 (37.4)	195 (27.9)	442 (63.1)
West	1,077 (21.0)	333 (20.2)	180 (54.2)	133 (40.1)	106 (31.8)	205 (61.7)
Urbanicity (n = 5,091)§§§						
Urban	4,241 (83.3)	1,313 (79.6)	761 (58.0)	544 (41.4)	440 (33.5)	866 (66.0)
Rural	850 (16.7)	322 (19.5)	158 (49.1)	87 (27.1)	56 (17.4)	178 (55.2)

See table footnotes on the next page.

TABLE. (*Continued*) Prevalence of symptoms of anxiety or depression, substance use, and suicidal ideation among adults with disabilities, by disability status and other characteristics — United States, February 16–March 8, 2021

Abbreviations: N/A = not applicable; USD = U.S. dollars.

* Weighted rounded counts and percentages might not sum to expected values.

† Symptoms of anxiety and depression were assessed via the four-item Patient Health Questionnaire (PHQ-4). Respondents who scored ≥3 out of 6 on the Generalized Anxiety Disorder (GAD-2) and Patient Health Questionnaire (PHQ-2) subscales were considered symptomatic for these respective conditions.

§ New or increased substance use was assessed by using the question, "Have you started or increased using substances to help you cope with stress or emotions during the COVID-19 pandemic? Substance use includes alcohol, legal or illegal drugs, or prescription drug use in any way not directed by a doctor."

¶ Suicidal ideation was assessed by using an item from the National Survey on Drug Use and Health (https://nsduhweb.rti.org/respweb/homepage.cfm) adapted to refer to the previous 30 days, "At any time in the past 30 days, did you seriously think about trying to kill yourself?"

** Adults who had a disability were defined as such based on a qualifying response to either one of two questions: "Are you limited in any way in any activities because of physical, mental, or emotional condition?" and "Do you have any health conditions that require you to use special equipment, such as a cane, wheelchair, special bed, or special telephone?" Respondents who completed only one of the two disability screening questions (limited by a physical, mental, or emotional condition: 17); limited by a health condition that requires special equipment: 12) were classified as living with only that disability. https://www.cdc.gov/brfss/questionnaires/pdf-ques/2015-brfss-questionnaire-12-29-14.pdf

†† Gender responses of "Transgender" (22; 0.4%) and "None of these" (15; 0.3%) are not shown because of small counts.

§§ The non-Hispanic, multiple/other race or multiple races category includes respondents who identified as not Hispanic and as more than one race or as American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, or any other race.

¶¶ Household income responses of "Prefer not to say" (225) are not shown because of an inability to sufficiently characterize these responses.

*** Adults who were in parental or unpaid caregiving roles were self-identified. For this analysis, the definition of unpaid caregivers of adults was having provided unpaid care to a relative or friend ≥18 years to help them take care of themselves at any time during the 3 months before the survey. The definition of someone in a parental role was having provided unpaid care to a relative or friend <18 years. Respondents answered these questions separately. During analysis, all respondents were categorized as being in a parental role only, caregivers of adults only, having both parental and caregiving roles, or having neither parental nor caregiving roles. Adults in parenting roles might not have been natural or legal parents of children in their care.

††† https://www2.census.gov/geo/pdfs/maps-data/maps/reference/us_regdiv.pdf

§§§ Invalid postcodes were provided by 28 respondents, for whom urbanicity was not categorized. https://www.hrsa.gov/rural-health/about-us/definition/datafiles.html

prevalent among adults with disabilities. These findings suggest value in enhanced mental health screening among adults with disabilities and in ensuring accessibility of routine and crisis services, particularly given that many adults reported that the COVID-19 pandemic had reduced mental health and substance use care or medication accessibility. Mental health disparities among adults with disabilities were observed across demographic groups, highlighting the importance of ensuring access to disaster distress[§§§] and suicide prevention[¶¶¶] resources in this population. Important strategies to prevent persons from becoming suicidal include strengthening economic supports, promoting connectedness, and teaching coping skills.[****] Health care providers could incorporate trauma-informed care, because adults with disabilities might have encountered stigma and trauma in previous health care interactions. Adults with disabilities more frequently reported prepandemic and past-month substance use to cope with stress or emotions compared with adults without disabilities. The substance with the largest increase in use was methamphetamine, which is particularly concerning given the increase in amphetamine overdoses[††††] (*7*). Drug overdose deaths rose in 2020, driven by synthetic opioids.[§§§§] Consistent with previous research, adults with disabilities disproportionately reported opioid use and nonopioid prescription drug misuse (*8*), highlighting the importance of educating patients and ensuring clinician access to prescription drug monitoring programs.[¶¶¶¶] Nearly one in ten adults with disabilities reported past-month opioid use, and opioid use among adults without disabilities increased. Policies that reduce barriers to evidence-based treatment, including recently updated buprenorphine practice guidelines,[*****] might improve access.

The findings in this report are subject to at least four limitations. First, self-reported mental health and substance use might be subject to social desirability biases and stigma, which could lead to underreporting. Second, because the surveys were English-language only and data were obtained using nonprobability–based sampling, despite quota sampling and survey weighting, the findings from this nonrandom sample might not be generalizable. However, the proportion and demographics of surveyed adults with disabilities were similar to those of recent samples from other sources with the same or similar screening questions (*1*,*2*,*4*), and prevalence estimates of symptoms of anxiety and depression were largely consistent with those from other sources for the U.S. adult population (*9*) and adults with disabilities (*4*) including the U.S. Census Bureau's probability-based Household Pulse Survey (64.3% among adults with disabilities compared with 27.4% among

§§§ Substance Abuse and Mental Health Services Administration National Helpline (https://www.samhsa.gov/find-help/national-helpline); Disaster Distress Helpline (https://www.samhsa.gov/disaster-preparedness).

¶¶¶ National Suicide Prevention Lifeline: 1–800–273-TALK for English, 1–888–628–9454 for Spanish, or Lifeline Crisis Chat (https://suicidepreventionlifeline.org/chat/).

**** https://www.cdc.gov/violenceprevention/pdf/suicideTechnicalPackage.pdf

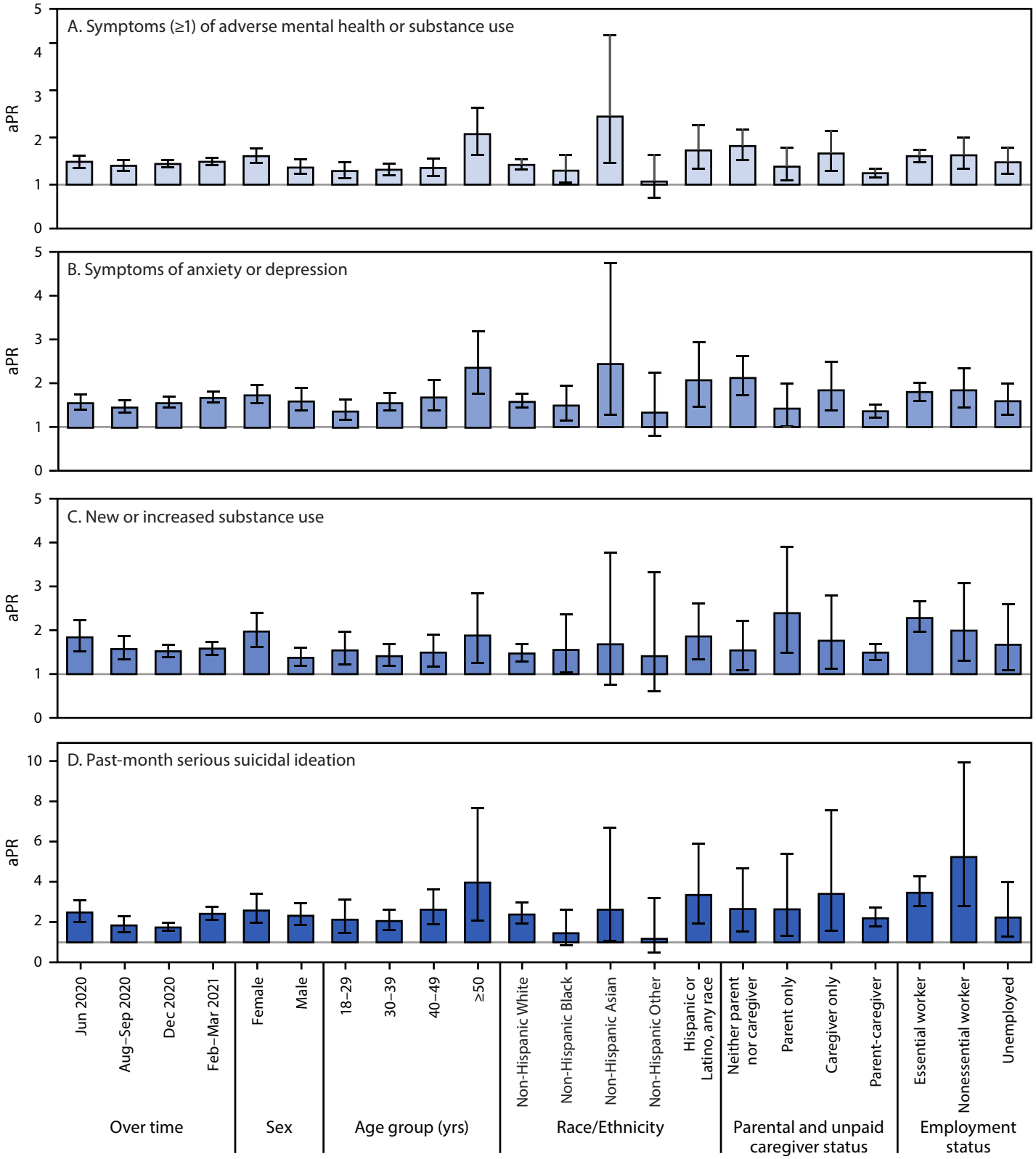
†††† https://emergency.cdc.gov/han/2020/han00438.asp

§§§§ https://www.cdc.gov/media/releases/2020/p1218-overdose-deaths-covid-19.html

¶¶¶¶ https://www.cdc.gov/drugoverdose/pdmp/states.html

***** https://www.federalregister.gov/documents/2021/04/28/2021-08961/practice-guidelines-for-the-administration-of-buprenorphine-for-treating-opioid-use-disorder

FIGURE 1. Adjusted prevalence ratios* and 95% confidence intervals† for ≥1 symptoms of adverse mental health or substance use (A), symptoms of anxiety or depression (B), new or increased substance use (C), and suicidal ideation (D) among adults with disabilities, compared with adults without disabilities (referent group)§ — United States, February 16–March 8, 2021¶



See figure footnotes on the next page.

FIGURE 1. (*Continued*) Adjusted prevalence ratios* and 95% confidence intervals† for ≥1 symptoms of adverse mental health or substance use (A), symptoms of anxiety or depression (B), new or increased substance use (C), and suicidal ideation (D) among adults with disabilities, compared with adults without disabilities (referent group)§ — United States, February 16–March 8, 2021¶

Abbreviations: aPR = adjusted prevalence ratio; CI = confidence interval.

* With 95% CIs indicated by error bars. Multivariable Poisson regression models included sex, age group in years, race/ethnicity, income, U.S. Census region, urbanicity, and parental or unpaid caregiving roles (parental roles were not assessed in June 2020; only unpaid caregiving roles were considered for this variable in the June 2020 models). Separate, additional models were run to estimate aPRs for the following employment statuses: essential worker, nonessential worker, and unemployed. Estimates were not made for retired or student employment statuses because of collinearity between these employment statuses and age.

† For panels A, B, and C, the y-axis range for aPR estimates is 0–5, which contains all aPRs and 95% CIs for these panels with maximal view of differences in model estimates. For panel D, given the relative rarity of suicidal ideation among some demographic subgroups that results in wide CIs for aPR estimates, the y-axis range is 0–10.

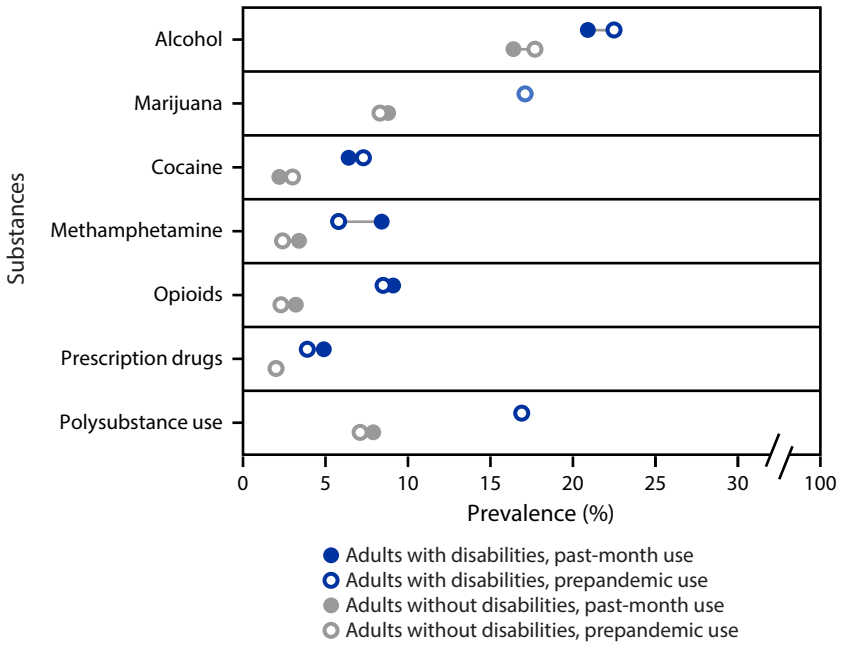
§ Within each subgroup, adults without disabilities are the reference group used to estimate aPRs for outcomes among adults with disabilities.

¶ Estimated aPRs are during February 16–March 8, 2021, except for the "over time" estimates, which also include estimates based on data collected during June 24–30, 2020, August 28–September 6, 2020, and December 6–27, 2020.

adults without disabilities in April 2021).†††††† Third, the respondents with disabilities might not be representative of all adults with disabilities, some of whom might lack access to hardware or assistive technologies required to independently complete the survey. Finally, adverse mental health symptoms might, in some cases, represent respondents' disabling mental health conditions, which could confound associations with other comorbid disabling conditions (e.g., physical, cognitive, sensory); however, sensitivity analyses excluding adults with disabilities who had mental health or substance use diagnoses yielded consistent findings.

Adults with disabilities have been disproportionately affected by adverse mental health symptoms and substance use during the COVID-19 pandemic, highlighting the importance of improved access to treatment for this population. Clinicians might consider screening all patients for mental health and substance use conditions during and after the pandemic.§§§§§ Behavioral health care providers might also consider facility, policy, and procedural pathway analyses to ensure accessibility for clients with physical, sensory, or cognitive disabilities.¶¶¶¶¶ Strategies designed to increase access to care and medication during public health emergencies, such as telehealth, might consider telemedicine platform and system accessibility for adults with disabilities (*10*); further research to identify and address health disparities among adults with disabilities could help guide additional evidence-based strategies.

FIGURE 2. Prevalence of prepandemic and past-month substance use to cope with stress or emotions among adults, by disability status and type of substance — United States, February 16–March 8, 2021*,†,§



* Overall, prepandemic and past-month use of any of these substances were reported by 39.7% and 40.6%, respectively, of adults with disabilities, and by 25.3% and 24.5%, respectively, of adults without disabilities.

† All differences between adults with disabilities and adults without disabilities were significant (chi-square p-value <0.05).

§ Circles for use of marijuana (among adults with disabilities), use of prescription drugs (among adults without disabilities), and polysubstance use (among adults with disabilities) might appear overlapping because of very small changes in reported prevalence (<1% in all cases).

Acknowledgments

Survey respondents; Mallory Colys, Sneha Baste, Daniel Chong, Rebecca Toll, Qualtrics, LLC; Rebecca Robbins, Matthew D. Weaver, Laura K. Barger, Brigham and Women's Hospital and Harvard Medical School; Elise R. Facer-Childs, Joshua F. Wiley, Monash University; Rashon I. Lane, CDC; CDC Foundation; BNY Mellon; Hopelab, Inc.; The Kinghorn Foundation; Australian-American Fulbright Commission.

†††††† https://www.cdc.gov/nchs/covid19/pulse/functioning-and-disability.htm

§§§§§ https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/drug-use-illicit-screening; https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/depression-in-adults-screening

¶¶¶¶¶ http://cct.org/wp-content/uploads/2015/08/2015ADAComplianceGuide.pdf

Summary

What is already known about this topic?

Adults with disabilities experience higher levels of mental health conditions and substance use than do adults without disabilities.

What is added by this report?

During February–March 2021, 64.1% of surveyed U.S. adults with disabilities reported adverse mental health symptoms or substance use; past-month substance use was higher than that among adults without disabilities (40.6% versus 24.5%, respectively). Among adults with a diagnosis of mental health or substance use conditions, adults with disabilities more frequently (43% versus 35%) reported pandemic-related difficulty accessing related care and medications.

What are the implications for public health practice?

During public health emergencies, including the COVID-19 pandemic, enhanced mental health and substance use screening among adults with disabilities and improved access to related health care services are critical.

Corresponding author: Amy Board, aboard@cdc.gov.

[1]Turner Institute for Brain and Mental Health and School of Psychological Sciences, Monash University, Melbourne, Australia; [2]Austin Health, Melbourne, Australia; [3]Brigham and Women's Hospital, Boston, Massachusetts; [4]Harvard Medical School, Boston, Massachusetts; [5]CDC COVID-19 Response Team; [6]National Center for Injury Prevention and Control, CDC; [7]Epidemic Intelligence Service, CDC; [8]University of Melbourne, Melbourne, Australia.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Charles A. Czeisler reports an institutional grant paid to Monash University from the CDC Foundation (funding provided by BNY Mellon); an institutional grant to Monash University from WHOOP, Inc.; being the incumbent of an endowed professorship provided to Harvard Medical School by Cephalon, Inc. in 2004; institutional support for Quality Improvement Initiative from Delta Airlines and Puget Sound Pilots; education/research support from Jazz Pharmaceuticals PLC, Inc., Philips Respironics, Inc., Regeneron Pharmaceuticals, and Sanofi S.A.; educational grant funding from ResMed, Teva Pharmaceuticals Industries Ltd., Australia and Vanda Pharmaceuticals, Inc.; royalty payments from Philips Respironics, Inc. on sales of the Actiwatch-2 and Actiwatch-Spectrum devices; personal consultancy and lecture fees from Physician's Seal, LLC, State of Washington Board of Pilotage Commissioners, Vanda Pharmaceuticals, Inc., Teva Pharmaceutical Industries, Ltd, Australia, Tencent Holdings, Ltd, and the National Sleep Foundation (Chair, Sleep Timing and Variability Consensus Panel); payment for expert witness testimony related to matters involving Aegis Chemical Solutions, Amtrak, Casper Sleep, Inc., Enterprise Rent-A-Car, Dallas Police Association, FedEx, PAR Electrical Contractors, Inc., Puget Sound Pilots, Schlumberger Technology Corp., Union Pacific Railroad, United Parcel Service, and Vanda Pharmaceuticals, Inc.; travel support from Tencent Holdings, Ltd., Aspen Brain Institute, Bloomage International Investment Group, Inc., Stanley Ho Medical Development Foundation, German National Academy of Sciences, National Safety Council, and the National Sleep Foundation; membership AARP advisory board, Children and Screens: Institute of Digital Media and Child Development, Klarman Family Foundation, and Biotechnology and Biological Sciences Research Council (U.K.); equity interest in Vanda Pharmaceuticals, Inc.; and institutional educational gifts to Brigham and Women's Hospital from Johnson & Johnson and Harmony Biosciences, LLC. Mark É. Czeisler reports institutional grants paid to Monash University from the CDC Foundation (funding provided by BNY Mellon), and from WHOOP, Inc.; funding from the Australian-American Fulbright Foundation (funding provided by the Kinghorn Foundation); and personal consultancy fees from Vanda Pharmaceuticals, Inc. Mark E. Howard and Shantha M.W. Rajaratnam report institutional grants paid to Monash University from the CDC Foundation (funding provided by BNY Mellon), and from WHOOP, Inc. Shantha M.W. Rajaratnam reports an institutional grant paid to Monash University from the Cooperative Research Centre for Alertness, Safety and Productivity; consulting fees paid to Monash University from Teva Pharmaceutical Industries, Ltd, Australia and Ukraine, Vanda Pharmaceuticals, Inc., BHP Billiton, and Herbert Smith Freehils; patent PTC/AU2021/050126 for Systems and Methods for Monitoring and Control of Sleep Patterns; and institutional consultancy fees from Circadian Therapeutics. No other potential conflicts of interest were disclosed.

