

Epidemiology of Dengue — Puerto Rico, 2010–2024

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Abstract

Dengue is a mosquito-borne viral illness that can cause acute febrile illness, severe disease, or death. Worldwide, the number of dengue cases is increasing. During the last dengue outbreaks in Puerto Rico throughout 2010–2013, dengue virus (DENV) serotype 1 (DENV-1) predominated, and the largest proportion of cases occurred among adolescents and young adults aged 10–19 years. Dengue case data from January 1, 2010–November 4, 2024, were obtained from the Puerto Rico Department of Health. Bivariate analyses were conducted to evaluate the distribution of cases by patient age, DENV serotype, and hospitalization status during three periods: 2010–2019, 2020–2022, and 2023–2024. During 2023–2024, the median age of dengue cases increased to 26 years (95% CI = 25–27 years) compared with that during 2020–2022 (17 years; 95% CI = 17–18 years) and 2010–2019 (19 years; 95% CI = 19–19 years). After >10 years of DENV-1 predominance, the proportions of DENV serotypes 2 (DENV-2) and 3 (DENV-3) increased significantly during 2023–2024, with DENV-3 replacing DENV-1 as the predominant serotype. In addition, the proportion of dengue patients who were hospitalized increased from 35.7% (2010–2019) to 53.5% (2023–2024). The current dengue outbreak in Puerto Rico marks a shift in serotype predominance to DENV-3 and increasing percentages of cases in older age groups (61.7% in adults aged ≥20 years), although a high proportion of cases still occur among adolescents aged 10–19 years (29.5%). The current dengue outbreak also has a higher rate of hospitalizations than those in previous years. Understanding the changing epidemiology of dengue is crucial to guiding public health strategies for dengue control, including clinical management, surveillance and health care system resilience, and public outreach and education.

Introduction

Dengue, a viral illness transmitted by mosquitoes (most commonly *Aedes aegypti* and *Aedes albopictus*), can cause asymptomatic infection, nonspecific acute febrile illness, or severe dengue, which includes severe bleeding, critical organ failure, or plasma leakage (1,2). With appropriate treatment, including early clinical and laboratory diagnosis and maintenance of adequate hydration, mortality is typically <1%.* Four distinct dengue virus (DENV) serotypes (DENV-1–4) cause illness. Infection with one serotype provides long-lasting immunity against that specific serotype, but only transient protection against the other three serotypes (3). Dengue prevention includes avoiding mosquito bites, using mosquito repellents, wearing protective clothing, (i.e., long sleeves and pants), and eliminating

* https://iris.who.int/bitstream/handle/10665/75303/9789241504034_eng.pdf

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water-holding containers that can serve as mosquito breeding sites. Dengvaxia,[†] a dengue vaccine recommended for persons aged 9–16 years with evidence of previous DENV infection and living in endemic areas, provides protection against all four DENV serotypes among persons with previous DENV infection; it is not recommended for persons without previous infection because of an increased risk for hospitalization or severe dengue. However, the vaccine is being discontinued by the manufacturer because of a lack of demand in the global market. In Puerto Rico, dengue is endemic, with outbreaks occurring every 3–7 years. This report describes dengue cases reported to the Puerto Rico Department of Health (PRDH) during January 1, 2010–November 4, 2024.

Methods

Patients meeting the Council of State and Territorial Epidemiologists' dengue case definition[§] were included in the analysis. Dengue cases were aggregated by period (2010–2019, 2020–2022, and 2023–2024), patient age (<20, 20–39, and ≥40 years), identified DENV serotype, and patient hospitalization status. Periods were selected based on dengue trends, with 2010–2019 including the 2010–2013 dengue outbreaks and subsequent low-prevalence years (2014–2019); 2020–2022, including the reintroduction and increased transmission of DENV; and 2023–2024, capturing the most recent outbreak

period. Differences in the median patient age by period were evaluated using Mood's median tests. Hospitalization rates by period, serotype, and age group were evaluated using logistic regression models; adjusted odds ratios and 95% CIs are reported. Analyses were conducted using R (version 4.4.0; R Foundation). This activity was reviewed by CDC, deemed not research and was conducted consistent with applicable federal law and CDC policy.[¶]

