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Zika-Associated Birth Defects Reported in Pregnancies with Laboratory Evidence of Confirmed or Possible Zika Virus Infection — U.S. Zika Pregnancy and Infant Registry, December 1, 2015–March 31, 2018

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Zika virus infection during pregnancy can cause serious birth defects of the brain and eyes, including intracranial calcifications, cerebral or cortical atrophy, chorioretinal abnormalities, and optic nerve abnormalities (*1*,*2*). The frequency of these Zika-associated brain and eye defects, based on data from the U.S. Zika Pregnancy and Infant Registry (USZPIR), has been previously reported in aggregate (*3*,*4*). This report describes the frequency of individual Zika-associated brain and eye defects among infants from pregnancies with laboratory evidence of confirmed or possible Zika virus infection. Among 6,799 live-born infants in USZPIR born during December 1, 2015–March 31, 2018, 4.6% had any Zika-associated birth defect; in a subgroup of pregnancies with a positive nucleic acid amplification test (NAAT) for Zika virus infection, the percentage was 6.1% of live-born infants. The brain and eye defects most frequently reported included microcephaly, corpus callosum abnormalities, intracranial calcification, abnormal cortical gyral patterns, ventriculomegaly, cerebral or cortical atrophy, chorioretinal abnormalities, and optic nerve abnormalities. Among infants with any Zika-associated birth defect, one third had more than one defect reported. Certain brain and eye defects in an infant might prompt suspicion of prenatal Zika virus infection. These findings can help target surveillance efforts to the most common brain and eye defects associated with Zika virus infection during pregnancy should a Zika virus outbreak reemerge, and might provide a signal to the reemergence of Zika virus, particularly in geographic regions without ongoing comprehensive Zika virus surveillance.

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To monitor the impact of the 2015–2017 Zika virus outbreak, CDC, in collaboration with state, local, and territorial health departments, established USZPIR to conduct mother-infant linked longitudinal surveillance of outcomes in pregnant women and infants with laboratory evidence of confirmed or possible Zika virus infection during pregnancy* in the 50 U.S. states, the District of Columbia (DC), U.S. territories, and freely associated states.† Data from this cohort have been published previously (*3*–*5*). Pregnancies with an outcome occurring during December 1, 2015–March 31, 2018, were included in USZPIR with data reported as of December 2020 included in this report. Jurisdictions collected prenatal, pregnancy outcome, and follow-up information for infants and children (from birth through age 5 years)§ from medical records in a standardized format.

All mother-infant data with an indication of a possible abnormality were reviewed by subject matter experts (which included CDC clinicians and researchers and external consultants); data reviewed included results from neuroimaging, ophthalmologic examinations, and clinical examinations for any criteria based on USZPIR surveillance case definition (*6*). Cases that met criteria for Zika-associated abnormalities were subsequently reviewed in detail by two or more clinicians (including pediatricians, obstetrician-gynecologists, and clinical geneticists), for confirmation and classification of the individual defect or defects. All discrepancies in classification were discussed and resolved among a panel of experts. Infants who had microcephaly and were not small for gestational age at birth underwent further review; those who met criteria for a potential birth head circumference measurement inaccuracy were not included as having microcephaly in USZPIR.¶ Infants with other abnormal radiographic findings (e.g., mineralizing vasculopathy, and isolated subependymal cysts), which were

* Maternal laboratory evidence of confirmed or possible Zika virus infection was defined as 1) Zika virus infection detected by a Zika virus RNA nucleic acid amplification test (NAAT) (e.g., reverse transcription–polymerase chain reaction [RT-PCR]) on any maternal, placental, fetal, or infant specimen (referred to as positive Zika virus NAAT) or 2) detection of recent Zika virus infection or recent unspecified flavivirus infection by serologic tests on a maternal, fetal, or infant specimen (i.e., either positive or equivocal Zika virus and immunoglobulin M [IgM] Zika virus plaque reduction neutralization test [PRNT] titer ≥10, regardless of dengue virus PRNT value; or negative Zika virus IgM, and positive or equivocal dengue virus IgM, and Zika virus PRNT titer ≥10, regardless of dengue virus PRNT titer). Infants with positive or equivocal Zika virus IgM are included, provided a confirmatory PRNT has been performed on a maternal or infant specimen. The use of PRNT for confirmation of Zika virus infection, including during pregnancy, in women and infants, is not routinely recommended in Puerto Rico; dengue virus is endemic and cross-reactivity is likely to occur in most cases (https://www.cdc.gov/zika/laboratories/lab-guidance.html). In Puerto Rico, detection of a positive Zika virus IgM result in a pregnant woman, fetus, or infant (within 48 hours after delivery) was considered sufficient to indicate possible Zika virus infection.

† U.S. territories in USZPIR are American Samoa, Puerto Rico, and the U.S. Virgin Islands; freely associated states are Federated States of Micronesia and the Marshall Islands.

§ Infants and children in Puerto Rico and the U.S. Virgin Islands are followed through age 5 years; infants and children in U.S. states and DC, and U.S. territories and freely associated states are followed through age 3 years.

¶ https://www.researchsquare.com/article/rs-1189991/v1

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deemed as having "unknown clinical significance" by experts, were not reported.

In this report, the number of infants with any Zika-associated birth defect and enumerated individual brain and eye defects identified in the entire cohort with laboratory evidence of confirmed or possible Zika virus infection from a maternal, placental, fetal, or infant specimen are presented. A subgroup of infants from pregnancies with confirmed Zika virus infection (i.e., positive Zika virus NAAT) are reported to examine whether findings are consistent with the entire cohort.** Zika-associated birth defects among pregnancy losses are reported separately.†† In addition, the frequency of Zika-associated birth defects by location of birth, trimester with first evidence of Zika virus exposure (based on symptom onset, travel history to a region with endemic Zika virus transmission, or positive laboratory results), maternal symptom status, and reported neuroimaging and ophthalmology examinations are presented. Analyses were conducted using SAS (version 9.4; SAS Institute). CIs were calculated using exact Poisson regression. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.§§

During December 1, 2015–March 31, 2018, among 6,799 live-born infants reported in USZPIR, 2,288 (33.7%) were born in U.S. states and DC and 4,511 (66.3%) in U.S. territories and freely associated states (Table 1). Zika virus exposure was reported for 2,121 (31.2%) pregnant women in the first trimester; 2,495 (36.7%) in the second trimester; and 2,039 (30.0%) in the third trimester. Symptoms compatible with Zika virus disease¶¶ were reported in 35% of these women.

Among live-born infants reported in USZPIR, 4.6% (315 of 6,799) had any Zika-associated birth defect. In the subgroup with positive Zika virus NAAT during pregnancy, 6.1% (138 of 2,257) infants had any Zika-associated birth defect. Among pregnancies with positive Zika virus NAAT results, and thus less likelihood of exposure misclassification, the frequency of any Zika-associated birth defect was higher among those with first*** (8.0%) and second (6.0%) trimester infections compared with third trimester infections (3.8%). Frequency of Zika-associated birth defects in infants was similar among those born to symptomatic (5.3%) and asymptomatic (4.2%) pregnant women; neuroimaging and ophthalmology examinations were reported for 4,086 (60.1%) and 2,456 (36.1%), respectively.

The most frequent structural defects reported among live-born infants and children were microcephaly; corpus callosum abnormalities; intracranial calcification; abnormal cortical gyral patterns; ventriculomegaly; cerebral or cortical atrophy; chorioretinal atrophy, scarring, or pigmentary changes; and optic nerve abnormalities (Table 2). A similar distribution of birth defects was observed in the total cohort and in the Zika virus NAAT-positive subgroup. Among infants with any Zika-associated birth defect, one third (110 of 315) had more than one birth defect identified.

Among 325 pregnancies with laboratory evidence of confirmed or possible Zika virus infection that resulted in a pregnancy loss, 13 (4.0%) fetuses had any reported Zika-associated birth defect. Defects included microcephaly, cerebral or cortical atrophy, abnormal cortical gyral patterns, corpus callosum abnormalities, cerebellar abnormalities, hydranencephaly, ventriculomegaly or hydrocephaly, and brainstem abnormalities (C Moore, CDC, unpublished data, 2022).

Discussion

During 2015–2017, large Zika virus outbreaks occurred throughout the United States (including U.S. territories and freely associated states). In the United States, infections during pregnancy were initially reported among U.S. travelers returning from affected countries.††† During 2016, widespread local transmission was documented in the territories of Puerto Rico and the U.S. Virgin Islands, and limited transmission was documented in some counties in Florida and Texas.§§§ Among completed pregnancies with laboratory evidence of Zika virus infection reported to USZPIR, 4.6% of live-born infants had any Zika-associated birth defect. Among the subgroup with NAAT-positive results, Zika-associated birth defects were reported with exposures throughout pregnancy but were more prevalent among infants born to mothers with exposure early in pregnancy. Approximately two thirds of pregnant women in this cohort reported asymptomatic infections.¶¶¶ The similar frequency of Zika-associated birth defects among

** Includes maternal, placental, fetal, or infant laboratory evidence of Zika virus infection based on the presence of Zika virus RNA by a positive NAAT (e.g., RT-PCR).

†† Pregnancy losses include spontaneous abortions, terminations, stillbirths, and pregnancy losses not specified. Information from prenatal or postnatal imaging and autopsy were used to determine presence of Zika-associated birth defects, although pregnancy losses often had less information reported and frequently lacked postnatal imaging that could verify prenatal findings and might identify additional abnormalities.

§§ 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.

¶¶ Signs and symptoms included fever, arthralgia, conjunctivitis, rash, and other clinical signs or symptoms that are consistent with Zika virus disease.

*** Zika virus infections that occurred during the periconceptual period, which is defined as 4 weeks before last menstrual period, are included in the first trimester.

††† https://www.cdc.gov/zika/reporting/index.html

§§§ https://wwwnc.cdc.gov/travel/page/zika-travel-information

¶¶¶ Because of the decline in the global incidence of Zika virus, testing is not currently recommended for asymptomatic pregnant persons with possible exposure (https://www.cdc.gov/zika/symptoms/diagnosis.html). However, during the 2015–2017 Zika virus outbreak in the Americas, widespread transmission and unknown impacts of Zika virus infection during pregnancy prompted CDC to recommend testing for potentially at-risk asymptomatic pregnant persons.

TABLE 1. Frequency of Zika-associated birth defects,* by selected characteristics among live-born infants from pregnancies with laboratory evidence of confirmed or possible Zika virus infection — U.S. Zika Pregnancy and Infant Registry, December 1, 2015–March 31, 2018

Characteristic	From pregnancies with laboratory evidence of confirmed or possible Zika virus infection†		From pregnancies with positive Zika virus NAAT result§	
	No./Total no.	% (95% CI)	No./Total no.	% (95% CI)
Total	**315/6,799**	**4.6 (4.1–5.2)**	**138/2,257**	**6.1 (5.1–7.2)**
Location of birth				
U.S. states and DC	124/2,288	5.4 (4.5–6.5)	38/374	10.2 (7.2–14.0)
U.S. territories and freely associated states¶	191/4,511	4.2 (3.7–4.9)	100/1,883	5.3 (4.3–6.5)
Trimester with first evidence of exposure,††				
1st§§	108/2,121	5.1 (4.2–6.2)	43/539	8.0 (5.8–10.8)
2nd	107/2,495	4.3 (3.5–5.2)	62/1,028	6.0 (4.6–7.7)
3rd	82/2,039	4.0 (3.2–5.0)	25/657	3.8 (2.5–5.6)
Maternal symptoms¶¶,***				
Signs/Symptoms of Zika virus disease	126/2,379	5.3 (4.4–6.3)	92/1,596	5.8 (4.7–7.1)
No signs/symptoms of Zika virus disease	186/4,382	4.2 (3.7–4.9)	46/661	7.0 (5.1–9.3)
Examinations reported				
Neuroimaging	258/4,086	6.3 (5.6–7.1)	120/1,595	7.5 (6.2–9.0)
Ophthalmology	167/2,456	6.8 (5.8–7.9)	79/1,072	7.4 (5.8–9.2)

Abbreviations: DC = District of Columbia; NAAT = nucleic acid amplification test; RT-PCR = reverse transcription–polymerase chain reactionreaction; USZPIR = U.S. Zika Pregnancy and Infant Registry.

* Zika-associated birth defects include selected congenital brain anomalies (intracranial calcifications, cerebral or cortical atrophy, abnormal cortical gyral patterns, corpus callosum abnormalities, cerebellar abnormalities, porencephaly, hydranencephaly, or ventriculomegaly/hydrocephaly); selected congenital eye anomalies (microphthalmia or anophthalmia; coloboma; cataract; intraocular calcifications; chorioretinal anomalies involving the macula, excluding retinopathy of prematurity; and optic nerve atrophy, pallor, and other optic nerve abnormalities); and/or microcephaly at birth (birth head circumference below the third percentile for infant sex and gestational age based on INTERGROWTH-21st online percentile calculator unless infants meet criteria of possible measurement inaccuracy. http://intergrowth21.ndog.ox.ac.uk/

† Includes maternal, placental, or infant laboratory evidence of confirmed or possible Zika virus infection during pregnancy based on presence of Zika virus RNA by a positive NAAT (e.g., RT-PCR), serologic evidence of a Zika virus infection, or serologic evidence of an unspecified flavivirus infection.

§ Includes maternal, placental, or infant laboratory evidence of confirmed Zika virus infection during pregnancy based on presence of Zika virus RNA by a positive NAAT (e.g., RT-PCR).

¶ U.S. territories in USZPIR are American Samoa, Puerto Rico, and the U.S. Virgin Islands; freely associated states are Federated States of Micronesia and the Marshall Islands.

** Among pregnancies in which birth occurred in the U.S. states and DC, symptom onset date, travel dates to an endemic region, or date of earliest laboratory evidence of Zika virus infection were used to calculate trimester of exposure. Among pregnancies where birth occurred in U.S. territories and freely associated states, symptom onset date or date of earliest laboratory evidence of Zika virus infection were used to calculate trimester of exposure.

†† Unknown trimester of exposure is not shown because of small cell sizes; 144 pregnancies were missing trimester of exposure.

§§ Zika virus infections that occurred during the periconceptual period, which is defined as 4 weeks before last menstrual period, are included in the first trimester of exposure.

¶¶ Maternal symptom status is not shown because of small cell sizes; 38 pregnancies were missing maternal symptom status.

*** Signs and symptoms included fever, arthralgia, conjunctivitis, rash, and other clinical signs or symptoms that are consistent with Zika virus disease.

asymptomatic and symptomatic pregnant women is consistent with previous findings (*3*,*5*).

Certain individual brain and eye defects associated with Zika virus infection were frequently reported in USZPIR cohort. A similar subset of Zika-associated birth defects was found to have significantly higher prevalence ratios in areas of widespread local transmission compared with areas without local transmission in the Zika Birth Defects Surveillance System.**** Given the short window for testing and that symptoms of Zika are often mild or absent, combining these two systems has identified the most prevalent Zika-associated birth defects. Using a surveillance system that monitored outcomes regardless of testing and a system that monitored outcomes among those possibly exposed to Zika virus has been critical to understanding the effects of Zika virus infection during pregnancy on infants and children.

