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Progress Toward Poliomyelitis Eradication — Pakistan, January 2022–June 2023

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Abstract

Since the establishment of the Global Polio Eradication Initiative in 1988, Pakistan remains one of only two countries (along with Afghanistan) with continued endemic transmission of wild poliovirus (WPV). This report describes Pakistan's progress toward polio eradication during January 2022–June 2023. During 2022, Pakistan reported 20 WPV type 1 (WPV1) cases, all of which occurred within a small geographic area encompassing three districts in south Khyber Pakhtunkhwa. As of June 23, only a single WPV1 case from Bannu district in Khyber Pakhtunkhwa province has been reported in 2023, compared with 13 cases during the same period in 2022. In addition, 11 WPV1 isolates have been reported from various environmental surveillance (ES) sewage sampling sites to date in 2023, including in Karachi, the capital of the southern province of Sindh. Substantial gaps remain in the quality of supplementary immunization activities (SIAs), especially in poliovirus reservoir areas. Despite the attenuation and apparently limited geographic scope of poliovirus circulation in Pakistan, the isolation of WPV1 from an ES site in Karachi is cause for concern about the actual geographic limits of transmission. Interrupting WPV1 transmission will require meticulous tracking and sustained innovative efforts to vaccinate children who are regularly missed during SIAs and rapidly responding to any new WPV1 isolations.

Introduction

Endemic transmission of indigenous wild poliovirus (WPV) type 1 (WPV1) has never been interrupted in Pakistan, which, along with Afghanistan, is one of two remaining countries where WPV1 remains endemic (*1*,*2*). Both countries share long borders with highly mobile populations and, as such, are considered a single epidemiologic block. The 2022–2026 Global Polio Eradication Initiative (GPEI) Strategic Plan's stated goal of interrupting all WPV1 transmission worldwide by the end of 2023 (*3*) could be jeopardized by continued poliovirus circulation in Pakistan. This report describes Pakistan's progress toward eliminating indigenous WPV1 transmission during January 2022–June 2023 and updates previous reports (*4*,*5*).

Methods

Poliovirus surveillance data and vaccination campaign information were provided by the Pakistan National Emergency Operations Center and by other GPEI partners, including UNICEF and the World Health Organization (WHO). Weekly polio surveillance reports from the country and regional teams, as well as vaccination campaign reports shared by the country team were reviewed, as were national and subnational presentations prepared by the Pakistan polio program

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and immunization coverage surveys sponsored by Gavi, the Vaccine Alliance (conducted by a third party). Genomic sequencing analysis results were reviewed to ascertain the genetic relationship among polioviruses identified in WPV1 patients' specimens and environmental sewage samples. A descriptive analysis of WPV1 patient characteristics, including age and essential immunization status, was conducted using Microsoft Excel.

Results

Immunization Activities

Essential (routine) immunization. For 2021, WHO and UNICEF estimated Pakistan's national coverage with 3 doses of oral poliovirus vaccine (OPV) and 1 dose of inactivated poliovirus vaccine (IPV) by age 12 months at 83% for each vaccine (*6*). A 2021 third-party survey sponsored by Gavi, the Vaccine Alliance, indicated that the percentage of children aged 12–23 months who had received 3 OPV doses ranged (by province) from 45.1% in Balochistan to 94.9% in Punjab. No districts in the provinces of Balochistan, Khyber Pakhtunkhwa, and Sindh achieved ≥80% coverage, compared with 31 (86%) of 36 districts in Punjab province.

Supplementary immunization activities. Following the declaration of eradication of WPV type 2 in 2015 (*3*), and the globally synchronized withdrawal of trivalent OPV (tOPV) (containing Sabin strain types 1, 2, and 3) by all OPV-using countries in 2016 (*7*), most polio supplementary immunization activities (SIAs)* in Pakistan have been implemented using bivalent OPV (bOPV) (containing Sabin strain types 1 and 3). In response to circulating vaccine-derived poliovirus (cVDPV) type 2 (cVDPV2)† outbreaks during 2019–2021, SIAs were implemented with tOPV and monovalent OPV type 2. During 2022, two national immunization days (NIDs) and six subnational immunization days (SNIDs) were conducted using bOPV. NIDs in Pakistan typically target approximately 44 million children aged <5 years, whereas SNIDs target smaller populations, depending on the areas identified by ongoing risk assessments. In addition, bOPV case-response vaccination activities were implemented following WPV1 isolation in south Khyber Pakhtunkhwa during March, April, and June 2022. Fractional-dose IPV (dose-sparing intradermal administration of IPV using one fifth of the regular intramuscular dose) was administered to eligible children along with OPV in south Khyber Pakhtunkhwa in SIAs that took place during June and August 2022. To date in 2023, one NID was conducted in January, and four SNIDs were conducted in February, March, May, and June.

Approximately 1.1 million vaccine-eligible children aged <5 years reside in the seven districts of south Khyber Pakhtunkhwa. Approximately 50,000 children in the region are

* SIAs are mass house-to-house vaccination campaigns targeting children aged <5 years with OPV, regardless of the child's vaccination history.

† cVDPV, which can lead to paralysis, emerges as a result of attenuated OPV virus regaining neurovirulence after prolonged circulation in underimmunized populations.

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regularly missed during OPV SIAs, including 19,500 children in the Mehsud tribal area of South Waziristan, where local health workers have been intimidated and prevented from vaccinating eligible children by militants since August 2022. The program has further been battling repeated boycotts by some communities during SIAs for reasons mostly unrelated to polio, such as requests for electricity services. Lot quality assurance sampling[§] surveys, which assess SIA quality, continue to indicate substantial quality gaps in districts of south Khyber Pakhtunkhwa. Based on a 90% pass threshold, and surveyed using finger-marking, wherein a child's fingernail is marked with indelible ink by vaccinators as a program indicator of receipt of OPV, the proportion of union councils (the lowest governmental administrative level) in south Khyber Pakhtunkhwa that reached the threshold ranged from 56% to 80% for SIAs conducted during August 2022–February 2023. Nationally, an estimated 505,750 eligible children were missed during NIDs in January 2023, including 22,466 (4%) refusals. In some areas, SIA quality assessments could potentially overestimate the actual proportion of children vaccinated because of the practice of fake finger-marking, wherein a child's fingernail is marked by the vaccination team even though the child was not actually vaccinated.

Summary

What is already known about this topic?

Transmission of wild poliovirus type 1 (WPV1) has never been interrupted in Pakistan, one of two countries with ongoing endemic transmission.

What is added by this report?

Twenty WPV1 cases were reported in Pakistan during 2022, and one case during 2023 (as of June 2023), all clustered within a small geographic area in the southern region of Khyber Pakhtunkhwa province, an area with considerable security challenges and a history of vaccine hesitancy. Recent isolation of WPV1 from sewage in Karachi suggests surveillance gaps and improvements needed in immunization campaign quality.

What are the implications for public health practice?

To interrupt WPV1 circulation, the Pakistan polio program needs to meticulously track and sustain innovative efforts to vaccinate children who are regularly missed during polio vaccination activities, especially in reservoir areas affected by conflict and insecurity.

Poliovirus Surveillance

Acute flaccid paralysis surveillance. Pakistan reported a national nonpolio acute flaccid paralysis (NPAFP)[¶] rate of 18.9 cases per 100,000 persons aged <15 years in 2022 (Table); provincial rates ranged from 10.7 to 28.6, exceeding the recommended surveillance sensitivity benchmark of ≥2 cases per 100,000 persons aged <15 years. As of May 16, 2023, the annualized 2023 national NPAFP rate is 15.3. Stool specimen adequacy[**] during 2022 and 2023 exceeded the target ≥80% indicator nationally and in all provinces. District-level performance indicators also generally improved compared with those in previous years. For example, the NPAFP rate in seven districts of south Khyber Pakhtunkhwa improved from 17.7 in 2021 to 24.9 in 2022. The program undertook internal reviews across all provinces and continues to implement surveillance-strengthening plans.

Environmental surveillance. A network of 114 environmental surveillance (ES) sewage collection sites in 80 districts serves as an ancillary means for detecting poliovirus circulation. Sewage samples collected monthly at these sites are tested for polioviruses and other (nonpolio) enteroviruses. During 2022, 37 (4%) of 1,024 sewage samples tested positive for WPV1, compared with 65 (8%) of 846 samples in 2021. In 2023 to date, 11 (1%) of 1,119 sewage samples have tested positive for WPV1, including samples from Lahore district in Punjab province (two); Dera Ismail Khan, Hangu, Peshawar, and South Waziristan districts in Khyber Pakhtunkhwa province (eight); and Karachi in Sindh province (one).

Epidemiology of poliovirus cases. Twenty WPV1 cases were reported in Pakistan in 2022, compared with one case during 2021, 84 in 2020, and 147 in 2019 (Figure 1) (Figure 2) (*4*,*5*). As of June 23, 2023, a single WPV1 case has been reported in 2023. The case occurred in Bannu district, Khyber Pakhtunkhwa province, with paralysis onset on February 20, 2023 (Figure 2). All 20 WPV1 cases reported in 2022 occurred in three districts of south Khyber Pakhtunkhwa: North Waziristan (17), Lakki Marwat (two), and South Waziristan (one). Among the 21 WPV1 cases identified during the entire reporting period, patient ages ranged from 3 to 197 months (16 years) (median = 15 months); 17 (81%) had never received OPV through essential immunization; the remaining four (19%) had received 1–3 doses of OPV through essential

[§] Lot quality assurance sampling (LQAS) uses a small sample to assess the quality of vaccination activities after SIAs in union councils (referred to as "lots"). LQAS surveys seek evidence of vaccination (finger marking) by randomly selecting 60 children within each lot. If the number of unvaccinated children in the sample exceeds three, then the union council SIA is classified as having failed at a threshold of ≥90%, and additional vaccination activities in those areas are recommended. If the threshold of ≥90% (three or fewer unvaccinated children) is met, the union council SIA is classified as having passed.