Results

Dengue Case Characteristics

A total of 39,094 dengue cases were reported to PRDH during 2010–2024, including 30,517 (78.1%) during 2010–2019; 2,695 (6.9%) during 2020–2022; and 5,882 (15.0%) during 2023–2024 (Figure). Large dengue outbreaks occurred in 2010 (10,967 cases), 2012 (6,583), and 2013 (10,351), followed by an unusually low number of cases during 2016–2019 (365), likely associated with temporary crossreactive protective immunity from the Zika virus disease outbreak in 2016 (Supplementary Figure, <https://stacks.cdc.gov/view/cdc/174510>). The median patient age across the full study period was 20 years (range = 0–102 years). The median age during 2010–2019 was 19 years, declined to 17 years during 2020–2022, and then increased to 26 years during 2023–2024.

[†] <https://www.fda.gov/media/124379/download>

[§] <https://ndc.services.cdc.gov/case-definitions/dengue-virus-infections-2015/>

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

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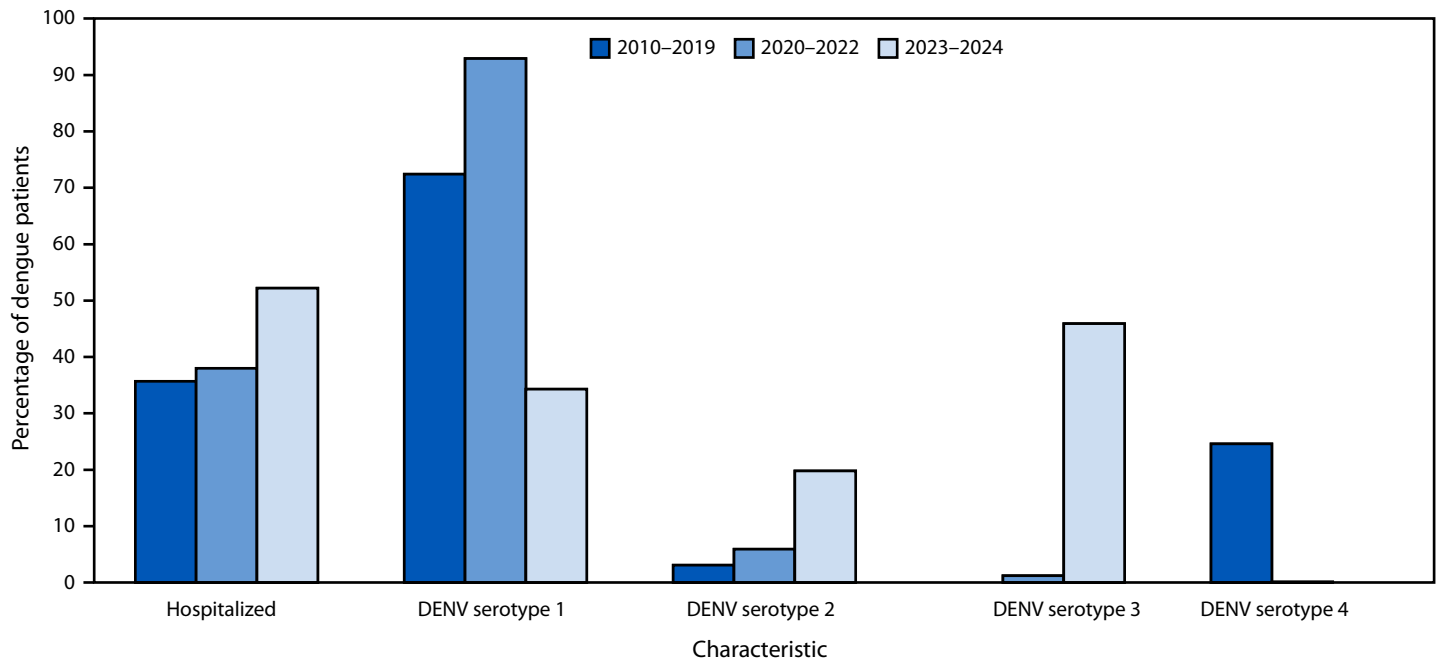
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FIGURE. Percentage of dengue patients hospitalized and percent distribution of infecting serotype,* by surveillance period (N = 39,094) — Puerto Rico Department of Health, Puerto Rico, 2010–2024



Abbreviation: DENV = dengue virus.