The findings in this report are subject to at least five limitations. First, these data are based on information abstracted from medical records. Although CDC provided specific guidance for evaluation of all infants born from pregnancies with possible Zika virus exposure during pregnancy (*7*), these evaluations might not have been feasible, were not always conducted, or were not found in records (*4*). Zika-associated birth defects, especially individual brain and eye defects might not have been detected without occurrence and reporting of neuroimaging and ophthalmologic examinations. Second, these findings are only applicable to live births. Pregnancy losses are likely underreported to USZPIR, and among those reported, postnatal studies to verify prenatal findings or identify additional defects are often lacking. Third, although routine testing during pregnancy occurred in areas with local Zika virus transmission, a potential bias could have been introduced in areas without local transmission, as differential testing might have occurred in

**** https://www.researchsquare.com/article/rs-1189990/v1

TABLE 2. Individual Zika-associated birth defects among live-born infants from pregnancies with laboratory evidence of confirmed or possible Zika virus infection — U.S. Zika Pregnancy and Infant Registry, December 1, 2015–March 31, 2018

Birth defect	No. of infants (%)	
	From pregnancies with laboratory evidence of confirmed or possible Zika virus infection* (n = 6,799)	From pregnancies with positive Zika virus NAAT result† (n = 2,257)
Any Zika-associated birth defect§	**315 (4.6)**	**138 (6.1)**
Brain abnormalities/Microcephaly¶		
Any brain abnormality/microcephaly	275 (4.0)	126 (5.6)
Microcephaly**,††	214 (3.1)	100 (4.4)
Corpus callosum abnormalities	64 (0.9)	40 (1.8)
Intracranial calcifications	58 (0.9)	27 (1.2)
Abnormal cortical gyral patterns	56 (0.8)	29 (1.3)
Ventriculomegaly/Hydrocephaly	53 (0.8)	34 (1.5)
Cerebral or cortical atrophy	43 (0.6)	24 (1.1)
Cerebellar abnormalities	27 (0.4)	15 (0.7)
Fetal brain disruption sequence	12 (0.2)	10 (0.4)
Brainstem abnormalities	8 (0.1)	6 (0.3)
Porencephaly/Hydranencephaly	5 (0.1)	3 (0.1)
Eye abnormalities		
Any eye abnormality	76 (1.1)	34 (1.5)
Chorioretinal atrophy, scarring, or pigmentary changes	47 (0.7)	25 (1.1)
Optic nerve abnormalities	34 (0.5)	13 (0.6)
Coloboma	7 (0.1)	5 (0.2)
Congenital cataract	7 (0.1)	3 (0.1)
Microphthalmia	5 (0.1)	1 (—)
Other brain and eye abnormality patterns		
Multiple brain or eye abnormalities	110 (1.6)	55 (2.4)
Brain and eye abnormalities	36 (0.5)	22 (1.0)
One or more brain abnormalities only	239 (3.5)	104 (4.6)
One brain abnormality or microcephaly only	173 (2.5)	72 (3.2)
Microcephaly only§§	144 (2.1)	58 (2.6)
Microcephaly only and SGA	98 (1.4)	37 (1.6)
One or more eye abnormalities only	40 (0.6)	12 (0.5)
One eye abnormality only	32 (0.5)	11 (0.5)

Abbreviations: NAAT = nucleic acid amplification test; RT-PCR = reverse transcription–polymerase chain reaction; SGA = small for gestational age.

* Includes maternal, placental, or infant laboratory evidence of confirmed or possible Zika virus infection during pregnancy based on presence of Zika virus RNA by a positive NAAT (e.g., RT-PCR), serologic evidence of a Zika virus infection, or serologic evidence of an unspecified flavivirus infection.

† Includes maternal, placental, or infant laboratory evidence of confirmed Zika virus infection during pregnancy based on presence of Zika virus RNA by a positive NAAT.

§ Zika-associated birth defects include selected congenital brain anomalies (intracranial calcifications, cerebral or cortical atrophy, abnormal cortical gyral patterns, corpus callosum abnormalities, cerebellar abnormalities, porencephaly, hydranencephaly, or ventriculomegaly/hydrocephaly); selected congenital eye anomalies (microphthalmia or anophthalmia; coloboma; cataract; intraocular calcifications; chorioretinal anomalies involving the macula, excluding retinopathy of prematurity; and optic nerve atrophy, pallor, and other optic nerve abnormalities); and/or microcephaly at birth (birth head circumference below the third percentile for infant sex and gestational age based on INTERGROWTH-21st online percentile calculator unless infants meet criteria of possible measurement inaccuracy. http://intergrowth21.ndog.ox.ac.uk/

¶ Among infants with brain abnormalities, microcephaly, or both, 24 (0.4%) and 11 (0.5%) infants also had arthrogryposis among pregnancies with laboratory evidence of confirmed or possible Zika virus infection during pregnancy and NAAT-confirmed Zika virus infection, respectively.

** Infants with birth head circumference below the third percentile based on INTERGROWTH-21st. http://intergrowth21.ndog.ox.ac.uk/

†† Among infants with microcephaly, 141 and 64 also had a birthweight below the 10th percentile (SGA) among pregnancies with laboratory evidence of confirmed or possible Zika virus infection during pregnancy and NAAT-confirmed Zika virus infection, respectively.

§§ Neuroimaging was available for 66.0% and 29.2% of infants with microcephaly only from pregnancies with laboratory evidence of confirmed or possible Zika virus infection during pregnancy and NAAT-confirmed Zika virus infection, respectively.

women reporting possible Zika virus exposure related to travel or sex or when birth defects were detected in the fetus or infant. Fourth, USZPIR surveillance case definition includes infants with microcephaly based on head circumference measurement at birth alone, and only one third of these had sufficient information to be evaluated for possible measurement error. Thus, misclassification of infants with microcephaly based on birth head circumference alone might still exist. Finally, pregnancies in persons with possible Zika virus exposure, including those with evidence of unspecified flavivirus infection were included; therefore, some might not have had Zika virus infection during pregnancy. Analysis of the subgroup with NAAT-positive results indicated higher frequency of any Zika-associated birth defects, but the distribution of individual defects was generally consistent between the total cohort and this subgroup.

Summary

What is already known about this topic?

Zika virus infection during pregnancy can cause serious brain and eye birth defects.

What is added by this report?

This study describes the frequency of individual Zika-associated birth defects from the U.S. Zika Pregnancy and Infant Registry (USZPIR). Approximately 5% of infants in USZPIR had any Zika-associated brain or eye defect. Several individual brain and eye defects were more commonly reported. One third of infants with any Zika-associated birth defect had more than one defect reported.

What are the implications for public health practice?

Certain brain and eye defects in infants might prompt suspicion of prenatal Zika virus infection and might provide a signal to the reemergence of Zika virus, particularly in geographic regions without ongoing comprehensive Zika virus surveillance.

Much has been learned since the first infant with Zika-associated birth defects was identified in the United States. This report is the first to describe Zika-associated birth defects from USZPIR with data combined from the U.S. states, DC, and U.S. territories and freely associated states. The study provides a description of the frequency of individual Zika-associated birth defects reported among infants from pregnancies with laboratory evidence of confirmed or possible Zika virus infection. Additional study is needed to define the full spectrum of Zika-associated outcomes, including any specific defects or combination of defects that might predict the presence of Zika virus infection and Zika virus circulation. Further monitoring of these infants for neurodevelopmental abnormalities is ongoing. Infants exposed to Zika virus infection in utero, but without structural birth defects, might also have neurologic sequelae and developmental delay (*4*,*8*). Zika virus outbreaks are tracked globally; Zika virus infection remains a nationally reportable disease in the United States.†††† These findings can help to target surveillance efforts to the most common brain and eye defects associated with Zika virus infection during pregnancy should a Zika virus outbreak reemerge, and might provide a signal to the reemergence of Zika virus, particularly in geographic regions without ongoing comprehensive Zika virus surveillance

†††† https://ndc.services.cdc.gov/case-definitions/zika-virus-disease-and-zika-virus-infection-2016-06-01/

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Use of Recombinant Zoster Vaccine in Immunocompromised Adults Aged ≥19 Years: Recommendations of the Advisory Committee on Immunization Practices — United States, 2022

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Zoster Vaccine Recombinant, Adjuvanted (Shingrix, GlaxoSmithKline [GSK]) is a 2-dose (0.5 mL each) subunit vaccine containing recombinant glycoprotein E in combination with adjuvant ($AS01_B$) that was licensed in the United States for prevention of herpes zoster for adults aged ≥50 years by the Food and Drug Administration (FDA) and recommended for immunocompetent adults aged ≥50 years by the Advisory Committee on Immunization Practices (ACIP) in 2017* (*1*). On July 23, 2021, the FDA expanded the indication for recombinant zoster vaccine (RZV) to include adults aged ≥18 years who are or will be at increased risk for herpes zoster because of immunodeficiency or immunosuppression caused by known disease or therapy (*2*). On October 20, 2021, ACIP recommended 2 doses of RZV for the prevention of herpes zoster and related complications in adults aged ≥19 years† who are or will be immunodeficient or immunosuppressed because of disease or therapy. RZV is the first herpes zoster vaccine approved for use in immunocompromised persons. With moderate to high vaccine efficacy and an acceptable safety profile, RZV has the potential to prevent considerable herpes zoster incidence and related complications. This report updates previous ACIP recommendations for the prevention of herpes zoster (*1*,*3*).

Herpes zoster is a painful, cutaneous eruption, usually involving one to three adjacent dermatomes,§ resulting from reactivation of latent varicella-zoster virus. The incidence of herpes zoster and related complications (including the most common complication of postherpetic neuralgia) increase with age (*3*–*5*). The risk for herpes zoster and related complications is generally higher in immunocompromised compared with immunocompetent adults, although there is heterogeneity within and across immunocompromised groups (*6*,*7*). The risk for herpes zoster among younger adults with certain immunocompromising conditions can be comparable to or higher than that in the general adult population aged >50 years (*6*,*7*). Because immunosuppression and immunodeficiency were contraindications for the previously available vaccine, zoster vaccine live,¶ and RZV was originally recommended for immunocompetent adults aged ≥50 years, there has been an unmet need for vaccination against herpes zoster in immunocompromised adults.

During December 2017–October 2021, the ACIP Herpes Zoster Work Group participated in monthly or bimonthly teleconferences to review herpes zoster epidemiology and evidence for the efficacy and safety of RZV in immunocompromised adults. These topics were discussed during four ACIP meetings in 2021. To guide its deliberations, ACIP used the Evidence to Recommendations Framework and the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach (*8*) to evaluate possible benefits (prevention of herpes zoster, postherpetic neuralgia, and herpes zoster-related hospitalizations) and harms (serious adverse events [SAEs],** immune-mediated disease, graft-versus-host-disease, graft rejection, and reactogenicity) associated with RZV.††

Prevention of herpes zoster and occurrence of SAEs were deemed critical outcomes by the work group. Five studies in four immunocompromised groups§§ evaluated herpes zoster as an outcome (*9*–*13*). Estimates of vaccine efficacy (VE) came from three studies, with VE of 68.2% (95% CI = 55.6%–77.5%) for autologous hematopoietic cell transplant recipients (*11*), and 87.2% (44.3%–98.6%) and 90.5% (73.5%–97.5%) in post hoc efficacy analyses for patients with hematologic malignancies (*12*) and potential immune-mediated diseases (*13*), respectively. SAEs were evaluated in seven studies (*9*–*15*) in six immunocompromised groups (2,541 RZV recipients).¶¶ Overall, rates of SAEs were

* This recommendation became official CDC policy in January 2018.

† On October 20, 2021 ACIP voted 15–0 in favor of the recommendation for use of RZV for the prevention of herpes zoster and related complications in adults aged ≥19 years (to align with the age range in the adult immunization schedule) who are or will be immunodeficient or immunosuppressed because of disease or therapy.

§ A dermatome is a cutaneous area of skin supplied by one spinal nerve.

¶ Zoster vaccine live is no longer available for use in the United States, as of November 18, 2020.

** Serious adverse event is defined as an undesirable experience associated with the vaccine that results in death, hospitalization, disability or requires medical or surgical intervention to prevent a serious outcome.

†† https://www.cdc.gov/vaccines/acip/recs/grade/recombinant-zoster-immunocompromised.html

§§ Autologous hematopoietic cell transplant recipients, patients with hematologic malignancies, patients living with HIV aged ≥18 years, and patients with potential immune-mediated diseases aged ≥50 years.

¶¶ Autologous hematopoietic cell transplant recipients, patients living with HIV, patients with hematologic malignancies, patients with solid tumors, renal transplant recipients aged ≥18 years, and patients with potential immune-mediated diseases aged ≥50 years.

comparable between RZV and placebo recipients (risk ratios ranged from 0.79 to 1.99). SAEs deemed to be related to vaccination by study investigators ranged from 0% to 1.6% in the RZV group and 0% to 0.76% in the placebo group. The level of certainty for prevention of herpes zoster and occurrence of SAEs was type 2 (moderate).***

In addition to the critical outcomes (prevention of herpes zoster and SAEs), the remaining outcomes were deemed important by the work group. One study among hematopoietic cell transplant recipients (*11*) reported VE of 89% (95% CI = 22%–100%) for prevention of postherpetic neuralgia and 85% (32%–97%) for prevention of herpes zoster-related hospitalization (certainty type 3 [low]). Immune-mediated diseases were evaluated in six studies (*9*,*11*–*15*) in five immunocompromised groups††† and were not increased among RZV recipients (certainty type 4 [very low]). One study in patients with hematologic malignancies (*12*) reported on graft-versus-host-disease among hematopoietic cell transplant recipients and did not identify an increased risk among RZV recipients (certainty type 4 [very low]). One study among renal transplant patients (*15*) reported on graft rejection and did not identify an increased risk among RZV recipients (certainty type 3). Local and systemic grade 3 reactions§§§ were evaluated in six studies (*9*–*12*,*14*,*15*) in five immunocompromised groups.¶¶¶ Local grade 3 reactions occurred in 10.7% to 14.2% of RZV recipients, and systemic grade 3 reactions occurred in 9.9% to 22.3% of RZV recipients, compared with 0% to 0.3% and 6.0% to 15.5%, respectively, among placebo recipients (certainty type 2).

Additional data reviewed within the Evidence to Recommendations Framework supported the use of RZV in immunocompromised adults.**** Two economic studies assessed RZV use (versus no vaccination) among immunocompromised adults (*16*). Both studies focused on hematopoietic cell transplant patients as the base case and found that vaccination was cost-saving, and eight to 10 persons receiving complete vaccination were needed to avert an episode of herpes zoster. Additional analyses assessed vaccination among persons with other immunocompromising conditions†††† and found that vaccination would cost <$99,000 per quality-adjusted life-year gained for most scenarios and could be cost-saving in several scenarios. Vaccination among patients with autoimmune and inflammatory conditions yielded the highest estimate of $208,000 per quality-adjusted life-year gained. Variations in results across scenarios were likely due to differences in estimated costs of health care, VE, and incidence of herpes zoster across different immunocompromising conditions.

Overall, the work group determined that herpes zoster in immunocompromised adults is of public health importance; the desirable anticipated effects of RZV in immunocompromised adults are large and the undesirable effects are small, which favors the intervention; immunocompromised adults probably feel that the desirable effects of vaccination with RZV are large relative to the undesirable effects and that there is probably not important uncertainty or variability in how patients value these outcomes. Use of RZV in immunocompromised adults is acceptable to stakeholders and a reasonable and efficient allocation of resources; health equity would probably be increased; and the intervention would be feasible to implement. On October 20, 2021, with this input from the work group, ACIP unanimously approved the recommendation.

With moderate to high VE among several immunocompromised groups and an acceptable safety profile across a range of immunocompromised groups, RZV has the potential to prevent considerable herpes zoster incidence and related complications. Recommending vaccination of immunocompromised adults aged ≥19 years will enable providers to vaccinate patients at a time most appropriate for their immunocompromising condition or therapy.

Clinical Guidance§§§§

Dosing schedule. Two RZV doses are necessary, regardless of previous history of herpes zoster or previous receipt of zoster vaccine live. The second RZV dose should typically be given 2–6 months after the first; for persons who are or will be immunodeficient or immunosuppressed and who would benefit from a shorter vaccination schedule, the second dose can be administered 1–2 months after the first (*2*). If the second RZV dose is given sooner than 4 weeks after the first, a valid second dose should be repeated at least 4 weeks after the dose given too early. The vaccine series does not need to be restarted if more than 6 months have elapsed since the first dose.

*** Grading of Recommendations, Assessment, Development and Evaluation (GRADE) level of certainty scale: type 1 = high certainty, type 2 = moderate certainty, type 3 = low certainty, and type 4 = very low certainty.