References

1. Okoro CA, Hollis ND, Cyrus AC, Griffin-Blake S. Prevalence of disabilities and health care access by disability status and type among adults—United States, 2016. MMWR Morb Mortal Wkly Rep 2018;67:882–7. PMID:30114005 https://doi.org/10.15585/mmwr.mm6732a3
2. Cree RA, Okoro CA, Zack MM, Carbone E. Frequent mental distress among adults, by disability status, disability type, and selected characteristics—United States, 2018. MMWR Morb Mortal Wkly Rep 2020;69:1238–43. PMID:32914770 https://doi.org/10.15585/mmwr.mm6936a2
3. Okoro CA, McKnight-Eily LR, Strine TW, Crews JE, Holt JB, Balluz LS. State and local area estimates of depression and anxiety among adults with disabilities in 2006. Disabil Health J 2011;4:78–90. PMID:21419371 https://doi.org/10.1016/j.dhjo.2010.05.001
4. Okoro CA, Strine TW, McKnight-Eily L, Verlenden J, Hollis ND. Indicators of poor mental health and stressors during the COVID-19 pandemic, by disability status: a cross-sectional analysis. Disabil Health J 2021;101110:101110. PMID:33962896 https://doi.org/10.1016/j.dhjo.2021.101110
5. Czeisler MÉ, Lane RI, Wiley JF, Czeisler CA, Howard ME, Rajaratnam SMW. Follow-up survey of US adult reports of mental health, substance use, and suicidal ideation during the COVID-19 pandemic, September 2020. JAMA Netw Open 2021;4:e2037665. https://doi.org/10.1001/jamanetworkopen.2020.37665
6. Gleason J, Ross W, Fossi A, Blonsky H, Tobias J, Stephens M. The devastating impact of Covid-19 on individuals with intellectual disabilities in the United States. NEJM Catalyst [Commentary] 2021. https://catalyst.nejm.org/doi/full/10.1056/CAT.21.0051.
7. Liu S, Scholl L, Hoots B, Seth P. Nonfatal drug and polydrug overdoses treated in emergency departments—29 states, 2018–2019. MMWR Morb Mortal Wkly Rep 2020;69:1149–55. PMID:32853194 https://doi.org/10.15585/mmwr.mm6934a1

8. Lauer EA, Henly M, Brucker DL. Prescription opioid behaviors among adults with and without disabilities—United States, 2015–2016. Disabil Health J 2019;12:519–22. PMID:30594480 https://doi.org/10.1016/j.dhjo.2018.12.001
9. Vahratian A, Blumberg SJ, Terlizzi EP, Schiller JS. Symptoms of anxiety or depressive disorder and use of mental health care among adults during the COVID-19 pandemic—United States, August 2020–February 2021. MMWR Morb Mortal Wkly Rep 2021;70:490–4. PMID:33793459 https://doi.org/10.15585/mmwr.mm7013e2
10. Annaswamy TM, Verduzco-Gutierrez M, Frieden L. Telemedicine barriers and challenges for persons with disabilities: COVID-19 and beyond. Disabil Health J 2020;13:100973. PMID:32703737 https://dx.doi.org/10.1016/j.dhjo.2020.100973

Morbidity and Mortality Weekly Report

New COVID-19 Cases and Hospitalizations Among Adults, by Vaccination Status — New York, May 3–July 25, 2021

Eli S. Rosenberg, PhD[1,2]; David R. Holtgrave, PhD[2]; Vajeera Dorabawila, PhD[1]; MaryBeth Conroy, MPH[1]; Danielle Greene, DrPH[1]; Emily Lutterloh, MD[1,2]; Bryon Backenson, MS[1,2]; Dina Hoefer, PhD[1]; Johanne Morne, MS[1]; Ursula Bauer, PhD[1]; Howard A. Zucker, MD, JD[1]

On August 18, 2021, this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

Data from randomized clinical trials and real-world observational studies show that all three COVID-19 vaccines currently authorized for emergency use by the Food and Drug Administration* are safe and highly effective for preventing COVID-19–related serious illness, hospitalization, and death (*1*,*2*). Studies of vaccine effectiveness (VE) for preventing new infections and hospitalizations attributable to SARS-CoV-2, the virus that causes COVID-19), particularly as the B.1.617.2 (Delta) variant has become predominant, are limited in the United States (*3*). In this study, the New York State Department of Health linked statewide immunization, laboratory testing, and hospitalization databases for New York to estimate rates of new laboratory-confirmed COVID-19 cases and hospitalizations by vaccination status among adults, as well as corresponding VE for full vaccination in the population, across all three authorized vaccine products. During May 3–July 25, 2021, the overall age-adjusted VE against new COVID-19 cases for all adults declined from 91.7% to 79.8%. During the same period, the overall age-adjusted VE against hospitalization was relatively stable, ranging from 91.9% to 95.3%. Currently authorized vaccines have high effectiveness against COVID-19 hospitalization, but effectiveness against new cases appears to have declined in recent months, coinciding with the Delta variant's increase from <2% to >80% in the U.S. region that includes New York and relaxation of masking and physical distancing recommendations. To reduce new COVID-19 cases and hospitalizations, these findings support the implementation of a layered approach centered on vaccination, as well as other prevention strategies such as masking and physical distancing.

Four databases (the Citywide Immunization Registry, New York State Immunization Information System, Electronic Clinical Laboratory Reporting System, and Health Electronic Response Data System [HERDS]) were linked to construct a surveillance-based cohort of adults aged ≥18 years residing in New York by using individual name-based identifiers, date of birth, and zip code of residence. The Citywide Immunization Registry and the New York State Immunization Information System are used to collect and store all COVID-19 provider vaccination data for persons residing in New York City and the rest of the state, respectively (excluding selected settings such as Veterans Affairs and military health care facilities); persons were considered fully vaccinated ≥14 days after receipt of the final vaccine dose.† The Electronic Clinical Laboratory Reporting System collects all reportable COVID-19 test results (nucleic acid amplification test [NAAT] or antigen) in New York (*4*); a new COVID-19 case was defined as the receipt of a new positive SARS-CoV-2 NAAT or antigen test result, but not within 90 days of a previous positive result. HERDS includes a statewide, daily electronic survey of all inpatient facilities in New York; new admissions with a laboratory-confirmed COVID-19 diagnosis are entered into HERDS daily by trained hospital staff members.

After a period of phased COVID-19 vaccine eligibility based on age, occupation, setting, or comorbidities beginning in December 2020, all New York residents aged ≥60 years were eligible for vaccination by March 10, 2021; eligibility was expanded to persons aged ≥30 years by March 30, and to all adults aged ≥18 years by April 6.§ To allow time for a large portion of vaccinated persons to achieve full immunity, this study was restricted to the week beginning May 3 through the week beginning July 19, 2021.

Breakthrough infections were defined as new cases among persons who were fully vaccinated on the day of specimen collection. Hospitalizations among persons with breakthrough infection were defined as new hospital admissions among persons fully vaccinated on the reporting day. The total adult state population that was fully vaccinated and unvaccinated¶ was assessed for each day and stratified by age group (18–49 years, 50–64 years, and ≥65 years). Persons who were partially vaccinated were excluded from analyses. For each week and age group, the rates of new cases and hospitalizations were calculated among fully vaccinated and unvaccinated persons, by respectively dividing the counts for each group by the fully vaccinated and unvaccinated person-days in that week. Age-adjusted VE each week was estimated

*As of the publication date of this report, COVID-19 vaccines by Pfizer-BioNTech, Moderna, and Janssen (Johnson & Johnson) have been authorized by the Food and Drug Administration under Emergency Use Authorization.

† Final dose was the second dose for Pfizer-BioNTech and Moderna vaccines, first dose for Janssen vaccine.

§ https://www.governor.ny.gov/news/governor-cuomo-announces-new-yorkers-30-years-age-and-older-will-be-eligible-receive-covid-19

¶ The total adult state population that was unvaccinated was calculated as the total U.S. Census population, minus fully or partially vaccinated persons. Persons who were partially vaccinated were defined as those who initiated a vaccine series but did not complete it or were within 14 days after completion.

as the population-weighted mean of the age-stratified VE.** The interval between completing vaccination and positive SARS-CoV-2 test result date was summarized using the median, interquartile range (IQR), and percentage tested ≥7 days from being fully vaccinated.†† The ratio of hospitalizations to cases was computed for each vaccination group to understand the relative severity of cases. Statistical testing was not performed because the study included the whole population of interest and was not a sample.

By July 25, 2021, a total of 10,175,425 (65.8%) New York adults aged ≥18 years were fully vaccinated; 1,603,939 (10.4%) were partially vaccinated. Among fully vaccinated adults, 51.3% had received Pfizer-BioNTech, 39.8% had received Moderna, and 8.9% had received Janssen (Johnson & Johnson) vaccines. During May 3–July 25, a total of 9,675 new cases (1.31 per 100,000 person-days) occurred among fully vaccinated adults, compared with 38,505 (10.69 per 100,000 person-days) among unvaccinated adults (Table). Most (98.1%) new cases among fully vaccinated persons occurred ≥7 days after being classified fully vaccinated (median = 85 days; IQR = 58–113). During May 3–July 25, case rates among fully vaccinated persons were generally similar across age groups, as were case rates among unvaccinated persons, declining through the end of June before increasing in July (Figure 1). Weekly estimated VE against new laboratory-confirmed infection during May 3–July 25 for all age groups generally declined, ranging from 90.6% to 74.6% for persons aged 18–49 years, 93.5% to 83.4% for persons aged 50–64 years, and 92.3% to 88.9% for persons aged ≥65 years. During May 3–July 25, the overall, age-adjusted VE against infection declined from 91.7% to 79.8% (Figure 1) (Table).

A total of 1,271 new COVID-19 hospitalizations (0.17 per 100,000 person-days) occurred among fully vaccinated adults, compared with 7,308 (2.03 per 100,000 person-days) among unvaccinated adults (Table). Hospitalization rates generally declined through the week of July 5, but increased the weeks of July 12 and July 19, and were higher among fully vaccinated and unvaccinated persons aged ≥65 years compared with younger age groups (Figure 2). Age group–specific estimated VE against hospitalization remained stable, ranging from 90.8% to 97.5% for persons aged 18–49 years, from 92.4% to 97.0% for persons aged 50–64 years, and from 92.3% to 96.1% for persons aged ≥65 years. During May 3–July 25, the overall, age-adjusted VE against hospitalization was generally stable from 91.9% to 95.3% (Figure 2) (Table). The ratio of hospitalizations to cases was moderately lower among fully vaccinated (13.1 hospitalizations per 100 cases) compared with unvaccinated (19.0 hospitalizations per 100 cases) groups.

** For both outcomes, VE at each week and age group was calculated as 1-(Rate$_{vaccinated}$ / Rate$_{unvaccinated}$).

†† The percentage tested ≥7 days from being fully vaccinated was included to inform possible undiagnosed infection before full vaccination was achieved.

TABLE. Vaccination coverage, new COVID-19 cases, and new hospitalizations with laboratory-confirmed COVID-19 among fully vaccinated and unvaccinated adults, and estimated vaccine effectiveness — New York, May 3–July 25, 2021

	Population*			New cases†					New hospitalizations§				
				Fully vaccinated		Unvaccinated			Fully vaccinated		Unvaccinated		
Week starting	Average no. fully vaccinated¶	Average no. unvaccinated	Full vaccination coverage, %	No.	Rate*	No.	Rate*	Estimated vaccine effectiveness, %	No.	Rate*	No.	Rate*	Estimated vaccine effectiveness, %
May 3	6,255,275	5,367,527	40.4	700	1.60	7,387	19.66	91.7	154	0.35	1,478	3.93	95.3
May 10	6,948,727	4,938,120	44.9	589	1.21	5,839	16.89	92.7	149	0.31	1,145	3.31	95.0
May 17	7,641,098	4,642,464	49.4	555	1.04	4,106	12.63	91.9	134	0.25	968	2.98	96.2
May 24	8,222,099	4,444,612	53.1	431	0.75	2,757	8.86	92.0	140	0.24	748	2.40	93.8
May 31	8,691,229	4,289,385	56.2	364	0.60	2,092	6.97	91.6	87	0.14	549	1.83	95.1
Jun 7	9,034,873	4,226,865	58.4	341	0.54	1,504	5.08	89.7	95	0.15	448	1.51	93.3
Jun 14	9,272,840	4,165,878	59.9	340	0.52	1,233	4.23	87.9	88	0.14	324	1.11	91.9
Jun 21	9,516,612	4,022,274	61.5	396	0.59	1,201	4.27	85.8	60	0.09	283	1.01	94.6
Jun 28	9,747,395	3,913,256	63.0	535	0.78	1,421	5.19	83.8	69	0.10	288	1.05	93.9
Jul 5	9,911,987	3,870,504	64.1	928	1.34	2,223	8.20	82.4	72	0.10	270	1.00	94.4
Jul 12	10,034,269	3,818,600	64.8	1,703	2.42	3,242	12.13	78.2	89	0.13	340	1.27	94.8
Jul 19	10,135,322	3,742,197	65.5	2,793	3.94	5,500	21.00	79.8	134	0.19	467	1.78	95.3
Total	—	—	—	**9,675**	**1.31**	**38,505**	**10.69**	—	**1,271**	**0.17**	**7,308**	**2.03**	—

* Population sizes fully vaccinated and unvaccinated were computed daily. For display purposes, the average populations fully vaccinated and unvaccinated are shown for each week. Rate calculations were conducted using daily population sizes and are expressed per 100,000 person-days. Persons partially vaccinated were excluded from analyses.

† New cases were defined as a new positive SARS-CoV-2 nucleic acid amplification test or antigen test result, not within 90 days of a previous positive result, reported to the Electronic Clinical Laboratory Reporting System, which collects all reportable COVID-19 test results in New York.

§ New hospitalizations were determined by a report of a hospital admission with a confirmed COVID-19 diagnosis, entered into the Health Electronic Response Data System, which includes a statewide, daily electronic survey of all inpatient facilities in New York.

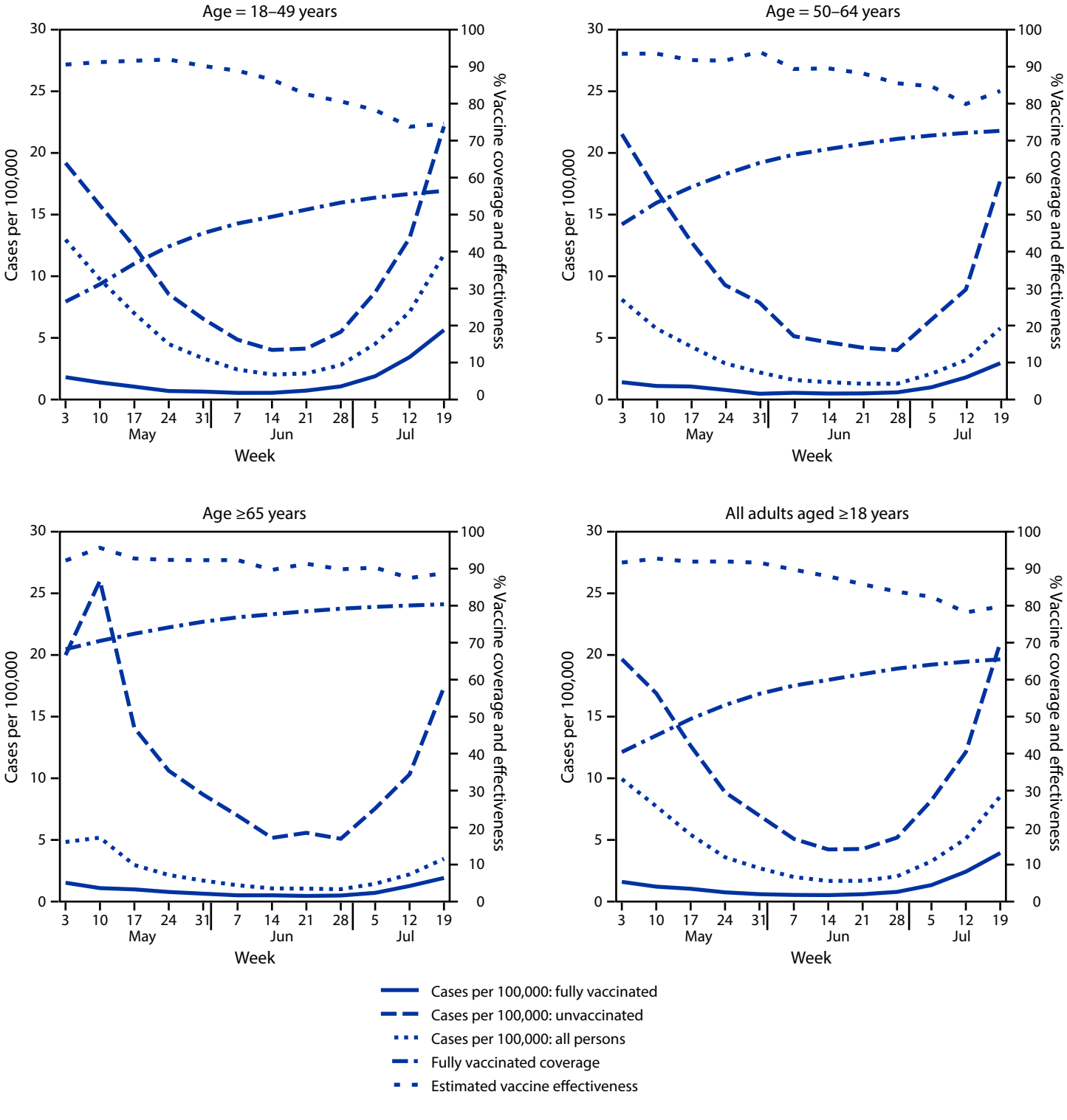
¶ Persons were determined to be fully vaccinated following 14 days after final vaccine-series dose receipt, per the Citywide Immunization Registry and the New York State Immunization Information System, which collect and store all COVID-19 vaccine receipt data by providers for persons residing in New York City and the rest of New York, respectively.

Discussion

In this study, current COVID-19 vaccines were highly effective against hospitalization (VE >90%) for fully vaccinated New York residents, even during a period during which prevalence of the Delta variant increased from <2% to >80% in the U.S. region that includes New York, societal public health restrictions eased,[§§] and adult full-vaccine coverage in

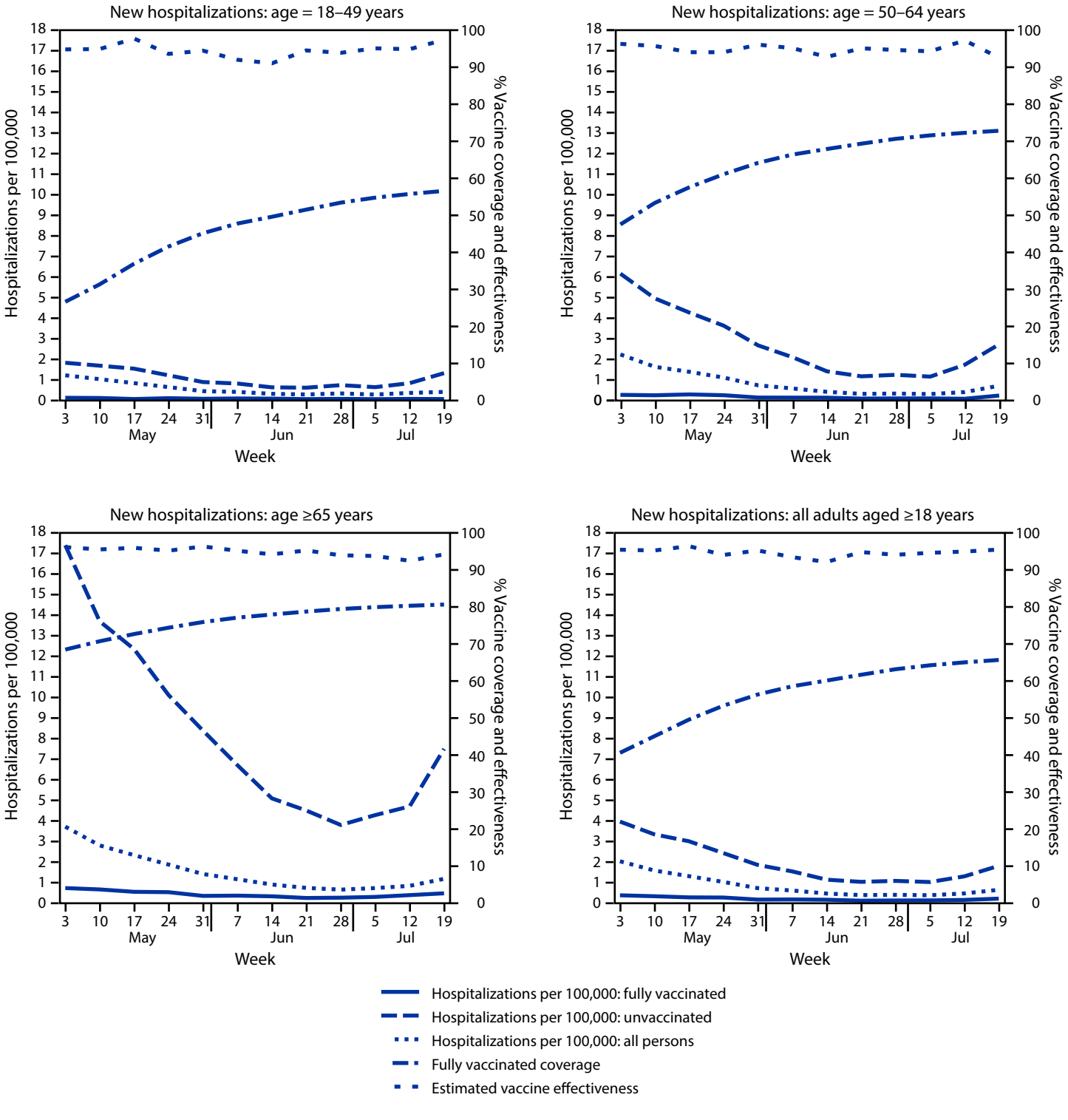
[§§] https://covid.cdc.gov/covid-data-tracker/#variant-proportions

FIGURE 1. New COVID-19 cases among fully vaccinated and unvaccinated adults, vaccine coverage, and estimated vaccine effectiveness, by age — New York, May 3–July 25, 2021



New York neared 65%. However, during the assessed period, rates of new cases increased among both unvaccinated and fully vaccinated adults, with lower relative rates among fully vaccinated persons. Moreover, VE against new infection declined from 91.7% to 79.8%. To reduce new COVID-19 cases and hospitalizations, these findings support the implementation of a layered approach centered on vaccination, as well as other prevention strategies.

FIGURE 2. New hospitalizations with laboratory-confirmed COVID-19 among fully vaccinated and unvaccinated adults, vaccine coverage, and estimated vaccine effectiveness, by age — New York, May 3–July 25, 2021



Summary

What is already known about this topic?

Real-world studies of population-level vaccine effectiveness against laboratory-confirmed SARS-CoV-2 infection and COVID-19 hospitalizations are limited in the United States.

What is added by this report?

During May 3–July 25, 2021, the overall age-adjusted vaccine effectiveness against hospitalization in New York was relatively stable (91.9%–95.3%). The overall age-adjusted vaccine effectiveness against infection for all New York adults declined from 91.7% to 79.8%.

What are the implications for public health practice?

These findings support the implementation of multicomponent approach to controlling the pandemic, centered on vaccination, as well as other prevention strategies such as masking and physical distancing.

The findings from this study are consistent with those observed in other countries. Israel has reported 90% VE for the Pfizer-BioNTech vaccine against hospitalization; however, a decline in VE against new diagnosed infections occurred during June 20–July 17 (decreasing to <65%) (*5*). Another study in the United Kingdom found higher VE against infection with the Delta variant for Pfizer-BioNTech (88%), which was lower than VE against the B.1.1.7 (Alpha) variant (94%) (*6*).

The factors driving the apparent changes in VE, including variations by age, are uncertain. Changes in immune protection from current vaccine product dosing regimens are under investigation,¶¶ with additional doses being considered (*7*). Increased Delta variant viral load might underpin its increased transmissibility and could potentially lead to reduced vaccine-induced protection from infection (*8*). Further, variations from clinical trial findings could be because the trials were conducted during a period before the emergence of new variants and when nonpharmaceutical intervention strategies (e.g., wearing masks and physically distancing) were more stringently implemented, potentially lessening the amount of virus to which persons were exposed. Other factors that could influence VE include indirect protective effects of unvaccinated persons by vaccinated persons and an increasing proportion of unvaccinated persons acquiring some level of immunity through infection (*9*).