* Number of dengue cases with information on infecting serotype divided by total dengue cases: 2010–2019 = 20,783 / 30,517; 2020–2022 = 1,512 / 2,695; and 2023–2024 = 4,753 / 5,882. Percentages were calculated among patients for whom serotype was known.

Incidence increased among persons aged 20–39 years from 78.9 cases per 100,000 population during 2010–2019 to 101.9 during 2023–2024, and among persons aged ≥40 years, from 43.3 to 53.9 (Table 1). Fewer than one half (45.6%) of patients were female. A total of 94 (0.2%) fatal dengue cases were reported during 2010–2024.

Dengue Serotype Trends

Among 27,048 (69.2%) cases with an identified serotype during 2010–2024, DENV-1 accounted for two thirds (18,072; 66.8%); DENV-2, DENV-3, and DENV-4 accounted for 6.2% (1,664), 8.2% (2,206), and 18.9% (5,106) cases, respectively (Figure). During 2010–2019, DENV-1 was identified in 15,039 (72.4%) cases, with DENV-2 and DENV-4 identified in 635 (3.1%) and 5,104 (24.6%) cases, respectively. During 2020–2022, DENV-1 predominance increased to 92.9%, with low percentages of DENV-2 (5.9%) and DENV-3 (1.2%) identified. During 2023–2024, DENV-3 emerged as the predominant serotype (45.9%) accompanied by a reduction in the prevalence of DENV-1 (34.3%) and an increase in the prevalence of DENV-2 (19.8%). DENV-4 prevalence declined from 24.6% during 2010–2019, to 0.1% during 2020–2022, to 0% during 2023–2024. During these periods, no coinfections with more than one serotype were identified.

TABLE 1. Estimated average annual dengue incidence,* by age group and period — Puerto Rico, 2010–2024

Age group, yrs	Average annual incidence*		
	2010–2019	2020–2022	2023–2024
<20	184.4	79.7	196.1
20–39	78.9	27.8	101.9
≥40	43.3	9.5	53.9

* Cases per 100,000 population, calculated using the number of dengue cases reported to the Puerto Rico Department of Health and U.S. Census Bureau data. <https://www.census.gov/data.html>

Hospitalizations and Deaths

Among all dengue cases reported during 2010–2024, a total of 15,077 (38.6%) patients were hospitalized (Table 2). The highest rates of hospitalization were among patients with DENV-3 (60.9%) identified, followed by those with DENV-2 (50.2%); the lowest rates were among patients with DENV-1 (37.3%). Higher dengue hospitalization rates were also reported among patients aged <20 years (42.8%) than among those aged 20–39 (33.0%) and ≥40 years (36.3%). Just over one third of patients with dengue reported during 2010–2019 and 2020–2022 were hospitalized (35.7% and 38.0%, respectively); during 2023–2024 more than one half (53.5%) of patients with dengue were hospitalized. Among patients aged <20 years, hospitalization rates increased from 40.3% during 2010–2019 to 59.0% during 2023–2024.

TABLE 2. Age group, pregnancy status, and infecting serotype among all dengue patients and hospitalized dengue patients — Puerto Rico Department of Health, Puerto Rico, 2010–2019, 2020–2022, and 2023–2024