††† Autologous hematopoietic cell transplant recipients, patients with hematologic malignancies, patients with solid tumors, and renal transplant recipients aged ≥18 years, and patients with potential immune-mediated diseases aged ≥50 years.

§§§ Grade 3 reactions are defined as reactions related to vaccination severe enough to prevent normal activities.

¶¶¶ Autologous hematopoietic cell transplant recipients, patients living with HIV, patients with hematologic malignancies, patients with solid tumors, and renal transplant recipients aged ≥18 years.

**** https://www.cdc.gov/vaccines/acip/recs/grade/recombinant-zoster-immunocompromised-etr.html

†††† Patients with hematologic malignancies, solid organ transplant recipients, patients living with HIV, patients with breast cancer, and patients with autoimmune and inflammatory conditions.

§§§§ https://www.cdc.gov/shingles/vaccination/immunocompromised-adults.html

Timing of vaccination. When possible, patients should be vaccinated before becoming immunosuppressed. Otherwise, providers should consider timing vaccination when the immune response is likely to be most robust (i.e., during periods of lower immunosuppression and stable disease). RZV may be administered to patients who previously received varicella vaccine. RZV is not a live virus vaccine; therefore, RZV may be administered while patients are taking antiviral medications.

Coadministration with other vaccines. Recombinant and adjuvanted vaccines, such as RZV, can be administered concomitantly, at different anatomic sites, with other adult vaccines, including COVID-19 vaccines (*17*). Concomitant administration of RZV with other adult vaccines[¶¶¶¶] has been studied, and there was no evidence for interference in the immune response to either vaccine or of safety concerns (*18*–*20*). Coadministration of RZV with adjuvanted influenza vaccine (Fluad) and COVID-19 vaccines is being studied.

Counseling for reactogenicity. Before vaccination, providers should counsel patients about expected local and systemic reactogenicity, including grade 3 reactions. It is generally not recommended to take antipyretic or analgesic medications prophylactically before vaccination; however, antipyretic or analgesic medications may be taken for the treatment of postvaccination local or systemic symptoms. Patients should be encouraged to complete the series even if they experienced a (nonanaphylactic) grade 1–3 reaction after receipt of the first RZV dose.

Special Populations[*****]

Persons with a history of herpes zoster. Herpes zoster can recur. Persons with a history of herpes zoster should receive RZV.

Persons with no documented history of varicella, varicella vaccination, or herpes zoster. Persons who have neither experienced varicella nor received varicella vaccine are not at risk for herpes zoster. More than 99% of Americans born before 1980 have had varicella (*21*). Children and adolescents who have received live-attenuated varicella vaccines are at lower risk for herpes zoster than are those who experienced varicella (*22,23*). RZV is not indicated and has not been studied for the prevention of varicella. For immunocompromised persons, evidence of immunity to varicella (confirming need for RZV) includes documented receipt of 2 doses of varicella vaccine, laboratory evidence of immunity or laboratory confirmation of disease, or diagnosis or verification of a history of varicella or herpes zoster by a health care provider. For immunocompromised adults with no documented history of varicella, varicella vaccination, or herpes zoster, providers should refer to the ACIP varicella vaccine recommendations for further guidance, including postexposure prophylaxis guidance (*24*).

Pregnancy. There is currently no ACIP recommendation for RZV use in pregnancy; therefore, providers should consider delaying RZV until after pregnancy. There is no recommendation for pregnancy testing before vaccination.

Breastfeeding. Recombinant vaccines such as RZV pose no known risk to mothers who are breastfeeding or to their infants (*17*). Clinicians may consider vaccination without regard to breastfeeding status if RZV is otherwise indicated.

Summary

What is already known about this topic?

Immunocompromised persons experience a higher incidence of herpes zoster and related complications. On July 23, 2021, the Food and Drug Administration expanded the indication for use of recombinant zoster vaccine (RZV) to include immunodeficient or immunosuppressed adults.

What is added by this report?

On October 20, 2021, the Advisory Committee on Immunization Practices recommended 2 RZV doses for prevention of herpes zoster and related complications in immunodeficient or immunosuppressed adults aged ≥19 years.

What are the implications for public health practice?

RZV is the first herpes zoster vaccine approved for use in immunocompromised persons. With moderate to high vaccine efficacy and an acceptable safety profile, RZV has the potential to prevent considerable herpes zoster incidence and related complications.

Contraindications

Allergy. RZV should not be administered to persons with a history of severe allergic reaction, such as anaphylaxis, to any component of this vaccine.

Precautions

Moderate or severe acute illness with or without fever. In general, vaccination should be delayed for patients experiencing moderate or severe acute illness (*17*).

Current episode of herpes zoster. RZV is not a treatment for herpes zoster or postherpetic neuralgia. If a person is experiencing an episode of herpes zoster, vaccination should be delayed until the acute stage of the illness is over and symptoms abate (*17*).

[¶¶¶¶] Fluarix Quadrivalent (influenza vaccine), 23-valent pneumococcal polysaccharide vaccine (PPSV23, Pneumovax23), tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis vaccine (Tdap, Boostrix).

[*****] https://www.cdc.gov/shingles/vaccination/immunocompromised-adults.html

Reporting of Vaccine Adverse Events

Adverse events following vaccination can be reported to the Vaccine Adverse Events Reporting System (VAERS). Reporting is encouraged for any clinically significant adverse event even if it is uncertain whether the vaccine caused the event. Information on how to submit a report to VAERS is available at https://vaers.hhs.gov/index.html or by telephone at 1-800-822-7967.

Future Research and Monitoring Priorities

CDC will monitor adverse events following RZV immunization through VAERS, the Vaccine Safety Datalink, and observational studies. This is particularly important given the heterogeneity of herpes zoster risk within and across immunocompromised groups and the novel adjuvant and high rates of reactogenicity of the vaccine. Limited data for outcomes deemed important by the work group (e.g., possible graft rejection, graft-versus-host-disease, immune-mediated disease) highlight the need for additional research. Additional postmarketing monitoring will include studies conducted by GSK and reported to FDA. Continued monitoring of the impact of the U.S. varicella and herpes zoster vaccination programs on herpes zoster epidemiology will be important to guide future herpes zoster vaccination recommendations.

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Progress Toward Poliomyelitis Eradication — Afghanistan, January 2020–November 2021

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Wild poliovirus types 2 and 3 were declared eradicated in 2015 and 2019, respectively, and, since 2017, transmission of wild poliovirus type 1 (WPV1) has been detected only in Afghanistan and Pakistan. In 2020, these countries reported their highest number of WPV1 cases since 2014 and experienced outbreaks of type 2 circulating vaccine-derived poliovirus (cVDPV2)* (*1*); in Afghanistan, the number of WPV1 cases reported increased 93%, from 29 in 2019 to 56 in 2020, with 308 cVDPV2 cases reported. This report describes the activities and progress toward polio eradication in Afghanistan during January 2020–November 2021 and updates previous reports (*2–4*). Despite restrictions imposed by antigovernment elements since 2018, disruption of polio eradication efforts by the COVID-19 pandemic, and civil and political instability, eradication activities have resumed. During January–November 2021, four WPV1 cases and 43 cVDPV2 cases were detected, representing decreases of 93% from 56 and 85% from 281, respectively, during the same period in 2020. After the assumption of nationwide control by the current de facto government of Afghanistan during August 2021, health officials committed to oral poliovirus vaccine (OPV) campaigns nationwide, with the potential to vaccinate approximately 2.5 million children against poliovirus who were previously not accessible for ≥2 years. Although challenges remain, vigorous, sustained polio eradication efforts in Afghanistan could result in substantial progress toward eradication during 2022–2023.

Immunization Activities

The estimated national routine vaccination coverage with the third dose of bivalent OPV (bOPV containing Sabin types 1 and 3) (OPV3) among children aged 12 months was 73% during 2018 and 2019; the estimated 1-dose coverage with injectable inactivated poliovirus vaccine (IPV) during 2019 was 66% (*5*). Nationwide, during 2020 and 2021 to date, 27% of children aged 6–59 months with nonpolio acute flaccid paralysis (NPAFP; paralysis with no evidence of poliovirus infection, a proxy indicator of OPV3 coverage) had received 3 OPV doses through routine immunization services, based on caretaker recall. The percentage of children aged 6–59 months with NPAFP who never received OPV through routine or supplementary immunization activities (SIAs)† increased from 1% in 2019 to 4% in 2020, and to 6% in 2021, with the highest provisional percentages in 2021 in the southern provinces of Zabul (32%), Nimroz (13%), and Helmand (21%), and the western province of Badghis (19%). However, this proportion remained at or near 0% in most of the eastern provinces during 2019–2021 and decreased from 10% and 4.9% in the southeast provinces of Paktya and Khost to 0% and 2.4%, respectively.

During January 2020–November 2021, 10 OPV SIAs were conducted; eight were national immunization days (NIDs) and two were subnational immunization days (SNIDs) targeting children aged <5 years. In addition, four case-response campaigns with type 1-containing monovalent OPV (mOPV), bOPV, or trivalent OPV (tOPV containing Sabin types 1, 2, and 3) were implemented during July–November 2020. During January and February 2020, during IPV fixed-site campaigns, IPV was administered to 159,833 (93%) children targeted in the accessible districts in the eastern provinces of Kunar, Nangarhar, and Laghman, and the southeast province of Paktika.

Most districts of the southern and eastern provinces of Afghanistan were under control of antigovernment elements before assumption of full nationwide control by the de facto government of Afghanistan during August 2021. Children who are unvaccinated are classified as being inaccessible to vaccination or as accessible but missed.§ House-to-house SIAs, the optimal method for reaching every child for OPV vaccination, have been banned in all areas controlled by antigovernment elements since May 2018. Enhanced transit point and fixed-post vaccination at health facilities have been permitted since October 2019.

According to administrative data, an estimated 2,752,578 (28%) of the 9,999,227 children aged <5 years were inaccessible to vaccination during the January 2020 NID. In October

* cVDPV can emerge when attenuated OPV virus reverts to neurovirulence as a result of transmission in areas with low immunization coverage.

† SIAs are mass house-to-house campaigns targeting children aged <5 years with OPV, regardless of their vaccination history.

§ Children living in antigovernment element–held areas with insecurity or where SIAs were banned up to this time are classified as being inaccessible to vaccination. Children in areas that were fully accessible for OPV SIAs were classified as having been missed if they remained unvaccinated because of absence from home, refusal, or low-quality campaign implementation by vaccination teams.

2020, when SIAs recommenced after a 5-month suspension because of COVID-19, this number increased to 3,381,642 (34%) and peaked at approximately 4,000,000 (40%) during the March and June 2021 NIDs. During these SIAs, the proportion of children reported as accessible but missed ranged from 4% in February 2020 to 3% in October 2020.

Lot quality assurance sampling (LQAS)[¶] surveys assess SIA quality in accessible areas. On the basis of the number of unvaccinated children among those surveyed, SIAs in districts either passed (90%) or failed. The proportion of surveyed districts with failed SIAs during January 2020–June 2021 ranged from 40% in July 2020 to 12% in November 2020, January 2021, and June 2021.

Children aged ≤10 years are also targeted for vaccination along major travel routes throughout Afghanistan, and persons of all ages are targeted at border crossing points with Iran and Pakistan. During January 2020–November 2021, 14,899,633 doses of bOPV were administered to children at transit points and 1,432,964 doses to persons of all ages at border crossings.

[¶] LQAS is a rapid survey method to assess the quality of vaccination activities after SIAs in predefined areas, such as health districts (referred to as "lots"), using a sample size of 60. LQAS involves dividing the population into lots and ascertaining receipt of vaccination by randomly selecting children within each lot. If the number of unvaccinated persons in the sample exceeds three, then the SIA quality in that area is classified as failed (i.e., at a pass threshold of ≥90%) and mop-up activities are recommended. If the threshold of ≥90% is met, the SIA's quality for the area is classified as having passed, although mop-up activities might still be indicated in certain areas.

Poliovirus Surveillance

Acute flaccid paralysis surveillance. Detection of two or more NPAFP cases per 100,000 persons aged <15 years together with ≥80% of AFP cases having adequate stool specimens collected[**] indicate that surveillance is sufficiently sensitive to detect poliovirus cases. The Afghanistan AFP surveillance network includes 2,843 health facilities and 45,029 community- and health facility–based reporting volunteers. During 2020, the national NPAFP rate was 22 per 100,000 persons aged <15 years in accessible areas and 20 per 100,000 in inaccessible areas (regional range = 12–24) (Table). The percentages of AFP cases with adequate specimens were 95% and 92% in accessible and inaccessible areas, respectively (regional range = 86%–98%).

Environmental surveillance. Poliovirus surveillance in Afghanistan is supplemented by environmental surveillance (ES) conducted through the systematic sampling and virologic testing of sewage at 25 sites in 13 provinces. During 2019, WPV1 was detected in ES specimens from sites in Helmand

[**] The global standard surveillance performance indicator target is ≥80% of AFP cases with adequate stool specimens collected. Adequate stool specimens are defined as two stool specimens of sufficient quality for laboratory analysis, collected ≥24 hours apart, both within 14 days of paralysis onset, and arriving in good condition at a World Health Organization-accredited laboratory with reverse cold chain maintained, without leakage or desiccation, and with proper documentation.

TABLE. Acute flaccid paralysis surveillance performance indicators, reported cases of wild poliovirus and vaccine-derived poliovirus type 2,* and percentage of environmental samples with detection of wild poliovirus type 1, by region and period — Afghanistan, January 2020–November 2021[†]

	AFP surveillance indicators						No. of WPV1 cases reported			No. of cVDPV2 cases reported			No. (%) of ES samples with WPV1 detected[§]		
	No. of AFP cases		NPAFP rate (%)[¶]		% With adequate stool specimens**		2020		2021	2020		2021	2020		2021
Region	2020	2021	2020	2021	2020	2021	Jan–Jun	Jul–Dec	Jan–Nov	Jan–Jun	Jul–Dec	Jan–Nov	Jan–Jun	Jul–Dec	Jan–Nov
All regions	**3,972**	**3,009**	**18**	**17**	**93**	**94**	**34**	**22**	**4**	**54**	**254**	**43**	**22 (11)**	**13 (6)**	**1 (0.3)**
Badakhshan	83	61	12	10	89	93	1	0	0	1	0	0	0 (—)	0(—)	0 (—)
Central	734	658	15	17	98	98	0	0	0	0	17	4	0 (—)	1 (3)	0 (—)
Eastern	543	374	24	20	92	96	2	0	0	51	19	0	2 (2)	2 (3)	0 (—)
Northeastern	429	298	18	15	95	94	0	0	3	0	4	0	0 (—)	1 (20)	0 (—)
Northern	337	255	13	12	91	89	1	0	0	0	7	2	0 (—)	0 (—)	0 (—)
Southeastern	426	283	20	15	95	96	0	6	1	1	33	8	1 (8)	0 (—)	0 (—)
Southern	798	586	21	18	86	89	23	15	0	0	145	12	17 (26)	7 (9)	1 (0.8)
Western	622	494	20	20	93	93	7	1	0	1	29	17	2 (29)	2 (40)	0 (—)

Abbreviations: AFP = acute flaccid paralysis; cVDPV2 = circulating vaccine-derived poliovirus type 2; ES = environmental surveillance; NPAFP = nonpolio acute flaccid paralysis; WPV1 = wild poliovirus type 1.

* cVDPVs are genetically linked VDPV2 isolates for which there is evidence of person-to-person transmission within the community.

[†] Data as of January 11, 2022.

[§] Total number of ES samples by period: January 2020–June 2020 = 208, July 2020–December 2020 = 205, and January 2021–November 2021 = 341. WPV-1–positive ES samples were detected in 2020 in Kabul (central), Nangarhar (eastern), Kunduz (northeastern), Khost (southeastern), and Helmand and Kandahar (southern) provinces, and in 2021 in Helmand (southern) province. Percentages indicate specimens testing positive for WPV1 for the total number of specimens collected for all regions and the specific region during that period.

[¶] Cases per 100,000 persons aged <15 years. The surveillance performance indicator target is ≥2 NPAFP cases per 100,000 persons aged <15 years.