The findings in this report are subject to at least six limitations. First, although limiting the analysis period to after universal adult vaccine eligibility and age stratification likely helped to reduce biases, residual differences between fully vaccinated and unvaccinated groups have the potential to reduce estimated VE. Second, the analysis excluded partially vaccinated persons, to robustly assess VE for fully vaccinated compared with that of unvaccinated persons. A supplementary sensitivity analysis that included partially vaccinated persons as unvaccinated yielded conservative VE for laboratory-confirmed infection (declining from 88.7% to 72.1%) and for hospitalizations (ranging from 89.7% to 93.0%). Third, exact algorithms were used to link databases; some persons were possibly not linked because matching variables were entered differently in the respective systems. Fourth, this study did not estimate VE by vaccine product, and persons were categorized fully vaccinated at 14 days after final dose, per CDC definitions; however, the Janssen vaccine might have higher efficacy at 28 days.*** Given that Janssen vaccine recipients accounted for 9% of fully vaccinated persons and the observed time period from full vaccination to infection (median 85 days), this would minimally affect the findings. Fifth, information on reasons for testing and hospitalization, including symptoms, was limited. However, a supplementary analysis found that among 1,271 fully vaccinated adults and 7,308 unvaccinated adults, 545 (42.9%) and 4,245 (58.1%), respectively, were reported to have been admitted for COVID-19 by hospital staff members using nonstandardized definitions. A sensitivity analysis of hospitalization VE limited to those admitted for COVID-19, found similar results (VE range = 93.9%–97.4%), suggesting that the extent of bias was limited. Finally, data were too sparse to reliably estimate VE for COVID-19-related deaths.

This study's findings suggest currently available vaccines have high effectiveness for preventing laboratory-confirmed SARS-CoV-2 infection and COVID-19 hospitalization. However, VE against infection appears to have declined in recent months in New York, coinciding with a period of easing societal public health restrictions††† and increasing Delta variant circulation (*8*). These findings support a multipronged approach to reducing new COVID-19 hospitalizations and cases, centered on vaccination, and including other approaches such as masking and physical distancing.

¶¶ https://www.medrxiv.org/content/10.1101/2021.07.28.21261159v1

*** https://www.fda.gov/media/146338/download

††† https://coronavirus.jhu.edu/data/state-timeline/new-confirmed-cases/new-york/205

Acknowledgments

Steven Davis, Rebecca Hoen, New York State Department of Health; Citywide Immunization Registry Program, New York City Department of Health and Mental Hygiene.

Corresponding author: Eli Rosenberg, eli.rosenberg@health.ny.gov.

[1]New York State Department of Health; [2]University at Albany School of Public Health, State University of New York, Rensselaer, New York.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

References

1. Food and Drug Administration. COVID-19 vaccines. Silver Spring, MD: US Department of Health and Human Services; Food and Drug Administration; 2021. Accessed July 29, 2021. https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/covid-19-vaccines.
2. Pilishvili T, Fleming-Dutra KE, Farrar JL, et al.; Vaccine Effectiveness Among Healthcare Personnel Study Team. Interim estimates of vaccine effectiveness of Pfizer-BioNTech and Moderna COVID-19 vaccines among health care personnel—33 U.S. sites, January–March 2021. MMWR Morb Mortal Wkly Rep 2021;70:753–8. PMID:34014909 https://doi.org/10.15585/mmwr.mm7020e2
3. CDC. COVID-19 vaccine breakthrough case investigation and reporting. Atlanta, GA: US Department of Health and Human Services, CDC; 2021. Accessed July 29, 2021. https://www.cdc.gov/vaccines/covid-19/health-departments/breakthrough-cases.html
4. Rosenberg ES, Dufort EM, Blog DS, et al.; New York State Coronavirus 2019 Response Team. COVID-19 testing, epidemic features, hospital outcomes, and household prevalence, New York State—March 2020. Clin Infect Dis 2020;71:1953–9. PMID:32382743 https://doi.org/10.1093/cid/ciaa549
5. Israel Ministry of Health. Decline in vaccine effectiveness against infection and symptomatic illness. Jerusalem, Israel: Israel Ministry of Health; 2021. Accessed July 29, 2021. https://www.gov.il/en/departments/news/05072021-03.
6. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of Covid-19 vaccines against the B.1.617.2 (Delta) variant. N Engl J Med 2021. Epub July 21, 2021. PMID:34289274 https://doi.org/10.1056/NEJMoa2108891
7. Kamar N, Abravanel F, Marion O, Couat C, Izopet J, Del Bello A. Three doses of an mRNA Covid-19 vaccine in solid-organ transplant recipients. N Engl J Med 2021. Epub June 23, 2021. PMID:34161700 https://doi.org/10.1056/NEJMc2108861
8. Brown CM, Vostok J, Johnson H, et al. Outbreak of SARS-CoV-2 infections, including COVID-19 vaccine breakthrough infections, associated with large public gatherings—Barnstable County, Massachusetts, July 2021. MMWR Morb Mortal Wkly Rep 2021l;70:1059–62. PMID:34351882 https://doi.org/10.15585/mmwr.mm7031e2
9. Patel MK, Bergeri I, Bresee JS, et al. Evaluation of post-introduction COVID-19 vaccine effectiveness: summary of interim guidance of the World Health Organization. Vaccine 2021;39:4013–24. PMID:34119350 https://doi.org/10.1016/j.vaccine.2021.05.099

Sustained Effectiveness of Pfizer-BioNTech and Moderna Vaccines Against COVID-19 Associated Hospitalizations Among Adults — United States, March–July 2021

Mark W. Tenforde, MD, PhD[1,*]; Wesley H. Self, MD[2,*]; Eric A. Naioti, MPH[1]; Adit A. Ginde, MD[3]; David J. Douin, MD[3]; Samantha M. Olson, MPH[1]; H. Keipp Talbot, MD[2]; Jonathan D. Casey, MD[2]; Nicholas M. Mohr, MD[4]; Anne Zepeski, PharmD[4]; Manjusha Gaglani, MBBS[5,6]; Tresa McNeal, MD[5]; Shekhar Ghamande, MD[5]; Nathan I. Shapiro, MD[7]; Kevin W. Gibbs, MD[8]; D. Clark Files, MD[8]; David N. Hager, MD, PhD[9]; Arber Shehu, MD[9]; Matthew E. Prekker, MD[10]; Heidi L. Erickson, MD[10]; Michelle N. Gong, MD[11]; Amira Mohamed, MD[11]; Daniel J. Henning, MD[12]; Jay S. Steingrub, MD[13]; Ithan D. Peltan, MD[14]; Samuel M. Brown, MD[14]; Emily T. Martin, PhD[15]; Arnold S. Monto, MD[15]; Akram Khan, MD[16]; Catherine L. Hough, MD[16]; Laurence W. Busse, MD[17]; Caitlin C. ten Lohuis, ACNP-BC[17]; Abhijit Duggal, MD[18]; Jennifer G. Wilson, MD[19]; Alexandra June Gordon, MD[19]; Nida Qadir, MD[20]; Steven Y. Chang, MD, PhD[20]; Christopher Mallow, MD[21]; Carolina Rivas[21]; Hilary M. Babcock, MD[22]; Jennie H. Kwon, DO[22]; Matthew C. Exline, MD[23]; Natasha Halasa, MD[2]; James D. Chappell, MD, PhD[2]; Adam S. Lauring, MD, PhD[24]; Carlos G. Grijalva, MD[2]; Todd W. Rice, MD[2]; Ian D. Jones, MD[2]; William B. Stubblefield, MD[2]; Adrienne Baughman[2]; Kelsey N. Womack, PhD[2]; Christopher J. Lindsell, PhD[2]; Kimberly W. Hart, MA[2]; Yuwei Zhu, MD[2]; Meagan Stephenson, MPH[1]; Stephanie J. Schrag, DPhil[1]; Miwako Kobayashi, MD[1]; Jennifer R. Verani, MD[1]; Manish M. Patel, MD[1]; IVY Network Investigators

On August 18, 2021, this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

Real-world evaluations have demonstrated high effectiveness of vaccines against COVID-19–associated hospitalizations (*1*–*4*) measured shortly after vaccination; longer follow-up is needed to assess durability of protection. In an evaluation at 21 hospitals in 18 states, the duration of mRNA vaccine (Pfizer-BioNTech or Moderna) effectiveness (VE) against COVID-19–associated hospitalizations was assessed among adults aged ≥18 years. Among 3,089 hospitalized adults (including 1,194 COVID-19 case-patients and 1,895 non–COVID-19 control-patients), the median age was 59 years, 48.7% were female, and 21.1% had an immunocompromising condition. Overall, 141 (11.8%) case-patients and 988 (52.1%) controls were fully vaccinated (defined as receipt of the second dose of Pfizer-BioNTech or Moderna mRNA COVID-19 vaccines ≥14 days before illness onset), with a median interval of 65 days (range = 14–166 days) after receipt of second dose. VE against COVID-19–associated hospitalization during the full surveillance period was 86% (95% confidence interval [CI] = 82%–88%) overall and 90% (95% CI = 87%–92%) among adults without immunocompromising conditions. VE against COVID-19– associated hospitalization was 86% (95% CI = 82%–90%) 2–12 weeks and 84% (95% CI = 77%–90%) 13–24 weeks from receipt of the second vaccine dose, with no significant change between these periods (p = 0.854). Whole genome sequencing of 454 case-patient specimens found that 242 (53.3%) belonged to the B.1.1.7 (Alpha) lineage and 74 (16.3%) to the B.1.617.2 (Delta) lineage. Effectiveness of mRNA vaccines against COVID-19–associated hospitalization was sustained over a 24-week period, including among groups at higher risk for severe COVID-19; ongoing monitoring is needed as new SARS-CoV-2 variants emerge. To reduce their risk for hospitalization, all eligible persons should be offered COVID-19 vaccination.

Evaluations of authorized mRNA COVID-19 vaccines (Pfizer-BioNTech and Moderna) have consistently demonstrated high VE across diverse populations (*1*,*5*). Because COVID-19 vaccines were initially authorized in the United States in December 2020, evaluations of real-world effectiveness have been subject to a short period of postvaccination follow-up. Monitoring durability of protection after COVID-19 vaccination can help determine whether booster vaccines might be indicated, particularly with continued emergence of new variants that might overcome vaccine-induced immunity. In real-world settings, durability of protection has commonly been measured by comparing the odds of vaccination in laboratory-confirmed case-patients and control-patients who tested negative for infection, by time since vaccination (*6*,*7*).

During March 11–July 14, 2021, adults aged ≥18 years admitted to 21 hospitals in 18 states were included in an analysis of durability of vaccine-induced protection. Case-patients had COVID-19–like illness[†] and had received a positive SARS-CoV-2 reverse transcription–polymerase chain reaction (RT-PCR) or antigen test result. A first group of hospital-based control-patients had COVID-19–like illness and had negative SARS-COV-2 results by all tests, including at least one RT-PCR test. A second hospital-based control group of patients without COVID-19–like illness (and therefore unlikely to be hospitalized for COVID-19–like illness)

[*] These authors contributed equally to this report.

[†] COVID-19–like illness was defined as having one or more of the following: fever, cough, shortness of breath, loss of taste, loss of smell, use of respiratory support for the acute illness, or new pulmonary findings on chest imaging consistent with pneumonia.

was also enrolled (*4*). This second control group also received negative SARS-CoV-2 results by all tests, including at least one RT-PCR test. Eligibility for enrollment as a case-patient or one of these controls required SARS-CoV-2 testing within 10 days of symptom onset and hospital admission within 14 days of symptom onset. Final case/control status was determined using clinical testing results and central laboratory RT-PCR testing of upper respiratory specimens (nasal swabs or saliva) performed at a central laboratory (Vanderbilt University Medical Center, Nashville, Tennessee) (*4*). Specimens positive for SARS-CoV-2 with cycle threshold values <32 were sent to University of Michigan (Ann Arbor, Michigan) for whole genome sequencing and SARS-CoV-2 lineage determination (*4*).

Patients or their proxies were interviewed about baseline demographic characteristics, clinical history (including COVID-19–like signs or symptoms experienced and date of illness onset), and history of COVID-19 vaccination. Vaccine was considered to have been administered if vaccination dates and product names were verified through medical records, state immunization registries, vaccination record cards, or provider or pharmacy records, or if plausibly reported by patient or proxy with date and location of vaccination. A patient was considered to be fully vaccinated if both doses of an authorized mRNA COVID-19 vaccine were administered, with the second dose received ≥14 days before illness onset.[§] Participants were excluded from this analysis if they received only 1 dose of an mRNA COVID-19 vaccine, received 2 doses with the second dose <14 days before illness onset, received a non-mRNA COVID-19 vaccine, or received mixed products of an mRNA COVID-19 vaccine (i.e., a different product for each dose).

Vaccine effectiveness against COVID-19–associated hospitalization was estimated using logistic regression, comparing the odds of being fully vaccinated versus unvaccinated between case-patients and controls (including both control groups) using the equation VE = 100 × (1 − odds ratio) (*1*). VE over the full surveillance period was assessed, as well as among those with illness onset during March–May and June–July 2021, because of increased circulation of Delta variants in the United States during the latter period (*8*). Models were adjusted for potential confounders, including admission date (biweekly intervals), U.S. Department of Health and Human Services region, age, sex, and race/ethnicity. Time-varying VE models were then constructed. First, a binary model was constructed by adding a categorical term (2–12 weeks versus 13–24 weeks) for interval from receipt of the second vaccine dose (among vaccinated participants) and illness onset. Unvaccinated patients were assigned values of zero days since vaccination. In additional analyses, other specifications of time were considered, including using linear and natural cubic spline terms. Bootstrapping with 1,000 replications was used to estimate 95% CIs. Subgroup analyses included adults aged ≥65 years, patients with immunocompromising conditions,[¶] and patients with three or more categories of chronic medical conditions. A sensitivity analysis was also performed including each of the two control groups in models rather than combining them. Significance of association between VE and time since vaccination was assessed using a likelihood-ratio chi-square test with p-values <0.05 considered statistically significant. Analyses were conducted using R statistical software (version 4.0.3; R Foundation). This activity was determined to be public health surveillance by each participating site and CDC and was conducted consistent with applicable federal law and CDC policy.[**]

After excluding 722 ineligible patients (461 who were not fully vaccinated or unvaccinated, 127 who received a non-mRNA COVID-19 vaccine or mixed vaccines, and 134 who did not meet other inclusion criteria), 3,089 patients were included in the final analysis (1,194 case-patients and 1,895 in the combined control groups) (Table). The median patient age was 59 years (interquartile range = 46–69 years), 48.7% were female, 56.7% were non-Hispanic White, and 21.1% had an immunocompromising condition. Among case-patients, 141 (11.8%) were fully vaccinated as were 988 (52.1%) controls. Among 454 case-patient specimens with SARS-CoV-2 lineage determined, 242 (53.3%) were identified as Alpha and 74 (16.3%) as Delta (Figure 1). Delta variants became the dominant virus in mid-June. Overall VE against hospitalization for COVID-19 was 86% (95% CI = 82%–88%) over the full surveillance period, including 90% (95% CI = 87%–92%) among patients without immunocompromising conditions and 63% (95% CI = 44%–76%) among patients with immunocompromising conditions. VE among patients with illness onset during March–May was 87% (95% CI = 83%–90%), and among those with illness onset during June–July was 84% (95% CI = 79%–89%). In models considering time since vaccination, VE was 86% (95% CI = 82%–90%)

[§] The date of illness onset was used for cases and controls with COVID-19–like illness with median value imputed if missing. For controls without COVID-19–like illness, the date of admission minus the median number of days between illness onset and admission for patients with COVID-19 was used for a date of illness onset, also referred to as "illness onset" for this report.

[¶] Immunocompromising conditions included having one or more of the following: active solid organ cancer (active cancer defined as treatment for the cancer or newly diagnosed cancer in the past 6 months), active hematologic cancer (such as leukemia, lymphoma, or myeloma), HIV infection without AIDS, AIDS, congenital immunodeficiency syndrome, previous splenectomy, previous solid organ transplant, immunosuppressive medication, systemic lupus erythematosus, rheumatoid arthritis, psoriasis, scleroderma, or inflammatory bowel disease, including Crohn's disease or ulcerative colitis.

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

TABLE. Characteristics of COVID-19 case-patients and controls among hospitalized adults — 21 academic medical centers in 18 states, March–July 2021

Characteristic	No. (%)			P-value*
	Overall (N = 3,089)	Cases (n = 1,194)	Controls (n = 1,895)	
Median age, yrs (IQR)	59 (46–69)	56 (42–66)	62 (48–71)	<0.001
Age group, yrs				<0.001
18–49	950 (30.8)	445 (37.3)	505 (26.7)	
50–64	1,008 (32.6)	424 (35.5)	584 (30.8)	
≥65	1,131 (36.6)	325 (27.2)	806 (42.5)	
Sex				
Female	1,504 (48.7)	580 (48.6)	924 (48.8)	0.921
Race/Ethnicity				<0.001
White, non-Hispanic	1,752 (56.8)	548 (45.9)	1,204 (63.5)	
Black, non-Hispanic	693 (22.4)	312 (26.1)	381 (20.1)	
Hispanic, any race	467 (15.1)	245 (20.5)	222 (11.7)	
Other, non-Hispanic	140 (4.5)	67 (5.6)	73 (3.9)	
Unknown	37 (1.2)	22 (1.8)	15 (0.8)	
Region†				<0.001
Northeast	432 (14.0)	165 (13.8)	267 (14.1)	
South	1,151 (37.3)	459 (38.4)	692 (36.5)	
Midwest	818 (26.5)	265 (22.2)	553 (29.2)	
West	688 (22.3)	305 (25.5)	383 (20.2)	
Resident in long-term care facility (100 unknown)	141 (4.7)	29 (2.5)	112 (6.1)	<0.001
Previous hospitalization in last year (231 unknown)	1,297 (45.4)	319 (30.0)	978 (54.5)	<0.001
No. of baseline conditions (2 unknown)§				<0.001
0	552 (17.9)	301 (25.2)	251 (13.3)	
1	736 (23.8)	310 (26.0)	426 (22.5)	
2	766 (24.8)	260 (21.8)	506 (26.7)	
≥3	1,033 (33.5)	322 (27.0)	711 (37.5)	
Specific chronic conditions				
Cardiovascular disease (1 unknown)	1,900 (61.5)	647 (54.2)	1,253 (66.2)	<0.001
Pulmonary disease (1 unknown)	804 (26.0)	257 (21.5)	547 (28.9)	<0.001
Diabetes mellitus (1 unknown)	952 (30.8)	348 (29.2)	604 (31.9)	0.108
Immunocompromising condition* (2 unknown)¶	652 (21.1)	205 (17.2)	447 (23.6)	<0.001
Fully vaccinated**	1,129 (36.6)	141 (11.8)	988 (52.1)	<0.001
Vaccine product received (among fully vaccinated persons)				0.030
Pfizer-BioNTech	666 (59.0)	95 (67.4)	571 (57.8)	
Moderna	463 (41.0)	46 (32.6)	417 (42.2)	
If fully vaccinated, median (IQR) days from second vaccine dose and onset of symptoms	65 (41–93)	60 (36–94)	66 (42–93)	0.509

Abbreviation: IQR = interquartile range.

* P-values determined using the Wilcoxon rank-sum test for continuous variables and by chi-square test of independence for categorical variables.

† Hospitals by region included *Northeast*: Baystate Medical Center (Springfield, Massachusetts), Beth Israel Deaconess Medical Center (Boston, Massachusetts), Montefiore Medical Center (Bronx, New York); *South*: Vanderbilt University Medical Center (Nashville, Tennessee), University of Miami Medical Center (Miami, Florida), Emory University Medical Center (Atlanta, Georgia), Johns Hopkins Hospital (Baltimore, Maryland), Wake Forest University Baptist Medical Center (Winston-Salem, North Carolina), Baylor Scott and White Health (Temple, Texas); *Midwest*: University of Iowa Hospitals (Iowa City, Iowa), University of Michigan Hospital (Ann Arbor, Michigan), Hennepin County Medical Center (Minneapolis, Minnesota), Barnes-Jewish Hospital (St. Louis, Missouri), Cleveland Clinic (Cleveland, Ohio), Ohio State University Wexner Medical Center (Columbus, Ohio); *West*: Stanford University Medical Center (Stanford, California), UCLA Medical Center (Los Angeles, California), UCHealth University of Colorado Hospital (Aurora, Colorado), Oregon Health & Science University Hospital (Portland, Oregon), Intermountain Medical Center (Murray, Utah), University of Washington (Seattle, Washington).

§ Chronic condition categories included the following: cardiovascular disease, neurologic disease, pulmonary disease, gastrointestinal disease, endocrine disease, renal disease, hematologic disease, malignancy, immunosuppression not captured in other categories, autoimmune condition, or other condition (sarcoidosis, amyloidosis, or unintentional weight loss ≥10 pounds in the last 90 days).

¶ Immunocompromising conditions included having one or more of the following: active solid organ cancer (active cancer defined as treatment for the cancer or newly diagnosed cancer in the past 6 months), active hematologic cancer (such as leukemia, lymphoma, or myeloma), HIV infection without AIDS, AIDS, congenital immunodeficiency syndrome, previous splenectomy, previous solid organ transplant, immunosuppressive medication, systemic lupus erythematosus, rheumatoid arthritis, psoriasis, scleroderma, or inflammatory bowel disease, including Crohn's disease or ulcerative colitis.