[¶] Acute flaccid paralysis (AFP) cases that are discarded as not having laboratory or other proof of poliovirus as the cause are considered NPAFP cases. The expected background rate of NPAFP illnesses is ≥2 per 100,000 persons aged <15 years per year, the standard WHO performance indicator target for sufficiently sensitive surveillance to detect a case of poliomyelitis.

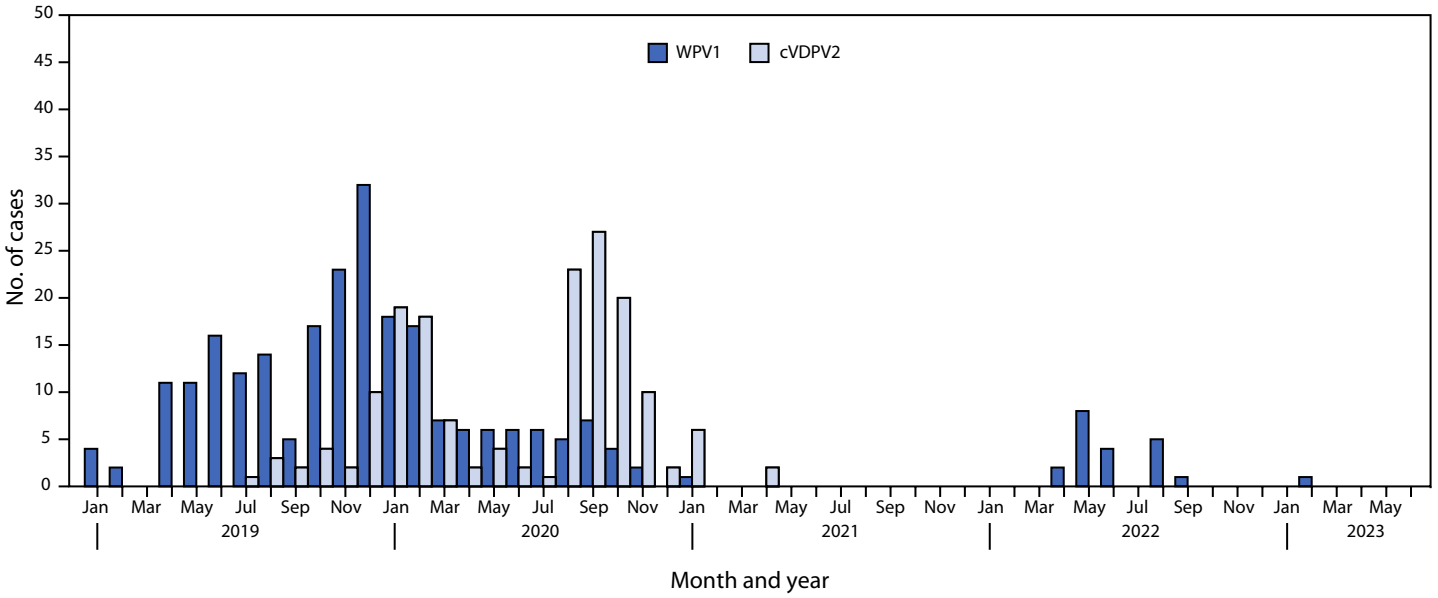
[**] Stool specimens are considered adequate if two specimens are collected ≥24 hours apart within 14 days of paralysis onset and arrive at a WHO-accredited laboratory with reverse cold chain maintained and without leakage or desiccation. The standard WHO stool specimen indicator target is adequate stool specimen collection from ≥80% of AFP cases.

TABLE. Acute flaccid paralysis surveillance indicators and number of wild poliovirus and circulating vaccine-derived poliovirus cases reported, by province and surveillance period — Pakistan, January 2022–June 2023

Region	AFP surveillance indicators: No. of AFP cases (nonpolio AFP rate)* 2022	AFP surveillance indicators: No. of AFP cases (nonpolio AFP rate)* 2023§	AFP surveillance indicators: Adequate stool specimens, %† 2022	AFP surveillance indicators: Adequate stool specimens, %† 2023	No. of poliovirus cases: Reported WPV1 cases Jan–Jun 2022	Jul–Dec 2022	Jan–Jun 2023	Total	Reported cVDPV2 cases Jan–Jun 2022	Jul–Dec 2022	Jan–Jun 2023	Total
Azad Jammu and Kashmir	500 (26.4)	128 (15.5)	90.6	89.1	0	0	0	**0**	0	0	0	**0**
Gilgit-Baltistan	170 (24.9)	52 (17.4)	85.3	82.7	0	0	0	**0**	0	0	0	**0**
Islamabad	287 (28.6)	89 (31.9)	83.3	85.4	0	0	0	**0**	0	0	0	**0**
Khyber Pakhtunkhwa	4,659 (23.4)	1,258 (16.4)	83.7	87.3	14	6	1	**21**	0	0	0	**0**
Punjab	9,474 (18.3)	2,668 (15.5)	86.4	86.9	0	0	0	**0**	0	0	0	**0**
Balochistan	637 (10.7)	192 (8.0)	83.8	89.1	0	0	0	**0**	0	0	0	**0**
Sindh	3,300 (14.6)	1,104 (13.1)	83.8	87.3	0	0	0	**0**	0	0	0	**0**
Total	**19,027 (18.9)**	**5,491 (15.3)**	**85.2**	**87.1**	**14**	**6**	**1**	**21**	**0**	**0**	**0**	**0**

Abbreviations: AFP = acute flaccid paralysis; cVDPV2 = circulating vaccine-derived poliovirus type 2; WHO = World Health Organization; WPV1 = wild poliovirus type 1.
* Nonpolio AFP cases per 100,000 persons aged <15 years.
† Stool specimens are considered adequate if two specimens are collected ≥24 hours apart within 14 days of paralysis onset and arrive at a WHO-accredited laboratory with reverse cold chain maintained and without leakage or desiccation. The standard WHO stool specimen indicator target is adequate stool specimen collection from ≥80% of AFP cases.
§ Annualized.

FIGURE 1. Wild poliovirus type 1 and circulating vaccine-derived poliovirus type 2 cases, by month — Pakistan, January 2019–June 2023

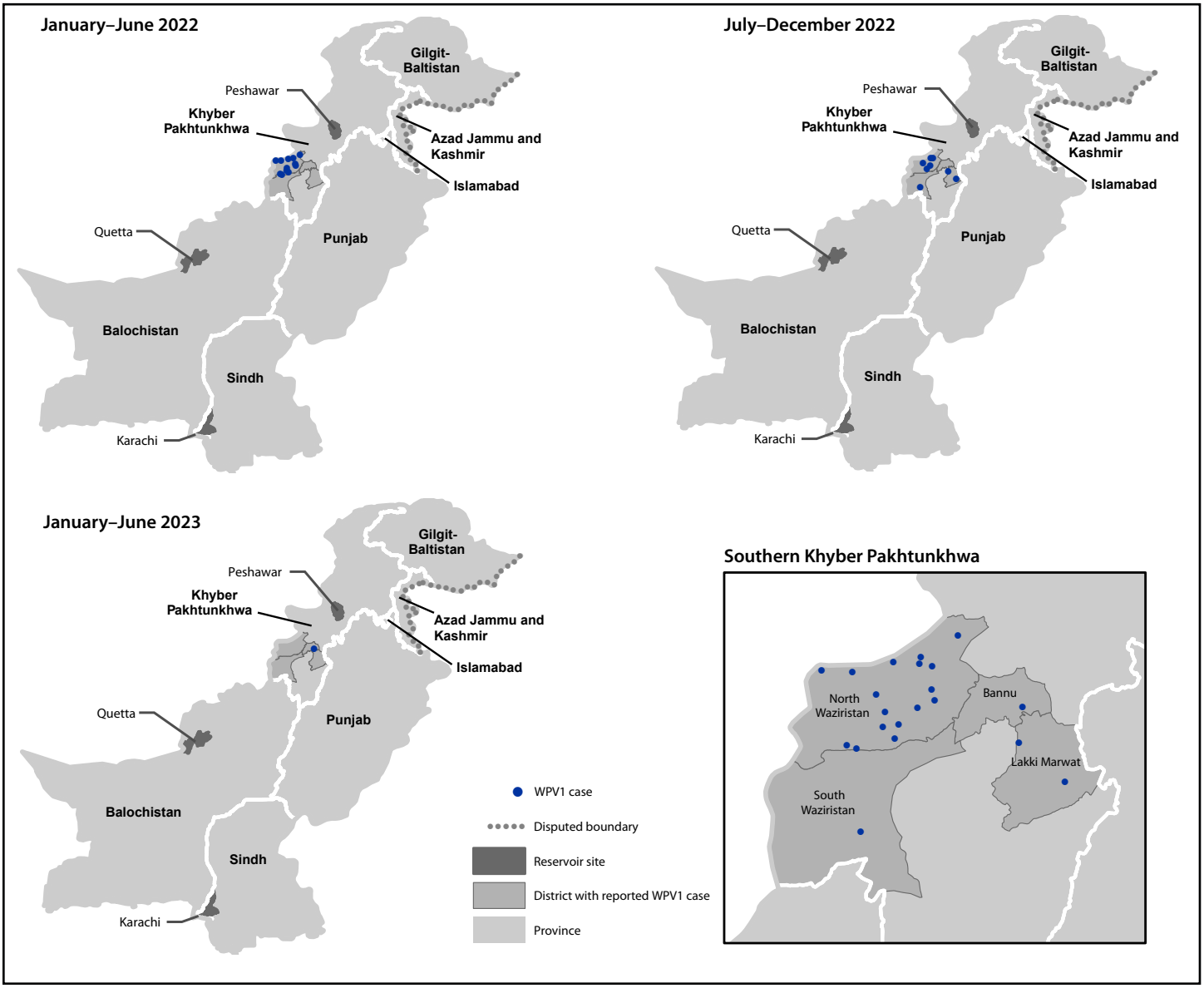


Abbreviations: cVDPV2 = circulating vaccine-derived poliovirus type 2; WPV1 = wild poliovirus type 1.

immunization. No cVDPV2 has been reported in Pakistan since April 23, 2021, when the last of 165 cVDPV2 cases that occurred during July 2019–April 2021 was reported (Table) (Figure 1).