** Surveillance performance indicator target is ≥80% of AFP cases have adequate stool specimens collected. Adequate stool specimens are defined as two stool specimens of sufficient quality for laboratory analysis, collected ≥24 hours apart, both within 14 days of paralysis onset, and arriving in good condition at a World Health Organization-accredited laboratory with reverse cold chain maintained, without leakage or desiccation, and with proper documentation.

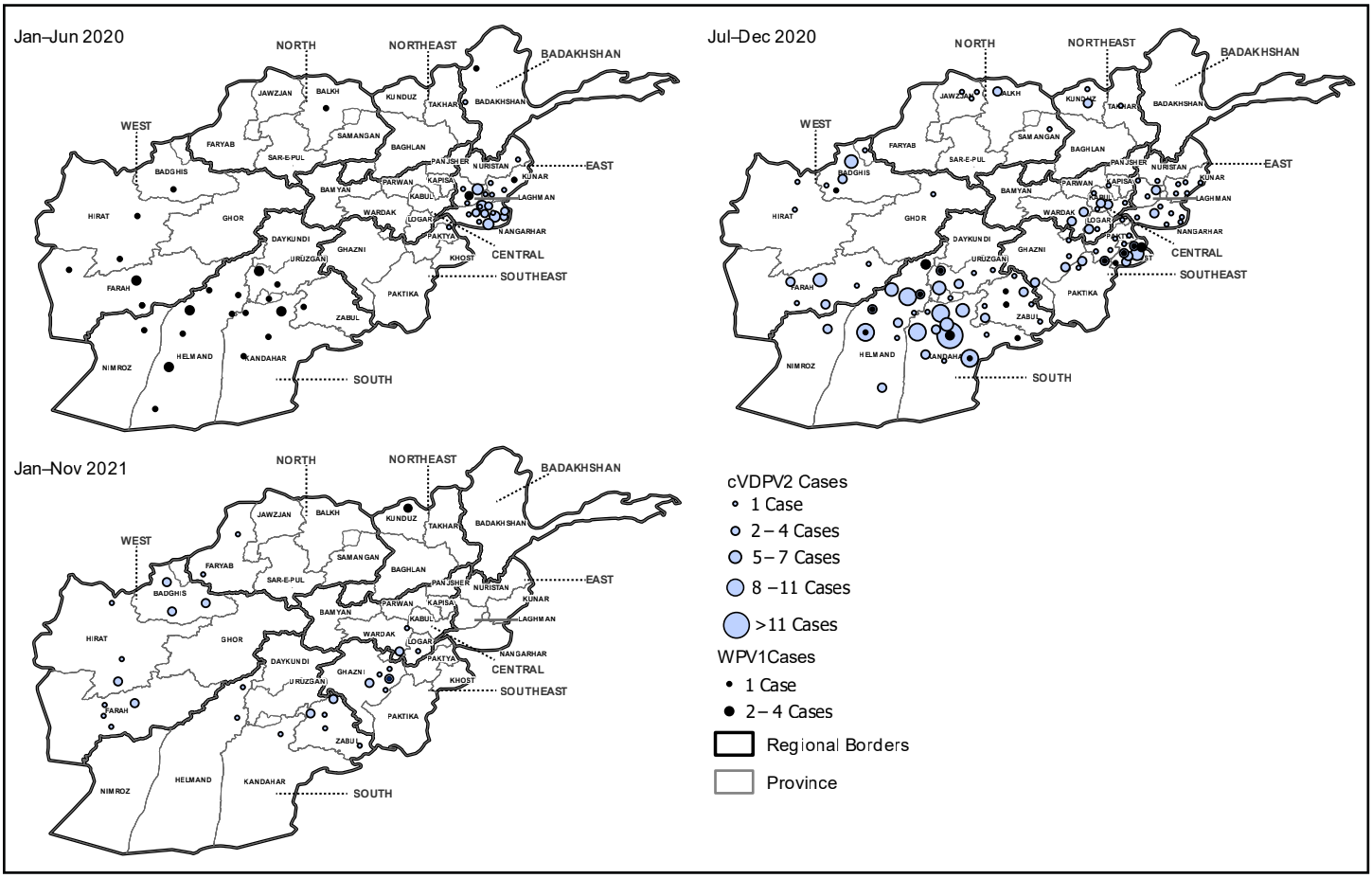
and Kandahar in the southern region and Nangarhar in the eastern region. During 2020, detection of WPV1-postitive ES specimens expanded in geographic scope to include Khost in the southeastern, Kabul in the central, Herat in the western, and Kunduz in the northeastern regions. One WPV1 ES-positive sample was detected during January–November 2021, a 97% decrease compared with 34 detected during the same period in 2020. Regarding cVDPV2[††] isolations, ES specimens in 2020 tested positive from sites in 10 provinces: Helmand and Kandahar southern provinces; Nangarhar, Kunar, and Laghman eastern provinces; Khost and Paktika southeastern provinces; and Kabul in central, Herat in western, and Kunduz in northwestern provinces. During 2021, cVDPV2-positive ES specimens were detected in only six provinces: Helmand, Kandahar, Nangarhar, Kabul, Herat, and Kunduz.

[††] cVDPV2s are genetically linked VDPV2 isolates for which there is evidence of person-to-person transmission in the community.

Epidemiology of Poliovirus Cases and Genomic Sequence Analysis of Poliovirus Isolates

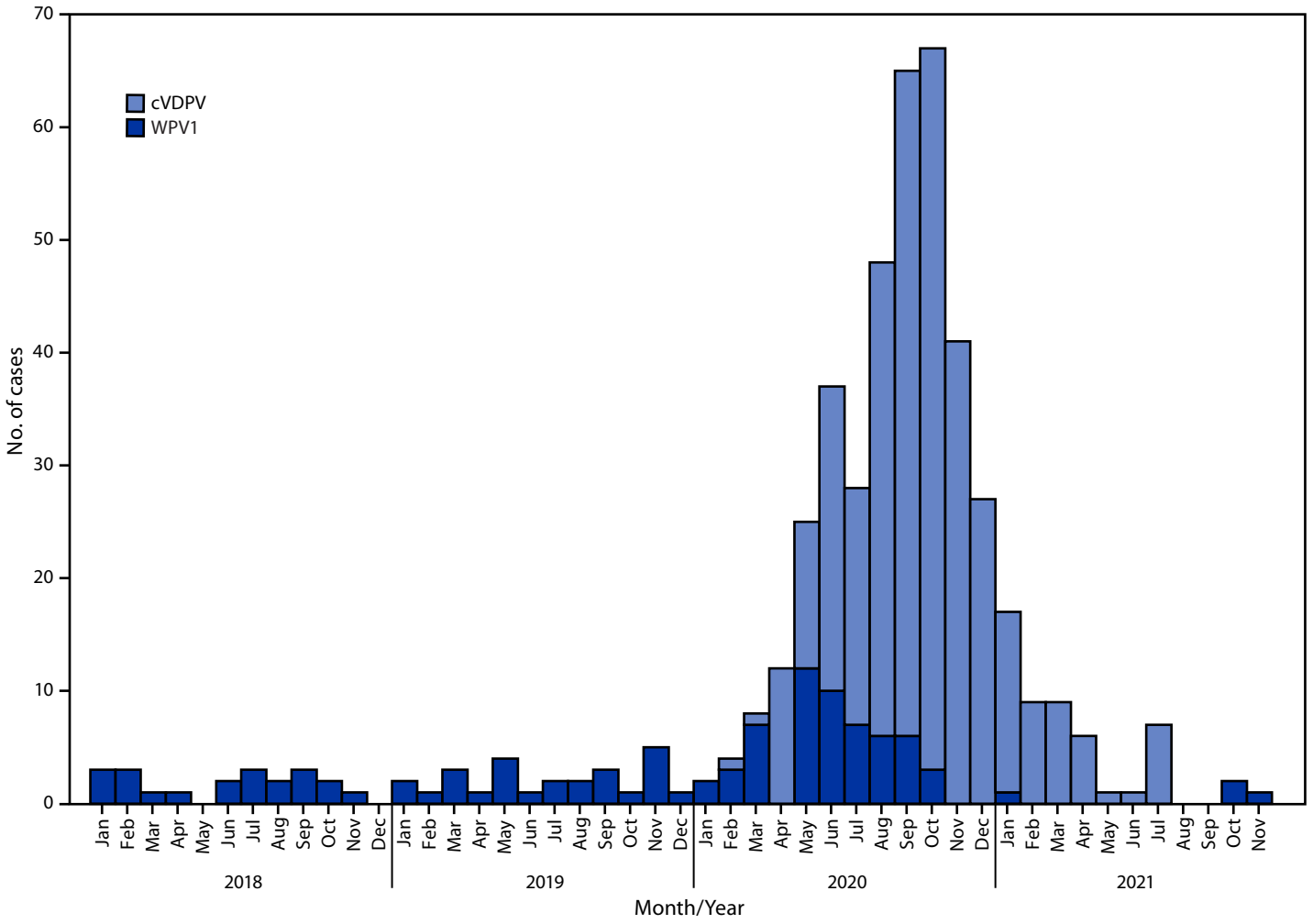
During 2020, WPV1 cases increased in number and geographic distribution compared with 2019: 56 WPV1 cases were reported from 38 districts in 14 provinces in 2020, compared with 29 WPV1 cases reported from 20 districts in 10 provinces in 2019. During January–November 2021 (as of January 11, 2022), only four WPV1 cases were reported (Table) (Figure 1) (Figure 2). Twenty-one (35%) of 60 patients with WPV1 cases reported between January 2020 and November 2021 had never received OPV, 14 (23%) had received 1 or 2 doses, and 24 (40%) had received ≥3 doses; 23 (38%) had

FIGURE 1. Cases of wild poliovirus type 1 and circulating vaccine-derived poliovirus type 2,[*,†] by province and period — Afghanistan, January 2020–November 2021[§]



Abbreviations: cVDPV2 = circulating vaccine-derived poliovirus type 2; WPV1 = wild poliovirus type 1.
* cVDPVs are genetically linked VDPV2 isolates for which there is evidence of person-to-person transmission in the community.
† Total cases by period: January–June 2020 = 34 WPV1 and 54 cVDPV2; July–December 2020 = 22 WPV1 and 254 cVDPV2; and January–November 2021 = 4 WPV1 and 43 cVDPV2.
§ Data as of January 11, 2022.

FIGURE 2. Number of wild poliovirus type 1 cases (n = 60) and circulating vaccine-derived poliovirus type 2* cases, by month of onset of paralysis (n = 351) — Afghanistan, January 2020–November 2021†



Abbreviations: cVDPV2 = circulating vaccine-derived poliovirus type 2; WPV1 = wild poliovirus type 1.
* cVDPVs are genetically linked VDPV2 isolates for which there is evidence of person-to-person transmission in the community.
† Data as of January 11, 2022.

never received OPV through routine immunization but had received ≥1 SIA doses.

Genomic sequence analysis of the VP1 capsid protein of poliovirus isolates provided evidence for multiple episodes of cross-border transmission between Afghanistan and Pakistan during 2018–2021, with sustained local transmission in both countries. During January 2020–November 2021, nine (15%) of 60 WPV1 isolates from AFP patients and nine (25%) of 36 WPV1 ES isolates in Afghanistan had the closest genetic links to WPV1 isolates from Pakistan; the remaining were most closely linked to AFP and ES isolates from within Afghanistan (Table). During the same period, five WPV1 genetic clusters (groups of viruses sharing ≥95% VP1 sequence identity) were detected among AFP cases. Although transmission in the eastern and southern provinces is mostly from distinct genetic clusters, two WPV1 isolates were identified in the south from clusters originally identified in the east. Sixteen orphan WPV1 viruses[§§] were isolated from ES or AFP cases, signaling gaps in AFP surveillance during this period, but similar in percentage to the report for the overlapping period of January 2019–July 2020 (*2*).

During January 2020–November 2021, with importation of cVDPV2 from Pakistan and new emergences seeded after mOPV2 use in Afghanistan (*6*), 351 cVDPV2 cases were reported from 131 districts in 28 provinces; 225 (64%) of those occurred among children aged <36 months. Of the 351 cVDPV2 cases, 225 (64%) were genetically related to

[§§] Orphan viruses are ≥1.5% divergent from their closest genetic match (i.e., ≤98.5% identity).

Summary

What is already known about this topic?

Wild poliovirus circulation continues only in Afghanistan and Pakistan.

What is added by this report?

Despite an increase in the numbers of inaccessible children in Afghanistan in 2021 and disruption of polio eradication activities caused by the COVID-19 pandemic and abrupt changes in government, the number of wild poliovirus type 1 cases and percentage of positive sewage samples have markedly decreased by 93% and 97%, respectively, from the same period in 2020.

What are the implications for public health practice?

Although challenges remain, prospects for vaccination of previously inaccessible children along with sustained, robust polio eradication efforts in Afghanistan could result in substantial progress toward eradication during 2022–2023.

the PAK-GB-1 emergence first detected in Gilgit-Baltistan, Pakistan, 127 (36%) were related to the AFG-NGR-1 emergence first detected in Afghanistan's Nangarhar province, and four (1%) were related to the cVDPV2 AFG-HLD-1 emergence first detected in Helmand province (*7*).

Discussion

Afghanistan and Pakistan remain the only countries with endemic WPV1 transmission; substantive progress in these countries represents progress toward global polio eradication. Although the overall number of WPV1 cases in Afghanistan was high in 2020, there was a marked decrease in cases from the first to the second half of the year and case numbers declined further during 2021. Although the number of inaccessible, and therefore unvaccinated, children markedly increased in 2021, WPV1 transmission decreased, possibly because of decreased population mixing and movement during the early phases of the COVID-19 pandemic and rapid return to quality SIAs.

The findings in this report are subject to at least two limitations. First, for the November 2021 SIA, the accuracy of the reported coverage data and LQAS surveys data is uncertain because many of these are reported by inexperienced officers selected by the de facto government without other oversight. Second, the quality of AFP surveillance likely suffered since the beginning of the COVID-19 pandemic and might also remain reduced from potential disruptions since the transition in government; however, a decrease in the proportion of WPV1-positive ES isolates in 2021 to date suggests that the current AFP surveillance data are consistent with decreased transmission.

In addition to the four WPV1 cases reported from Afghanistan during 2021, as of January 11, 2022, only one WPV1 case has been reported from Pakistan, further evidence for decreased transmission within the shared epidemiologic block. Because the de facto government of Afghanistan has resumed intensive OPV vaccination, the number of inaccessible children should be greatly decreased. House-to-house polio vaccination resumed in portions of the country with the involvement of female frontline workers in November 2021, and a second campaign took place in December 2021 synchronized with Pakistan. If future efforts are robust, sustained, and implemented countrywide, substantial progress toward interrupting WPV1 transmission in Afghanistan is possible during 2022–2023.

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Use of the Janssen (Johnson & Johnson) COVID-19 Vaccine: Updated Interim Recommendations from the Advisory Committee on Immunization Practices — United States, December 2021

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On February 27, 2021, the Food and Drug Administration (FDA) issued an Emergency Use Authorization (EUA) for the adenovirus-vectored COVID-19 vaccine (Janssen Biotech, Inc., a Janssen Pharmaceutical company, Johnson & Johnson), and on February 28, 2021, the Advisory Committee on Immunization Practices (ACIP) issued an interim recommendation for its use as a single-dose primary vaccination in persons aged ≥18 years (*1*,*2*). On April 13, 2021, CDC and FDA recommended a pause in the use of Janssen COVID-19 vaccine after reports of thrombosis with thrombocytopenia syndrome (TTS), a rare condition characterized by low platelets and thrombosis, including at unusual sites such as the cerebral venous sinus (cerebral venous sinus thrombosis [CVST]), after receipt of the vaccine.* ACIP rapidly convened two emergency meetings to review reported cases of TTS, and 10 days after the pause commenced, ACIP reaffirmed its interim recommendation for use of the Janssen COVID-19 vaccine in persons aged ≥18 years, but included a warning regarding rare clotting events after vaccination, primarily among women aged 18–49 years (*3*). In July, after review of an updated benefit-risk assessment accounting for risks of Guillain-Barré syndrome (GBS) and TTS, ACIP concluded that benefits of vaccination with Janssen COVID-19 vaccine outweighed risks. Through ongoing safety surveillance and review of reports from the Vaccine Adverse Event Reporting System (VAERS), additional cases of TTS after receipt of Janssen COVID-19 vaccine, including deaths, were identified. On December 16, 2021, ACIP held an emergency meeting to review updated data on TTS and an updated benefit-risk assessment. At that meeting, ACIP made a recommendation for preferential use of mRNA COVID-19 vaccines over the Janssen COVID-19 vaccine, including both primary and booster doses administered to prevent COVID-19, for all persons aged ≥18 years. The Janssen COVID-19 vaccine may be considered in some situations, including for persons with a contraindication to receipt of mRNA COVID-19 vaccines.