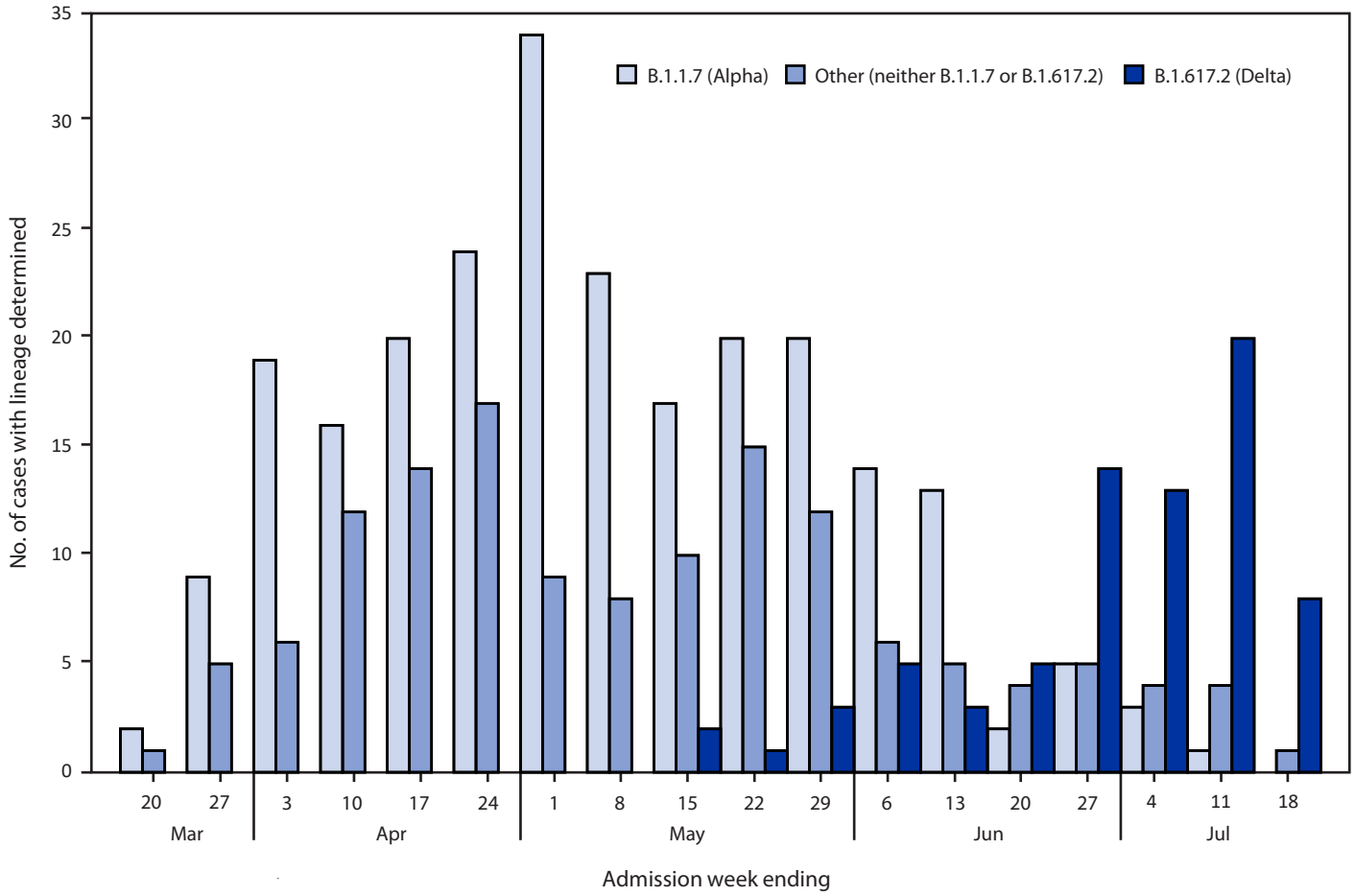
** COVID-19 vaccination status included unvaccinated, defined as no receipt of any SARS CoV-2 vaccine, and fully vaccinated, defined as receipt of both doses of a 2-dose mRNA vaccine with the second dose received ≥14 days before illness onset.

during the 2–12 weeks after the second vaccine dose and 84% (95% CI = 77%–90%) 13–24 weeks after the second dose; there was no significant difference in VE between these two periods (p = 0.854). Models treating time since vaccination as linear and as a natural cubic spline with a knot at the median and boundary knots at the 10th and 90th percentiles also showed no significant change in VE over a 24-week period (linear p = 0.400, spline p = 0.234) (Supplementary Figure, https://stacks.cdc.gov/view/cdc/108758). No significant change in VE over a 24-week period was observed within subgroups (all p>0.05) (Figure 2). In sensitivity analyses, results were similar using individual control groups and combined controls.

Discussion

In a multistate network that enrolled adults hospitalized during March–July 2021, effectiveness of 2 doses of mRNA vaccine against COVID-19–associated hospitalization was sustained over a follow-up period of 24 weeks (approximately 6 months). These findings of sustained VE were consistent among subgroups at highest risk for severe outcomes from COVID-19, including older adults, adults with three or more

FIGURE 1. Whole genome sequencing lineage determination among adults hospitalized with COVID-19 — 21 academic medical centers in 18 states,*,† March–July 2021



* Specimens with SARS-CoV-2 detected by reverse transcription–polymerase chain reaction and with a cycle threshold <32 for at least one of two nucleocapsid gene targets tested underwent whole genome sequencing. SARS-CoV-2 lineages were assigned with >80% coverage using Pangolin genomes. Results are presented for B.1.1.7 (Alpha) variants, B.1.617.2 (Delta) variants, and other (neither B.1.1.7 or B.1.617.2) variant with lineage determined by whole genome sequencing. Of 74 Delta variants sequenced, four belonged to the AY.3 Delta sublineage. The histogram provides the number of viruses sequenced by week of hospital admission.

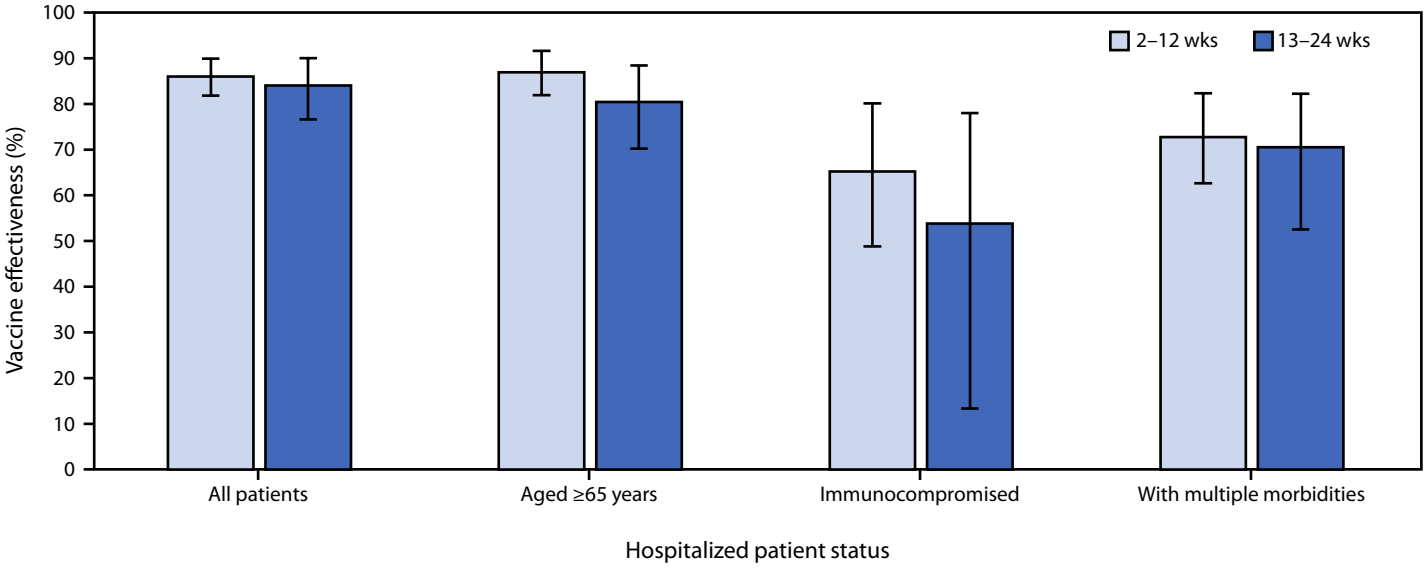
† Hospitals by region included *Northeast*: Baystate Medical Center (Springfield, Massachusetts), Beth Israel Deaconess Medical Center (Boston, Massachusetts), Montefiore Medical Center (Bronx, New York); *South*: Vanderbilt University Medical Center (Nashville, Tennessee), University of Miami Medical Center (Miami, Florida), Emory University Medical Center (Atlanta, Georgia), Johns Hopkins Hospital (Baltimore, Maryland), Wake Forest University Baptist Medical Center (Winston-Salem, North Carolina), Baylor Scott and White Health (Temple, Texas); *Midwest*: University of Iowa Hospitals (Iowa City, Iowa), University of Michigan Hospital (Ann Arbor, Michigan), Hennepin County Medical Center (Minneapolis, Minnesota), Barnes-Jewish Hospital (St. Louis, Missouri), Cleveland Clinic (Cleveland, Ohio), Ohio State University Wexner Medical Center (Columbus, Ohio); *West*: Stanford University Medical Center (Stanford, California), UCLA Medical Center (Los Angeles, California), UCHealth University of Colorado Hospital (Aurora, Colorado), Oregon Health & Science University Hospital (Portland, Oregon), Intermountain Medical Center (Murray, Utah), University of Washington (Seattle, Washington).

chronic medical conditions, and those with immunocompromising conditions. Overall VE in adults with immunocompromising conditions was lower than that in those without immunocompromising conditions but was sustained over time in both populations.

These data provide evidence for sustained high protection from severe COVID-19 requiring hospitalization for up to 24 weeks among fully vaccinated adults, which is consistent with data demonstrating mRNA COVID-19 vaccines have the capacity to induce durable immunity, particularly in limiting the severity of disease (*9,10*). Alpha variants were the predominant viruses sequenced, although Delta variants became dominant starting in mid-June, consistent with national surveillance data (*8*). Because of limited sequenced virus, Delta-specific VE was not assessed. VE was similar during June–July when circulation of Delta increased in the United States compared with VE during March–May when Alpha variants predominated, although further surveillance is needed.

The findings in this report are subject to at least six limitations. First, the follow-up period was limited to approximately 24 weeks since receipt of full vaccination because of the recent authorization of mRNA COVID-19 vaccines in the United States. Additional analyses with longer duration of follow-up since vaccination are warranted. Second, effectiveness over time from authorized non-mRNA COVID-19 vaccines, including Janssen's (Johnson & Johnson) vaccine product, was not assessed because of limited use of this vaccine during the surveillance period. Third, time-varying VE was not assessed

FIGURE 2. Sustained vaccine effectiveness* against COVID-19 among hospitalized adults, by patient status†,§ and interval since vaccination — 21 medical centers in 18 states,¶ March–July 2021



Abbreviation: VE = vaccine effectiveness.

* VE was estimated using logistic regression comparing the odds of being fully vaccinated with an authorized mRNA COVID-19 vaccine with being unvaccinated in case patients and controls using the equation VE = 100 × (1 – odds ratio). Models were adjusted for date of hospital admission (biweekly intervals), U.S. Department of Health and Human Services region of hospital, age group (18–49, 50–64, or ≥65 years), sex, and race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic of any race, non-Hispanic Other, or unknown). Analyses restricted to adults aged ≥65 years adjusted for age in years as a continuous variable. Binary time since second dose of mRNA vaccine was added to the model with results for 2–12 weeks and 13–24 weeks shown. 95% confidence intervals shown by error bars.

† Immunocompromising conditions included having one or more of the following: active solid organ cancer (active cancer defined as treatment for the cancer or newly diagnosed cancer in the past 6 months), active hematologic cancer (such as leukemia, lymphoma, or myeloma), HIV infection without AIDS, AIDS, congenital immunodeficiency syndrome, previous splenectomy, previous solid organ transplant, immunosuppressive medication, systemic lupus erythematosus, rheumatoid arthritis, psoriasis, scleroderma, or inflammatory bowel disease, including Crohn's disease or ulcerative colitis.

§ Multiple morbidities were defined as having chronic conditions within three or more of the following condition categories: cardiovascular disease, neurologic disease, pulmonary disease, gastrointestinal disease, endocrine disease, renal disease, hematologic disease, malignancy, immunosuppression not captured in other categories, autoimmune condition, or other condition (sarcoidosis, amyloidosis, or unintentional weight loss ≥10 pounds in the last 90 days).

¶ Hospitals by region included *Northeast:* Baystate Medical Center (Springfield, Massachusetts), Beth Israel Deaconess Medical Center (Boston, Massachusetts), Montefiore Medical Center (Bronx, New York); *South:* Vanderbilt University Medical Center (Nashville, Tennessee), University of Miami Medical Center (Miami, Florida), Emory University Medical Center (Atlanta, Georgia), Johns Hopkins Hospital (Baltimore, Maryland), Wake Forest University Baptist Medical Center (Winston-Salem, North Carolina), Baylor Scott and White Health (Temple, Texas); *Midwest:* University of Iowa Hospitals (Iowa City, Iowa), University of Michigan Hospital (Ann Arbor, Michigan), Hennepin County Medical Center (Minneapolis, Minnesota), Barnes-Jewish Hospital (St. Louis, Missouri), Cleveland Clinic (Cleveland, Ohio), Ohio State University Wexner Medical Center (Columbus, Ohio); *West:* Stanford University Medical Center (Stanford, California), UCLA Medical Center (Los Angeles, California), UCHealth University of Colorado Hospital (Aurora, Colorado), Oregon Health & Science University Hospital (Portland, Oregon), Intermountain Medical Center (Murray, Utah), University of Washington (Seattle, Washington).

Summary

What is already known about this topic?

COVID-19 mRNA vaccines provide strong protection against severe COVID-19; however, the duration of protection is uncertain.

What is added by this report?

Among 1,129 patients who received 2 doses of a mRNA vaccine, no decline in vaccine effectiveness against COVID-19 hospitalization was observed over 24 weeks. Vaccine effectiveness was 86% 2–12 weeks after vaccination and 84% at 13–24 weeks. Vaccine effectiveness was sustained among groups at risk for severe COVID-19.

What are the implications for public health practice?

mRNA vaccine effectiveness against COVID-19–associated hospitalizations was sustained over 24 weeks; ongoing monitoring is needed as new SARS-CoV-2 variants emerge. To reduce hospitalization, all eligible persons should be offered COVID-19 vaccination.

by lineage because of sample size. Fourth, residual confounding might have been present, although the analysis adjusted for potential confounders, including calendar time and patient age. Fifth, this analysis did not consider VE over time among persons aged <18 years or partially vaccinated persons. Finally, the current analysis only included hospitalized adults and did not include persons with asymptomatic SARS-CoV-2 infection or COVID-19 who did not require hospitalization.

Protection against severe COVID-19 resulting in hospitalization was sustained through 24 weeks after vaccination with mRNA COVID-19 vaccines. To reduce their risk for hospitalization, all eligible persons should be offered COVID-19 vaccination. Continued monitoring of VE against infection and severe disease is needed as the elapsed time since vaccination increases and new SARS-CoV-2 variants emerge.

IVY Network

Nicole Calhoun, Baylor Scott & White Health; Kempapura Murthy, Baylor Scott & White Health; Judy Herrick, Baylor Scott & White Health; Amanda McKillop, Baylor Scott & White Health; Eric Hoffman, Baylor Scott & White Health; Martha Zayed, Baylor Scott & White Health; Michael Smith, Baylor Scott & White Health; Natalie Settele, Baylor Scott & White Health; Jason Ettlinger, Baylor Scott & White Health; Elisa Priest, Baylor Scott & White Health; Jennifer Thomas, Baylor Scott & White Health; Alejandro Arroliga, Baylor Scott & White Health; Madhava Beeram, Baylor Scott & White Health; Ryan Kindle, Baystate Medical Center; Lori-Ann Kozikowski, Baystate Medical Center; Lesley De Souza, Baystate Medical Center; Scott Ouellette, Baystate Medical Center; Sherell Thornton-Thompson, Baystate Medical Center; Patrick Tyler, Beth Israel Deaconess Medical Center; Omar Mehkri, Cleveland Clinic; Kiran Ashok, Cleveland Clinic; Susan Gole, Cleveland Clinic; Alexander King, Cleveland Clinic; Bryan Poynter, Cleveland Clinic; Nicholas Stanley, Emory University; Audrey Hendrickson, Hennepin County Medical Center; Ellen Maruggi, Hennepin County Medical Center; Tyler Scharber, Hennepin County Medical Center; Jeffrey Jorgensen, Intermountain Medical Center; Robert Bowers, Intermountain Medical Center; Jennifer King, Intermountain Medical Center; Valerie Aston, Intermountain Medical Center; Brent Armbruster, Intermountain Medical Center; Richard E. Rothman, Johns Hopkins University; Rahul Nair, Montefiore Medical Center; Jen-Ting (Tina) Chen, Montefiore Medical Center; Sarah Karow, Ohio State University; Emily Robart, Ohio State University; Paulo Nunes Maldonado, Ohio State University; Maryiam Khan, Ohio State University; Preston So, Ohio State University; Joe Levitt, Stanford University; Cynthia Perez, Stanford University; Anita Visweswaran, Stanford University; Jonasel Roque, Stanford University; Adreanne Rivera, University of California, Los Angeles; Trevor Frankel, University of California, Los Angeles; Michelle Howell, UCHealth University of Colorado Hospital; Jennifer Friedel, UCHealth University of Colorado Hospital; Jennifer Goff, UCHealth University of Colorado Hospital; David Huynh, UCHealth University of Colorado Hospital; Michael Tozier, UCHealth University of Colorado Hospital; Conner Driver, UCHealth University of Colorado Hospital; Michael Carricato, UCHealth University of Colorado Hospital; Alexandra Foster, UCHealth University of Colorado Hospital; Paul Nassar, University of Iowa; Lori Stout, University of Iowa; Zita Sibenaller, University of Iowa; Alicia Walter, University of Iowa; Jasmine Mares, University of Iowa; Logan Olson, University of Iowa; Bradley Clinansmith, University of Iowa; Carolina Rivas, University of Miami; Hayley Gershengorn, University of Miami; EJ McSpadden, University of Michigan; Rachel Truscon, University of Michigan; Anne Kaniclides, University of Michigan; Lara Thomas, University of Michigan; Ramsay Bielak, University of Michigan; Weronika Damek Valvano, University of Michigan; Rebecca Fong, University of Michigan; William J. Fitzsimmons, University of Michigan; Christopher Blair, University of Michigan; Andrew L. Valesano, University of Michigan; Julie Gilbert, University of Michigan; Christine D. Crider, University of Washington; Kyle A. Steinbock, University of Washington; Thomas C. Paulson, University of Washington; Layla A. Anderson, University of Washington; Christy Kampe, Vanderbilt University Medical Center; Jakea Johnson, Vanderbilt University Medical Center; Rendie McHenry, Vanderbilt University Medical Center; Marcia Blair, Vanderbilt University Medical Center; Douglas Conway, Vanderbilt University Medical Center; Mary LaRose, Wake Forest University; Leigha Landreth, Wake Forest University; Madeline Hicks, Wake Forest University; Lisa Parks, Wake Forest University; Jahnavi Bongu, Washington University; David McDonald, Washington University; Candice Cass, Washington University; Sondra Seiler, Washington University; David Park, Washington University; Tiffany Hink, Washington University; Meghan Wallace, Washington University; Carey-Ann Burnham, Washington University; Olivia G. Arter, Washington University.

Corresponding author: Mark W. Tenforde, media@cdc.gov.

[1]CDC COVID-19 Response Team; [2]Vanderbilt University Medical Center, Nashville, Tennessee; [3]University of Colorado School of Medicine, Aurora, Colorado; [4]University of Iowa, Iowa City, Iowa; [5]Baylor Scott & White Health, Temple, Texas; [6]Texas A&M University College of Medicine, Temple, Texas; [7]Beth Israel Deaconess Medical Center, Boston, Massachusetts; [8]Wake Forest University Baptist Medical Center, Winston-Salem, North Carolina; [9]Johns Hopkins Hospital, Baltimore, Maryland; [10]Hennepin County Medical Center, Minneapolis, Minnesota; [11]Montefiore Healthcare Center, Albert Einstein College of Medicine, Bronx, New York; [12]University of Washington School of Medicine, Seattle, Washington; [13]Baystate Medical Center, Springfield, Massachusetts; [14]Intermountain Medical Center and University of Utah, Salt Lake City, Utah; [15]University of Michigan School of Public Health, Ann Arbor, Michigan; [16]Oregon Health & Science University Hospital, Portland, Oregon; [17]Emory University School of Medicine, Atlanta, Georgia; [18]Cleveland Clinic, Cleveland, Ohio; [19]Stanford University School of Medicine, Palo Alto, California; [20]Ronald Reagan-UCLA Medical Center, Los Angeles, California; [21]University of Miami, Miami, Florida; [22]Washington University, St. Louis, Missouri; [23]Ohio State University Wexner Medical Center, Columbus, Ohio; [24]University of Michigan School of Medicine, Ann Arbor, Michigan.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Samuel M. Brown reports personal fees from Hamilton, institutional fees from Faron Pharmaceuticals and Sedana, grants from Janssen, the National Institutes of Health (NIH), and the Department of Defense (DoD), book royalties from Oxford University and Brigham Young University, outside the submitted work. Jonathan D. Casey reports grants from NIH, outside the submitted work. Steven Y. Chang was a speaker for La Jolla Pharmaceuticals in 2018 and consulted for PureTech Health in 2020. James D. Chappell reports grants from NIH during the conduct of the study. Matthew C. Exline reports support from Abbott Labs for sponsored talks, outside the submitted work. D. Clark Files reports personal consultant fees from Cytovale and is a data and safety monitoring board (DSMB) member from Medpace, outside the submitted work. Adit A. Ginde reports grants from NIH, DoD, AbbVie, and Faron Pharmaceuticals, outside the submitted work. Michelle N. Gong reports grants from NIH and the Agency for Healthcare Research and Quality (AHRQ), DSMB membership fees from Regeneron, and personal fees from Philips Healthcare, outside the submitted work. Carlos G. Grijalva reports consultancy fees from Pfizer, Merck, and Sanofi-Pasteur; grants from Campbell Alliance/Syneos Health, NIH, the Food and Drug Administration, AHQR, and Sanofi, outside the submitted work. David N. Hager reports salary support from Incyte Corporation, the Marcus Foundation, and EMPACT Precision Medicine via Vanderbilt University Medical Center, outside the submitted work. Natasha Halasa reports grants and nonfinancial support from Sanofi, and Quidel outside the submitted work. Daniel J. Henning reports personal consultant fees from Cytovale and Opticyte. Akram Khan reports grants from United Therapeutics, Johnson & Johnson, 4D Medical, Lung LLC, and Reata Pharmaceuticals, outside the submitted work. Adam S. Lauring reports personal fees from Sanofi and Roche, outside the submitted work. Christopher J. Lindsell reports grants from NIH, DoD, and the Marcus Foundation; contract fees from bioMerieux, Endpoint LLC, and Entegrion Inc, outside the submitted work and has a patent for risk stratification in sepsis and septic shock issued. Emily T. Martin reports personal fees from Pfizer and grants from Merck, outside the submitted work. Arnold S. Monto reports consulting fees from Sanofi-Pasteur and Seqirus outside the submitted work. Ithan D. Peltan reports grants from NIH and Janssen Pharmaceuticals and institutional support from Asahi Kasei Pharma and Regeneron, outside the submitted work. Todd W. Rice reports personal fees from Cumberland Pharmaceuticals, Inc. and personal fees from Avisa Pharma, LLC and Sanofi, outside the submitted work. Wesley H. Self reports consulting fees from Aeprio Pharmaceuticals and Merck outside the submitted work. No other potential conflicts of interest were disclosed.