Genomic sequence analysis of WPV1 isolates. Analyses of the region coding the viral capsid protein VP1 indicated that the viruses of WPV1 cases all belong to a single genetic cluster sharing ≥95% sequence identity (the YB3C cluster). Among 11 environmental sample isolates for which sequencing results were available, three belonged to the YB3C cluster, which is endemic in Pakistan, whereas eight belonged to the YB3A cluster, currently circulating in eastern Afghanistan. The most recent isolation from Karachi also belonged to the YB3A cluster and differed by 5.3% in its VP1 coding region from its closest relative isolated from a sample collected in Karachi in January 2021. The level of deviation from its closest relative was much higher than the "orphan" virus criterion of ≥1.5%, indicating long-term undetected transmission of one lineage in Karachi missed by acute flaccid paralysis (AFP) surveillance and ES in the area.

FIGURE 2. Location of cases of wild poliovirus type 1, by province and period — Pakistan, January 2022–June 2023



Abbreviation: WPV1 = wild poliovirus type 1.

Discussion

The Pakistan polio program has made substantial progress toward the elimination of WPV1 transmission. The 21 WPV1 cases reported during January 2022–June 2023 represent a substantial reduction from the 84–147 WPV1 cases reported annually during 2019–2020 (*4*,*5*). Cases have been identified only in a small geographic area in south Khyber Pakhtunkhwa in districts afflicted by persistent insecurity and varying levels of community resistance. The genetic diversity of circulating WPV1 has narrowed from 10 clusters during 2019–2020 (*8*) to two indigenous clusters during the period under review.

Despite this progress, considerable obstacles to interrupting WPV1 transmission in Pakistan by the end of 2023 or the near future remain. AFP surveillance indicators have rebounded to or exceeded prepandemic levels nationally and provincially; however, continued isolation of WPV1 from ES sites in districts in south Khyber Pakhtunkhwa suggest ongoing gaps in AFP surveillance. WPV1 isolations from ES sampling sites in Lahore, Peshawar, and Hangu districts were genetically linked to WPV1 strains circulating in eastern Afghanistan, underscoring the ongoing risk for cross-border transmission as long as WPV1 circulation continues in Afghanistan. The "orphan" WPV1 ES isolate in Karachi highlights the current

limitations of poliovirus surveillance and the challenges faced in reaching a substantial proportion of susceptible children in high-risk areas of Karachi.

To address these issues, meticulous microplanning of SIAs and systematic tracking of repeatedly missed children are needed, including among high-risk mobile populations moving across the shared border with Afghanistan. Wherever feasible, vaccination activities should be synchronized with Afghanistan in coordination with officials in that country and integrated with the delivery of other essential health services to gain the trust of hesitant communities. The safety and morale of frontline workers should remain a critical priority for the polio program, especially in light of occasional targeted attacks on polio workers and their accompanying security personnel.

Limitations

The findings in this report are subject to at least one limitation. With refusals typically accounting for <5% of children missed for vaccination in most areas during polio SIAs, operational issues continue to account for the vast majority of continually missed children. A substantial limitation of this report is that estimates of vaccination coverage might be distorted by caregiver recall. Even when a given child's finger is marked as evidence of vaccination during polio campaigns, the mark might not accurately reflect the true vaccination status because of the practice of fake finger-marking by some vaccinators.

Implications for Public Health Practice

The 2021–2022 WPV1 outbreak in southeastern Africa linked to importation from Pakistan is apparently winding down (*9*); thus, the focus of GPEI partners remains on interrupting endemic WPV1 transmission in Pakistan and Afghanistan, as well as containing cVDPV outbreaks (*10*). Any new detection of poliovirus circulation in Pakistan would require an urgent response to facilitate prompt interruption of virus transmission. Halting the spread of WPV1 in Pakistan requires that the country maintain its strong commitment to ensuring that every child is reached, vaccinated, and protected from the debilitating effects of paralytic polio.

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Effectiveness of Monovalent and Bivalent mRNA Vaccines in Preventing COVID-19–Associated Emergency Department and Urgent Care Encounters Among Children Aged 6 Months–5 Years — VISION Network, United States, July 2022–June 2023

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Abstract

On June 19, 2022, the original monovalent mRNA COVID-19 vaccines were approved as a primary series for children aged 6 months–4 years (Pfizer-BioNTech) and 6 months–5 years (Moderna) based on safety, immunobridging, and limited efficacy data from clinical trials. On December 9, 2022, CDC expanded recommendations for use of updated bivalent vaccines to children aged ≥6 months. mRNA COVID-19 vaccine effectiveness (VE) against emergency department or urgent care (ED/UC) encounters was evaluated within the VISION Network during July 4, 2022–June 17, 2023, among children with COVID-19–like illness aged 6 months–5 years. Among children aged 6 months–5 years who received molecular SARS-CoV-2 testing during August 1, 2022–June 17, 2023, VE of 2 monovalent Moderna doses against ED/UC encounters was 29% (95% CI = 12%–42%) ≥14 days after dose 2 (median = 100 days after dose 2; IQR = 63–155 days). Among children aged 6 months–4 years with a COVID-19–like illness who received molecular testing during September 19, 2022–June 17, 2023, VE of 3 monovalent Pfizer-BioNTech doses was 43% (95% CI = 17%–61%) ≥14 days after dose 3 (median = 75 days after dose 3; IQR = 40–139 days). Effectiveness of ≥1 bivalent dose, comparing children with at least a complete primary series and ≥1 bivalent dose to unvaccinated children, irrespective of vaccine manufacturer, was 80% (95% CI = 42%–96%) among children aged 6 months–5 years a median of 58 days (IQR = 32–83 days) after the dose. All children should stay up to date with recommended COVID-19 vaccines, including initiation of COVID-19 vaccination immediately when they are eligible.

Introduction

As of June 2023, SARS-CoV-2 had resulted in more than 2 million COVID-19 cases, more than 20,000 hospitalizations, and more than 400 deaths among U.S. children aged 6 months–4 years (*1*,*2*). The original monovalent mRNA vaccines were authorized in June 2022 for children aged 6 months–4 years (Pfizer-BioNTech*) and 6 months–5 years (Moderna†) based on safety, immunobridging, and limited efficacy data from clinical trials, with recommendations expanded to include bivalent vaccines in December 2022 (*3*–*5*). Because efficacy data were limited, postauthorization vaccine effectiveness (VE) data are necessary to understand how well the vaccines work and to help guide development of future vaccine policy for this age group.

Methods

VISION,§ a multisite, electronic health care record–based network, evaluated VE against COVID-19–associated emergency department or urgent care (ED/UC) encounters, across six sites in eight states. VISION VE methods have been previously described (*6*). VISION assessed VE among immunocompetent (*7*) children aged 6 months–4 years (monovalent Pfizer-BioNTech, 3-dose primary series) and 6 months–5 years (monovalent Moderna, 2-dose primary series) who visited a

* Pfizer-BioNTech is recommended as 3 3-μg doses, with ≥3–8 weeks between doses 1 and 2 and ≥8 weeks between doses 2 and 3.

† Moderna is recommended as 2 25-μg doses separated by ≥4–8 weeks.

§ Sites from the CDC-funded VISION Network that contributed data for this analysis were Columbia University (New York), HealthPartners and Children's Minnesota (Minnesota and Wisconsin), Intermountain Healthcare (Utah), Kaiser Permanente Northern California (California), Kaiser Permanente Northwest (Oregon and Washington), and University of Colorado (Colorado).

participating ED/UC during July 4, 2022–June 17, 2023, with a COVID-19–like illness[¶] and who received SARS-CoV-2 nucleic acid amplification testing during the 14 days preceding, or up to 72 hours after, the ED/UC encounter. Patients were classified on the index date[**] as unvaccinated (no COVID-19 vaccine doses received), vaccinated with 1 or 2 monovalent Moderna doses or 1, 2, or 3 monovalent Pfizer-BioNTech doses, or vaccinated with ≥1 bivalent dose. ED/UC encounters were excluded if the most recent vaccine dose was received <14 days before the index date, if the child had received a combination of Moderna and Pfizer-BioNTech vaccine doses, or if a vaccination schedule that was not authorized in the study population had been used (e.g., 4 monovalent Pfizer-BioNTech doses or 3 monovalent Moderna doses). Children who had received bivalent doses were only included if they had a complete primary series (either monovalent or bivalent doses).

VE, stratified by vaccine product and number of doses received, was estimated using a test-negative case-control study design, comparing odds of COVID-19 vaccination versus being unvaccinated in case-patients (those who received a positive SARS-CoV-2 test result) and control-patients (those who received a negative test result).[††] Analysis periods varied for each product and dose combination based on differences in recommended schedules for Moderna and Pfizer-BioNTech vaccines.[§§] Children became eligible for inclusion in each analysis 2 weeks after the initial date a child could have received each product and dose combination. Analyses were conducted using R software (version 4.2.2; R Foundation). This study was reviewed and approved by institutional review boards at participating sites or under a reliance agreement with the Institutional Review Board of Westat and was conducted consistent with applicable federal law and CDC policy.[¶¶]

Results

The 90,905 ED/UC encounters in children aged 6 months–5 years eligible for inclusion in the Moderna monovalent analysis included 4,934 (5.4%) case-patients and 85,971 (94.6%) control-patients (Table 1). An additional 96 encounters occurred among control-patients who received ≥1 bivalent Moderna dose. The 81,077 ED/UC encounters in children aged 6 months–4 years eligible for inclusion in the Pfizer-BioNTech monovalent analysis included 4,642 (5.7%) case-patients and 76,435 (94.3%) control-patients. An additional 222 encounters occurred among children who received ≥1 bivalent Pfizer-BioNTech dose; 219 of these were control-patients, and three were case-patients.