Since June 2020, ACIP has convened 23 public meetings to review data on the epidemiology of COVID-19 and the use of COVID-19 vaccines, including nine during which Janssen COVID-19 vaccine-related data were reviewed. The ACIP COVID-19 Vaccines Work Group, comprising experts in infectious diseases, vaccinology, vaccine safety, public health, and ethics, has held weekly meetings to review COVID-19 surveillance data, evidence for vaccine efficacy and safety, and implementation considerations for COVID-19 vaccines. In addition, the COVID-19 Vaccines Safety Technical Work Group (VaST), consisting of independent vaccine safety experts and established to provide expert consultation on COVID-19 vaccine safety issues, has reviewed safety data from the COVID-19 vaccination program during weekly meetings. After TTS was first identified in the United States in April 2021, a benefit-risk assessment for the use of the Janssen COVID-19 vaccine was presented to ACIP using an adapted Evidence to Recommendations (EtR) framework.† In the setting of limited COVID-19 vaccine supply in the United States at that time, ACIP reaffirmed its interim recommendations for the use of the Janssen COVID-19 vaccine in persons aged ≥18 years under FDA's EUA, which was updated to include a warning that rare clotting events might occur after vaccination, primarily among women aged 18–49 years (*3*). Updates to the benefit-risk assessment were also reviewed by ACIP in June 2021, after an increased risk for myocarditis, particularly in males aged 12–29 years, was observed after receipt of mRNA COVID-19 vaccines; and again, in July 2021, after an increased number of cases of GBS were identified following administration of Janssen COVID-19 vaccine (*4*,*5*). After each review, ACIP determined that the benefits of COVID-19 vaccination in preventing COVID-19 morbidity and associated mortality outweighed the risks for these rare, but serious adverse events; however, the balance of benefits and risks varied by age and sex. Ongoing postauthorization safety surveillance identified additional TTS cases and associated deaths after Janssen COVID-19 vaccination, and updated safety data were reviewed by VaST in December 2021. The COVID-19 Vaccines Work Group also reviewed an updated benefit-risk assessment of

* https://emergency.cdc.gov/han/2021/han00442.asp

† https://www.cdc.gov/vaccines/acip/recs/grade/downloads/acip-evidence-recs-framework.pdf

COVID-19 vaccines in the setting of new safety findings and sufficient COVID-19 vaccine supply in the United States. In addition, FDA updated the EUA fact sheets with additional TTS data in December 2021.[§] A summary of the data reviewed and discussions from both VaST and the ACIP COVID-19 Vaccines Work Group were presented to ACIP during their emergency meeting on December 16, 2021.

TTS is a rare but potentially life-threatening syndrome associated with adenoviral-vectored COVID-19 vaccination that involves acute venous or arterial thrombosis and new onset thrombocytopenia (*6*). Based on the distinctive clinical and laboratory features of the syndrome, epidemiologic clustering in time after receipt of adenoviral-vectored COVID-19 vaccines, and plausible pathogenic mechanisms, the evidence supports a causal relationship between TTS and the Janssen COVID-19 vaccine (*6*). Potential adverse events, including cases of TTS, are reported to VAERS (*7*), the national passive vaccine safety monitoring system. Physicians at CDC and FDA confirmed whether each report met the CDC case definition for TTS[¶] through medical record review, with input from Clinical Immunization Safety Assessment Project investigators,[**] including hematologists. A detailed review of TTS cases with vaccination occurring before August 31, 2021, including a description of rates, patient characteristics, and clinical course, was presented to ACIP and used in the benefit-risk analysis (*8*).

Overall, 54 cases of TTS were identified in persons who received the Janssen COVID-19 vaccine during March 2–August 31, 2021; 37 (69%) patients were women, 45 (83%) were White non-Hispanic persons, and the median age was 44.5 years (range = 18–70 years). Most patients (39; 72%) received the Janssen COVID-19 vaccine before the pause on April 13, 2021; 15 (28%) cases occurred in persons who were vaccinated after the pause was lifted on April 23, 2021. Whereas most (13 of 15; 87%) patients with TTS identified through April 2021 were women aged 18–49 years, approximately one half (26 of 54; 48%) of all patients with TTS after receipt of Janssen COVID-19 vaccine identified through August 2021 were women aged 18–49 years.

Approximately 14.1 million doses of the Janssen COVID-19 vaccine were administered in the United States through August 31, 2021, resulting in an overall TTS reporting rate of 3.83 cases per million doses administered. TTS rates were highest among women aged 30–39 years (10.6 per million doses) and 40–49 years (9.0 per million doses) (Table 1). Among persons who received primary Janssen COVID-19 vaccination by August 31, 2021, eight TTS deaths occurred[††] (*8*). Six deaths occurred in women, and two in men. The overall reporting rate for TTS deaths was 0.6 per million Janssen COVID-19 vaccine doses administered; the highest rates were among women aged 30–39 years (1.9 per million doses) and 40–49 years (1.8 per million doses). Among the patients who died with TTS, six had a diagnosis of CVST, and two had clinical characteristics compatible with CVST; all eight had presenting features associated with poor short-term prognosis (e.g., cerebral hemorrhage, intracranial edema, and mass effect) (*9*). Although public health messaging concerning the risk associated with the Janssen COVID-19 vaccine and clinical guidance for management and treatment of TTS[§§] was provided in April 2021, the proportion of deaths among reported TTS cases did not decline (five deaths among 39 [13%] TTS patients vaccinated before the pause and three deaths among 15 patients (20%) vaccinated after the pause), likely due to the rapidity of progression of severe CVST.

ACIP reviewed an updated benefit-risk assessment of COVID-19 vaccines to determine whether the interim recommendations for the use of the Janssen COVID-19 vaccine in the United States should be updated. This assessment considered 1) the incidence of TTS and case characteristics, 2) current COVID-19 epidemiology, 3) an individual benefit-risk analysis to quantify COVID-19 hospitalizations prevented by Janssen COVID-19 vaccination in the United States and possible vaccine-associated adverse events, 4) data from jurisdictional COVID-19 vaccination programs describing use of Janssen COVID-19 vaccine, and 5) administration of Janssen COVID-19 vaccine by age and sex. ACIP reviewed the benefits and risks of Janssen COVID-19 vaccination compared with no COVID-19 vaccination. Given the current widespread availability of mRNA COVID-19 vaccines, the analysis also included the differential benefits and risks of the Janssen COVID-19 vaccine compared with mRNA COVID-19 vaccines, using methods similar to those used previously.[¶¶]

The benefits of Janssen and mRNA COVID-19 vaccination over 180 days per million fully vaccinated persons[***]

[§] https://www.fda.gov/emergency-preparedness-and-response/coronavirus-disease-2019-covid-19/janssen-covid-19-vaccine#additional

[¶] CDC case definition for TTS. Tier 1: thrombosis in an unusual location for a thrombus (i.e., cerebral vein, visceral artery or vein, extremity artery, central artery or vein) and new onset thrombocytopenia (i.e., platelet count <150,000 per microliter [μL]) occurring any time after receipt of a COVID-19 vaccine. Tier 2: new-onset thrombocytopenia, thrombosis in an extremity vein or pulmonary artery in the absence of thrombosis at a Tier 1 location, and a positive antiplatelet factor (PF)4 antibody enzyme-linked immunosorbent assay test result or functional heparin-induced thrombocytopenia (HIT) platelet test occurring any time after receipt of a COVID-19 vaccine.

[**] https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/cisa/index.html

[††] An additional death was reported in a woman aged 18–29 years who had received the Janssen COVID-19 vaccine after August 31, 2021.

[§§] https://www.hematology.org/covid-19/vaccine-induced-immune-thrombotic-thrombocytopenia

[¶¶] https://www.cdc.gov/vaccines/covid-19/info-by-product/janssen/risk-benefit-analysis.html

[***] https://www.cdc.gov/coronavirus/2019-ncov/vaccines/fully-vaccinated.html

TABLE 1. Number of cases and deaths attributed to thrombosis with thrombocytopenia syndrome reported to the Vaccine Adverse Event Reporting System following administration of Janssen (Johnson & Johnson) COVID-19 vaccine, total Janssen COVID-19 vaccine doses administered, and reporting rate per million Janssen COVID-19 vaccine doses administered, by sex and age group — United States, March–August 2021

Sex/Age group, yrs	No. of TTS cases	No. of TTS deaths*	No. of Janssen COVID-19 vaccine doses administered	No. of TTS cases per million Janssen COVID-19 vaccine doses administered	No. of TTS deaths per million Janssen COVID-19 vaccine doses administered
Women					
18–49	26	4	3,235,530	8.0	1.2
18–29	5	0	1,089,649	4.6	0
30–39	11	2	1,037,386	10.6	1.9
40–49	10	2	1,108,495	9.0	1.8
50–64	9	2	2,002,984	4.5	1.0
≥65	2	0	1,096,923	1.8	0
Men					
18–49	12	2	4,402,102	2.7	0.5
18–29	3	1	1,565,212	1.9	0.6
30–39	3	0	1,443,900	2.1	0
40–49	6	1	1,392,990	4.3	0.7
50–64	5	0	2,338,263	2.1	0
≥65	0	0	1,004,285	0	0
Total	**54**	**8**	**14,080,087**	**3.8**	**0.6**

Abbreviation: TTS = thrombosis with thrombocytopenia syndrome.
* An additional death was reported in a woman aged 18–29 years who received the Janssen COVID-19 vaccine after August 31, 2021.

aged ≥18 years were assessed, including 1) COVID-19 hospitalizations prevented, based on rates during the week ending November 13, 2021[†††] and 2) age- and vaccine-specific vaccine effectiveness estimates from the Influenza and Other Viruses in the Acutely Ill (IVY) Network, a hospital-based platform that monitors effectiveness of influenza and COVID-19 vaccines.[§§§] The risks assessed for Janssen COVID-19 vaccination were 1) updated TTS rates through August 31, 2021 and 2) GBS rates through June 30, 2021, reported previously to ACIP[¶¶¶] (*5*). The risks for mRNA COVID-19 vaccination were based on myocarditis rates through October 6, 2021, previously reported to ACIP.[****] Each benefit-risk assessment was stratified by sex and age group (18–49, 50–64, and ≥65 years). An additional aspect of the benefit-risk assessment included a review of the severity of vaccine-associated adverse events, including myocarditis, TTS, and GBS. Among 47 patients aged 12–29 years with myocarditis after mRNA COVID-19 vaccination and health care provider follow-up ≥3 months after diagnosis, preliminary data showed that 91% were deemed by their health care provider to have fully or probably recovered; further follow-up is ongoing.[††††] Among fully reviewed deaths reported to VAERS, there have been no confirmed deaths due to myocarditis after mRNA COVID-19 vaccination. Among 130 patients with preliminary reports of GBS after Janssen COVID-19 vaccination through July 24, 2021, one (0.8%) patient died, and 18 (14%) had respiratory compromise or failure (*10*). Among 54 TTS cases after Janssen COVID-19 vaccination, eight (15%) patients died, and an additional nine (17%) required discharge to postacute care or a rehabilitation facility (*8*). The estimated benefits of the Janssen COVID-19 vaccine outweighed the risks when compared with no vaccine for all persons aged ≥18 years (Table 2). However, when compared with the benefit-risk balance for mRNA COVID-19 vaccines, the Janssen COVID-19 vaccine prevented fewer COVID-19 hospitalizations. In addition, potentially more severe, long-term health impacts from TTS and GBS after Janssen COVID-19 vaccination were noted, compared with the apparently less severe myocarditis-associated outcomes after receipt of mRNA COVID-19 vaccines.

ACIP also reviewed population-level data, including current use of the Janssen COVID-19 vaccine. As of December 15, 2021,

[†††] https://gis.cdc.gov/grasp/COVIDNet/COVID19_3.html. Data were used for the most recent week not subject to reporting delays before the ACIP meeting.

[§§§] Vaccine effectiveness (VE) estimates from https://www.cdc.gov/mmwr/volumes/70/wr/mm7038e1.htm. Estimates are adjusted for continuous age in years, calendar date (biweekly), U.S. Department of Health and Human Services region, sex, and race/ethnicity. A combined VE estimate for both mRNA COVID-19 vaccines was used in the benefit-risk analysis: 18–49 years = 92%; 50–64 years = 92%; ≥65 years = 88%. VE estimates for Janssen COVID-19 vaccine: 18–49 years = 73%; 50–64 years = 69%; ≥65 years = 76%.

[¶¶¶] Presumptive reports of GBS were not verified by medical record review. An interim analysis in the Vaccine Safety Datalink also found the risk for GBS (confirmed by medical record review) after Janssen COVID-19 vaccine was elevated during the 1–42 days after vaccination. https://www.medrxiv.org/content/10.1101/2021.12.03.21266419v1

[****] https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-10-20-21/07-COVID-Su-508.pdf

[††††] https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2021-11-2-3/04-COVID-Oster-508.pdf

TABLE 2. Estimated COVID-19 hospitalizations prevented during 180 days after administration of 1-dose Janssen (Johnson & Johnson) COVID-19 vaccine and 2-dose mRNA COVID-19 vaccine, number of cases of Guillain-Barré syndrome and thrombosis with thrombocytopenia syndrome cases expected per million Janssen vaccine doses administered and number of myocarditis cases expected per million second mRNA vaccine doses administered, by sex and age group — United States, 2021

	Benefits	Harms	
Vaccine/Sex/Age group, yrs	No. of COVID-19 hospitalizations prevented*	No. of adverse events*	
Janssen COVID-19 vaccine		No. of GBS cases	No. of TTS cases
Women			
18–49	3,729	5	8
50–64	11,181	7	5
≥65	24,149	9	2
Men			
18–49	2,421	6	3
50–64	12,189	16	2
≥65	32,801	8	0
mRNA COVID-19 vaccines (Pfizer-BioNTech or Moderna)	**No. of COVID-19 hospitalizations prevented***	**No. of myocarditis cases**	
Women			
18–49	4,700	2	
50–64	14,908	1	
≥65	27,962	0	
Men			
18–49	3,052	13	
50–64	16,251	1	
≥65	37,980	1	

Abbreviations: GBS = Guillain-Barré syndrome; TTS = thrombosis with thrombocytopenia syndrome.
* Per million doses administered

among approximately 488 million COVID-19 primary series doses and 56 million COVID-19 booster doses administered, only 17 million (3.5%) and 800,000 (1.6%), respectively, were Janssen COVID-19 vaccines.[§§§§] According to 46 jurisdictional immunization programs that voluntarily completed an online form shared with jurisdictions during December 12–15, 2021, the Janssen COVID-19 vaccine was offered widely and was available among other COVID-19 vaccines to nearly all populations; however, in some transitional settings (e.g., correctional facilities, homeless shelters, or airports), it might have been the only vaccine offered.