References

1. Tenforde MW, Olson SM, Self WH, et al.; IVY Network; HAIVEN Investigators. Effectiveness of Pfizer-BioNTech and Moderna vaccines against COVID-19 among hospitalized adults aged ≥65 years—United States, January–March 2021. MMWR Morb Mortal Wkly Rep 2021;70:674–9. PMID:33956782 https://doi.org/10.15585/mmwr.mm7018e1
2. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of the Pfizer-BioNTech and Oxford-AstraZeneca vaccines on covid-19 related symptoms, hospital admissions, and mortality in older adults in England: test negative case-control study. BMJ 2021;373:n1088. PMID:33985964 https://dx.doi.org/10.1136%2Fbmj.n1088
3. Haas EJ, Angulo FJ, McLaughlin JM, et al. Impact and effectiveness of mRNA BNT162b2 vaccine against SARS-CoV-2 infections and COVID-19 cases, hospitalisations, and deaths following a nationwide vaccination campaign in Israel: an observational study using national surveillance data. Lancet 2021;397:1819–29. PMID:33964222 https://doi.org/10.1016/S0140-6736(21)00947-8
4. Tenforde MW, Patel MM, Ginde AA, et al. Effectiveness of SARS-CoV-2 mRNA vaccines for preventing Covid-19 hospitalizations in the United States. Clin Infect Dis. In press 2021.
5. Thompson MG, Burgess JL, Naleway AL, et al. Prevention and attenuation of Covid-19 with the BNT162b2 and mRNA-1273 vaccines. N Engl J Med 2021;385:320–9. PMID:34192428 https://doi.org/10.1056/NEJMoa2107058
6. Ferdinands JM, Gaglani M, Martin ET, et al. Waning vaccine effectiveness against influenza-associated hospitalizations among adults, 2015–2016 to 2018–2019, US Hospitalized Adult Influenza Vaccine Effectiveness Network. Clin Infect Dis 2021. Epub January 19, 2021. PMID:33462610 https://doi.org/10.1093/cid/ciab045
7. Feng S, Chiu SS, Chan ELY, et al. Effectiveness of influenza vaccination on influenza-associated hospitalisations over time among children in Hong Kong: a test-negative case-control study. Lancet Respir Med 2018;6:925–34. PMID:30442587 https://doi.org/10.1016/S2213-2600(18)30419-3
8. CDC. COVID data tracker. Atlanta, GA: US Department of Health and Human Services, CDC; 2021. Accessed August 5, 2021. https://covid.cdc.gov/covid-data-tracker/#datatracker-home
9. Turner JS, O'Halloran JA, Kalaidina E, et al. SARS-CoV-2 mRNA vaccines induce persistent human germinal centre responses. Nature 2021;596:109–13. PMID:34182569 https://doi.org/10.1038/s41586-021-03738-2
10. Cromer D, Juno JA, Khoury D, et al. Prospects for durable immune control of SARS-CoV-2 and prevention of reinfection. Nat Rev Immunol 2021;21:395–404. PMID:33927374 https://doi.org/10.1038/s41577-021-00550-x

Effectiveness of Pfizer-BioNTech and Moderna Vaccines in Preventing SARS-CoV-2 Infection Among Nursing Home Residents Before and During Widespread Circulation of the SARS-CoV-2 B.1.617.2 (Delta) Variant — National Healthcare Safety Network, March 1–August 1, 2021

Srinivas Nanduri, MD[1,*]; Tamara Pilishvili, PhD[1,*]; Gordana Derado, PhD[1]; Minn Minn Soe, MBBS[1]; Philip Dollard, MPH[1]; Hsiu Wu, MD[1]; Qunna Li, MSPH[1]; Suparna Bagchi, DrPH[1]; Heather Dubendris, MSPH[1,2]; Ruth Link-Gelles, PhD[1]; John A. Jernigan, MD[1]; Daniel Budnitz, MD[1]; Jeneita Bell, MD[1]; Andrea Benin, MD[1]; Nong Shang, PhD[1]; Jonathan R. Edwards, MStat[1*]; Jennifer R. Verani, MD[1,*]; Stephanie J. Schrag, DPhil[1,*]

On August 18, 2021, this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

Nursing home and long-term care facility residents live in congregate settings and are often elderly and frail, putting them at high risk for infection with SARS-CoV-2, the virus that causes COVID-19, and severe COVID-19–associated outcomes; therefore, this population was prioritized for early vaccination in the United States (*1*). Following rapid distribution and administration of the mRNA COVID-19 vaccines (Pfizer-BioNTech and Moderna) under an Emergency Use Authorization by the Food and Drug Administration (*2*), observational studies among nursing home residents demonstrated vaccine effectiveness (VE) ranging from 53% to 92% against SARS-CoV-2 infection (*3*–*6*). However, concerns about the potential for waning vaccine-induced immunity and the recent emergence of the highly transmissible SARS-CoV-2 B.1.617.2 (Delta) variant† highlight the need to continue to monitor VE (*7*). Weekly data reported by the Centers for Medicaid & Medicare (CMS)–certified skilled nursing facilities or nursing homes to CDC's National Healthcare Safety Network (NHSN)§ were analyzed to evaluate effectiveness of full vaccination (2 doses received ≥14 days earlier) with any of the two currently authorized mRNA COVID-19 vaccines during the period soon after vaccine introduction and before the Delta variant was circulating (pre-Delta [March 1–May 9, 2021]), and when the Delta variant predominated¶ (Delta [June 21–August 1, 2021]). Using 17,407 weekly reports from 3,862 facilities from the pre-Delta period, adjusted effectiveness against infection for any mRNA vaccine was 74.7% (95% confidence interval [CI] = 70.0%–78.8%). Analysis using 33,160 weekly reports from 11,581 facilities during an intermediate period (May 10–June 20) found that the adjusted effectiveness was 67.5% (95% CI = 60.1%–73.5%). Analysis using 85,593 weekly reports from 14,917 facilities during the Delta period found that the adjusted effectiveness was 53.1% (95% CI = 49.1%–56.7%). Effectiveness estimates were similar for Pfizer-BioNTech and Moderna vaccines. These findings indicate that mRNA vaccines provide protection against SARS-CoV-2 infection among nursing home residents; however, VE was lower after the Delta variant became the predominant circulating strain in the United States. This analysis assessed VE against any infection, without being able to distinguish between asymptomatic and symptomatic presentations. Additional evaluations are needed to understand protection against severe disease in nursing home residents over time. Because nursing home residents might remain at some risk for SARS-CoV-2 infection despite vaccination, multiple COVID-19 prevention strategies, including infection control, testing, and vaccination of nursing home staff members, residents, and visitors, are critical. An additional dose of COVID-19 vaccine might be considered for nursing home and long-term care facility residents to optimize a protective immune response.

Effectiveness of mRNA COVID-19 vaccines against laboratory-confirmed SARS-CoV-2 infection among nursing home residents was evaluated using data reported to NHSN. CMS-certified nursing homes are required to report aggregate weekly numbers of new laboratory-confirmed SARS-CoV-2 infections among residents, by vaccination status (product and number of doses received), to NHSN. Vaccination status of cases was categorized as 1) unvaccinated (no COVID-19 vaccine doses); 2) fully vaccinated with an mRNA vaccine (2 doses ≥14 days before collection of a SARS-CoV-2–positive specimen), and 3) "other" (single dose of mRNA or Janssen [Johnson & Johnson] vaccine or received unspecified vaccines). Nursing homes also reported weekly on the number of residents by vaccination status; reporting on resident vaccination status was voluntary during the pre-Delta period but was required by CMS starting on June 6, 2021.

Facility-level weekly records for the analysis combined case counts by vaccination status in each week with the weekly number of residents by vaccination status 2 weeks previously. This ensured that residents were counted as fully vaccinated only after ≥14 days from receipt of a second dose. Weekly reports of case counts were excluded if a facility did not report resident counts by vaccination status for the corresponding week 2 weeks earlier.

* These authors contributed equally to this report.
† https://www.cdc.gov/coronavirus/2019-ncov/variants/delta-variant.html
§ https://www.cdc.gov/nhsn/ltc/covid19/index.html
¶ https://covid.cdc.gov/covid-data-tracker/#variant-proportions

Records from facilities with case data during March 1–August 1, 2021, and the corresponding data on resident vaccination status during February 15–July 18, 2021, were combined for an overall 22-week study period. During the study period, 15,254 facilities sent 330,864 weekly reports with case counts to NHSN; of these, 15,236 facilities (99.9%) sent 144,334 (43.6%) weekly reports with counts of residents by vaccination status.

A generalized linear mixed effects model was used with a zero-inflated Poisson distribution (used to model data that have an excess of zero counts) for case counts by vaccination status, offset by resident counts, to estimate the ratio of infection rates among fully vaccinated and unvaccinated residents. To account for variability across sites, facility was included as a random effect. Because of potential for confounding by time, calendar week was modeled as a fixed effect covariate. Nonlinearity of infection rates over calendar weeks was modeled with cubic splines. To evaluate the effect of circulating SARS-CoV-2 variants on VE, the study period was stratified into three periods: 1) pre-Delta (March 1–May 9); 2) intermediate, the period when Delta circulation was documented but not predominant (May 10–June 20); and 3) Delta, when ≥50% of SARS-CoV-2 viruses sequenced were the Delta variant (June 21–August 1), with an interaction term between this categorical time variable and vaccination status to obtain VE estimates for each period. The following characteristics were evaluated as potential confounders of VE: 1) facility-level cumulative SARS-CoV-2 infection rates combined for staff members and residents from May 8, 2020, through the week of reporting; 2) weekly local county incidence of SARS-CoV-2 infections; and 3) CDC Social Vulnerability Index score** for each facility's county. The change-in-estimate criterion for the regression coefficient with a 10% cutoff was used to evaluate covariates; none met this criterion. VE was estimated as 1 minus the rate ratio multiplied by 100, adjusted for calendar week and facility as a random effect. VE for the "other" category is not presented because this group combines different categories, and estimates would not be meaningful. Data analysis was conducted using SAS (version 9.4; SAS Institute) and R (version 4.0.4; R Foundation); statistical significance was defined as $p<0.05$. This activity was reviewed by CDC and was conducted consistent with federal laws and institutional policies.††

After applying exclusion criteria and combining facility-level weekly case and corresponding resident counts, the analysis included 136,160 reports from 14,997 facilities (median of eight reports per facility; interquartile range = 6–10), with 3,862 (25.8%) facilities reporting during the pre-Delta period, 11,581 (77.2%) during the intermediate period, and 14,917 (99.5%) during the Delta period. Overall, the analysis included 10,428,783 aggregate weekly resident counts, including 1,531,446 (14.7%) unvaccinated residents, 5,174,098 (49.6%) fully vaccinated with Pfizer-BioNTech, 2,633,700 (25.3%) fully vaccinated with Moderna, and 1,089,539 (10.4%) with "other" vaccination status. Overall, 6,879 COVID-19 cases were identified, including 2,113 (30.7%) in unvaccinated residents, 2,603 (37.8%) in residents fully vaccinated with Pfizer-BioNTech, 1,302 (18.9%) in residents fully vaccinated with Moderna, and 861 (12.5%) in residents with "other" vaccination status.

During the pre-Delta period, adjusted VE against infection among those fully vaccinated (versus unvaccinated) was 74.7% for any mRNA vaccine, 74.2% for Pfizer-BioNTech, and 74.7% for Moderna (Table). During the Delta period, adjusted VE against infection among those fully vaccinated was 53.1% for any mRNA vaccine, 52.4% for Pfizer-BioNTech, and 50.6% for Moderna. VE estimates for the Delta period were significantly lower than those for the pre-Delta period ($p<0.001$). VE point estimates during the intermediate period were lower than those during the pre-Delta period; however, the estimates were not significantly different ($p = 0.06$) (Table).

Discussion

Analysis of nursing home COVID-19 data from NHSN indicated a significant decline in effectiveness of full mRNA COVID-19 vaccination against laboratory-confirmed SARS-CoV-2 infection, from 74.7% during the pre-Delta period (March 1–May 9, 2021) to 53.1% during the period when the Delta variant predominated in the United States. This study could not differentiate the independent impact of the Delta variant from other factors, such as potential waning of vaccine-induced immunity. Further research on the possible impact of both factors on VE among nursing home residents is warranted. Because nursing home residents might remain at some risk for SARS-CoV-2 infection despite vaccination, multipronged COVID-19 prevention strategies, including infection control,§§ testing, and vaccination of nursing home staff members, residents, and visitors are critical.

These results (pre-Delta 74.7%; Delta 53.1%) fall within the range of findings from other studies of COVID-19 mRNA VE in nursing home residents conducted before the Delta variant was prevalent, with estimates against infection ranging from 53% to 92% (*3*–*6*). Variability in VE estimates across studies can result from differences in underlying populations, SARS-CoV-2 testing practices and diagnostics, prevalence of previous infections, analytic methods, and virus variant strains in circulation.

** https://www.atsdr.cdc.gov/placeandhealth/svi/data_documentation_download.html

†† 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.

§§ https://www.cdc.gov/coronavirus/2019-ncov/hcp/long-term-care.html

TABLE. Effectiveness of full vaccination* with Pfizer-BioNTech or Moderna vaccines in preventing SARS-CoV-2 infection among nursing home residents, by period of B.1.617.2 (Delta) variant circulation — National Healthcare Safety Network, March 1–August 1, 2021

Vaccine type/Period†	Aggregate weekly count of residents	No. of cases	Vaccine effectiveness, % (95% CI)		p-value**
			Unadjusted§	Adjusted¶	
Any mRNA vaccine					
Period 1: pre-Delta	936,123	466	74.3 (69.5–78.4)	74.7 (70.0–78.8)	Ref
Period 2: intermediate	1,859,929	440	65.8 (58.5–71.9)	67.5 (60.1–73.5)	0.06
Period 3: Delta	5,011,746	2,999	52.8 (48.8–56.5)	53.1 (49.1–56.7)	<0.001
Pfizer-BioNTech					
Period 1: pre-Delta	679,288	348	74.7 (69.5–79.0)	74.2 (68.9–78.7)	Ref
Period 2: intermediate	1,246,078	316	63.5 (54.9–70.5)	66.5 (58.3–73.1)	0.07
Period 3: Delta	3,248,732	1,939	52.2 (47.7–56.3)	52.4 (48.0–56.4)	<0.001
Moderna					
Period 1: pre-Delta	256,835	118	72.6 (66.1–77.8)	74.7 (66.2–81.1)	Ref,
Period 2: intermediate	613,851	124	73.2 (66.8–78.3)	70.4 (60.1–78.0)	0.45
Period 3: Delta	1,763,014	1,060	48.4 (42.3–53.8)	50.6 (45.0–55.7)	<0.001
Unvaccinated					
Period 1: pre-Delta	217,534	447	Ref		NA
Period 2: intermediate	360,051	269			
Period 3: Delta	953,861	1,397			

Abbreviations: CI = confidence interval; NA = not applicable; Ref = referent group.

* Fully vaccinated cases were defined as infections in residents who received the second of 2 doses of either Pfizer-BioNTech or Moderna vaccines ≥14 days before SARS-CoV-2–positive specimen collection.

† Periods for analysis were stratified as follows: period 1 = pre-Delta (March 1–May 9, 2021); period 2 = intermediate (May 10–June 20, 2021); period 3 = Delta (June 21–August 1, 2021).

§ Results from a generalized linear mixed effects model with random effects for facility and zero-inflated Poisson distribution; vaccine effectiveness was estimated as 1 minus the rate ratio multiplied by 100, with rate ratio comparing rates among fully vaccinated to those among unvaccinated persons. Results for "other" category, which included those who received a single dose of Janssen (Johnson & Johnson) or mRNA vaccine, or those residents who received unspecified vaccines are not presented because this group combines the different categories and estimates will not be meaningful.

¶ Results from the same model controlling for calendar week of reporting of case counts.

** p-values for comparison of adjusted vaccine effectiveness estimates in period 2 and period 3 with estimates in period 1. The difference in estimates among periods was evaluated by adding an interaction between periods and vaccine status in the model.

Nursing home residents, who are often elderly and frail, might have a less robust response to vaccines, and are at higher risk for infection with SARS-CoV-2 and for severe COVID-19 (*8*). In addition, nursing home residents were among the earliest groups vaccinated in the United States; thus, if vaccine-induced immunity does wane over time, this decrease in VE might first be observed among nursing home residents. Because increased U.S. circulation of the Delta variant coincided with a period ≥6 months after vaccine introduction, the extent to which reduced vaccine protection against Delta and potential waning immunity contributed to the lower VE in the Delta period could not be determined by this study.

Nursing homes were aggressive in case ascertainment because of guidelines recommending weekly point prevalence surveys if a single SARS-CoV-2 infection in a staff member or resident was identified.¶¶ This analysis assessed VE against any infection, without being able to distinguish between asymptomatic and symptomatic infections. Additional evaluations are needed to understand protection against severe disease in nursing home residents over time.

The findings in this report are subject to at least five limitations. First, resident-level demographic or clinical data were not reported to NHSN. Therefore, the analysis could not control for potential confounders, such as age, presence of underlying health conditions, or the influence of previous SARS-CoV-2 infections on VE. Second, vaccination dates were not available and time since vaccination could not be measured to evaluate potential waning of protection. Third, staff member vaccination data were not sufficiently complete to assess as a potential confounder. Fourth, before June 7, 2021, weekly reporting of resident vaccination status was voluntary, and missing data limited inclusion of facility records during this period. Although the magnitude of potential bias introduced by missing data could not be assessed, a bias indicator analysis was conducted, which indicated that VE was likely underestimated during the pre-Delta period (COVID-19 Vaccine Effectiveness Team, CDC, unpublished data, 2021). Finally, the study assessed only nursing home residents and is not generalizable to the broader population.

Both Pfizer-BioNTech and Moderna mRNA vaccines were highly effective in preventing SARS-CoV-2 infection in nursing home residents early after vaccine introduction. However, the effectiveness among this population in recent months has been significantly lower. To prevent transmission of SARS-CoV-2 in nursing homes, these findings highlight the critical importance of COVID-19 vaccination of staff members, residents,

¶¶ https://www.cms.gov/files/document/qso-20-38-nh.pdf

Summary

What is already known about this topic?

Early observational studies among nursing home residents showed mRNA vaccines to be 53% to 92% effective against SARS-CoV-2 infection.

What is added by this report?

Two doses of mRNA vaccines were 74.7% effective against infection among nursing home residents early in the vaccination program (March–May 2021). During June–July 2021, when B.1.617.2 (Delta) variant circulation predominated, effectiveness declined significantly to 53.1%.

What are the implications for public health practice?

Multicomponent COVID-19 prevention strategies, including vaccination of nursing home staff members, residents, and visitors, are critical. An additional dose of COVID-19 vaccine might be considered for nursing home and long-term care facility residents to optimize a protective immune response.

and visitors and adherence to rigorous COVID-19 prevention strategies. An additional dose of COVID-19 vaccine might be considered for nursing home and long-term care facility residents to optimize a protective immune response.***

*** https://www.cdc.gov/vaccines/acip/meetings/slides-2021-08-13.html

Corresponding author: Srinivas Nanduri, snanduri@cdc.gov.

[1]CDC COVID-19 Response Team; [2]Lantana Consulting Group, East Thetford, Vermont.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflicts of interest were disclosed.

References

1. Dooling K, Marin M, Wallace M, et al. The Advisory Committee on Immunization Practices' updated interim recommendation for allocation of COVID-19 vaccine—United States, December 2020. MMWR Morb Mortal Wkly Rep 2021;69:1657–60. PMID:33382671 https://doi.org/10.15585/mmwr.mm695152e2
2. Gharpure R, Patel A, Link-Gelles R. First-dose COVID-19 vaccination coverage among skilled nursing facility residents and staff. JAMA 2021;325:1670–1. PMID:33625464 https://doi.org/10.1001/jama.2021.2352
3. Monge S, Olmedo C, Alejos B, Lapeña MF, Sierra MJ, Limia A. Direct and indirect effectiveness of mRNA vaccination against SARS-CoV-2 infection in long-term care facilities in Spain. Emerg Infect Dis 2021. Epub July 27, 2021.
4. Mazagatos C, Monge S, Olmedo C, et al.; Working Group for the surveillance and control of COVID-19 in Spain. Effectiveness of mRNA COVID-19 vaccines in preventing SARS-CoV-2 infections and COVID-19 hospitalisations and deaths in elderly long-term care facility residents, Spain, weeks 53 2020 to 13 2021. Euro Surveill 2021;26:2100452. PMID:34142647 https://doi.org/10.2807/1560-7917.ES.2021.26.24.2100452
5. Britton A, Jacobs Slifka KM, Edens C, et al. Effectiveness of the Pfizer-BioNTech COVID-19 vaccine among residents of two skilled nursing facilities experiencing COVID-19 outbreaks—Connecticut, December 2020–February 2021. MMWR Morb Mortal Wkly Rep 2021;70:396–401. PMID:33735160 https://doi.org/10.15585/mmwr.mm7011e3
6. Emborg H-D, Valentiner-Branth P, Schelde AB, et al. Vaccine effectiveness of the BNT162b2 mRNA COVID-19 vaccine against RT-PCR confirmed SARS-CoV-2 infections, hospitalisations and mortality in prioritised risk groups. medRxiv [Preprint posted online June 2, 2021]. https://www.medrxiv.org/content/10.1101/2021.05.27.21257583v1
7. Puranik A, Lenehan PJ, Silvert E, et al. Comparison of two highly-effective mRNA vaccines for COVID-19 during periods of Alpha and Delta variant prevalence. medRxiv [Preprint posted online August 9, 2021]. https://www.medrxiv.org/content/10.1101/2021.08.06.21261707v2
8. Bagchi S, Mak J, Li Q, et al. Rates of COVID-19 among residents and staff members in nursing homes—United States, May 25–November 22, 2020. MMWR Morb Mortal Wkly Rep 2021;70:52–5. PMID:33444301 https://doi.org/10.15585/mmwr.mm7002e2

Effectiveness of COVID-19 Vaccines in Preventing SARS-CoV-2 Infection Among Frontline Workers Before and During B.1.617.2 (Delta) Variant Predominance — Eight U.S. Locations, December 2020–August 2021

Ashley Fowlkes, ScD[1]; Manjusha Gaglani, MBBS[2]; Kimberly Groover, PhD[3]; Matthew S. Thiese, PhD[4]; Harmony Tyner, MD[5]; Katherine Ellingson, PhD[6]; HEROES-RECOVER Cohorts

On August 24, 2021, this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

During December 14, 2020–April 10, 2021, data from the HEROES-RECOVER Cohorts,* a network of prospective cohorts among frontline workers, showed that the Pfizer-BioNTech and Moderna mRNA COVID-19 vaccines were approximately 90% effective in preventing symptomatic and asymptomatic infection with SARS-CoV-2, the virus that causes COVID-19, in real-world conditions (*1,2*). This report updates vaccine effectiveness (VE) estimates including all COVID-19 vaccines available through August 14, 2021, and examines whether VE differs for adults with increasing time since completion of all recommended vaccine doses. VE before and during SARS-CoV-2 B.1.617.2 (Delta) variant predominance, which coincided with an increase in reported COVID-19 vaccine breakthrough infections, were compared (*3,4*).