To better understand coverage in this population, receipt of monovalent and bivalent doses among all children aged 6 months–5 years, regardless of dose or product received, including children aged 5 years who received a Pfizer-BioNTech dose, was assessed. Among all 5,131 case-patients identified during July 4, 2022–June 17, 2023, a total of 340 (6.6%) had received ≥1 monovalent doses, and three (0.06%) had received ≥1 bivalent dose, regardless of manufacturer. Among all 92,777 control-patients identified during July 4, 2022–June 17, 2023, a total of 11,195 (12.1%) had received ≥1 monovalent dose, and 384 (0.4%) had received ≥1 bivalent dose, irrespective of manufacturer.

VE of a single monovalent Moderna vaccine dose (partial primary series) in children aged 6 months–5 years was 23% ≥14 days after the dose (median = 64 days after the dose), although the 95% CI included the null value (Table 2). VE of 2 monovalent Moderna vaccine doses (complete primary series) in children aged 6 months–5 years was 46% in the 14–59 days after vaccination (median = 38 days). VE of 2 monovalent

[¶] Medical events with a discharge code consistent with COVID-19–like illness were included using *International Classification of Diseases, Tenth Revision* (ICD-10) discharge codes: COVID-19 pneumonia: J12.81 and J12.82; influenza pneumonia: J09.X1, J10.0, J10.00, J10.01, J10.08, J11.0, J11.00, and J11.08; other viral pneumonia: J12*; bacterial and other pneumonia: J13, J14, J15*, J16*, J17, and J18*; influenza disease: J09*, J10.1, J10.2, J10.8*, J11.1, J11.2, and J11.8*; acute respiratory distress syndrome: J80; asthma acute exacerbation: J45.21, J45.22, J45.31, J45.32, J45.41, J45.42, J45.51, J45.52, J45.901, and J45.902; respiratory failure: J96.0*, J96.2*, and R09.2; other acute lower respiratory tract infections: J20*, J21*, J22, J40, J41*, J42, J43*, J47*, J85, J85.0, J85.1, J85.2, J85.3, and J86*; acute and chronic sinusitis: J01*; acute upper respiratory tract infections: J00*, J02*, J03*, J04*, J05*, and J06*; acute respiratory illness signs and symptoms: R04.2, R05, R05.1, R05.2, R05.4, R05.8, R05.9, R06.00, R06.02, R06.03, R06.1, R06.2, R06.8, R06.81, R06.82, R06.89, R07.1, R09.0*, R09.1, R09.2, R09.3, and R09.8*; acute febrile illness signs and symptoms: R50* and R68.83; viral infection, not otherwise specified: B34.9; cause-unspecified gastroenteritis and colitis, unspecified: A09 and K52.9; thrombosis: I82.210, I82.290, I82.220, I82.4*, I82.6*, I82.A1*, I82.B1*, and I82.C1*; acute myocarditis: I40.0, I40.1, I40.8, and I40.9. All ICD-10 codes with * include all child codes under the specific parent code.

[**] The index date for each encounter was defined as either the date of collection of a respiratory specimen associated with the most recent positive or negative SARS-CoV-2 test result before the encounter or the date of the encounter (if testing occurred only after the encounter date).

[††] VE was calculated as (1 – adjusted odds ratio) x 100%. Odds ratios and 95% CIs were estimated using multivariable logistic regression controlling for age, race and ethnicity, sex, calendar day (days since January 1, 2021), and geographic region. Calendar day was modeled as natural cubic splines. Odds ratios in strata with sparse data were calculated using unadjusted exact methods.

[§§] Children became eligible for inclusion 14 days after receiving the dose at different times: 1 dose of Moderna and Pfizer-BioNTech on July 4, 2022; 2 doses of Pfizer-BioNTech on July 25, 2022; 2 doses of Moderna on August 1, 2022; 3 doses of Pfizer-BioNTech on September 19, 2022; and bivalent doses on December 24, 2022.

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

TABLE 1. Characteristics of emergency department and urgent care visits among children aged 6 months–5 years with COVID-19–like illness, by SARS-CoV-2 test result — eight U.S. states, July 4, 2022–June 17, 2023

Characteristic	SARS-CoV-2 test result, no. (column %)			
	Moderna analyses*		Pfizer analyses†	
	Positive (case-patients)	Negative (control-patients)	Positive (case-patients)	Negative (control-patients)
All ED/UC encounters (row %)	**4,934 (5.4)**	**86,067 (94.6)**	**4,645 (5.7)**	**76,654 (94.3)**
Variant-predominant period§				
BA.4/BA.5-related	4,022 (81.5)	63,518 (73.8)	3,756 (80.9)	56,526 (73.7)
XBB-related	912 (18.5)	22,549 (26.2)	889 (19.1)	20,128 (26.3)
Site				
Columbia University	376 (7.6)	10,240 (11.9)	346 (7.4)	9,037 (11.8)
HealthPartners and Children's Minnesota	801 (16.2)	14,196 (16.5)	763 (16.4)	13,197 (17.2)
Intermountain Healthcare	1,825 (37.0)	24,046 (27.9)	1,737 (37.4)	21,718 (28.3)
KPNW	250 (5.1)	4,584 (5.3)	237 (5.1)	3,949 (5.2)
KPNC	1,212 (24.6)	23,629 (27.5)	1,133 (24.4)	20,665 (27.0)
University of Colorado	470 (9.5)	9,372 (10.9)	429 (9.2)	8,088 (10.6)
Age				
6–12 mos	1,531 (31.0)	11,866 (13.8)	1,536 (33.1)	11,968 (15.6)
1 yr	1,402 (28.4)	20,188 (23.5)	1,416 (30.5)	20,624 (26.9)
2 yrs	732 (14.8)	16,117 (18.7)	741 (16.0)	16,397 (21.4)
3 yrs	510 (10.3)	14,857 (17.3)	516 (11.1)	15,066 (19.7)
4 yrs	431 (8.7)	12,194 (14.2)	436 (9.4)	12,599 (16.4)
5 yrs	328 (6.6)	10,845 (12.6)	NA	NA
Sex				
Female	2,203 (44.6)	38,735 (45.0)	2,089 (45.0)	34,297 (44.7)
Male	2,731 (55.4)	47,332 (55.0)	2,556 (55.0)	42,357 (55.3)
Race and ethnicity¶				
Black or African American, non-Hispanic	430 (8.7)	9,261 (10.8)	389 (8.4)	8,012 (10.5)
White, non-Hispanic	1,744 (35.3)	30,379 (35.3)	1,633 (35.2)	27,184 (35.5)
Hispanic or Latino	1,647 (33.4)	28,844 (33.5)	1,567 (33.7)	25,529 (33.3)
Other, non-Hispanic	782 (15.8)	12,195 (14.2)	744 (16.0)	11,163 (14.6)
Unknown	331 (6.7)	5,388 (6.3)	312 (6.7)	4,766 (6.2)
Period**				
Jul 4–31, 2022	914 (18.5)	4,145 (4.8)	847 (18.2)	3,784 (4.9)
Aug–Sep 18, 2022	898 (18.2)	8,569 (10.0)	829 (17.8)	7,658 (10.0)
Sep 19–Dec 23, 2022	1,755 (35.6)	42,680 (49.6)	1,638 (35.3)	37,583 (49.0)
Dec 24, 2022–May 3, 2023	1,250 (25.3)	26,359 (30.6)	1,221 (26.3)	23,815 (31.1)
May 4–June 17, 2023	117 (2.4)	4,314 (5.0)	110 (2.4)	3,814 (5.0)
Medical condition††				
Asthma	124 (2.5)	5,266 (6.1)	102 (2.2)	4,353 (5.7)
Prematurity	11 (0.2)	248 (0.3)	12 (0.3)	227 (0.3)
Chronic lung disease of prematurity	4 (0.1)	125 (0.2)	5 (0.1)	110 (0.2)

See table footnotes on the next page.

Moderna vaccine doses was 21% ≥60 days after vaccination (median = 120 days), although the 95% CI included the null value.

VE of a single monovalent Pfizer-BioNTech dose (partial primary series) in children aged 6 months–4 years was 7% ≥14 days after the dose (median = 58 days), although the 95% CI included the null value. VE of 2 doses (partial primary series) was 46% during the 14–59 days after the second dose (median = 37 days). VE of 2 doses was 27% ≥60 days after vaccination (median = 106 days), although the 95% CI included the null value. VE of 3 doses (complete primary series) was 70% during the 14–59 days after vaccination (median = 35 days). VE of 3 doses was 24% ≥60 days after vaccination (median = 124 days), although the 95% CI included the null value. VE of ≥1 bivalent dose, irrespective of manufacturer or age group in children aged 6 months–5 years with a complete primary series was 80% ≥14 days after receipt of the last dose (median = 58 days).