Characteristic	2010–2019*		2020–2022*			2023–2024*			Total 2010–2024*		
	No. of dengue cases	No. (%) of hospitalized dengue patients	No. of dengue cases	No. (%) of hospitalized dengue patients	Adjusted* OR (95% CI)	No. of dengue cases	No. (%) of hospitalized dengue patients	Adjusted* OR (95% CI)	Total no. of dengue cases	No. (%) of hospitalized dengue patients	Adjusted* OR (95% CI)
Age group, yrs [†]											
<20	15,508	6,254 (40.3)	1,490	658 (44.2)	1.2 (1.0–1.3)	2,255	1,330 (59.0)	1.5 (1.3–1.7) [§]	19,253	8,242 (42.8)	1.6 (1.5–1.7) [§]
20–39	7,142	2,121 (29.7)	692	222 (32.1)	1.1 (1.0–1.3)	1,681	801 (47.7)	1.8 (1.6–2.1) [§]	9,515	3,144 (33.0)	Ref
≥40	7,489	2,457 (32.8)	511	145 (28.4)	0.8 (0.6–0.9) [§]	1,946	1,013 (52.1)	1.8 (1.6–2.0) [§]	9,946	3,615 (36.3)	1.2 (1.1–1.2) [§]
Unknown	378	76 (20.1)	2	0 (—)	—	0	0 (—)	—	380	76 (20.0)	—
Total	30,517	10,908 (35.7)	2,695	1,025 (38.0)	1.1 (1.0–1.2)	5,882	3,144 (53.5)	1.7 (1.5–1.8)[§]	39,094	15,077 (38.6)	—
Pregnant patients	276	103 (37.3)	20	6 (30.0)	—	22	8 (36.4)	—	318	117 (36.8)	—
Serotype [†]											
DENV-1	15,039	5,360 (35.6)	1,404	521 (37.1)	1.1 (1.0–1.2)	1,629	855 (52.5)	2.2 (2.0–2.4) [§]	18,072	6,736 (37.3)	Ref
DENV-2	635	173 (27.2)	89	37 (41.6)	1.9 (1.2–3.0) [§]	940	626 (66.6)	5.3 (4.3–6.7) [§]	1,664	836 (50.2)	1.5 (1.3–1.7) [§]
DENV-3	5	1 (20.0)	18	9 (50.0)	4.2 (0.5–93.0)	2,183	1,333 (61.1)	6.6 (1.0–130.6)	2,206	1,343 (60.9)	1.8 (1.6–2.0) [§]
DENV-4	5,104	1,743 (34.1)	1	1 (100.0)	—	1	0 (—)	—	5,106	1,744 (34.2)	1.0 (0.9–1.0)
Unknown	9,734	3,631 (37.3)	1,183	457 (38.6)	—	1,129	330 (29.2)	—	12,046	4,418 (36.7)	—
Total	30,517	10,908 (35.7)	2,695	1,025 (38.0)	1.1 (1.0–1.2)	5,882	3,144 (53.5)	1.7 (1.5–1.8)[§]	39,094	15,077 (38.6)	—

Abbreviations: DENV = dengue virus; OR = odds ratio; Ref = referent group.

* Each row in the first three columns (2010–2019, 2020–2022, and 2023–2024) represents the number and percentage of hospitalizations among cases in each age group or serotype, with adjusted ORs comparing proportions in 2020–2022 and 2023–2024 with those from 2010–2019 (Ref). Age group ORs are adjusted by serotype. Serotype ORs are adjusted by age group. The “Total (2010–2024)” column represents a separate analysis comparing all hospitalized dengue patients during 2010–2024 with Ref categories for age group (20–39 years) and serotype (DENV-1).

[†] Percentages of overall hospitalized dengue patients are calculated among those for whom information on age and DENV serotype were known.

[§] Statistically significant increase or decrease in odds of hospitalization compared with 2010–2019.

Similarly, among patients aged 20–39 years, hospitalization rates increased from 29.7% during 2010–2019 to 47.7% during 2023–2024. Among patients aged ≥40 years, approximately one third (32.8%) were hospitalized during 2010–2019; this percentage decreased to 28.4% during 2020–2022, but then increased to 52.1% during 2023–2024.

During 2010–2024, a total of 318 (0.8%) of 39,094 dengue cases occurred in pregnant persons, including 276 (0.7%) during 2010–2019, 20 (0.1%), during 2020–2022, and 22 (0.1%) during 2023–2024. Hospitalization rates among pregnant patients with dengue during these periods were 37.3%, 30.0%, and 36.4%, respectively.