Methods for the HEROES-RECOVER Cohorts have been published previously (*1,2,5*). Health care personnel, first responders, and other essential and frontline workers in eight U.S. locations across six states were tested weekly for SARS-CoV-2 infection by reverse transcription–polymerase chain reaction (RT-PCR)† and upon the onset of any COVID-19–like illness. Weeks when the Delta variant accounted for ≥50% of viruses sequenced, based on data from each respective location, were defined as weeks of Delta variant predominance. Vaccination was documented by self-report and verified by provision of vaccine cards or extraction from electronic medical records or state immunization registries. Among 4,217 participants, 3,483 (83%) were vaccinated; 2,278 (65%) received Pfizer-BioNTech, 1,138 (33%) Moderna, and 67 (2%) Janssen (Johnson & Johnson) COVID-19 vaccines. Cox proportional hazards models were used to calculate ratios of unvaccinated to fully vaccinated (≥14 days after receipt of all recommended COVID-19 vaccine doses) infection rates, adjusted for occupation, site, and local viral circulation (*6*), and weighted for inverse probability of vaccination using sociodemographic characteristics, health information, frequency of close social contact, and mask use. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.§

During the 35-week study period, 4,136 participants with no previous laboratory-documented SARS-CoV-2 infection contributed a median of 20 unvaccinated days per participant (interquartile range [IQR] = 8–45 days; total = 181,357 days), during which 194 SARS-CoV-2 infections were identified; 89.7% of these infections were symptomatic. A total of 2,976 participants contributed a median of 177 fully vaccinated days (IQR = 115–195 days; total = 455,175 days) with 34 infections, 80.6% of which were symptomatic. Adjusted VE against SARS-CoV-2 infection was 80% (95% confidence interval [CI] = 69%–88%). The VE point estimate was 85% among participants for whom <120 days had elapsed since completion of full vaccination compared with 73% among those for whom ≥150 days had elapsed; however the VE 95% CI were overlapping, indicating the difference was not statistically significant (Table).

During Delta variant–predominant weeks at study sites, 488 unvaccinated participants contributed a median of 43 days (IQR = 37–69 days; total = 24,871 days) with 19 SARS-CoV-2 infections (94.7% symptomatic); 2,352 fully vaccinated participants contributed a median of 49 days (IQR = 35–56 days; total = 119,218 days) with 24 SARS-CoV-2 infections (75.0% symptomatic). Adjusted VE during this Delta predominant period was 66% (95% CI = 26%–84%) compared with 91% (95% CI = 81%–96%) during the months preceding Delta predominance.

During December 14, 2020–August 14, 2021, full vaccination with COVID-19 vaccines was 80% effective in preventing RT-PCR–confirmed SARS-CoV-2 infection among frontline workers, further affirming the highly protective benefit of full vaccination up to and through the most recent summer U.S. COVID-19 pandemic waves. The VE point estimates declined from 91% before predominance of the SARS-CoV-2 Delta

* Arizona Healthcare, Emergency Response and Other Essential Workers Surveillance Study (HEROES) conducted in Phoenix, Tucson, and other noncentrally located areas in Arizona; Research on the Epidemiology of SARS-CoV-2 in Essential Response Personnel (RECOVER) conducted in Miami, Florida; Duluth, Minnesota; Portland, Oregon; Temple, Texas; and Salt Lake City, Utah.

† RT-PCR was conducted using the Quidel Lyra SARS-CoV-2 Assay (before November 2020) or TaqPath COVID-19 Combo Kit (Applied Biosystems) at the Marshfield Clinic Research Institute (Marshfield, WI).

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

TABLE. Effectiveness of COVID-19 vaccines against any SARS-CoV-2 infection among frontline workers, by B.1.617.2 (Delta) variant predominance and time since full vaccination — eight U.S. locations, December 2020–August 2021

Period and vaccination status	No. of contributing participants*	Total no. of person-days	Median days (IQR)	No. of SARS-CoV-2 infections	Adjusted VE,† % (95% CI)
Full cohort to date					
Unvaccinated	4,136	181,357	20 (8–45)	194	N/A
Fully vaccinated§	2,976	454,832	177 (115–195)	34	80 (69–88)
14–119 days after full vaccination	2,923	284,617	106 (106–106)	13	85 (68–93)
120–149 days after full vaccination	2,369	66,006	30 (30–30)	3	81 (34–95)
≥150 days after full vaccination	2,129	104,174	52 (37–64)	18	73 (49–86)
Pre-Delta variant predominance					
Unvaccinated	4,137	156,626	19 (8–43)	175	N/A
Fully vaccinated	2,875	329,865	124 (95–149)	10	91 (81–96)
Delta variant predominance					
Unvaccinated	488	24,871	43 (37–69)	19	N/A
Fully vaccinated	2,352	119,218	49 (35–56)	24	66 (26–84)

Abbreviations: CI = confidence interval; IQR = interquartile range; N/A = not applicable; SMD = standardized mean difference; VE = vaccine effectiveness.

* Person-days between the date of any dose of COVID-19 vaccine and fully vaccinated status were excluded from VE models because of indeterminate immune status. Participants with SARS-CoV-2 infection during this period were also excluded; in the pre-Delta period, 47 participants were excluded, and in the Delta period, two participants were excluded. Contributing participants in vaccination categories also do not equal the total number of participants in the cohort.

† Adjusted VE was inversely weighted for probability of being vaccinated and adjusted for local virus circulation, study location, and occupation. Delta variant models were additionally adjusted for ethnicity. All Cox regression models met the proportional hazards assumption. To calculate the probability of being vaccinated for each period, boosted regression models were fit including covariates for site, sociodemographic characteristics, health information, frequency of close social contact, mask use, and local virus circulation. In the full cohort to date and the pre-Delta cohort, all covariates met balance criteria of SMD<0.2 after weighting except mask use at work (SMD = 0.227 and 0.207, respectively) but was not found to change VE estimates by ≥3% when added to the models. In the Delta predominant cohort occupation, ethnicity, influenza vaccination, and mask use at work did not meet balance criteria (SMD range = 0.206–0.288); influenza vaccination and mask use at work did not change VE estimates by ≥3%; however, occupation and ethnicity did change VE by ≥3% and were therefore included as covariates in the Cox regression model for VE.

§ Fully vaccinated was defined as ≥14 days after receipt of all recommended COVID-19 vaccine doses.

variant to 66% since the SARS-CoV-2 Delta variant became predominant at the HEROES-RECOVER cohort study sites; however, this trend should be interpreted with caution because VE might also be declining as time since vaccination increases and because of poor precision in estimates due to limited number of weeks of observation and few infections among participants. As with all observational VE studies, unmeasured and residual confounding might be present. Active surveillance through the cohort is ongoing and VE estimates will be monitored continuously. Although these interim findings suggest a moderate reduction in the effectiveness of COVID-19 vaccines in preventing infection, the sustained two thirds reduction in infection risk underscores the continued importance and benefits of COVID-19 vaccination.

Acknowledgments

Mark G. Thompson, Lauren Grant, Julie Mayo Lamberte, Young M. Yoo, Gregory Joseph, Josephine Mak, Monica Dickerson, Suxiang Tong, John Barnes, Eduardo Azziz-Baumgartner, Melissa L. Arvay, Preeta Kutty, Alicia M. Fry, Lenee Blanton, Jill Ferdinands, Anthony Fiore, Aron Hall, Adam MacNeil, L. Clifford McDonald, Mary Reynolds, Sue Reynolds, Stephanie Schrag, Nong Shang, Robert Slaughter, Matthew J. Stuckey, Natalie Thornburg, Jennifer Verani, Vic Veguilla, Rose Wang, Bao-Ping Zhu, William Brannen, Stephanie Bialek, CDC; Jefferey L. Burgess, Karen Lutrick, Shawn Beitel, Patrick Rivers, Xiaoxiao Sun, Joe K. Gerald, Janko Nikolich-Žugich, Genesis Barron, Dimaye Calvo, Esteban Cardona, Andrea Carmona, Alissa Coleman, Zoe Baccam, Emily Cooksey, Kiara Earley, Natalie Giroux, Sofia Grijalva, Allan Guidos, Adrianna Hernandez, James Hollister, Theresa Hopkins, Rezwana Islam, Krystal Jovel, Olivia Kavanagh, Jonathan Leyva, Sally Littau, Amelia Lobos, James Lopez, Veronica Lugo, Jeremy Makar, Taylor Maldonado, Enrique Marquez, Allyson Munoz, Assumpta Nsengiyunva, Joel Parker, Jonathan Perez Leyva, Alexa Roy, Saskia Smidt, Isabella Terrazas, Tahlia Thompson, Heena Timsina, Erica Vanover, Mandie White, April Yingst, Kenneth Komatsu, Elizabeth Kim, Karla Ledezma, University of Arizona, Arizona Department of Health Services; David Engelthaler, Translational Genomics Research Institute; Lauren E.W. Olsho, Danielle R. Hunt, Laura J. Edwards, Meredith G. Wesley, Meghan K. Herring, Tyler C. Morrill, Brandon P. Poe, Brian Sokol, Andrea Bronaugh, Tana Brummer, Hala Deeb, Rebecca Devlin, Sauma Doka, Tara Earl, Jini Etolue, Deanna Fleary, Jessica Flores, Chris Flygare, Isaiah Gerber, Louise Hadden, Jenna Harder, Lindsay LeClair, Nancy McGarry, Peenaz Mistry, Steve Pickett, Khaila Prather, David Pulaski, Rajbansi Raorane, Meghan Shea, John Thacker, Matthew Trombley, Pearl Zheng, Chao Zhou, Abt Associates; Kayan Dunnigan, Spencer Rose, Tnelda Zunie, Michael E. Smith, Kempapura Murthy, Nicole Calhoun, Claire Mathenge, Arundhati Rao, Manohar Mutnal, Linden Morales, Shelby Johnson, Alejandro Arroliga, Madhava Beeram, Joel Blais, Jason Ettlinger, Angela Kennedy, Natalie Settele, Rupande Patel, Elisa Priest, Jennifer Thomas, Baylor Scott & White Health; Allison L. Naleway, Holly C. Groom, Jennifer L. Kuntz, Yolanda Prado, Daniel Sapp, Mi Lee, Chris Eddy,

Matt Hornbrook, Danielle Millay, Dorothy Kurdyla, Ambrosia Bass, Kristi Bays, Kimberly Berame, Cathleen Bourdoin, Carlea Buslach, Jennifer Gluth, Kenni Graham, Tarika Holness Enedina Luis, Abreeanah Magdaleno, DeShaun Martin, Joyce Smith-McGee, Martha Perley, Sam Peterson, Aaron Piepert, Krystil Phillips, Joanna Price, Sperry Robinson, Katrina Schell, Emily Schield, Natosha Shirley, Anna Shivinsky, Britta Torgrimson-Ojerio, Brooke Wainwright, Shawn Westaway, Kaiser Permanente Northwest; Jennifer Meece, Elisha Stefanski, Lynn Ivacic, Jake Andreae, Adam Bissonnette, Krystal Boese, Michaela Braun, Cody DeHamer, Timothy Dziedzic, Joseph Eddy, Heather Edgren, Wayne Frome, Nolan Herman, Mitchell Hertel, Erin Higdon, Rosebud Johnson, Steve Kaiser, Tammy Koepel, Sarah Kohn, Taylor Kent, Thao Le, Carrie Marcis, Megan Maronde, Isaac McCready, Nidhi Mehta, Daniel Miesbauer, Anne Nikolai, Brooke Olson, Lisa Ott, Cory Pike, Nicole Price, Christopher Reardon, Logan Schafer, Rachel Schoone, Jaclyn Schneider, Tapan Sharma, Melissa Strupp, Janay Walters, Alyssa Weber, Reynor Wilhorn, Ryan Wright, Benjamin Zimmerman, Marshfield Clinic Research Laboratory; Angela Hunt, Jessica Lundgreen, Karley Respet, Jennifer Viergutz, Daniel Stafki, St. Luke's Regional Health Care System; Alberto J. Caban-Martinez, Natasha Schaefer-Solle, Paola Louzado Feliciano, Carlos Silvera, Karla Montes, Cynthia Beaver, Katerina Santiago, University of Miami; Sarang K. Yoon, Kurt Hegmann, Andrew L. Phillips, Rachel T. Brown, Camie Schaefer, Arlyne Arteaga, Matthew Bruner, Daniel Dawson, Emilee Eden, Jenna Praggastis, Joseph Stanford, Jeanmarie Mayer, Marcus Stucki, Riley Campbell, Kathy Tran, Madeleine Smith, Braydon Black, Madison Tallman, Chapman Cox, Derrick Wong, Michael Langston, Adriele Fugal, Fiona Tsang, Maya Wheeler, Gretchen Maughan, Taryn Hunt-Smith, Nikki Gallacher, Anika DSouza, Trevor Stubbs, Iman Ibrahim, Ryder Jordin, University of Utah; Marilyn J. Odean, Whiteside Institute for Clinical Research; Allen Bateman, Erik Reisdorf, Kyley Guenther, Erika Hanson, Wisconsin State Laboratory of Hygiene; the HEROES-RECOVER participants.

Corresponding author: Ashley Fowlkes, afowlkes@cdc.gov

[1]CDC COVID-19 Response Team; [2]Baylor Scott and White Health, Texas A&M University College of Medicine, Temple, Texas; [3]Abt Associates, Inc., Rockville, Maryland; [4]University of Utah, Salt Lake City, Utah; [5]St. Luke's Regional Health Care System, Duluth, Minnesota; [6]Mel and Enid Zuckerman College of Public Health, University of Arizona, Tucson, Arizona.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Matthew S. Thiese reports grants and personal fees from Reed Group and the American College of Occupational and Environmental Medicine, outside the submitted work. No other potential conflicts of interest were disclosed.

References

1. Thompson MG, Burgess JL, Naleway AL, et al. Prevention and attenuation of Covid-19 with the BNT162b2 and mRNA-1273 vaccines. N Engl J Med 2021;385:320–9. PMID:34192428 https://doi.org/10.1056/NEJMoa2107058
2. Thompson MG, Burgess JL, Naleway AL, et al. Interim estimates of vaccine effectiveness of BNT162b2 and mRNA-1273 COVID-19 vaccines in preventing SARS-CoV-2 infection among health care personnel, first responders, and other essential and frontline workers—eight U.S. locations, December 2020–March 2021. MMWR Morb Mortal Wkly Rep 2021;70:495–500. PMID:33793460 https://doi.org/10.15585/mmwr.mm7013e3
3. Herlihy R, Bamberg W, Burakoff A, et al. Rapid increase in circulation of the SARS-CoV-2 B.1.617.2 (Delta) variant—Mesa County, Colorado, April–June 2021. MMWR Morb Mortal Wkly Rep 2021;70:1084–7. PMID:34383734 https://doi.org/10.15585/mmwr.mm7032e2
4. Brown CM, Vostok J, Johnson H, et al. Outbreak of SARS-CoV-2 infections, including COVID-19 vaccine breakthrough infections, associated with large public gatherings—Barnstable County, Massachusetts, July 2021. MMWR Morb Mortal Wkly Rep 2021;70:1059–62. PMID:34351882 https://doi.org/10.15585/mmwr.mm7031e2
5. Lutrick K, Ellingson KD, Baccam Z, et al. COVID-19 infection, reinfection, and vaccine effectiveness in a prospective cohort of Arizona frontline/essential workers: the AZ HEROES research protocol. JMIR Res Protoc 2021. Epub May 26, 2021. PMID:34057904 https://doi.org/10.2196/28925
6. US Department of Health and Human Services. HHS protect public data hub. Washington, DC: US Department of Health and Human Services; 2021. Accessed August 16, 2021. https://protect-public.hhs.gov/

SARS-CoV-2 Infections and Hospitalizations Among Persons Aged ≥16 Years, by Vaccination Status — Los Angeles County, California, May 1–July 25, 2021

Jennifer B. Griffin, PhD[1]; Meredith Haddix, MPH[1]; Phoebe Danza, MPH[1]; Rebecca Fisher, MPH[1]; Tae Hee Koo, MPH[1]; Elizabeth Traub, MPH[1]; Prabhu Gounder, MD[1]; Claire Jarashow, PhD[2]; Sharon Balter, MD[1]

On August 24, 2021, this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

COVID-19 vaccines fully approved or currently authorized for use through Emergency Use Authorization from the Food and Drug Administration are critical tools for controlling the COVID-19 pandemic; however, even with highly effective vaccines, a proportion of fully vaccinated persons will become infected with SARS-CoV-2, the virus that causes COVID-19 (*1*). To characterize postvaccination infections, the Los Angeles County Department of Public Health (LACDPH) used COVID-19 surveillance and California Immunization Registry 2 (CAIR2) data to describe age-adjusted infection and hospitalization rates during May 1–July 25, 2021, by vaccination status. Whole genome sequencing (WGS)–based SARS-CoV-2 lineages and cycle threshold (Ct) values from qualitative reverse transcription–polymerase chain reaction (RT-PCR) for two SARS-CoV-2 gene targets, including the nucleocapsid (N) protein gene region and the open reading frame 1 ab (ORF1ab) polyprotein gene region,* were reported for a convenience sample of specimens. Among 43,127 reported SARS-CoV-2 infections in Los Angeles County residents aged ≥16 years, 10,895 (25.3%) were in fully vaccinated persons, 1,431 (3.3%) were in partially vaccinated persons, and 30,801 (71.4%) were in unvaccinated persons. Much lower percentages of fully vaccinated persons infected with SARS-CoV-2 were hospitalized (3.2%), were admitted to an intensive care unit (0.5%), and required mechanical ventilation (0.2%) compared with partially vaccinated persons (6.2%, 1.0%, and 0.3%, respectively) and unvaccinated persons (7.6%, 1.5%, and 0.5%, respectively) (p<0.001 for all comparisons). On July 25, the SARS-CoV-2 infection rate among unvaccinated persons was 4.9 times and the hospitalization rate was 29.2 times the rates among fully vaccinated persons. During May 1–July 25, the percentages of B.1.617.2 (Delta) variant infections estimated from 6,752 samples with lineage data increased among fully vaccinated persons (from 8.6% to 91.2%), partially vaccinated persons (from 0% to 88.1%), and unvaccinated persons (from 8.2% to 87.1%). In May, there were differences in median Ct values by vaccination status; however, by July, no differences were detected among specimens from fully vaccinated, partially vaccinated, and unvaccinated persons by gene targets. These infection and hospitalization rate data indicate that authorized vaccines were protective against SARS-CoV-2 infection and severe COVID-19 during a period when transmission of the Delta variant was increasing. Efforts to increase COVID-19 vaccination, in coordination with other prevention strategies, are critical to preventing COVID-19–related hospitalizations and deaths.

LACDPH analyzed data for laboratory-confirmed cases of SARS-CoV-2 reported from testing laboratories to LACDPH during May 1–July 25, 2021, which included a total of 9,651,332 Los Angeles County residents (excluding Pasadena and Long Beach residents).† A laboratory-confirmed SARS-CoV-2 infection was defined as a first detection§ of SARS-CoV-2 RNA or antigen in a respiratory specimen. Vaccination status was ascertained by matching SARS-CoV-2 case surveillance and CAIR2 data on person-level identifiers using an algorithm with both deterministic and probabilistic passes. Persons were considered fully vaccinated ≥14 days after receipt of the second dose in a 2-dose series (Pfizer-BioNTech or Moderna COVID-19 vaccines) or after 1 dose of the single-dose Janssen (Johnson & Johnson) COVID-19 vaccine¶; partially vaccinated ≥14 days after receipt of the first dose and <14 days after the second dose in a 2-dose series; and unvaccinated <14 days after receipt of the first dose of a 2-dose series or 1 dose of the single-dose vaccine or if no CAIR2 vaccination data were available. COVID-19–associated hospitalizations were defined as hospital admissions occurring ≤14 days after a first SARS-CoV-2 infection. COVID-19–associated deaths were defined as deaths occurring ≤60 days after the date of a first laboratory-confirmed SARS-CoV-2 infection or deaths with COVID-19 listed as a cause of or contributing condition to death.

* Gene targets for RT-PCR testing included the N protein gene region and the ORF1ab polyprotein gene region. The N gene targets were analyzed separately for two laboratories because Ct values are not directly comparable across different testing laboratories; these N gene targets were designated SARS-CoV-2 nucleocapsid (SC2N) and N to differentiate between the two participating laboratory partners. Gene targets were selected based on testing platforms used by LACDPH laboratory partners.

† The population of Los Angeles County residents is based on 2018 population estimates prepared for Los Angeles County Internal Services Department. These population estimates exclude the populations of Pasadena and Long Beach because they have independent public health departments.

§ Cases were limited to first laboratory-confirmed infections and excluded reinfections.

¶ https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated-guidance.html

Differences in the percentages of infections by vaccination status were calculated using chi-square tests for categorical variables and Kruskal-Wallis tests for medians; p-values <0.05 were considered statistically significant. Age-adjusted rolling 7-day SARS-CoV-2 infection and hospitalization rates were estimated by vaccination status.** Using convenience samples, WGS lineage data from all available sequencing results (6,752)†† and Ct values from diagnostic qualitative RT-PCR assays targeting two genes (SARS-CoV-2 nucleocapsid [SC2N; 5,179], ORF1ab [1,041], and N [1,062]) from two laboratories were reported over time by vaccination status. Analyses were conducted using SAS (version 9.4; SAS Institute). This activity was determined by LACDPH's Institutional Review Board (IRB) to be a surveillance activity necessary for public health work and therefore did not require IRB review.