Discussion

In this multisite analysis from the VISION Network, complete primary mRNA COVID-19 vaccination helped protect against ED/UC encounters in young children, although protection waned in patterns similar to those seen in older children and adults (*7*,*8*). In this analysis, receipt of ≥1 bivalent vaccine dose, irrespective of the manufacturer, provided 80% protection for children who had received a complete primary

TABLE 1. (*Continued*) Characteristics of emergency department and urgent care visits among children aged 6 months–5 years with COVID-19–like illness, by SARS-CoV-2 test result — eight U.S. states, July 4, 2022–June 17, 2023

Characteristic	SARS-CoV-2 test result, no. (column %)			
	Moderna analyses*		Pfizer analyses†	
	Positive (case-patients)	Negative (control-patients)	Positive (case-patients)	Negative (control-patients)
Vaccination status,§§ total no. of doses, vaccine				
Unvaccinated	4,791 (97.1)	81,573 (94.8)	4,469 (96.2)	71,147 (92.8)
1 dose total, MV Moderna	47 (1.0)	968 (1.1)	NA	NA
2 doses total, MV Moderna	96 (1.9)	3,430 (4.0)	NA	NA
2 doses total, BV Moderna	0 (—)	0 (—)	NA	NA
2 doses total, 1 MV Moderna, 1 BV Moderna	0 (—)	2 (—)	NA	NA
3 doses total, 2 MV Moderna, 1 BV Moderna	0 (—)	94 (0.1)	NA	NA
1 dose total, MV Pfizer-BioNTech	NA	NA	75 (1.6)	1,451 (1.9)
2 doses total, MV Pfizer-BioNTech	NA	NA	70 (1.5)	2,437 (3.2)
3 doses total, MV Pfizer-BioNTech	NA	NA	28 (0.6)	1,400 (1.8)
3 doses total, BV Pfizer-BioNTech	NA	NA	0 (—)	0 (—)
3 doses total, 2 MV Pfizer-BioNTech, 1 BV Pfizer-BioNTech	NA	NA	3 (0.1)	205 (0.3)
3 doses total, 1 MV Pfizer-BioNTech, 2 BV Pfizer-BioNTech	NA	NA	0 (—)	2 (—)
4 doses total, 3 MV Pfizer-BioNTech, 1 BV Pfizer-BioNTech	NA	NA	0 (—)	12 (—)
Received ≥1 bivalent dose, irrespective of manufacturer	0 (—)	96 (0.1)	3 (0.1)	219 (0.3)

Abbreviations: BV = bivalent; ED = emergency department; ICD-10 = *International Classification of Diseases, Tenth Revision*; KPNC = Kaiser Permanente Northern California; KPNW = Kaiser Permanente Northwest; MV = monovalent; NA = not applicable; UC = urgent care; VE = vaccine effectiveness.

* Children who received Pfizer-BioNTech COVID-19 vaccine were excluded from the Moderna VE analyses. Ninety-six Moderna bivalent dose recipients are included in the table but were excluded from the monovalent Moderna-specific primary series analyses.

† Children who received Moderna COVID-19 vaccine were excluded from the Pfizer-BioNTech VE analyses. A total of 226 recipients of Pfizer-BioNTech bivalent doses are included in the table but were excluded from the monovalent Pfizer-BioNTech–specific primary series analyses.

§ Variant predominance was defined as the period during which a variant accounted for ≥50% of all sequenced specimens in the U.S. Department of Health and Human Services region where the site is located. XBB-related sublineages predominated at Columbia University beginning December 31, 2022; at Intermountain Healthcare and University of Colorado beginning January 28, 2023; at HealthPartners and Children's Minnesota and KPNC beginning February 4, 2023; and at KPNW beginning February 11, 2023.

¶ Children whose caregiver reported non-Hispanic ethnicity and any of the following for race were classified as other, non-Hispanic: American Indian or Alaska Native, Asian, Native Hawaiian or other Pacific Islander, or other race, or whose caregiver reported not Hispanic with no corresponding race chosen. Children whose caregiver did not report race and ethnicity were classified as unknown.

** Periods were divided based on when children were eligible for inclusion in analyses according to updates to primary series vaccination policy as follows: July 4, 2022 = 14 days after recommendation of the monovalent primary series; August 1, 2022 = first children eligible for inclusion in analyses of second dose of Pfizer-BioNTech or Moderna monovalent vaccine; September 19, 2022 = first children eligible for inclusion in analyses of third dose of Pfizer-BioNTech monovalent vaccine; December 24, 2022 = first children eligible for inclusion in analyses of bivalent vaccines; and May 4 = first children eligible for inclusion after receipt of bivalent primary series doses. https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us-appendix.html

†† Asthma included children with the following ICD-10 discharge code: J45*; prematurity included children with the following ICD-10 discharge code: P07*; chronic lung disease of prematurity included children with the following ICD-10 discharge code: P27.1. Data on chronic lung disease of prematurity were not available from one site.

§§ Vaccination status categories are mutually exclusive. Percentages reflect column percentages among analytic sample and because of exclusion criteria do not reflect vaccine coverage in the population of children with ED/UC encounters. Among all control-children aged 6–23 months, 2–4 years, and 5 years (including children aged 5 years who received the Pfizer-BioNTech 10-μg dose), 10.2%, 13.1%, and 13.4% received ≥1 COVID-19 vaccine dose, respectively. Ten children who received a bivalent dose but did not complete a primary series were dropped, including two children who received 1 bivalent Moderna dose only, four children who received 1 monovalent Pfizer-BioNTech and 1 bivalent Pfizer-BioNTech dose, three children who received 1 monovalent Pfizer-BioNTech dose only, and one child who received 2 bivalent Pfizer-BioNTech doses.

series ≥14 days earlier compared with unvaccinated children; however, few children had received a bivalent dose, so the estimate was imprecise. In addition, the median interval since receipt of the bivalent dose was only 58 days, meaning there was little time for waning to be observed.

A single dose (i.e., an incomplete primary series) of either monovalent Moderna or Pfizer-BioNTech did not provide protection. VE of 2 doses of monovalent vaccine ≥14 days after the second dose was 37% among children aged 6 months–4 years (Pfizer-BioNTech) and 29% among those aged 6 months–5 years (Moderna), aligning with previous data showing effectiveness of ≥2 vaccine doses in young children (*9*). Of note, the predominantly circulating SARS-CoV-2 variants had evolved substantially from the strain included in the original monovalent COVID-19 vaccines by the time young children became eligible, highlighting the importance of receiving an updated vaccine.

To date, limited VE data are available for young children. A previous analysis of national pharmacy testing data showed generally similar patterns of VE by number of doses and time since vaccination in children aged 3–5 years, but higher VE than in the current analysis (*9*). This finding might be related to several factors that might have affected the control populations, including differences among children who are tested at

TABLE 2. Vaccine effectiveness* against laboratory-confirmed COVID-19–associated emergency department and urgent care encounters among children aged 6 months–4 years (Pfizer-BioNTech analyses) and 6 months–5 years (Moderna analyses), by vaccine product, number of doses, and time since last dose — eight U.S. states, July 2022–June 2023

Vaccine product, age group, analysis period,† no. of doses (time since last dose)	Total	Positive SARS-CoV-2 test result, no. (%)	Median interval since last dose, days (IQR)	VE§ (95% CI)
Monovalent Moderna vaccine, aged 6 mos–5 yrs				
1-dose VE analysis, Jul 4, 2022–Jun 17, 2023				
Unvaccinated (Ref)	**86,364**	4,791 (5.5)	NA	Ref
1 dose only (≥14 days)	**1,015**	47 (4.6)	64 (29 to 117)	23 (−4 to 43)
2-dose VE analysis, Aug 1, 2022–Jun 17, 2023				
Unvaccinated (Ref)	**81,373**	3,887 (4.8)	NA	Ref
2 doses (≥14 days)	**3,526**	96 (2.7)	100 (63 to 155)	29 (12 to 42)
2 doses (14–59 days)	**806**	23 (2.9)	38 (26 to 49)	46 (17 to 64)
2 doses (≥60 days)	**2,720**	73 (2.7)	120 (89 to 178)	21 (−1 to 38)
Monovalent Pfizer-BioNTech COVID-19 vaccine, aged 6 mos–4 yrs				
1-dose VE analysis, Jul 4, 2022 – Jun 17, 2023				
Unvaccinated (Ref)	**75,616**	4,469 (5.9)	NA	Ref
1 dose only (≥14 days)	**1,526**	75 (4.9)	58 (28 to 106)	7 (−18 to 26)
2-dose VE analysis, Jul 25, 2022–Jun 17, 2023				
Unvaccinated (Ref)	**72,101**	3,828 (5.3)	NA	Ref
2 doses only (≥14 days)	**2,507**	70 (2.8)	67 (40 to 115)	37 (19 to 51)
2 doses (14–59 days)	**1,105**	32 (2.9)	37 (25 to 47)	46 (22 to 62)
2 doses (≥60 days)	**1,402**	38 (2.7)	106 (81 to 155)	27 (−2 to 47)
3-dose VE analysis, Sep 19, 2022–Jun 17, 2023				
Unvaccinated (Ref)	**62,977**	2,829 (4.5)	NA	Ref
3 doses only (≥14 days)	**1,428**	28 (2.0)	75 (40 to 139)	43 (17 to 61)
3 doses (14–59 days)	**563**	6 (1.1)	35 (25 to 46)	70 (34 to 87)
3 doses (≥60 days)	**865**	22 (2.5)	124 (86 to 170)	24 (−17 to 51)
≥1 bivalent vaccine among children who received at least a complete primary series, irrespective of manufacturer, aged 6 mos–5 yrs¶				
Dec 24, 2022–Jun 17, 2023				
Unvaccinated (Ref)	**30,146**	1,328 (4.4)	NA	Ref
≥1 bivalent dose (≥14 days)	**318**	3 (0.9)	58 (32 to 83)	80 (42 to 96)**

Abbreviations: NA = not applicable; Ref = referent group; VE = vaccine effectiveness.

* VE was calculated as (1 − adjusted odds ratio) x 100%, estimated using a test-negative case-control design, adjusted for age, sex, race and ethnicity, geographic region, and calendar time (days since January 1, 2021).

† Different analysis periods were used for each product and dose number because vaccinated children became eligible to be included 14 days after the dose at different times: 1 dose of Moderna and Pfizer-BioNTech on July 4, 2022; 2 doses of Pfizer-BioNTech on July 25, 2022; 2 doses of Moderna on August 1, 2022; 3 doses of Pfizer-BioNTech on September 19, 2022; and bivalent doses on December 24, 2022.