Based on a comprehensive review of existing data, ACIP concluded that 1) because of both higher vaccine effectiveness of mRNA COVID-19 vaccines and more serious rare safety issues associated with the Janssen vaccine, the benefit-risk balance for mRNA COVID-19 vaccines is more favorable than that for Janssen COVID-19 vaccine, 2) a preferential recommendation for mRNA COVID-19 vaccines over the Janssen COVID-19 vaccine is warranted, 3) the benefits of Janssen COVID-19 vaccine continue to outweigh the risks of remaining unvaccinated, and 4) if Janssen COVID-19 vaccine is the only vaccine offered to some harder-to-reach populations, an inequitable distribution of risk for TTS and GBS might occur. These considerations were in the context of wide U.S. availability of mRNA COVID-19 vaccines. ACIP voted unanimously (15 to zero) for a recommendation for preferential use of mRNA COVID-19 vaccines over the Janssen COVID-19 vaccine for the prevention of COVID-19 for all persons aged ≥18 years.

ACIP members discussed concerns about the clinical severity of the very rare risk for TTS and GBS after Janssen COVID-19 vaccination. However, they highlighted that there might be some situations where Janssen COVID-19 vaccine could be offered, including to persons with a contraindication to mRNA COVID-19 vaccines (e.g., severe allergic reaction after a previous dose or to a component of an mRNA COVID-19 vaccine). In such situations, providing information concerning the risk for these rare but serious adverse events after Janssen COVID-19 vaccination will be critical to ensuring that vaccine recipients are making an informed decision. In addition, vaccine providers should be encouraged to start a 2-dose mRNA COVID-19 vaccine primary series, even if there is uncertainty about when or in what setting the patient will receive the second dose. Prioritizing availability of mRNA vaccines for use in hard-to-reach populations or in transitional settings and continued expansion of infrastructures affording mRNA vaccine access will be critical to ensuring equity in the opportunity to receive a preferentially recommended mRNA vaccine. Additional detailed clinical considerations for use of COVID-19 vaccines are available at https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html.

CDC has updated patient education and communication materials reflecting the preferential recommendation for mRNA COVID-19 vaccines[¶¶¶¶]; timely updates of these materials are important to ensure that vaccine providers are aware of updated COVID-19 vaccine recommendations, that Janssen COVID-19 vaccine recipients are aware of these risks, and that they know to seek care if they experience concerning symptoms. CDC and FDA will continue to closely monitor reports of serious adverse events after both mRNA and Janssen COVID-19 vaccines and will present any additional data to ACIP for consideration. As demonstrated at the December 16, 2021, ACIP meeting, the benefit-risk analyses

[§§§§] https://covid.cdc.gov/covid-data-tracker/#vaccinations_vacc-people-onedose-pop-5yr

[¶¶¶¶] https://www.cdc.gov/vaccines/covid-19/info-by-product/janssen/index.html

Summary

What is already known about this topic?

Cases of thrombosis with thrombocytopenia syndrome and Guillain-Barré syndrome have been reported after receipt of Janssen COVID-19 vaccine.

What is added by this report?

On December 16, 2021, after reviewing updated vaccine effectiveness and safety data, the Advisory Committee on Immunization Practices made a preferential recommendation for the use of mRNA COVID-19 vaccines over the Janssen adenoviral-vectored COVID-19 vaccine in all persons aged ≥18 years in the United States.

What are the implications for public health practice?

Pfizer-BioNTech or Moderna mRNA COVID-19 vaccines are preferred over the Janssen COVID-19 vaccine for primary and booster vaccination. The Janssen COVID-19 vaccine may be considered in some situations, including for persons with a contraindication to receipt of mRNA COVID-19 vaccines.

and ACIP recommendations for COVID-19 vaccines can be updated to reflect additional information as the COVID-19 pandemic evolves. All persons aged ≥5 years are recommended to receive a COVID-19 primary series vaccination with a preferred mRNA COVID-19 vaccine, and an mRNA COVID-19 booster dose, if eligible, particularly given the recent emergence of the highly transmissible B.1.1.529 (Omicron) variant.

Reporting of Vaccine Adverse Events

FDA requires that immunization providers report vaccine administration errors, serious adverse events, cases of multisystem inflammatory syndrome, and cases of COVID-19 that result in hospitalization or death after administration of COVID-19 vaccine under an EUA.***** Adverse events that occur after receipt of any COVID-19 vaccine should be reported to VAERS (https://vaers.hhs.gov or 1-800-822-7967). Any person who administers or receives a COVID-19 vaccine is encouraged to report any clinically noteworthy adverse event, whether or not it is clear that a vaccine caused the adverse event. In addition, CDC has developed a new, voluntary smartphone-based online tool (v-safe) that uses text messaging and online surveys to provide near real-time health check-ins after receipt of a COVID-19 vaccine (https://www.cdc.gov/vsafe).

***** https://vaers.hhs.gov/reportevent.html

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Morbidity and Mortality Weekly Report

Racial and Ethnic Disparities in Receipt of Medications for Treatment of COVID-19 — United States, March 2020–August 2021

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On January 14, 2022, this report was posted as an MMWR *Early Release on the* MMWR *website (https://www.cdc.gov/mmwr).*

The COVID-19 pandemic has magnified longstanding health care and social inequities, resulting in disproportionately high COVID-19–associated illness and death among members of racial and ethnic minority groups (*1*). Equitable use of effective medications (*2*) could reduce disparities in these severe outcomes (*3*). Monoclonal antibody (mAb) therapies against SARS-CoV-2, the virus that causes COVID-19, initially received Emergency Use Authorization (EUA) from the Food and Drug Administration (FDA) in November 2020. mAbs are typically administered in an outpatient setting via intravenous infusion or subcutaneous injection and can prevent progression of COVID-19 if given after a positive SARS-CoV-2 test result or for postexposure prophylaxis in patients at high risk for severe illness.† Dexamethasone, a commonly used steroid, and remdesivir, an antiviral drug that received EUA from FDA in May 2020, are used in inpatient settings and help prevent COVID-19 progression§ (*2*). No large-scale studies have yet examined the use of mAb by race and ethnicity. Using COVID-19 patient electronic health record data from 41 U.S. health care systems that participated in the PCORnet, the National Patient-Centered Clinical Research Network,¶ this study assessed receipt of medications for COVID-19 treatment by race (White, Black, Asian, and Other races [including American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, and multiple or Other races]) and ethnicity (Hispanic or non-Hispanic). Relative disparities in mAb** treatment among all patients†† (805,276) with a positive SARS-CoV-2 test result and in dexamethasone and remdesivir treatment among inpatients§§ (120,204) with a positive SARS-CoV-2 test result were calculated. Among all patients with positive SARS-CoV-2 test results, the overall use of mAb was infrequent, with mean monthly use at 4% or less for all racial and ethnic groups. Hispanic patients received mAb 58% less often than did non-Hispanic patients, and Black, Asian, or Other race patients received mAb 22%, 48%, and 47% less often, respectively, than did White patients during November 2020–August 2021. Among inpatients, disparities were different and of lesser magnitude: Hispanic inpatients received dexamethasone 6% less often than did non-Hispanic inpatients, and Black inpatients received remdesivir 9% more often than did White inpatients. Vaccines and preventive measures are the best defense against infection; use of COVID-19 medications postexposure or postinfection can reduce morbidity and mortality and relieve strain on hospitals but are not a substitute for COVID-19 vaccination. Public health policies and programs centered around the specific needs of communities can promote health equity (*4*). Equitable receipt of outpatient treatments, such as mAb and antiviral medications, and implementation of prevention practices are essential to reducing existing racial and ethnic inequities in severe COVID-19–associated illness and death.

* These authors contributed equally to this report.

† Fact sheets for healthcare providers for FDA emergency use authorization are available from https://www.fda.gov/media/145611/download for REGEN-COV (casirivimab and imdevimab) and https://www.fda.gov/media/145802/download for bamlanivimab and etesevimab. The SARS-CoV-2 B.1.1.529 (Omicron) variant is not neutralized by bamlanivimab and etesevimab or casirivimab and imdevimab, the mAb-based COVID-19 treatments that were most frequently prescribed before the emergence of Omicron.

§ https://www.covid19treatmentguidelines.nih.gov/management/clinical-management/

¶ PCORnet is a national network-of-networks developed to conduct patient-centered outcomes research. The PCORnet infrastructure supports large-scale studies using its distributed data network. https://doi.org/10.1016/j.jclinepi.2020.09.036

** mAbs included in this study include bamlanivimab, bamlanivimab and etesevimab, casirivimab, and imdevimab, and unspecified monoclonal antibodies. Medications are prescribed or administered in the 14 days before or after the index event.

†† All patients include 78.8% outpatient, 10.9% inpatient, and 10.3% with no associated care setting for mAbs. Care setting was designated with the test.

§§ Care setting was classified as the highest care setting within 16 days of a positive test result but does not necessarily reflect the care setting in which medications were provided. Patients initially tested in the outpatient setting would be assigned to the inpatient setting if they were admitted within 16 days of receipt of a positive test result.

The PCORnet-distributed data infrastructure was queried,[¶¶] and 41 sites[***] returned data on monthly receipt of medications for COVID-19 treatment during March 2020–August 2021. The monthly percentage of patients with a positive SARS-CoV-2 test result who received mAb (November 2020–August 2021) and of inpatients with a SARS-CoV-2 positive test result who received dexamethasone or remdesivir (March 2020–August 2021) was calculated separately by race and by ethnicity (as aggregated in PCORnet) for adults aged ≥20 years. Differences in treatment by race and ethnicity were assessed in two ways. First, pairwise Wilcoxon signed rank tests, with p-values indicated as p_w, were used to assess whether treatment receipt differed systematically over time (systematic temporal differences) by race or ethnicity. Second, relative monthly treatment disparities were calculated as the difference in percentage of patients treated between racial or ethnic minority (Black, Asian, Other for race; Hispanic ethnicity) and majority (White; non-Hispanic) groups divided by the percentage treated in the majority groups for each month.[†††] The grand means (means of relative monthly treatment disparities) were calculated, and t-tests for statistical difference from zero, with p-values indicated as p_t, were used to assess presence of overall relative treatment disparities. Results were considered statistically significant for p-values <0.05. GraphPad Prism software (version 9.3.0; GraphPad Software, Inc) was used for analyses and visualization. This activity was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.[§§§]

During March 2020–August 2021, a total of 5,918,199 patients in PCORnet health care systems were tested[¶¶¶] for SARS-CoV-2, and 805,276 (13.6%) test results were positive (Table 1), representing approximately 3.0% of all positive results reported to CDC (Supplementary Table, https://stacks.cdc.gov/view/cdc/113252). These patients are similar demographically to those included in CDC case data by age, sex, race, and ethnicity. Geographically, patients in the Census Pacific division are underrepresented whereas those in the Mountain division are overrepresented. Among patients with a positive test result, 2.9% were Asian, 15.7% Black, 61.2% White, and 10.9% Other race; 18.6% were Hispanic and 71.7% were non-Hispanic ethnicity (Table 1). Compared with all persons with a positive SARS-CoV-2 test result, a higher proportion of patients with high-risk comorbidities[****] were treated with mAb. Critical care[††††] was required by 3.4% of all persons with positive test results compared with 1.8% of those treated with mAb.

Mean monthly mAb use among all patients with positive SARS-CoV-2 test results who were White, Black, Asian, or Other race was 4.0%, 2.8%, 2.2%, and 2.2%, respectively; among patients of Hispanic or non-Hispanic ethnicity, mAb use was 1.8% and 4.0%, respectively. Patients who were Black, Asian, or Other race received mAb 22.4%, 48.3%, and 46.5%, respectively, less often than did White patients (Table 2); systematic temporal differences in mAb receipt were observed by race (all $p_w<0.01$) (Figure). SARS-CoV-2 positive patients of Hispanic ethnicity received mAb 57.7% less often ($p_t<0.001$) than did non-Hispanic patients; systematic temporal differences in mAb receipt were observed by ethnicity ($p_w = 0.002$).

Mean monthly dexamethasone use among inpatients who were White, Black, Asian, or Other race was 35.8%, 33.8%, 31.4%, and 34.2%, respectively; among patients of Hispanic or non-Hispanic ethnicity, dexamethasone use was 32.5% and 35.4%, respectively. Relative disparities in dexamethasone receipt by race were not statistically significant (Table 2); however, small but systematic temporal differences in dexamethasone receipt were observed among White inpatients and Black and Asian inpatients (both $p_w<0.05$) (Supplementary Figure, https://stacks.cdc.gov/view/cdc/113252). Hispanic inpatients were treated with dexamethasone 6.2% less often than were non-Hispanic inpatients and systematic temporal treatment differences were also observed ($p_w = 0.005$).

¶¶ A query is a single statistical SAS package that runs at sites to generate the data required. This study used a modular program that generated aggregate data at the site level and combined all results returned to the coordinating center, resulting in a single aggregate report on data across all responding sites.

*** Forty-one sites include Duke University, Medical University of South Carolina, University of North Carolina, Vanderbilt University Medical Center, Wake Forest Baptist Health, Allina Health, Intermountain Healthcare, Medical College of Wisconsin, University of Iowa Healthcare, University of Kansas, University of Nebraska, University of Texas SW Medical Center, University of Utah, University Medical Center New Orleans, Children's Hospital Colorado, Children's Hospital of Philadelphia, Cincinnati Children's Hospital, Nationwide Children's Hospital, Nemours Children's Hospital, Seattle Children's Hospital, St. Louis Children's Hospital, Columbia, Montefiore, Mount Sinai Health System, New York University Langone Medical Center, Weill Cornell Medicine, Lurie Children's Hospital, Northwestern University, Fenway Health, Health Choice Network, OCHIN, Inc, Johns Hopkins University, Ohio State University, Penn State College of Medicine and Penn State Health Milton S. Hershey Medical Center, Temple University, University of Michigan, University of Pittsburgh Medical Center, AdventHealth, Orlando Health System, University of Florida Health, and University of Miami. These sites represent academic and community hospitals; are located across all 50 states, Washington, D.C., Puerto Rico, U.S. Virgin Islands, U.S. Armed forces, and Guam; serve patients who are self-pay, public or privately insured; and total 3.0% of COVID-19 cases (as compared with CDC case surveillance.)

††† https://pubmed.ncbi.nlm.nih.gov/16032956/

§§§ 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.

¶¶¶ Testing was by polymerase chain reaction or antigen test; a positive, detected, or presumptive positive result was considered to be a positive test.

**** High-risk criteria defined by the FDA include age ≥65 years, obesity, pregnancy, chronic kidney disease, diabetes, immunosuppression, cardiovascular disease, and lung disease, along with other underlying conditions that are not explicitly listed in the EUAs for these treatments.

†††† Critical care services are identified by *International Classification of Diseases, Tenth Revision* critical care codes (99291 and 99292) for the evaluation and management of the critically ill or critically injured patient.