The percentage of fully vaccinated Los Angeles County residents increased from 27% on May 1, 2021, to 51% on July 25, 2021. During the same period, 43,127 cases of SARS-CoV-2 infection among residents aged ≥16 years were reported to LACDPH, including 10,895 (25.3%) in fully vaccinated persons, 1,431 (3.3%) in partially vaccinated persons, and 30,801 (71.4%) in unvaccinated persons (Table). The largest percentages of cases across all groups were among adults aged 30–49 years and 18–29 years, females, and Hispanic persons. Among fully vaccinated persons on July 25, 55.2% had received the Pfizer-BioNTech vaccine, 28.0% had received the Moderna vaccine, and 16.8% had received the Janssen vaccine. Lower percentages of fully vaccinated persons were hospitalized (3.2%), were admitted to an intensive care unit (0.5%), and required mechanical ventilation (0.2%) compared with partially vaccinated persons (6.2%, 1.0%, and 0.3%, respectively) and unvaccinated persons (7.6%, 1.5%, and 0.5%, respectively) (p<0.001). Among hospitalized persons and persons admitted to an intensive care unit, the median age was higher among vaccinated persons (median = 64 years, interquartile range [IQR] = 53.0–76.0 years; median = 64 years, IQR = 54.0–76.0 years, respectively) and partially vaccinated persons (median = 59, IQR = 46.0–72.0; median = 65, IQR = 57.0–80.0, respectively) than among unvaccinated persons (median = 49, IQR = 35.0–62.0; median = 56, IQR = 41.0–66.0, respectively) (p<0.001). A lower percentage of fully vaccinated (1.2%) and partially vaccinated (2.0%) persons were admitted to a hospital after their SARS-CoV-2 positive test result date compared with unvaccinated persons (4.2%). A lower percentage of deaths (0.2%, 24) occurred among fully vaccinated persons than among partially vaccinated (0.5%, seven) and unvaccinated (0.6%, 176) persons (p<0.001). Death investigations determined that six of the 24 fully vaccinated persons who died had immunocompromising conditions, including HIV infection, cancer (i.e., prostate, pancreatic, lung, or leukemia), and liver transplantation, and that the median age was higher among vaccinated (median = 78 years, IQR = 63.5–87.5 years) and partially vaccinated (median = 74, IQR = 58.0–80.0) persons than among unvaccinated persons (median = 63, IQR = 51.5–79.5) (p = 0.01).

Among all Los Angeles County residents, the age-adjusted 7-day incidence and hospitalization rates increased exponentially among unvaccinated, fully vaccinated, and partially vaccinated persons, with the highest rates among unvaccinated persons in late June (Figure 1). On May 1, in unvaccinated persons, the age-adjusted incidence (35.2 per 100,000 population) was 8.4 times and the age-adjusted hospitalization rate (4.6 per 100,000 population) was 10.0 times the rates in fully vaccinated persons (4.2 and 0.46, respectively). Partially vaccinated persons had a similar incidence (4.1) and hospitalization rate (0.27) as fully vaccinated persons. On July 25, the age-adjusted incidence in unvaccinated persons (315.1) was 4.9 times that in fully vaccinated persons (63.8); the rate among partially vaccinated persons was 46.8. The age-adjusted hospitalization rate in unvaccinated persons (29.4) was 29.2 times the rate in fully vaccinated persons (1.0); the hospitalization rate was similar in partially vaccinated persons (0.90) (Supplementary Table; https://stacks.cdc.gov/view/cdc/109087).

During May 1–July 25, the percentages of residents aged ≥16 years with SARS-CoV-2 Delta variant infections increased from 8.6% to 91.2% in fully vaccinated persons (1,667), from 0% to 88.1% in partially vaccinated persons (198), and from 8.2% to 87.1% in unvaccinated persons (4,887) (Figure 2). In May, median Ct values were lower in specimens from unvaccinated persons than in those from partially vaccinated and fully vaccinated persons for the ORF1ab gene target (22.8, 36.6, and 27.7, respectively) and N gene target (24.0, 36.0, and 30.6, respectively); however, in July, no differences were found by vaccination status among the gene targets (SC2N = 19.3, 20.2, and 19.4; ORF1ab = 18.8, 17.8, and 19.0; N = 19.3, 18.6, and 19.5, respectively) (Figure 2).

** Adjusted rates were calculated using 2018 population estimates and were standardized using the year 2000 U.S. standard population (https://www.cdc.gov/cancer/uscs/technical_notes/stat_methods/rates.htm). Rolling 7-day incidence was calculated by summing the total number of persons or hospitalizations during a 7-day period and dividing by the total population at the end of the 7-day period.

†† WGS lineage data were from all sequencing results reported to LACDPH or sequenced after specimens were referred to LACDPH laboratories.

TABLE. Number of SARS-CoV-2 cases among persons aged ≥16 years, by selected characteristics and vaccination status* — Los Angeles County, California,† May 1–July 25, 2021

Characteristic	Vaccination status, no. (%)				p-value
	Total	Fully vaccinated	Partially vaccinated	Unvaccinated	
Total no. of cases	**43,127**	**10,895**	**1,431**	**30,801**	—
Vaccine manufacturer					
Janssen (Johnson & Johnson)	—	1,830 (16.8)	—	—	—
Moderna	—	3,047 (28.0)	—	—	—
Pfizer-BioNTech	—	6,018 (55.2)	—	—	—
Median interval between final vaccine dose and infection, no. of days (IQR)	—	98 (74–120)	—	—	—
Median age, yrs (IQR)	**34 (26–46)**	37 (28–52)	35 (27–51)	32 (26–44)	<0.001
Age group, yrs					
16–17	**1,120 (2.6)**	107 (1.0)	34 (2.4)	979 (3.2)	<0.001
18–29	**14,758 (34.2)**	3,017 (27.7)	432 (30.2)	11,309 (36.7)	
30–49	**18,106 (42.0)**	4,649 (42.7)	582 (40.7)	12,875 (41.8)	
50–64	**6,418 (14.9)**	2,025 (18.6)	255 (17.8)	4,138 (13.4)	
65–79	**2,101 (4.9)**	857 (7.9)	95 (6.6)	1,149 (3.7)	
≥80	**624 (1.4)**	240 (2.2)	33 (2.3)	351 (1.1)	
Sex					
Female	**21,743 (50.4)**	5,514 (50.6)	757 (52.9)	15,472 (50.2)	<0.001
Male	**20,425 (47.4)**	5,249 (48.2)	659 (46.1)	14,517 (47.1)	
Other or unknown	**959 (2.2)**	132 (1.2)	15 (1.0)	812 (2.6)	
Race/Ethnicity					
American Indian or Alaska Native	**70 (0.2)**	17 (0.2)	2 (0.1)	51 (0.2)	<0.001
Asian	**1,970 (4.6)**	905 (8.3)	104 (7.3)	961 (3.1)	
Black or African American	**5,574 (12.9)**	681 (6.3)	138 (9.6)	4,755 (15.4)	
Hispanic or Latino	**14,144 (32.8)**	3,450 (31.7)	511 (35.7)	10,183 (33.1)	
Multiple race	**823 (1.9)**	272 (2.5)	32 (2.2)	519 (1.7)	
Native Hawaiian or Other Pacific Islander	**210 (0.5)**	41 (0.4)	8 (0.6)	161 (0.5)	
Other	**3,998 (9.3)**	778 (7.1)	112 (7.8)	3,108 (10.1)	
White	**9,338 (21.7)**	3,397 (31.2)	321 (22.4)	5,620 (18.2)	
Missing	**7,000 (16.2)**	1,354 (12.4)	203 (14.2)	5,443 (17.7)	
Hospitalized	**2,794 (6.5)**	350 (3.2)	89 (6.2)	2,355 (7.6)	<0.001
Admitted to ICU	**536 (1.2)**	55 (0.5)	15 (1.0)	466 (1.5)	<0.001
Required mechanical ventilation	**189 (0.4)**	19 (0.2)	5 (0.3)	165 (0.5)	<0.001
Admitted to hospital after positive SARS-CoV-2 test date	**1,454 (3.4)**	136 (1.2)	29 (2.0)	1,289 (4.2)	<0.001
Died	**207 (0.5)**	**24 (0.2)**	**7 (0.5)**	**176 (0.6)**	**<0.001**

Abbreviations: ICU = intensive care unit; IQR = interquartile range.

* Persons were considered fully vaccinated ≥14 days after receipt of the second dose in a 2-dose series (Pfizer-BioNTech or Moderna COVID-19 vaccines) or after 1 dose of the single-dose Janssen (Johnson & Johnson) COVID-19 vaccine; partially vaccinated ≥14 days after receipt of the first dose and <14 days after the second dose in a 2-dose series; and unvaccinated <14 days receipt of the first dose of a 2-dose series or 1 dose of the single-dose vaccine or if no vaccination registry data were available.

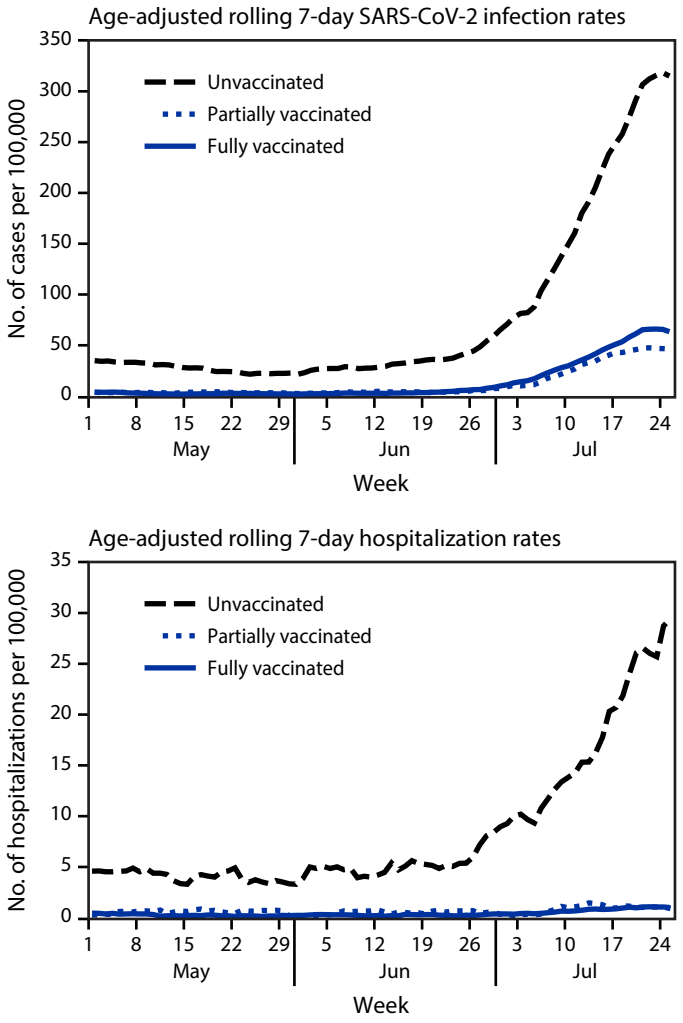
† Among residents of Los Angeles County; excludes Pasadena and Long Beach.

Discussion

The results of this population-based analysis using linked SARS-CoV-2 infection surveillance and vaccination registry data indicate that fully vaccinated persons aged ≥16 years with SARS-CoV-2 infection were less likely than unvaccinated persons to be hospitalized, to be admitted to an intensive care unit, to require mechanical ventilation, or to die from SARS-CoV-2 infection during a period when the Delta variant became predominant. Although age-adjusted hospitalization rates in partially vaccinated persons were similar to those in fully vaccinated persons, age-adjusted incidences were slightly lower in partially vaccinated persons than in fully vaccinated persons. These data indicate that authorized vaccines protect against SARS-CoV-2 infection and severe COVID-19, even with increased community transmission of the newly predominant Delta variant (*2*).

The SARS-CoV-2 Delta variant is highly transmissible (*3*) and became the predominant variant in Los Angeles County during May–July 2021. During this period, SARS-CoV-2 cases and hospitalizations increased substantially, most notably among unvaccinated persons. In May, specimens from fully vaccinated and partially vaccinated persons had higher Ct values for two gene targets compared with unvaccinated persons; however, by July, median Ct values had decreased and were similar in all gene regions in specimens from fully vaccinated, partially vaccinated, and unvaccinated persons.

FIGURE 1. Age-adjusted rolling 7-day SARS-CoV-2 infection and hospitalization rates,* by vaccination status† — Los Angeles County, California, May 1–July 25, 2021



* Rolling 7-day incidence was calculated by summing the total number of persons or hospitalizations during a 7-day period and dividing by the total population at the end of the 7-day period.

† Persons were considered fully vaccinated ≥14 days after receipt of the second dose in a 2-dose series (Pfizer-BioNTech or Moderna COVID-19 vaccines) or after 1 dose of the single-dose Janssen (Johnson & Johnson) COVID-19 vaccine; partially vaccinated ≥14 days after receipt of the first dose and <14 days after the second dose in a 2-dose series; and unvaccinated <14 days receipt of the first dose of a 2-dose series or 1 dose of the single-dose vaccine or if no vaccination registry data were available.

Summary

What is already known about this topic?

Although COVID-19 vaccines are highly effective, some fully vaccinated persons will be infected with SARS-CoV-2.

What is added by this report?

During May 1–July 25, 2021, among 43,127 SARS-CoV-2 infections in residents of Los Angeles County, California, 10,895 (25.3%) were in fully vaccinated persons, 1,431 (3.3%) were in partially vaccinated persons, and 30,801 (71.4%) were in unvaccinated persons. On July 25, infection and hospitalization rates among unvaccinated persons were 4.9 and 29.2 times, respectively, those in fully vaccinated persons. In July, when the Delta variant was predominant, cycle threshold values were similar for unvaccinated, partially vaccinated, and vaccinated persons.

What are the implications for public health practice?

Efforts to enhance COVID-19 vaccination coverage, in coordination with other prevention strategies, are critical to preventing COVID-19–related hospitalizations and deaths.

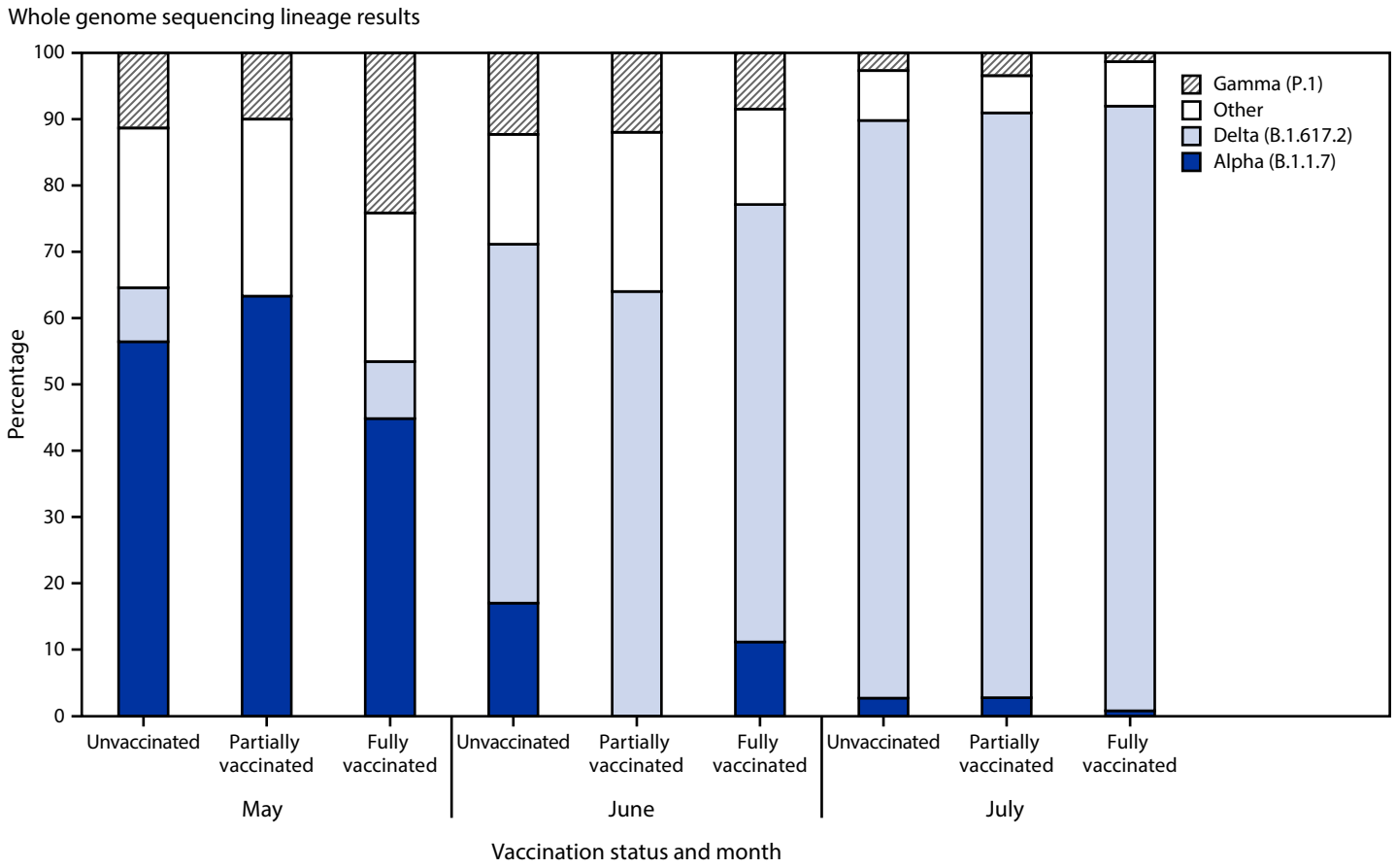
These findings are similar to those from a recent study showing no difference in Ct values in specimens from vaccinated and unvaccinated persons during a large outbreak (*4*). Ct values are correlated with the amount of viral nucleic acid present; however, Ct values are an imperfect proxy for viral nucleic acid load, are not standardized across testing platforms, vary by specimen type and time from specimen collection, and should be limited to assessing differences at the population level, not the person level.[§§]

The findings in this report are subject to at least six limitations. First, vaccination data for persons who lived in Los Angeles County at the time of their laboratory-confirmed infection but who were vaccinated outside of California were unavailable, leading to misclassification of their vaccination status; if vaccinated persons without accessible records were considered to be unvaccinated, the incidence in unvaccinated persons could be underestimated. Second, case ascertainment is based on passive surveillance, with known underreporting that might differ by vaccination status. Similarly, screening and testing behaviors might differ among groups. Third, COVID-19–associated hospitalizations were determined based on hospital admission and SARS-CoV-2 test dates alone, leading to the inclusion of incidental hospitalizations that were not associated with COVID-19. Fourth, COVID-19–associated deaths included deaths occurring ≤60 days after a first SARS-CoV-2 positive test date; therefore, some COVID-19–associated deaths might have been from other causes (excluding trauma). In addition, certain COVID-19–associated deaths might have been a result of long-term sequelae after 60 days and were not included. Fifth, lineage and Ct values were available only for a convenience sample of SARS-CoV-2 cases. Finally, all the assays used to generate Ct values for comparison were qualitative, and none is approved for use in quantitating the amount of viral nucleic acid present.

The findings in this report are similar to those from recent studies indicating that COVID-19 vaccination

§§ Additional information on Ct values and their limitations is available: https://www.idsociety.org/globalassets/idsa/public-health/covid-19/idsa-amp-statement.pdf and https://www.cdc.gov/coronavirus/2019-ncov/lab/faqs.html.

FIGURE 2. SARS-CoV-2 whole genome sequencing lineage results* and reverse transcription–polymerase chain reaction cycle threshold values† for two gene targets,§ by vaccination status¶ and month — Los Angeles County, California, May 1–July 25, 2021



See footnotes on the next page.

protects against severe COVID-19 in areas with increasing prevalence of the SARS-CoV-2 Delta variant (*5*,*6*). Efforts to increase COVID-19 vaccination coverage, in coordination with other prevention strategies, are critical to preventing COVID-19–related hospitalizations and deaths. Ongoing surveillance to characterize postvaccination infections, hospitalizations, and deaths will be important to monitor vaccine effectiveness, particularly as new variants emerge.

Acknowledgments

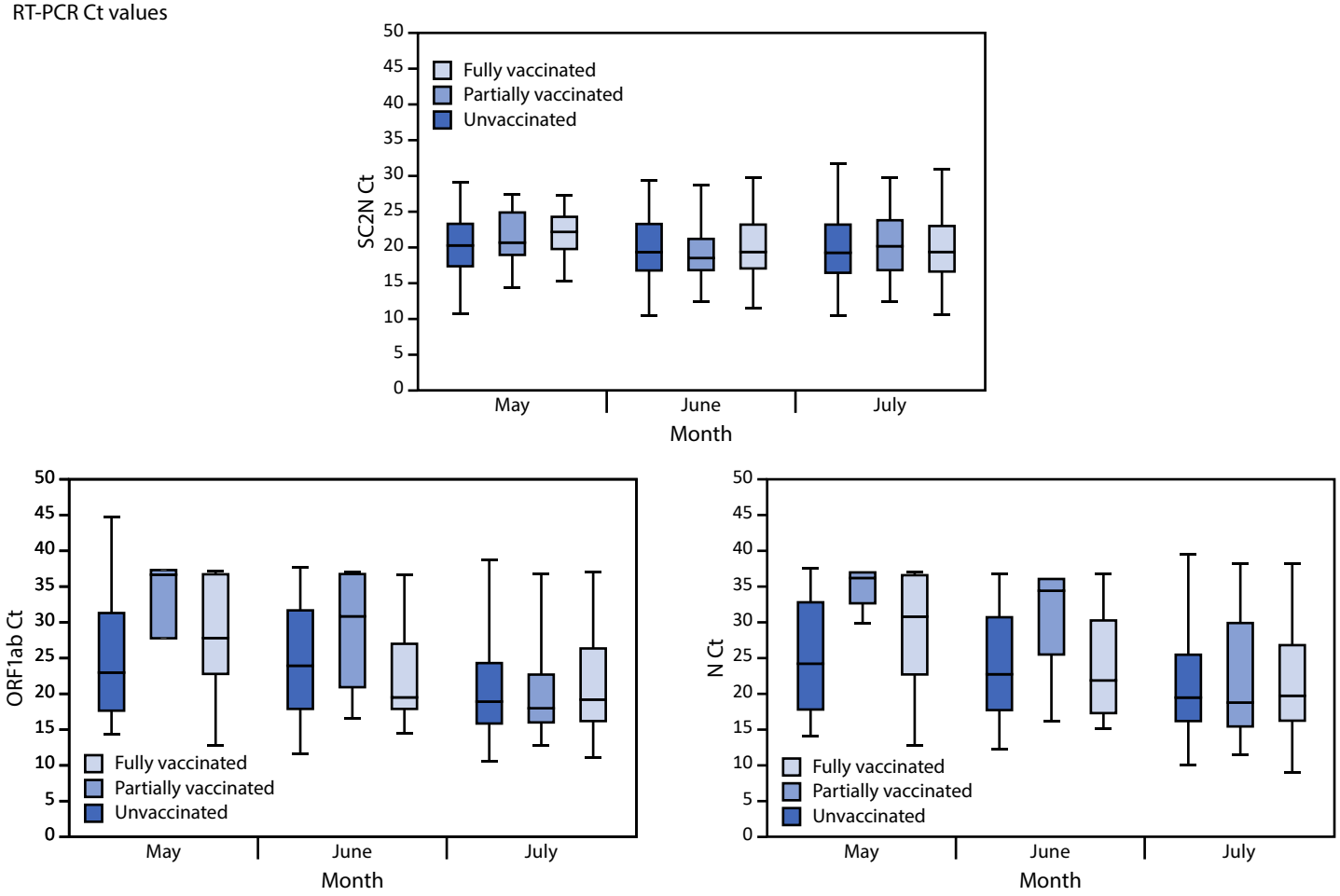
Kelsey Oyong; Heidi Sato; Rebecca Lee; Mireille Ibrahim; Kathleen Poortinga; Mirna Ponce-Jewell; Dulmini Wilson; Emmanuel Mendoza.