§ Some estimates are imprecise, which might be due to a relatively small number of persons in each level of vaccination or case status. This imprecision indicates that the actual VE could be substantially different from the point estimate shown, and estimates should therefore be interpreted with caution. Additional data accrual could increase precision and allow more precise interpretation.

¶ Children included in this estimate were either unvaccinated (received zero COVID-19 vaccine doses) or had received ≥1 bivalent vaccine dose from either manufacturer. Among those who received a bivalent vaccine dose, any combination of monovalent and bivalent doses was included, but at a minimum children had to have received 2 Moderna doses or 3 Pfizer-BioNTech doses (i.e., a complete primary series).

** This estimate was calculated using unadjusted exact methods because of the small number of vaccinated case-patients. All three vaccinated case-patients received bivalent Pfizer-BioNTech doses; vaccinated control-patients included those who received both bivalent Moderna (96) and Pfizer-BioNTech (223) doses.

pharmacies compared with those who are treated in an ED/UC, different analysis periods leading to different abilities to assess waning of VE, differences in circulating SARS-CoV-2 subvariants between the two analyses, and differences in circulation of other viruses, including respiratory syncytial virus and influenza.

The median interval since receipt of the most recent dose among children who had not completed their primary series was longer than expected based on the recommended dosing intervals: a median of 64 days since Moderna dose 1 compared with the 4–8 weeks recommended between Moderna doses and a median of 58 days since receiving Pfizer-BioNTech dose 1 versus 3–8 weeks recommended between doses 1 and 2; this aligns with available national data showing that approximately 10% of children aged 2–4 years had received ≥1 COVID-19 vaccine dose and only 6.1% had completed the primary series as of May 2023,*** nearly a full year after vaccines were recommended for this age group.

Limitations

The findings in this report are subject to at least five limitations. First, VE estimates for Moderna and Pfizer-BioNTech are not directly comparable because of different dates of eligibility for completion of the primary series, which might affect

*** https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends (Accessed July 14, 2023).

Summary

What is already known about this topic?

The original monovalent COVID-19 mRNA vaccines were first recommended in the United States in June 2022 for young children; bivalent vaccines were recommended in December 2022. Postauthorization vaccine effectiveness data in this age group are limited.

What is added by this report?

Monovalent and bivalent mRNA vaccines helped provide protection against COVID-19–associated emergency department and urgent care visits among children aged 6 months–4 years (Pfizer-BioNTech) and 6 months–5 years (Moderna).

What are the implications for public health practice?

All children should stay up to date with recommended COVID-19 vaccines, including initiating COVID-19 vaccination immediately when they become eligible.

product-specific VE estimates. Different rates of SARS-CoV-2 infection in the population and different circulating subvariants during August 1–September 19, 2022 (when VE could only be assessed for a complete Moderna primary series) compared with September 19, 2022–June 17, 2023 (when VE of a complete primary series for both products could be assessed), likely also affects comparability. Second, vaccination coverage among young children, including those in this analysis, is low, and vaccinated children might systematically differ from unvaccinated children (or from those who initiated but did not complete the primary series) in COVID-19 risk or likelihood of seeking care, which could bias VE results. Third, the combination of low vaccination coverage, relatively low SARS-CoV-2 circulation during the study period, and low overall rates of hospitalization in this age group precluded the assessment of VE against more severe outcomes, which is the primary goal of the U.S. COVID-19 vaccination program. In addition, low bivalent vaccination coverage precluded the estimation of product-specific VE. Fourth, this analysis was not able to control for previous infection because of underreporting in the medical record, which might have resulted in biased estimates. By July–August 2022, among children aged 6–11 months, 12–23 months, and 2–4 years, 66%, 74%, and 83%, respectively, had evidence of infection-induced SARS-CoV-2 immunity.[†††] These findings should therefore be interpreted as the incremental benefit provided by COVID-19 vaccination in a population with a high prevalence of infection-induced immunity. Finally, because these data are from eight states, this analysis might not be representative of the entire U.S. population.

[†††] https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-COVID-Jones-508.pdf

Implications for Public Health Practice

Complete Moderna or Pfizer-BioNTech primary series vaccination helped protect against COVID-19–associated ED/UC visits in young children. Although bivalent vaccination coverage was low in this group, ≥1 dose of bivalent vaccine also helped provide protection. All children should stay up to date with recommended COVID-19 vaccines, including initiating COVID-19 vaccination immediately when children become eligible.[§§§]

[§§§] https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html

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Epidemiologic and Clinical Features of Mpox in Adults Aged >50 Years — United States, May 2022–May 2023

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Abstract

During May 2022–May 2023, approximately 30,000 mpox cases were reported in the United States, predominantly among young adult men. Persons aged >50 years might experience more severe mpox disease because of a higher prevalence of comorbidities. Conversely, they could have residual protection from childhood smallpox vaccination against monkeypox virus infection and severe mpox, as has been suggested by investigation of some previous mpox outbreaks. To examine the characteristics of mpox cases among adults aged >50 years, analysts compared mpox epidemiology and clinical outcomes among all adults aged ≥18 years, by age group. Further, outcomes were compared among adults aged >50 years by JYNNEOS vaccination status. During May 10, 2022–May 17, 2023, among 29,984 adults with probable or confirmed mpox reported to CDC, 2,909 (9.7%) were aged >50 years, 96.3% of whom were cisgender men. Compared with adults aged 18–50 years, adults aged >50 years had higher prevalences of immunocompromising conditions (p<0.001) and HIV infection (p<0.001). Among adults with mpox aged >50 years, 27.6% had received JYNNEOS vaccination; this group had lower prevalences of constitutional symptoms (p<0.001), pruritus (p<0.001), and hospitalization (p = 0.002) compared with those who had not received JYNNEOS vaccine. Currently recommended JYNNEOS vaccination among all adults at risk for mpox should be encouraged, irrespective of childhood smallpox vaccination status.

Introduction

During May 10, 2022–May 17, 2023, a total of 30,401 mpox cases* were reported in the United States, predominantly among young adult men. Adults aged >50 years likely received childhood smallpox vaccination, which was given routinely to children in the United States before being discontinued in 1971†; therefore, they might be less susceptible to monkeypox virus infection as a result of cross-protection (*1*). Childhood smallpox vaccination has been shown to provide partial protection against mpox, both in preventing monkeypox virus infection and severe mpox, in studies of earlier mpox outbreaks in the Democratic Republic of the Congo (*2*) and the United States (*3*). Because adults aged >50 years are likely to have more comorbidities than are younger adults, they might experience severe mpox disease, often with indications for treatment (*4*). This analysis described age group–specific epidemiologic characteristics and clinical mpox outcomes among adults and compared characteristics and outcomes among adults aged >50 years by recent JYNNEOS vaccination status.

Methods

Data on confirmed or probable mpox cases§ among persons aged ≥18 years collected by jurisdictional public health departments and electronically reported through the National Notifiable Disease Surveillance System¶ or via a standardized case report form** during May 10, 2022–May 17, 2023, were included in the analysis. Adults with mpox were categorized into two age groups: 18–50 years and >50 years. Age-stratified categorical data, including epidemiologic characteristics, particularly sociodemographic characteristics, sexual contact during the 3 weeks preceding illness onset, HIV status, immunocompromising comorbidities excluding HIV (e.g., having undergone organ or stem cell transplant, active cancer, or immunosuppressive therapies), receipt of JYNNEOS vaccine, and clinical outcomes were summarized as frequencies and compared using Pearson's chi-square or Fisher's exact tests; p-values <0.05 were considered statistically significant. Adults who received ≥1 dose of JYNNEOS vaccine during the 2022 mpox outbreak were classified as vaccinated for the purposes of this report. To control for the potential effect of JYNNEOS vaccination on mpox clinical outcomes, analysts excluded adults with mpox who had received JYNNEOS when age-stratified clinical outcomes were being compared. An additional analysis among adults aged >50 years with mpox compared epidemiologic characteristics and clinical outcomes by JYNNEOS vaccination status; in this analysis, adults aged >50 years with mpox with unknown or missing JYNNEOS vaccination status or unknown or missing vaccination date were excluded. All statistical analyses were conducted using

* Includes cases from all age groups. https://www.cdc.gov/poxvirus/mpox/response/2022/index.html (Accessed May 17, 2023).

† Routine childhood smallpox vaccination ended in 1971 in the United States, although vaccination continued for some persons because of implementation nuances and recommendations based on risk. https://www.cdc.gov/mmwr/preview/mmwrhtml/rr6402a1.htm

§ Cases include positive test results for either *Monkeypox virus* or *Orthopoxvirus*.

¶ https://www.cdc.gov/nndss/index.html

** https://www.cdc.gov/poxvirus/mpox/pdf/sCRF-Short-Form.pdf

SAS software (version 9.4; SAS Institute). This analysis was reviewed by CDC and was conducted consistent with federal law and applicable CDC policy.[††]

Results

Among 29,984 adults with mpox reported by May 17, 2023, 2,909 (9.7%) were aged >50 years, including 2,794 (96.3%) who were cisgender men (Table 1). Among those aged >50 years, 1,297 (47.3%) were non-Hispanic White (White), 561 (20.5%) were non-Hispanic Black or African American (Black), and 758 (27.7%) were Hispanic or Latino (Hispanic). Among the 27,075 adults with mpox aged 18–50 years, 7,085 (27.8%) were White, 8,733 (34.2%) were Black, and 7,878 (30.9%) were Hispanic (p<0.001). Reports of any sexual contact during the 3 weeks preceding illness onset was similar among adults with mpox aged 18–50 years (78.6%) and those aged >50 years (77.0%). Among cisgender men with mpox, who accounted for 95.2% and 96.3% of adults with mpox aged 18–50 years and >50 years, respectively, 96.6% of these contacts among those aged 18–50 years, and 97.0% among those aged >50 years, were with other cisgender men. Immunocompromising conditions were more prevalent overall among adults aged >50 years (15.0%) than among those aged 18–50 years (11.1%), as was receipt of JYNNEOS vaccine (27.6% and 21.3%, respectively). Examination of symptoms and outcomes among adults with mpox who had not received JYNNEOS vaccine found lower prevalences of gastrointestinal (rectal or abdominal)[§§] and constitutional symptoms[¶¶] among those aged >50 years (37.3% and 85.0%, respectively) than among those aged 18–50 years (50.3% and 91.2%, respectively); the prevalences of hospitalization and death were comparable between the two age groups.