TABLE 1. Demographic and medical risk characteristics of patients with positive SARS-CoV-2 test results, by clinical setting and medications received — 41 health care systems in the National Patient-Centered Clinical Research Network, United States, March 2020–August 2021

Characteristic	No. (%)*				
	All patients with positive SARS-CoV-2 test result	Patients receiving monoclonal antibodies	Inpatients with positive SARS-CoV-2 test result	Patients receiving dexamethasone	Patients receiving remdesivir
No. of unique patients	805,276	12,539	120,204	40,685	35,315
Demographics					
Age group, yrs					
20–39	312,680 (38.8)	1,639 (13.1)	20,966 (17.4)	4,966 (12.2)	3,354 (9.5)
40–54	209,202 (26.0)	2,933 (23.4)	23,296 (19.4)	8,285 (20.4)	6,885 (19.5)
55–64	128,550 (16.0)	3,045 (24.3)	24,025 (20.0)	8,874 (21.8)	7,779 (22.0)
65–74	86,848 (10.8)	3,075 (24.5)	24,267 (20.2)	9,124 (22.4)	8,257 (23.4)
75–84	47,047 (5.8)	1,425 (11.4)	18,016 (15.0)	6,420 (15.8)	6,056 (17.1)
≥85	20,949 (2.6)	422 (3.4)	9,634 (8.0)	3,016 (7.4)	2,967 (8.4)
Sex					
Female	437,651 (54.3)	6,709 (53.5)	59,583 (49.6)	19,262 (47.3)	16,607 (47.0)
Male	367,359 (45.6)	5,828 (46.5)	60,603 (50.4)	21,416 (52.6)	18,704 (53.0)
Other†/Missing§	264 (0.0)	3 (0.0)	17 (0.0)	8 (0.0)	3 (0.0)
Race					
Asian	22,968 (2.9)	206 (1.6)	4,396 (3.7)	1,219 (3.0)	1,003 (2.8)
Black or African American	126,166 (15.7)	1,904 (15.2)	28,403 (23.6)	8,879 (21.8)	8,172 (23.1)
White	493,181 (61.2)	9,366 (74.7)	59,212 (49.3)	22,910 (56.3)	19,318 (54.7)
Other¶	88,026 (10.9)	773 (6.2)	20,729 (17.2)	6,151 (15.1)	5,366 (15.2)
Missing§	74,935 (9.3)	280 (2.2)	7,449 (6.2)	1,511 (3.7)	1,443 (4.1)
Ethnicity					
Hispanic	149,565 (18.6)	1,006 (8.0)	25,953 (21.6)	7,557 (18.6)	6,895 (19.5)
Non-Hispanic	577,394 (71.7)	11,189 (89.2)	88,007 (73.2)	31,627 (77.7)	27,147 (76.9)
Other**	5,553 (0.7)	20 (0.2)	273 (0.2)	84 (0.2)	104 (0.3)
Missing§	72,764 (9.0)	318 (2.5)	5,955 (5.0)	1,410 (3.5)	1,161 (3.3)
Medical conditions associated with high risk††					
Anemia	72,830 (9.0)	2,187 (17.4)	28,645 (23.8)	9,762 (24.0)	8,553 (24.2)
Arrythmia	73,318 (9.1)	2,527 (20.2)	33,443 (27.8)	12,235 (30.1)	10,828 (30.7)
Asthma	60,080 (7.5)	1,890 (15.1)	14,542 (12.1)	5,301 (13.0)	4,944 (14.0)
COPD	26,636 (3.3)	879 (7.0)	13,447 (11.2)	5,551 (13.6)	5,513 (15.6)
Cancer	37,027 (4.6)	1,641 (13.1)	11,642 (9.7)	4,716 (11.6)	3,605 (10.2)
Chronic kidney disease	50,580 (6.3)	1,795 (14.3)	26,221 (21.8)	9,269 (22.8)	8,418 (23.8)
Chronic pulmonary disorders	100,625 (12.5)	3,219 (25.7)	28,994 (24.1)	11,282 (27.7)	10,582 (30.0)
Coagulopathy	33,374 (4.1)	985 (7.9)	18,908 (15.7)	7,442 (18.3)	6,469 (18.3)
Congestive heart failure	40,179 (5.0)	1,344 (10.7)	21,246 (17.7)	7,868 (19.3)	7,329 (20.8)
Coronary artery disease	54,051 (6.7)	2,074 (16.5)	25,308 (21.1)	9,305 (22.9)	8,607 (24.4)
Diabetes type 2	107,527 (13.4)	3,890 (31.0)	41,888 (34.8)	15,462 (38.0)	14,706 (41.6)
Hypertension	209,848 (26.1)	7,265 (57.9)	69,671 (58.0)	25,653 (63.1)	23,633 (66.9)
Mental health disorders	97,046 (12.1)	2,728 (21.8)	23,857 (19.8)	8,015 (19.7)	7,044 (19.9)
Peripheral vascular disorders	31,930 (4.0)	1,250 (10.0)	14,484 (12.0)	5,373 (13.2)	4,596 (13.0)
Severe obesity (BMI ≥40 kg/m^2)	60,052 (7.5)	2,430 (19.4)	17,716 (14.7)	7,781 (19.1)	6,891 (19.5)
Outcome§§					
Critical care	27,585 (3.4)	225 (1.8)	21,412 (17.8)	10,675 (26.2)	8,244 (23.3)

Abbreviations: BMI = body mass index; CDM = common data model; COPD = chronic obstructive pulmonary disease; PCORnet = National Patient-Centered Clinical Research Network.

* Percentages are simple summary numbers (column percentages) out of the total in each category. Strata are not expected to sum to the total because the small cell masking by the data partners before submission of data.

† For sex stratifications, Other includes all remaining PCORnet CDM values that are not male or female.

§ For sex, race, and ethnicity stratifications, Missing includes PCORnet CDM values of Refuse to answer, No Information, Unknown, and missing values.

¶ For race stratifications, Other includes PCORnet CDM values of Native Hawaiian or Other Pacific Islander, American Indian or Alaska Native, Multiple races, and Other.

** For ethnicity stratifications, Other includes PCORnet CDM values of Other.

†† Recorded history of the diagnoses in electronic health record (outpatient or inpatient) within 3 years before a positive test. Patients can have more than one condition.

§§ Fourteen days before to 30 days after a positive test result.

Mean monthly remdesivir use among inpatients who were White, Black, Asian, or Other race was 29.0%, 31.2%, 26.2%, and 30.6%, respectively; among patients of Hispanic or non-Hispanic ethnicity, remdesivir use was 30.4% and 29.3%, respectively. Black inpatients received remdesivir 9.3% more often ($p_t = 0.03$) than did White inpatients; systematic temporal differences were also observed ($p_w = 0.03$). Asian, Other race, and Hispanic inpatients did not experience significant relative disparities or systematic temporal differences in remdesivir treatment compared with White and non-Hispanic inpatients.

TABLE 2. Average monthly frequency and relative disparity in receipt of medications for treatment of COVID-19, by race and ethnicity — 41 health care systems in the National Patient-Centered Clinical Research Network, United States, March 2020–August 2021

Treatment/Race and ethnicity	Total no. eligible for treatment*	Total no. (%) treated	Mean of monthly percentage treated†	p_w†	Mean of monthly relative disparity,§ % (95% CI)	p_t§
Monoclonal antibodies (November 2020–August 2021)						
Race						
White	334,472	9,366 (2.8)	4.0	—	Ref.	—
Black	73,853	1,904 (2.6)	2.8	0.004	−22.4 (−38.7 to −6.1)	0.0125
Asian	14,744	206 (1.4)	2.2	0.002	−48.3 (−63.1 to −33.6)	<0.0001
Other	45,521	773 (1.7)	2.2	0.002	−46.5 (−51.1 to −41.9)	<0.0001
Ethnicity						
Non-Hispanic	387,403	11,189 (2.9)	4.0	—	Ref.	—
Hispanic	80,176	1,006 (1.3)	1.8	0.002	−57.7 (−66.6 to −48.9)	<0.0001
Dexamethasone (March 2020–August 2021)						
Race						
White	59,212	22,910 (38.7)	35.8	—	Ref.	—
Black	28,403	8,879 (31.3)	33.8	0.024	−1.9 (−7.8 to 3.9)	0.498
Asian	4,396	1,219 (27.7)	31.4	0.020	−2.0 (−17.3 to 13.2)	0.782
Other	20,729	6,151 (29.7)	34.2	0.106	−1.3 (−9.1 to 6.6)	0.735
Ethnicity						
Non-Hispanic	88,007	31,627 (35.9)	35.4	—	Ref.	—
Hispanic	25,953	7,557 (29.1)	32.5	0.005	−6.2 (−11.7 to −0.6)	0.032
Remdesivir (March 2020–August 2021)						
Race						
White	59,212	19,318 (32.6)	29.0	—	Ref.	—
Black	28,403	8,172 (28.8)	31.2	0.028	9.3 (0.9 to 17.7)	0.032
Asian	4,396	1,003 (22.8)	26.2	0.200	−15.1 (−30.3 to 0.1)	0.052
Other	20,729	5,366 (25.9)	30.6	0.323	1.7 (−9.4 to 12.8)	0.748
Ethnicity						
Non-Hispanic	88,007	27,147 (30.8)	29.3	—	Ref.	—
Hispanic	25,953	6,895 (26.6)	30.4	0.423	8.8 (−0.4 to 18.0)	0.060

Abbreviation: Ref. = referent group.

* For monoclonal antibody therapy, all patients with a positive SARS-CoV-2 test result were considered eligible for treatment. For dexamethasone and remdesivir, inpatients with a positive SARS-CoV-2 test result were considered eligible for treatment.

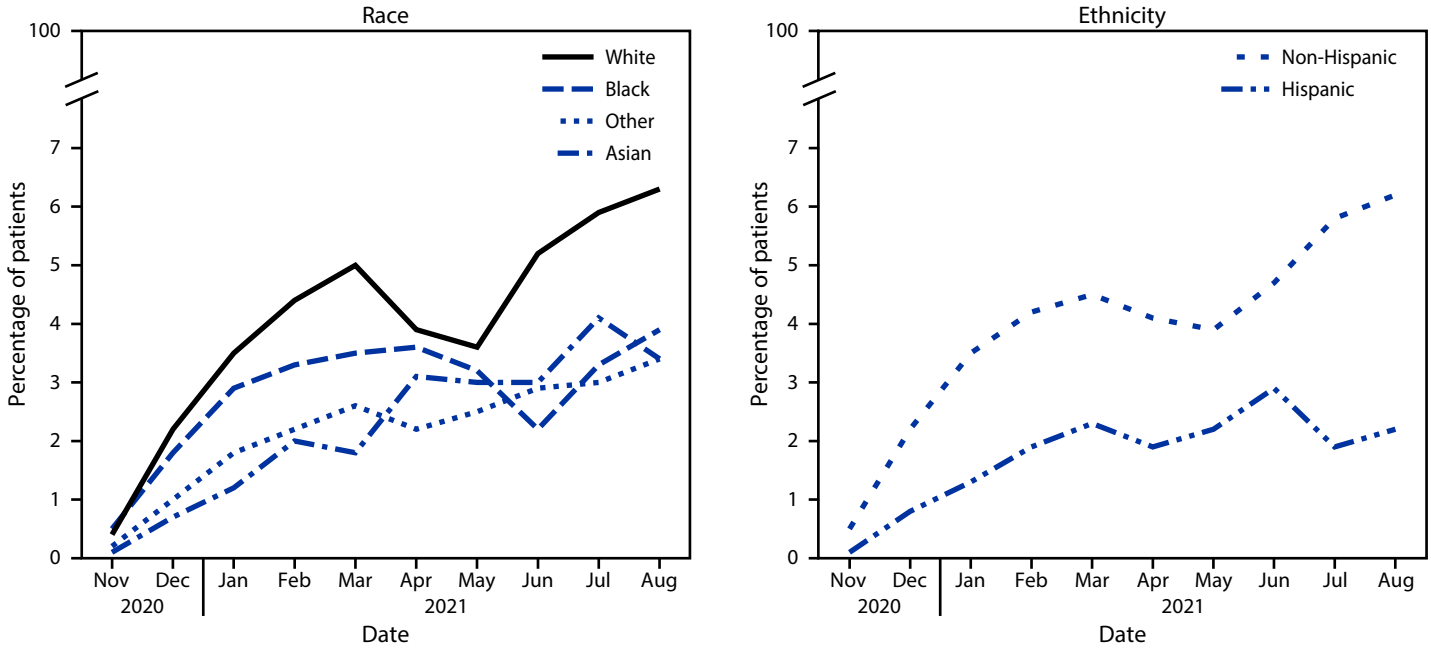
† Mean of monthly treated time series tested for differences using pairwise Wilcoxon signed rank tests with p value given as p_w. Mean of monthly percent treated = $[(\text{n treated / n eligible})_{\text{March 2020}} + (\text{n treated / n eligible})_{\text{April 2020}} + \ldots (\text{n treated / n eligible})_{\text{August 2021}}]$ / n total no. months.

§ The difference in percentage of patients treated among racial (Black, Asian, or Other races) or ethnic minority (Hispanic) and majority (White or non-Hispanic) groups divided by the percentage treated in the majority groups for each month. Assessed as nonzero using t tests with p-value given as p_t. Total number of months for dexamethasone and remdesivir = 18 and for monoclonal antibodies = 10. Mean of monthly relative disparity, % = $[(\text{Minority} - \text{majority / Majority})_{\text{March2020}} + (\text{minority} - \text{majority / Majority})_{\text{April 2020}} \ldots + (\text{Minority} - \text{majority / Majority})_{\text{August 2021}}]$ / Total no. of months.

Discussion

This large-scale study from 41 U.S. health care systems found disparate mAb treatment of COVID-19 in Hispanic, Black, Asian, and Other race patients relative to non-Hispanic and White patients. Large relative differences were noted for mAb treatment, yet absolute differences were small. Relative differences in treatment with dexamethasone and remdesivir were less apparent in hospital settings, which might be attributed to ease of medication access. mAb treatment must be administered by intravenous infusion or subcutaneous injection by a health care provider, typically in outpatient settings, soon after receipt of a positive test result and within 10 days of symptom onset. The finding of mAb treatment disparities is consistent with previous studies. A single-center study of kidney transplant patients found that Black and Hispanic patients infected with SARS-CoV-2 were less likely to receive mAb and more likely to be hospitalized (*5*). The current study did not identify the underlying causes for the observed disparities. mAb treatment disparities might reflect systemic factors such as limited access to testing and care because of availability constraints, inadequate insurance coverage, and transportation challenges; lack of a primary care provider to recommend treatment; variations in treatment supply and distribution; potential biases in prescribing practices; and limited penetration of messaging in some communities about mAb availability and effectiveness to prevent disease progression. Additional

FIGURE. Monthly* percentage of COVID-19 patients (n = 805,276) receiving monoclonal antibody treatment,† by race§ and ethnicity¶ — 41 health care systems in the National Patient-Centered Clinical Research Network — United States, November 2020–August 2021



* Systematic temporal differences in medication receipt by race and ethnicity were assessed by pairwise Wilcoxon signed rank test.
† mAbs require administration by intravenous infusion or subcutaneous injection.
§ White race is the referent group; p-values for Black, Asian, and Other races are 0.004, 0.002, and 0.002, respectively.
¶ Non-Hispanic ethnicity is the referent group; p = 0.002 for Hispanic ethnicity.

reasons might include hesitancy about receiving treatment; a previous study found patients who were non-Hispanic White and English-speaking accepted mAb treatment more often than did those who were non-White and Hispanic (*6*).

In inpatient settings, Black inpatients received remdesivir more often, and Black, Asian, and Hispanic inpatients received dexamethasone less often than did comparison groups. This could indicate racial and ethnic differences in clinical indications for medication use (e.g., age distribution and prevalence of comorbidities) or could be reflective of varying prescribing practices, protocols, and drug access by institutions that serve populations of different racial and ethnic distributions (*7*).

mAbs are authorized for use in persons at high-risk for severe COVID-19 with positive SARS-CoV-2 test results and as postexposure prophylaxis. In this study, a larger percentage of patients who received mAb had high-risk medical conditions, in accordance with current treatment guidelines. However, this study also found mAb treatments have been used relatively less commonly in racial and ethnic minority groups, amplifying the increased risk for severe COVID-19–associated outcomes, including death among these groups, as a consequence of their higher prevalence of preexisting conditions.[§§§§]

Reducing racial and ethnic disparities in COVID-19 treatment requires patient and clinician awareness of the problem and its solutions; resources; and action from government, private entities, and community- and faith-based organizations to implement effective interventions. Bringing health care to populations facing barriers in access to mAb via a mobile infusion unit or via telehealth providers has been shown to increase mAb use, decrease severe outcomes, and reduce costs (*8*,*9*). These examples of meeting persons in community venues can be helpful in delivering outpatient treatments, addressing pandemic disparities, and managing underlying chronic conditions affected by social determinants of health.[¶¶¶¶] Moreover, disparities in COVID-19 treatment are the latest example of longstanding unequal treatment of many medical

[§§§§] CDC data on SARS-CoV-2 hospitalization and death by race/ethnicity are available from COVID-NET, a population-based surveillance system collecting data through a network of 250 acute-care hospitals across 14 states (https://www.cdc.gov/coronavirus/2019-ncov/covid-data/investigations-discovery/hospitalization-death-by-race-ethnicity.html). CDC's National Center for Chronic Disease Prevention and Health Promotion data on 124 chronic disease indicators by race and ethnicity in the U.S. population are available online. https://www.cdc.gov/cdi/index.html

[¶¶¶¶] https://www.cdc.gov/chronicdisease/programs-impact/sdoh.htm

Summary

What is already known about this topic?