Corresponding author: Sharon Balter, sbalter@ph.lacounty.gov.

[1]Acute Communicable Disease Control Program, Los Angeles County Department of Public Health, California; [2]Vaccine Preventable Disease Control Program, Los Angeles County Department of Public Health, California.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. M. Claire Jarashow reports consulting fees from Uber outside the current work and unpaid board membership of two international nongovernmental organizations (C2C and Developing Communities) outside the current work. No other potential conflicts of interest were disclosed.

FIGURE 2. (*Continued*) SARS-CoV-2 whole genome sequencing lineage results* and reverse transcription–polymerase chain reaction cycle threshold values† for two gene targets,§ by vaccination status¶ and month — Los Angeles County, California, May 1–July 25, 2021



Abbreviations: Ct = cycle threshold; N = nucleocapsid; ORF1ab = open reading frame 1 ab; RT-PCR = reverse transcription–polymerase chain reaction; SC2N = SARS-CoV-2 nucleocapsid.

* SARS-CoV-2 infections among Los Angeles County residents aged ≥16 years with whole genome sequencing lineage results (n = 6,752) for fully vaccinated (n = 1,667), partially vaccinated (n = 198), and unvaccinated (n = 4,887) persons.

† Whiskers represent minimum and maximum observations; top of box represents the third quartile, bottom represents the first quartile, and box height represents the interquartile range. The midline is the median.

§ Ct values are correlated with the amount of viral nucleic acid present. Gene targets for RT-PCR testing included the N protein gene region and the ORF1ab polyprotein gene region. The N gene targets were analyzed separately for two laboratories because Ct values are not directly comparable across different testing laboratories; these N gene targets were designated SC2N and N to differentiate between the two participating laboratory partners. Gene targets were selected based on testing platforms used by Los Angeles County Department of Public Health laboratory partners. Analysis of SC2N Ct values is restricted to a Fulgent test result with a Ct value on the same day as person's first positive RT-PCR test result; SC2N gene target values (n = 5,179) are stratified for fully vaccinated (n = 1,248), partially vaccinated (n = 151), and unvaccinated (n = 3,780) persons. Analysis of ORF1ab and N Ct values is restricted to a Valencia Branch Laboratory test result with a Ct value on the same day as person's first positive RT-PCR test result. ORF1ab (n = 1,041) and N (n = 1,062) gene target values are stratified for fully vaccinated (n = 289 and n = 297, respectively), partially vaccinated (n = 36 and n = 41, respectively), and unvaccinated (n = 716 and n = 724, respectively) persons.

¶ Persons were considered fully vaccinated ≥14 days after receipt of the second dose in a 2-dose series (Pfizer-BioNTech or Moderna COVID-19 vaccines) or after 1 dose of the single-dose Janssen (Johnson & Johnson) COVID-19 vaccine; partially vaccinated ≥14 days after receipt of the first dose and <14 days after the second dose in a 2-dose series; and unvaccinated <14 days receipt of the first dose of a 2-dose series or 1 dose of the single-dose vaccine or if no vaccination registry data were available.

References

1. Birhane M, Bressler S, Chang G, et al.; CDC COVID-19 Vaccine Breakthrough Case Investigations Team. COVID-19 vaccine breakthrough infections reported to CDC—United States, January 1–April 30, 2021. MMWR Morb Mortal Wkly Rep 2021;70:792–3. PMID:34043615 https://doi.org/10.15585/mmwr.mm7021e3
2. Lopez Bernal J, Andrews N, Gower C, et al. Effectiveness of Covid-19 vaccines against the B.1.617.2 (Delta) variant. N Engl J Med 2021;385:585–94. PMID:34289274 https://doi.org/10.1056/NEJMoa2108891
3. Allen H, Vusirikala A, Flannagan J, et al.; Public Health England. Increased household transmission of COVID-19 cases associated with SARS-CoV-2 variant of concern B.1.617.2: a national case-control study. Knowledge Hub [Preprint posted online June 18, 2021]. https://khub.net/documents/135939561/405676950/Increased+Household+Transmission+of+COVID-19+Cases+-+national+case+study.pdf/7f7764fb-ecb0-da31-77b3-b1a8ef7be9aa
4. Brown CM, Vostok J, Johnson H, et al. Outbreak of SARS-CoV-2 infections, including COVID-19 vaccine breakthrough infections, associated with large public gatherings—Barnstable County, Massachusetts, July 2021. MMWR Morb Mortal Wkly Rep 2021;70:1059–62. PMID:34351882 https://doi.org/10.15585/mmwr.mm7031e2
5. Nasreen S, He S, Chung H, et al. Effectiveness of COVID-19 vaccines against variants of concern, Canada [Preprint posted online July 16, 2021]. https://www.medrxiv.org/content/10.1101/2021.06.28.21259420v2
6. Sheikh A, McMenamin J, Taylor B, Robertson C; Public Health Scotland and the EAVE II Collaborators. SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. Lancet 2021;397:2461–2. PMID:34139198 https://doi.org/10.1016/S0140-6736(21)01358-1

Notes from the Field

Illicit Benzodiazepines Detected in Patients Evaluated in Emergency Departments for Suspected Opioid Overdose — Four States, October 6, 2020–March 9, 2021

Kim Aldy, DO[1,2]; Desiree Mustaquim, PhD[3]; Sharan Campleman, PhD[1]; Alison Meyn, MPH[1]; Stephanie Abston[1]; Alex Krotulski, PhD[4]; Barry Logan, PhD[4,5]; Matthew R. Gladden, PhD[3]; Adrienne Hughes, MD[6]; Alexandra Amaducci, DO[7]; Joshua Shulman, MD[8]; Evan Schwarz, MD[9]; Paul Wax, MD[1,2]; Jeffrey Brent, MD, PhD[10]; Alex Manini, MD[11]; the Toxicology Investigators Consortium Fentalog Study Group

Illicit benzodiazepines are emerging drugs of abuse that are unlawfully manufactured in laboratories and have clinical side effects and toxicity that are not well understood. Although prescription and illicit benzodiazepines are structurally similar (*1*), illicit benzodiazepines can have different pharmacological properties; this contributes to concerns about their potential potency and clinical implications (*1*,*2*). Simultaneous exposure to both illicit benzodiazepines and opioids increases overdose risk (*3*). Although naloxone will reverse opioid overdose symptoms, it does not reverse overdoses resulting from nonopioid drugs. Therefore, in cases of co-exposure to opioids and benzodiazepines, including illicit benzodiazepines, symptoms of benzodiazepine intoxication (e.g., profound sedation) are unaffected by naloxone, leading to risk for respiratory failure or death (*1*). Rapid increases in the forensic and clinical detection of illicit benzodiazepines during 2020 have raised concerns about the drug's role in overdoses, but clinical descriptions of overdoses caused by illicit benzodiazepine co-exposure are limited (*4*–*6*). This report describes the detection of illicit benzodiazepine co-exposures among patients treated in emergency departments (EDs) with suspected opioid overdoses in selected states.

The Toxicology Investigators Consortium (ToxIC) Fentalog Study Group is conducting a study of patients aged >18 years evaluated in an ED following a suspected opioid overdose. Comprehensive toxicologic testing was performed on residual biologic samples via liquid chromatography quadrupole time-of-flight mass spectrometry for the presence of approximately 900 psychoactive substances, including 33 illicit benzodiazepines and metabolites. Additional case information was obtained through chart review.* This activity was reviewed by CDC and was conducted consistently with applicable federal law and CDC policy.†

During October 6, 2020–March 9, 2021, 141 biologic samples§ were analyzed from five clinical sites in four states (Missouri, New York, Oregon, and Pennsylvania).¶ The presence of illicit benzodiazepines was identified in 21 (14.9%) patients (Table); the substances identified included clonazolam (11 patients; 52.4%), etizolam (10; 47.6%), and flubromazolam (two; 9.5% [co-identified in patients with etizolam]). Among the 21 patients with illicit benzodiazepines detected, 12 (57.1%) were from Pennsylvania, six (28.6%) from Oregon, two (9.5%) from Missouri, and one (4.8%) from New York. Etizolam was confirmed in New York, Oregon, and Pennsylvania, and flubromazolam only in Oregon. At least one opioid was identified in 20 cases (95.2%), including methadone in 12 (60.0%). Either methamphetamine, amphetamine, or both were detected in 11 (52.4%) patients.

The mean patient age was 39 years (range = 25–63 years), and more than three quarters of patients (16; 76.2%) were men. The most commonly reported reason for opioid use was to induce euphoria (10; 47.6%), followed by use to prevent withdrawal (four; 19.0%). Naloxone was administered to 16 (76.2%) patients to reverse opioid overdose. In 15 cases for which the indication for naloxone administration was known, the most common indication was depressed consciousness (nine patients), followed by respiratory depression (seven patients). Of 13 patients for whom the response to naloxone was known, five showed no improvement after the first dose of naloxone. One patient, whose level of consciousness improved after the first dose, subsequently required 9 naloxone doses and ultimately received a naloxone infusion.

This report documents concerning co-exposure to both opioids and illicit benzodiazepines among patients evaluated for suspected opioid overdose from multiple geographically diverse U.S. EDs. Despite the fact that the sample was limited, this report's findings align with recent increases in the supply of illicit benzodiazepines in the United States (*4*–*6*). Even though the majority of these patients were discharged without apparent sequelae, in approximately one third of cases where response to naloxone was known, patients with simultaneous exposure

* The ToxIC Fentalog Study Group is conducting this study from 2020-2025. Data presented are part of an ongoing effort to assess the role and prevalence of novel substances in participating regions throughout the duration of this project. Chart review was performed via the patient's electronic medical record at the site by the medical toxicologist, the trained research assistant, or both. Reason for exposure was documented in the patients initial ED notes.

† 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.

§ All suspected opioid overdose cases from participating sites that met inclusion criteria were included in the study. Inclusion criteria were met for any patient aged >18 years with a suspected opioid overdose that had a leftover blood specimen for analysis. Exclusion criteria for cases were any cases in persons with trauma or burns, or if the patient was a prisoner, pregnant, or both.

¶ Pennsylvania had two study sites.

TABLE. Detection of illicit benzodiazepines and opioids, initial naloxone administration, and outcomes among patients with suspected opioid overdose (N = 21) — Toxicology Investigators Consortium Fentalog Study Group, four states, October 6, 2020–March 9, 2021

Characteristic	No. (%) of patients
Illicit benzodiazepines detected	
Clonazolam	11 (52.4)
Etizolam	10 (47.6)
Flubromazolam*	2 (9.5)
Opioids detected	
Co-detected opioids†	20 (95.2)
Methadone	12 (60.0)
Fentanyl	6 (30.0)
Heroin	4 (20.0)
Codeine	2 (10.0)
Para-fluorofentanyl	2 (10.0)
Buprenorphine	1 (5.0)
Acetyl fentanyl	1 (5.0)
Medical course and outcome	
Naloxone administration§	16 (76.2)
Only 1 dose administered	9 (56.3)
≥2 doses administered	7 (43.8)
Known naloxone indication¶	15 (71.4)
Depressed level of consciousness	9 (60.0)
Respiratory depression	7 (46.7)
Decreased oxygenation	3 (20.0)
Decreased carbon dioxide expiration	2 (13.3)
Known naloxone response**	13 (61.9)
Improved level of consciousness	6 (46.2)
Increased respiratory rate	4 (30.8)
Improved oxygenation	1 (7.7)
Precipitated withdrawal††	1 (7.7)
No response	5 (38.5)
Respiratory and cardiac intervention	
Endotracheal intubation/Mechanical ventilation	1 (4.8)
Cardiopulmonary resuscitation	1 (4.8)
Hospital course	
Discharge from emergency department	17 (81.0)
Admission to hospital floor	3 (14.3)
Admission to intensive care unit	1 (4.8)
Disposition	
Discharged without sequelae	18 (85.7)
Transferred to higher level of care	1 (4.8)
Transferred to substance use treatment	1 (4.8)
Left against medical advice	1 (4.8)
Died	0 (—)

* Flubromazolam was only detected in two of the cases that also included etizolam.
† At least one opioid was identified in 20 cases. More than one opioid might be noted for a given case. The percentages of specific opioids are calculated based on these 20 cases.
§ The percentages of number of doses of naloxone are calculated based on 16 cases with naloxone administration. Initial naloxone dose was administered either outside of the hospital (by emergency medical services in 10 cases, by bystanders in two cases, and unknown in one case) or in the hospital (three cases).
¶ Indications for initial dose of naloxone were known in 15 of 21 total cases. The percentages of naloxone indication categories are calculated based on these 15 cases. More than one indication might be noted for a given case.
** Response to initial dose of naloxone was known in 13 of 16 naloxone administrations (81.3%). More than one response might be noted for a given case. The percentages of clinical response categories are calculated based on these 13 cases.
†† Precipitated withdrawal is medication-induced withdrawal that can cause particularly intense symptoms, including agitation, nausea/vomiting, and muscle aches and pains, among other withdrawal symptoms.

to both opioids and illicit benzodiazepines did not respond to naloxone. Although other factors might be involved, such as naloxone dose or administration technique, the opioid effects among these patients might have been reversed; however, these patients possibly experienced additional sedative effects from illicit benzodiazepines. The widespread use of community naloxone programs highlights the importance of calling emergency medical services after administering naloxone, because patients with co-exposure might require additional medical care. The growing use of illicit benzodiazepines requires a better understanding of the synergistic toxicity when these drugs are used along with opioids. Raising awareness among clinical, public safety, and community partners about dangers associated with the use of illicit benzodiazepines, including co-use with opioids, is critical.

Corresponding author: Kim Aldy, kim.aldy@acmt.net.

[1]American College of Medical Toxicology, Phoenix, Arizona; [2]The University of Texas Southwestern Medical Center, Dallas, Texas; [3]National Center for Injury Prevention and Control, CDC; [4]Center for Forensic Science Research and Education at the Frederic Rieders Family Foundation, Willow Grove, Pennsylvania; [5]Toxicology Department, NMS Labs, Horsham, Pennsylvania; [6]Oregon Health & Science University Emergency Medicine, Portland, Oregon; [7]Lehigh Valley Health Network, Allentown, Pennsylvania; [8]University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania; [9]University of Washington School of Medicine, Seattle, Washington; [10]University of Colorado Denver School of Medicine, Aurora, Colorado; [11]Icahn School of Medicine at Mount Sinai, New York, New York.

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Jeffrey Brent reports support for the current work through a research grant from the National Institute of Drug Abuse. Sharan Campleman reports being the treasurer of the Public Health Research Institute of Southern California. No other potential conflicts of interest were disclosed.

References

1. Moosmann B, Auwärter V. Designer benzodiazepines: another class of new psychoactive substances. Handb Exp Pharmacol 2018;252:383–410. PMID:30367253 https://doi.org/10.1007/164_2018_154
2. Waters L, Manchester KR, Maskell PD, Haegeman C, Haider S. The use of a quantitative structure-activity relationship (QSAR) model to predict GABA-A receptor binding of newly emerging benzodiazepines. Sci Justice 2018;58:219–25. PMID:29685303 https://doi.org/10.1016/j.scijus.2017.12.004
3. Jones JD, Mogali S, Comer SD. Polydrug abuse: a review of opioid and benzodiazepine combination use. Drug Alcohol Depend 2012;125:8–18. PMID:22857878 https://doi.org/10.1016/j.drugalcdep.2012.07.004
4. Krotulski AJ, Walton SE, Mohr ALA, Logan BK. Trend report: Q1 2021: NPS benzodiazepines in the United States. Willow Grove, PA: Center for Forensic Science Research and Education, NPS Discovery; 2021. https://www.npsdiscovery.org/wp-content/uploads/2021/04/2021-Q1_NPS-Benzodiazepines_Trend-Report.pdf
5. Drug Enforcement Administration, Special Testing and Research Laboratory. Emerging threat report: annual 2020. Arlington, VA: US Department of Justice, Drug Enforcement Administration, Special Testing and Research Laboratory; 2021. https://cesar.umd.edu/sites/cesar.umd.edu/files/pubs/DEA-Emerging-Threat-Report-2020-Annual.pdf
6. Drug Enforcement Administration, Special Testing and Research Laboratory. Emerging threat report: annual 2019. Arlington, VA: US Department of Justice, Drug Enforcement Administration, Special Testing and Research Laboratory; 2020. https://cesar.umd.edu/sites/cesar.umd.edu/files/pubs/DEA-Emerging-Threat-Report-2019-Annual.pdf

Errata

Vol. 70, No. 21

In the report "Racial and Ethnic Disparities in Breastfeeding Initiation — United States, 2019," on page 774, the last sentence should have read, "Implementation of evidence-based maternity care policies and practices supportive of breastfeeding and targeted breastfeeding programs focusing on populations at highest risk for low breastfeeding initiation might help reduce racial/ethnic disparities in breastfeeding initiation, improve infant nutrition, and reduce maternal and infant **morbidity**."

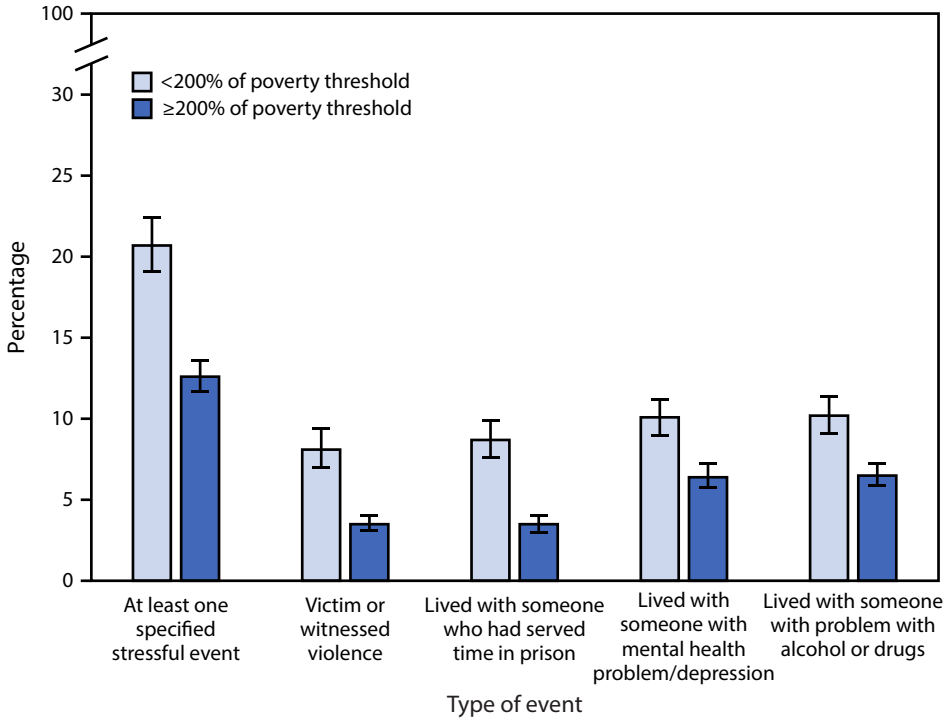
Vol. 70, No. 32

In the report "West Nile Virus and Other Domestic Nationally Notifiable Arboviral Diseases — United States, 2019," on pages 1072 and 1073, in Table 2, rates should have been **<0.01** for the following viruses and U.S. Census divisions: La Crosse virus for the West North Central Division; Eastern equine encephalitis for the South Atlantic division; and St. Louis encephalitis for the United States (total) and the West South Central division.

QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage* of Children and Adolescents Aged 0–17 Years Who Have Experienced a Specified Stressful Life Event,† by Type of Event and Poverty Status§ — National Health Interview Survey, United States, 2019¶



* With 95% confidence intervals indicated with error bars.
† Percentages for the specified stressful life events are based on the following questions: 1) "Has child ever been the victim of violence or witnessed violence in their neighborhood?"; 2) "Did child ever live with a parent or guardian who served time in jail or prison after child was born?"; 3) "Did child ever live with anyone mentally ill/depressed?"; 4) Did child ever live with anyone who had a problem with alcohol or drugs?" Having any stressful event was based on having answered "yes" to any of these four questions. The four stressful life event questions are part of a larger battery of questions called adverse childhood experiences.
§ Poverty status was based on family income and family size, using the U.S. Census Bureau's poverty thresholds. Family income was imputed when missing.
¶ Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population.

In 2019, 20.7% of children and adolescents in families with incomes <200% of the poverty threshold and 12.6% of children and adolescents in families with incomes ≥200% of the poverty threshold had experienced at least one specified stressful life event. Children and adolescents in families with incomes <200% of the poverty threshold were more likely than children and adolescents in families with incomes ≥200% of the poverty threshold to have been the victim or witnessed violence (8.1% versus 3.5%); lived with someone who had been in jail (8.7% versus 3.5%); lived with a person with problems with mental health or depression (10.1% versus 6.4%); or lived with a person with problems with alcohol or drugs (10.2% versus 6.5%).

Source: National Health Interview Survey, 2019. https://www.cdc.gov/nchs/nhis.htm

Reported by: Cynthia Reuben, MA, creuben@cdc.gov, 301-458-4458; Nazik Elgaddal, MS.

For more information on this topic, CDC recommends the following link: https://www.cdc.gov/injury/priority/aces.html

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

Readers who have difficulty accessing this PDF file may access the HTML file at https://www.cdc.gov/mmwr/index2021.html. Address all inquiries about the *MMWR* Series to Editor-in-Chief, *MMWR* Series, Mailstop V25-5, CDC, 1600 Clifton Rd., N.E., Atlanta, GA 30329-4027 or to mmwrq@cdc.gov.

ISSN: 0149-2195 (Print)