Among 1,020 adults with mpox aged >50 years with known JYNNEOS vaccination status, the prevalences of HIV and immunocompromising conditions were similar among those who did and did not receive JYNNEOS vaccine (Table 2). Among those aged >50 years, the prevalences of constitutional symptoms (64.9%), pruritus (44.1%), and hospitalization (1.2%) among those who had received JYNNEOS vaccine were lower than were those among persons who did not receive vaccine (81.3%, 56.9%, and 7.4%, respectively).

Discussion

Mpox might affect multiple organ systems; therefore, persons with comorbidities, including HIV and immunocompromising conditions, which are more prevalent among adults aged >50 years, might be at increased risk for more severe mpox disease (*4*). Most deaths and hospitalizations among adults with mpox in the United States during the recent outbreak occurred in persons with immunocompromising conditions (*5*,*6*). In this report, however, excluding adults who had received JYNNEOS vaccine, the prevalences of hospitalization and death among adults aged >50 years with mpox were similar to those in persons aged 18–50 years, and the prevalences of some symptoms were lower among adults aged >50 years than among those aged 18–50 years. Although the reasons for this finding are not clear, receipt of smallpox vaccine as part of childhood immunization before routine smallpox vaccination discontinued in the United States in 1971 might confer some level of protection against mpox in the current outbreak, with respect to whether the clinical presentation was atypical or asymptomatic (*7*).

The prevalences of pruritus, constitutional symptoms, and hospitalizations were lower among adults with mpox aged >50 years who received JYNNEOS vaccine than among those who did not receive the vaccine. Although childhood smallpox vaccination might confer some protection against monkeypox virus infection and might mitigate mpox disease severity, it is likely that receiving the currently recommended JYNNEOS vaccine provided additional protection. This finding is consistent with a study among adults who received JYNNEOS vaccine, wherein adults who received ≥1 dose of JYNNEOS vaccine had lower rates of hospitalization and symptoms (*8*). This finding underscores the importance that persons at risk

Summary

What is already known about this topic?

Childhood smallpox vaccination confers some cross-protection against mpox. Although persons aged >50 years likely received childhood smallpox vaccination, they might have more comorbidities and a higher risk for severe mpox compared with those aged ≤50 years. Information about waning cross-protective immunity and how this might affect risk for severe mpox is limited.

What is added by this report?

Among 29,984 adults with mpox, those aged >50 years had higher prevalences of immunocompromising conditions and HIV and lower prevalence of symptoms than did those aged ≤50 years. Among 1,020 adults aged >50 years with vaccination data, prevalences of pruritus, constitutional symptoms, and hospitalization were lower among those who received JYNNEOS vaccine than among those who had not.

What are the implications for public health practice?

All adults at risk for mpox should receive JYNNEOS vaccine, irrespective of childhood smallpox vaccination status.

[††] 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.
[§§] Includes rectal pain/bleeding, pus in the stool, proctitis, or tenesmus.
[¶¶] Includes fever, headache, malaise, myalgia, chills, or lymphadenopathy.

TABLE 1. Demographic and epidemiologic characteristics of adults with mpox, by age group (N = 29,984) — United States, May 10, 2022–May 17, 2023

Characteristic and clinical outcome	Age group, no. (column %)* 18–50 yrs n = 27,075	>50 yrs n = 2,909	p-value†
Gender identity			
Cisgender men	25,681 (95.2)	2,794 (96.3)	<0.001
Cisgender women	809 (3.0)	88 (3.0)	
Transgender men	55 (0.2)	0 (—)	
Transgender women	220 (0.8)	9 (0.3)	
Other gender identity	225 (0.8)	11 (0.4)	
Missing	85	7	
Race and ethnicity§			
Black or African American	8,733 (34.2)	561 (20.5)	<0.001
White	7,085 (27.8)	1,297 (47.3)	
Hispanic or Latino	7,878 (30.9)	758 (27.7)	
Other	1,684 (6.6)	120 (4.4)	
Multiracial	134 (0.5)	4 (0.1)	
Missing	1,561	169	
Any sexual contact during the 3 wks preceding illness onset			
Yes	15,495 (78.6)	1,618 (77.0)	0.083
No	4,216 (21.4)	484 (23.0)	
Missing	7,364	807	
Sexual partner among cisgender men¶			
Cisgender men only	12,561 (93.5)	1,393 (94.8)	0.201
Cisgender men and other genders	419 (3.1)	32 (2.2)	
Exclude cisgender men	454 (3.4)	45 (3.1)	
Missing	12,247	1,324	
HIV status			
HIV positive	4,798 (55.4)	552 (66.2)	<0.001
HIV negative	3,860 (44.6)	282 (33.8)	
Unknown HIV status or missing	18,417	2,075	
Immunocompromising condition**			
Yes	1,308 (11.1)	185 (15.0)	<0.001
No	10,466 (88.9)	1,045 (85.0)	
Missing	15,301	1,679	
Received ≥1 dose of JYNNEOS vaccine			
Yes	2,481 (21.3)	282 (27.6)	<0.001
No	9,177 (78.7)	738 (72.4)	
Missing	15,417	1,889	
Rash††			
Yes	6,867 (96.8)	563 (96.6)	0.72
No	224 (3.2)	20 (3.4)	
Missing	2,086	155	
Pruritus††			
Yes	2,972 (58.7)	221 (59.4)	0.78
No	2,092 (41.3)	151 (40.6)	
Missing	4,113	366	
Rectal symptoms††,§§ or abdominal pain			
Yes	2,719 (50.3)	134 (37.3)	<0.001
No	2,683 (49.7)	225 (62.7)	
Missing	3,775	379	
Constitutional symptoms††,¶¶			
Yes	6,103 (91.2)	424 (85.0)	<0.001
No	586 (8.8)	75 (15.0)	
Missing	2,488	239	
Hospitalization††			
Yes	657 (7.5)	58 (8.3)	0.459
No	8,110 (92.5)	644 (91.7)	
Missing	410	36	
Death††			
Yes	12 (0.2)	3 (0.6)	0.069
No	6,488 (99.8)	532 (99.4)	
Missing	2,677	203	

* Percentages were calculated using nonmissing data.
† Pearson's chi-square or Fisher's exact test.
§ Persons of Hispanic or Latino (Hispanic) origin might be of any race but are categorized as Hispanic; all racial groups are non-Hispanic.
¶ Only among cisgender men aged 18–40 years (25,681) and >50 years (2,794).
** Excluding HIV infection and AIDS.
†† Clinical outcomes were compared by age group after excluding adults who received JYNNEOS vaccine (2,763).
§§ Includes rectal pain/bleeding, pus in the stool, proctitis, or tenesmus.
¶¶ Includes fever, headache, malaise, myalgia, chills, or lymphadenopathy.

for mpox, particularly adults aged >50 years, receive currently recommended JYNNEOS vaccination. Immunologic studies have demonstrated some long-term immunologic memory from childhood smallpox vaccination that is cross-protective against mpox (*7*,*9*), but such immunity might have waned (*7*). JYNNEOS vaccination is recommended for all adults who are at risk for mpox irrespective of receipt of childhood smallpox vaccination (*10*).

Limitations

The findings in this report are subject to at least four limitations. First, data for some variables, such as HIV status, presence of immunocompromising conditions and mpox symptoms, and JYNNEOS vaccination status were frequently missing in national case surveillance data, which limits full characterization of the epidemiologic and clinical features among adults with mpox and could contribute to confounding bias. Second, some variables were self-reported, and might be subject to recall and social desirability biases. Third, receipt of smallpox vaccination was assumed for all adults aged >50 years despite nuances in implementation in the United States and other countries of origin of adults with mpox. Finally, this analysis was limited to confirmed and probable mpox cases reported to jurisdictional public health departments and might not represent all adults with mpox.

Implications for Public Health Practice

Hospitalization was less likely among adults aged >50 years with mpox who had received JYNNEOS vaccine than among those who had not. All adults who are at risk for acquiring mpox, regardless of childhood smallpox vaccination status, should receive 2 doses of JYNNEOS vaccine (*10*).

TABLE 2. Characteristics, symptoms, and clinical outcomes among adults aged >50 years with mpox and known JYNNEOS vaccination status,* by vaccination status (N = 1,020) — United States, May 10, 2022–May 17, 2023

Characteristic or outcome	Received JYNNEOS vaccine, no. (column %)†		
	No n = 738	Yes n = 282	p-value§
HIV status			
Positive	492 (66.8)	60 (61.9)	0.974
Negative	245 (33.2)	37 (38.1)	
Unknown or missing	1,994	81	
Immunocompromising condition¶			
Yes	172 (15.0)	13 (14.9)	0.356
No	971 (85.0)	74 (85.1)	
Missing	1,588	91	
Constitutional symptoms**			
Yes	1,320 (81.3)	74 (64.9)	<0.001
No	303 (18.7)	40 (35.1)	
Missing	1,108	64	
Rash			
Yes	1,928 (97.7)	123 (93.9)	0.895
No	45 (2.3)	8 (6.1)	
Missing	758	47	
Pruritus			
Yes	489 (56.9)	41 (44.1)	<0.001
No	371 (43.1)	52 (55.9)	
Missing	1,871	85	
Rectal symptoms†† or abdominal pain			
Yes	451 (36.3)	43 (43.0)	0.486
No	791 (63.7)	57 (57.0)	
Missing	1,489	78	
Hospitalization			
Yes	163 (7.4)	2 (1.2)	0.002
No	2,044 (92.6)	160 (98.8)	
Missing	524	16	
Death			
Yes	5 (0.3)	0 (—)	0.446
No	1,647 (99.7)	100 (100.0)	
Missing	1079	78	

* A total of 1,889 (65%) mpox patients were excluded because vaccination status (1662; 57%) or date (227; 8%) was missing or unknown.
† Percentages were calculated using nonmissing data.
§ Pearson's chi-square or Fisher's exact test.
¶ Excluding HIV infection and AIDS.
** Includes fever, headache, malaise, myalgia, chills, or lymphadenopathy.
†† Includes rectal pain/bleeding, pus in the stool, proctitis, or tenesmus.