Racial and ethnic disparities in SARS-CoV-2 infection risk and death from COVID-19 have been well documented.

What is added by this report?

Analysis of data from 41 health care systems participating in the PCORnet, the National Patient-Centered Clinical Research Network, found lower use of monoclonal antibody treatment among Black, Asian, and Other race and Hispanic patients with positive SARS-CoV-2 test results, relative to White and non-Hispanic patients. Racial and ethnic differences were smaller for inpatient administration of remdesivir and dexamethasone.

What are the implications for public health practice?

Equitable receipt of COVID-19 treatments by race and ethnicity along with vaccines and other prevention practices are essential to reduce inequities in severe COVID-19–associated illness and death.

conditions.***** Multicomponent, multisystem programs and policies can support health equity.††††† One such program is the COVID Response and Resilient Communities initiative, which places community health workers in communities to reduce long-standing disparities and deliver interventions to manage COVID-19.§§§§§ Future studies of COVID-19 treatment disparities should account for persons with high-risk conditions and include newer medications, such as the oral antiviral agents Paxlovid and molnupiravir, as well as sotrovimab,¶¶¶¶¶ which is the only mAb treatment currently available for early treatment of patients infected with the SARS-CoV-2 B.1.1.529 (Omicron) variant.******

The findings in this report are subject to at least five limitations. First, the aggregate data structure did not allow for adjustment of demographic or clinical factors that might be correlated with race and ethnicity. Second, all patients with a positive test result were used as the denominator for calculations of mAb treatment proportions because persons at risk for progression to severe illness could not be identified in aggregate data. Percentage use might be higher and relative disparities might be different if the denominator were specific to mAb prescribing guidelines. Third, missing race and ethnicity was more common among all patients with positive test results than among those treated; more work is needed to fully understand the implications of missing or inaccurate data (*10*). Fourth, mAb use was captured solely from electronic health records; disparities noted here might be restricted to patients who received mAb within a health care system because treatment received in non–health care settings (e.g., government-run infusion sites) is not likely to be recorded. Finally, PCORnet data are derived from a convenience sample of health care facilities, limiting generalizability to the U.S. population.

The COVID-19 pandemic has magnified and amplified inequities that must be addressed to achieve equitable health outcomes. The United States has surpassed 800,000 deaths from COVID-19 and is experiencing another case surge caused by Omicron.†††††† Vaccines and preventive measures are the best defense against infection; postinfection, COVID-19 medications reduce morbidity and mortality and relieve strain on hospitals. A lower proportion of persons of racial and ethnic minority groups received mAb outpatient treatment for preventing severe COVID-19. This finding highlights disparities as a priority for intervention and can guide strategies aimed at more equitable COVID-19 outcomes. Policies, resources, and programs addressing the specific needs of served populations, institutions, and places can accelerate progress towards health equity (4). Strategizing the equitable receipt of current and emerging outpatient treatments§§§§§§ by reducing barriers to accessing treatment might prevent disparities in severe COVID-19 outcomes. Efforts to reduce racial and ethnic disparities with equitable outpatient COVID-19 treatment access, practices, and supportive systems are urgently needed.

***** https://www.nap.edu/catalog/10260/unequal-treatment-confronting-racial-and-ethnic-disparities-in-health-care

††††† Public health policies and programs centered around the specific needs of communities can promote health equity, including health equity considerations for racial and ethnic minority groups. https://www.cdc.gov/coronavirus/2019-ncov/community/health-equity/race-ethnicity.html

§§§§§ COVID Response and Resilient Communities initiative provides financial support and technical assistance to 69 states, localities, territories, tribes, tribal organizations, urban Indian health organizations, and health service providers to tribes. Intended populations include those at high risk because of their race or ethnicity. https://www.cdc.gov/covid-community-health-workers/pdfs/CCR-fact-sheet-H.pdf

¶¶¶¶¶ Sotrovimab is a mAb authorized for use under an EUA from FDA in May 2021 for the treatment of mild to moderate COVID-19. It was not included in this analysis as it was less commonly used during the study period. The fact sheet for health care providers is available online. https://www.fda.gov/media/149534/download

****** https://www.covid19treatmentguidelines.nih.gov/therapies/statement-on-therapies-for-high-risk-nonhospitalized-patients/

†††††† https://covid.cdc.gov/covid-data-tracker

§§§§§§ https://emergency.cdc.gov/han/2021/han00461.asp

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Notes from the Field

Early Evidence of the SARS-CoV-2 B.1.1.529 (Omicron) Variant in Community Wastewater — United States, November–December 2021

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The United States designated the B.1.1.529 (Omicron) variant of SARS-CoV-2 (the virus that causes COVID-19) a variant of concern on November 30, 2021, and the first U.S. Omicron COVID-19 case was reported on December 1 (*1*). By December 18, Omicron was estimated to account for 37.9% of U.S. COVID-19 cases.* Early warning systems, such as sewage (wastewater) surveillance,† can help track the spread of SARS-CoV-2 variants across communities (*2*).

The National Wastewater Surveillance System (NWSS) comprises 43 health departments funded by CDC to provide data on presence of and trends in SARS-CoV-2 infections that are independent of clinical testing. In addition to total SARS-CoV-2 testing, some health departments track SARS-CoV-2 variants by detecting variant-associated mutations in wastewater. Health departments in four states (California, Colorado, New York, and Texas) were the first wastewater surveillance programs to detect evidence of Omicron in community wastewater. This report describes the initial detections in wastewater during November 21–December 16, 2021, and the interpretative framework for these types of data. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.§

California

The California Department of Public Health and academic partners use mutation-specific reverse transcription–polymerase chain reaction (RT-PCR) and sequencing to track variants in wastewater collected daily from 10 sewersheds.¶,** Omicron-associated mutations delHV69–70 (also seen with Alpha variant [B.1.1.7 and Q lineages])†† and del143–145 were detected in samples collected November 25 and November 30, 2021, from two Northern California communities (Table). Results from these samples were available on December 2; at that time, two clinical COVID-19 cases attributed to Omicron had been identified in California, but none from these communities. By December 17, del143–145 mutations were detected at all 10 sampled sewersheds in California communities.

Colorado

The Colorado Department of Public Health and Environment conducts biweekly SARS-CoV-2 wastewater testing at 21 sewersheds,§§ using sequencing to track variants. Thirteen Omicron-associated mutations were detected in a sample collected on December 2, 2021. At that time, only one travel-associated Omicron case had been reported in Colorado. No Omicron-associated mutations were detected in the samples collected on December 6; however, by December 16, Omicron-associated mutations were detected at 19 of 21 sewersheds.

New York City

The New York City Department of Environmental Protection tracks variants in wastewater by sequencing weekly samples collected from 14 sewersheds¶¶,*** (*3*). Twelve Omicron-associated mutations were detected in a sample collected on November 21. By December 4, the date the wastewater data were reported, one Omicron case had been identified in a resident of the sewershed. Samples collected on November 28 from this same sewershed and from another sewershed contained Omicron-associated mutations, as reported to the health department on December 17.

Houston, Texas

The Houston Health Department conducts weekly wastewater testing at 39 sewersheds in the city and uses sequencing to

* https://covid.cdc.gov/covid-data-tracker/#variant-proportions (Accessed January 10, 2022).
† https://www.cdc.gov/healthywater/surveillance/wastewater-surveillance/wastewater-surveillance.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.

¶ Quantitative SARS-CoV-2 measurements in untreated sewage can provide information on changes in total SARS-CoV-2 infection in the community contributing to that wastewater treatment plant. That area is known as the sewershed.
** https://www.protocols.io/view/quantification-of-sars-cov-2-variant-mutations-hv6-b2qmqdu6
†† https://www.researchsquare.com/article/rs-1083575/v1
§§ https://covid19.colorado.gov/covid-19-monitoring-in-wastewater
¶¶ https://www.medrxiv.org/content/10.1101/2021.03.21.21253978v1
*** https://www.medrxiv.org/content/10.1101/2021.07.26.21261142v1

TABLE. Detection of mutations associated with the SARS-CoV-2 B.1.1.529 (Omicron) variant in wastewater — California, Colorado, New York City, and Houston, Texas, November 21–December 16, 2021

Location	Sample date	Test method	Results
California			
Sewershed A	Nov 25, 2021	Mutation-specific RT-PCRs targeting delHV69–70 and del143–145*	Both mutations detected at <1,000 genomic copies/gram wastewater solids
Sewershed B	Nov 30, 2021	Mutation-specific RT-PCRs targeting delHV69–70 and del143–145*	Both mutations detected at <1,000 genomic copies/gram wastewater solids
	Dec 2, 2021	Mutation-specific RT-PCRs targeting delHV69–70 and del143–145*	Both mutations detected at <1,000 genomic copies/gram wastewater solids
		Partial sequencing of S-gene using ARTIC v4 73R, 74L primers	Detected 9 bp insertion mutation in s214EPE and 3 bp N211I deletion
Sewersheds (10 sites)	Dec 17, 2021 10 of 10 sites	Mutation-specific RT-PCR targeting del143–145*	Mutations detected at >4,500 genomic copies/gram wastewater solids
Colorado			
Sewersheds (21 sites)	Dec 2, 2021 One of 21 sites	SARS-CoV-2-enriched tiled amplicon sequencing	Detected 13 of 17 Omicron-associated mutations
	Dec 6, 2021 Zero of 21 sites	SARS-CoV-2-enriched tiled amplicon sequencing	No Omicron-associated mutations detected
	Dec 9, 2021 Five of 21 sites	SARS-CoV-2-enriched tiled amplicon sequencing	Detected between four and 13 of 17 Omicron-associated mutations depending on the site
	Dec 13, 2021 12 of 21 sites	SARS-CoV-2-enriched tiled amplicon sequencing	Detected between six and 14 of 17 Omicron-associated mutations, depending on the site
	Dec 16, 2021 19 of 21 sites	SARS-CoV-2-enriched tiled amplicon sequencing	Detected between 12 and 14 of 17 Omicron-associated mutations, depending on the site
New York City			
Sewershed A	Nov 21, 2021	Short-read sequencing of S-gene amplicon†,§	Detected 12 Omicron-associated mutations including eight mutations unique to Omicron
	Nov 28, 2021	Short-read sequencing of S-gene amplicon†,§	Detected 12 Omicron-associated mutations including eight mutations unique to Omicron
Sewershed B	Nov 28, 2021	Short-read sequencing of S-gene amplicon†,§	Detected 12 Omicron-associated mutations including eight mutations unique to Omicron
Houston, Texas			
Sewersheds (39 sites)	Nov 29, 2021 Seven of 39 sites	SARS-CoV-2-enriched tiled amplicon sequencing using ARTIC v3 primers¶	Detected six Omicron-associated mutations
	Dec 6, 2021 25 of 39 sites	SARS-CoV-2-enriched tiled amplicon sequencing using ARTIC v3 primers¶	Detected 14 Omicron-associated mutations
	Dec 13, 2021 35 of 39 sites	SARS-CoV-2-enriched tiled amplicon sequencing using ARTIC v3 primers¶	Detected 18 Omicron-associated mutations

Abbreviation: RT-PCR = reverse transcription–polymerase chain reaction.
* https://www.protocols.io/view/quantification-of-sars-cov-2-variant-mutations-hv6-b2qmqdu6
† https://www.medrxiv.org/content/10.1101/2021.03.21.21253978v1
§ https://www.medrxiv.org/content/10.1101/2021.07.26.21261142v1
¶ https://www.medrxiv.org/content/10.1101/2021.09.08.21263279v1

track variants.††† Sequencing detected six Omicron-associated mutations in samples collected on November 29 from seven sewersheds across the city. The first clinical detection of Omicron in the city was reported on December 1. The number of Omicron-positive sites, as well as the number of Omicron-associated mutations detected, increased over the subsequent 2 weeks.

Discussion

The wastewater surveillance programs in these four states were the first to detect evidence of Omicron in community wastewater. Variant tracking data from wastewater cannot confirm the presence of a specific variant because the methods used cannot determine whether all variant-defining mutations are present on a single genome. However, conditions that increase confidence in the results include detection of multiple variant-associated mutations; linked mutations (i.e., on the same sequence read), or unique mutations not shared by other known variants; RNA concentration data consistent with emergence (e.g., low initial concentrations, increasing over time); the reporting of clinical cases in the area; detections in consecutive samples or via multiple methods; and RNA concentration or sequence abundance data for multiple variant-associated mutations trending together. Limitations of variant tracking in wastewater include detections inconsistent with the current epidemiology, low quality sequence data, sporadic detections, detection of a single variant-associated mutation, and conflicting trends in concentration or abundance data for

††† https://www.medrxiv.org/content/10.1101/2021.09.08.21263279v1

mutations associated with the same variant. Reporting times >1 week can limit the usefulness of this data.

The detection of Omicron-associated mutations in community wastewater provides strong early evidence that the Omicron variant was likely present or more widely distributed in these communities than originally indicated by clinical testing alone; Omicron-associated mutations were documented during November 2021, at least a week before the first U.S. case identified via clinical testing on December 1. Variant tracking data from wastewater can be used as a complement to clinical testing for early detection of emerging variants, which can help guide decisions about allocation of clinical and public health resources, testing strategies, and public health messaging.

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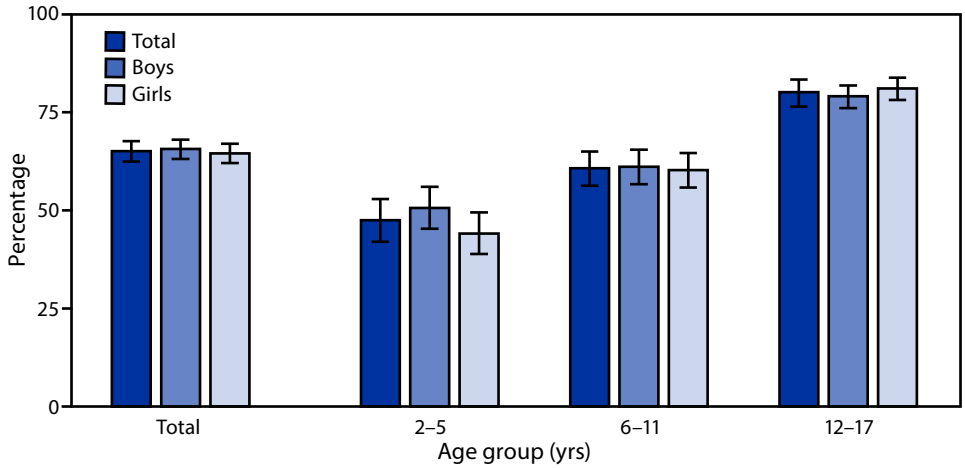
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage* of Children† Aged 2–17 Years With >2 Hours of Screen Time Per Weekday,§ by Sex and Age Group — National Health Interview Survey,¶ United States, 2020



* With 95% CIs indicated by error bars.
† Children are defined here as children and adolescents (i.e., persons aged 2–17 years).
§ Based on a response to the question, "On most weekdays, does (child's name) spend more than 2 hours a day in front of a TV, computer, cellphone, or other electronic device watching programs, playing games, accessing the Internet, or using social media?" Respondents were instructed not to include time spent for schoolwork.
¶ Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population.

Overall, 65.7% of boys and 64.6% of girls aged 2–17 years spent >2 hours of screen time per weekday, in addition to screen time spent for schoolwork. Among both boys and girls, the percentage of children who spent >2 hours of screen time increased with increasing age group from 47.5% for those aged 2–5 years to 80.2% for those aged 12–17 years.

Source: National Center for Health Statistics, National Health Interview Survey, 2020. https://www.cdc.gov/nchs/nhis/index.htm

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