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Notes from the Field

Outbreak of Norovirus Linked to a Food Establishment — Illinois, November 2022

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On November 26, 2022, the Tazewell (Illinois) County Health Department (TCHD) contacted the Illinois Department of Public Health (IDPH) concerning a large acute gastroenteritis outbreak linked to restaurant A in Illinois. TCHD conducted an outbreak investigation with the assistance of IDPH, including a case-control study that identified 317 norovirus infections among respondents (excluding the primary patient) who dined at restaurant A during November 19–26, 2022.

Investigation and Outcomes

A probable case was defined as the occurrence of diarrhea (three or more loose stools within 24 hours) or vomiting in a person who dined at restaurant A during November 19–26; probable cases with norovirus RNA detected in a stool specimen submitted to the IDPH laboratory were considered confirmed. Notification of the outbreak and requests for information from persons who had dined at restaurant A during November 19–26 were disseminated to the public by TCHD and restaurant A. The press also shared information about the outbreak on November 28, 2022, encouraging all persons who dined at restaurant A to report this to TCHD; after the release of news stories by the press, the number of reported ill persons doubled.

Overall, 317 case-patients (three with confirmed and 314 with probable norovirus infection) and 40 control patients (persons who dined at restaurant A during November 19–26 and did not become ill) were interviewed initially through an online form to identify epidemiologic links and common food exposures. When secondary phone interviews were conducted to confirm the illness onset date, pizza toppings, salad dressings, and condiments consumed, only 268 ill persons and 40 controls participated; the additional 49 ill persons were lost to follow-up. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.*

Although the outbreak originated in Tazewell County, ill persons resided in 10 additional Illinois counties and 12 other states; some secondary cases were reported within the households of restaurant patrons and were not included in the total of 317 case-patients. Restaurant patrons shared illness information and menu items consumed, via an online questionnaire and follow-up interview; among the 317 ill persons sharing information through the online questionnaire and phone calls, 268 (85%) participated in the secondary interview; 49 (15%) ill persons were lost to follow-up. Among the 268 interviewed persons with information on illness onset date, symptoms commenced during November 20–28, with 114 (43%) cases occurring on November 24 (Figure). The mean incubation period (interval from dining at restaurant A until symptom onset) was 22 hours (range = 3–45 hours), and the average illness duration was 37 hours (range = 3–96 hours). Nearly one third of cases (32%) occurred in persons aged 20–49 years (range = 6 months–83 years). Signs and symptoms reported by 317 case-patients through the online questionnaire included vomiting (84%), nausea (80%), diarrhea (68%), myalgias (40%), chills (38%), abdominal cramps (26%), and fever (19%). Seven persons were evaluated in an emergency department, and five visited an outpatient health care provider; no hospital admissions or deaths occurred.

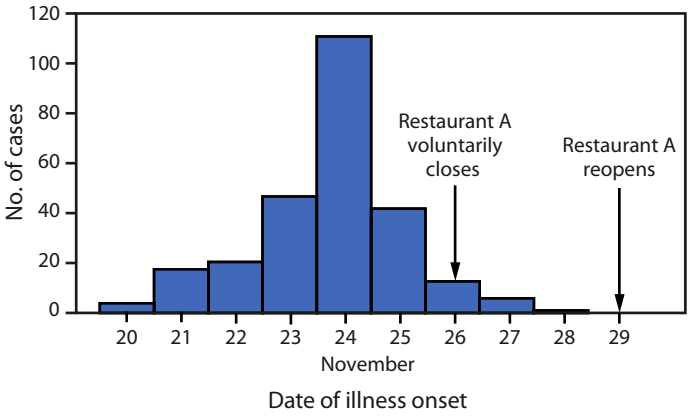
Preliminary Conclusions and Actions

Based on data obtained from the questionnaire, the suspected food vehicle was salad (odds ratio = 9.23; 95% CI = 4.48–18.99); 227 of 268 ill persons and 15 of 40 controls consumed salad. Twenty-seven ill persons did not eat salad but did consume additional sauces and dressings. Environmental and epidemiologic investigations indicated that contamination occurred throughout the food preparation process includes the division of the salad, toppings, and dressings into individual portions that are refrigerated for consumption on the following day. Preparation with ungloved hands by a food handler who had vomiting on November 22, and worked during November 21–23, likely served as a main contributor to the outbreak. The restaurant voluntarily closed on November 26 for disinfection and reopened on November 29, after a health inspection. TCHD provided education to food handlers on hand hygiene, staying home from work when ill with diarrhea or vomiting, and cleaning procedures.

Noroviruses are a leading cause of reported foodborne disease outbreaks associated with contamination of food in restaurants during preparation by infected food workers (*1*). A large restaurant-associated norovirus outbreak occurred through the main food vehicle of salad, likely following ungloved hand contact with the salad by an ill food handler during food preparation. Because a large number of persons had patronized the restaurant over the Thanksgiving holiday,

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

FIGURE. Norovirus cases among restaurant patrons associated with an ill food handler, by date of illness onset (N = 268)* — Illinois,† November 20–28, 2022



* Among 317 total reported cases, onset dates were not included for 49 ill persons with probable cases who were lost to follow-up.
† Although the outbreak originated in Tazewell County, Illinois, ill persons lived in 10 additional Illinois counties and 12 other states.

the ability to identify exact numbers of ill and well patrons was limited, and the number of cases is likely underreported.

The Food and Drug Administration's 2022 Food Code cites noroviruses as the leading cause of foodborne illness in the United States, and proper hand hygiene and exclusion of symptomatic employees are essential for preventing outbreaks† (*1*–*5*). Prevention or mitigation of future norovirus outbreaks in food service establishments depends upon reinforcing the need for proper handwashing, performing thorough environmental cleaning, using appropriate personal protective equipment, and excluding workers from the workplace when they are ill with vomiting and diarrhea and for at least 48 hours after resolution of symptoms (*2*–*4*).

† https://www.fda.gov/food/fda-food-code/food-code-2022

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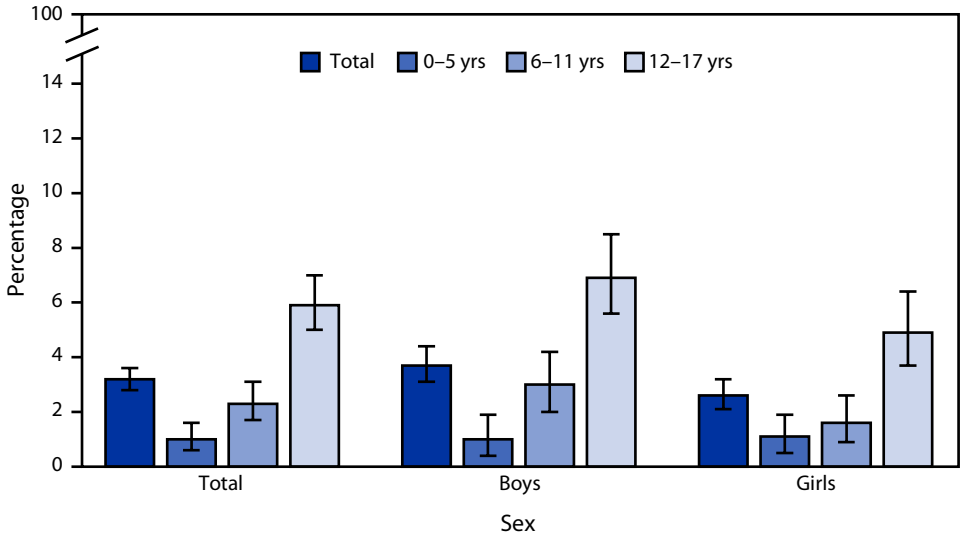
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Percentage* of Children and Adolescents Aged ≤17 Years Who Had Ever Received a Diagnosis of Concussion or Brain Injury,† by Sex and Age Group — National Health Interview Survey,§ United States, 2022



* With 95% CIs indicated by error bars.
† Based on parent or guardian responses to the questions, "Has (child) ever been checked for a concussion or brain injury by a doctor, nurse, athletic trainer, or other health professional?" and "Did a doctor, nurse, athletic trainer, or other health professional ever say that (child) had a concussion or brain injury?" Respondents who answered "no" to the first question were not asked about diagnosis but were included in the denominator. In 2022, 2.3 million children and adolescents aged ≤17 years had ever received a diagnosis of a concussion or brain injury.
§ Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population.

In 2022, 2.3 million (3.2%) children and adolescents aged ≤17 years had ever received a diagnosis of a concussion or brain injury. Diagnosis of a concussion or brain injury increased with age, from 1.0% among those aged 0–5 years to 2.3% among those aged 6–11 years, and 5.9% among those aged 12–17 years. Percentages were higher for boys than girls overall (3.7% versus 2.6%), among those aged 6–11 years (3.0% versus 1.6%), and those aged 12–17 years (6.9% versus 4.9%) but were similar by sex among those aged 0–5 years (1.0% versus 1.1%).

Source: National Center for Health Statistics, National Health Interview Survey, 2022. https://www.cdc.gov/nchs/nhis.htm

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

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