Hospitalization rates among patients infected with DENV-1 increased from 35.6% during 2010–2019 to 52.5% during 2023–2024. Similarly, among patients infected with DENV-2, hospitalization rates increased from 27.2% during 2010–2019 to 41.6% during 2020–2022, and to 66.6% during 2023–2024. The small numbers of DENV-3 and DENV-4 cases

limited analyses of hospitalization rates over time for patients infected with these serotypes.

The percentage of fatal dengue cases did not change significantly over time. The highest number of fatal cases (77; 0.3%) was reported during 2010–2019; eight (0.3%), and nine (0.2%) fatalities occurred during 2020–2022 and 2023–2024, respectively.

Discussion

These findings revealed a shift in the age distribution and percentage of hospitalized dengue patients during the analysis period, with an increase in the median patient age during the previous 2 years compared with both 2010–2019 and 2020–2022. This shift is likely the result of changing levels of population immunity, with lower levels of transmission during 2014–2019 after the large 2010–2013 outbreaks, resulting in lower levels of immunity among adults, driving a shift to slightly older age groups. In previous years, frequent exposure resulted in higher levels of protective immunity against DENV

among adults. A similar trend has been reported in other countries, including Bangladesh, Indonesia, Singapore, and Thailand, where the average age of patients with dengue has increased over time (4,5).

During 2023–2024, DENV-3 gained predominance in Puerto Rico. The lack of previous population exposure to DENV-2 and DENV-3 might be associated with higher infection and transmission rates, increasing the risk for an outbreak. The emergence of DENV-3 has resulted in multiple large outbreaks in recent years. In Brazil, DENV-3 reemerged in 2023, 15 years after the last DENV-3 outbreak, resulting in an unprecedented DENV-3 outbreak in 2024 (6). In Cuba, DENV-3 resulted in a large outbreak in 2022 (7), and in Mexico, increased numbers of cases attributed to DENV-3 occurred in 2024 (8).

Several factors likely contributed to the increased proportion of hospitalized patients during 2023–2024 in Puerto Rico. DENV-2 and DENV-3 have been associated with higher rates of severe disease and hospitalization compared with DENV-1 (9). However, PRDH also strengthened surveillance by expanding dengue testing in commercial laboratories and initiating interviews with all patients in 2023–2024, resulting in more complete case ascertainment. Population immunity could also affect disease severity; longer intervals between DENV infections have been associated with increased disease severity (10). The increase in median patient age could also play a role, because older populations might experience higher hospitalization rates owing to the presence of underlying comorbidities. Changes might also be related to health care provider testing and reporting practices if more severe cases have been more likely to be reported in recent years.

Limitations

The findings in this report are subject to at least five limitations. First, the associations evaluated across periods were not adjusted for confounders, such as comorbidities; patients with comorbidities might have higher hospitalization risk. Second, reported dengue cases do not include illnesses among persons who did not receive testing or did not seek health care services, likely underestimating the number of dengue cases in the community. Third, reporting biases could affect observed trends; hospitalized patients might have been more likely to be reported to public health authorities, inflating the proportion of hospitalized patients with dengue. Fourth, hospitalization practices might have changed over time; however, CDC recommendations** for hospitalization of persons with dengue have not changed throughout the analysis period. Finally,

** <https://www.cdc.gov/dengue/hcp/pocketguide/index.html>

Summary

What is already known about this topic?

Cases of dengue, a mosquito-borne viral illness, are increasing worldwide; during 2024, approximately 13 million cases have been reported in the Americas.

What is added by this report?

During 2023–2024, the median age of patients with dengue, the percentage of patients hospitalized, and the prevalences of serotypes 2 and 3 increased compared with the previous decade (2010–2019).

What are the implications for public health practice?

Understanding the changing epidemiology of dengue can help guide public health action, including providing clinical training, strengthening surveillance, ensuring health care system resilience, and raising public awareness.

increases in the percentage of older adults in Puerto Rico might affect the proportion of cases observed in older age groups; however, dengue incidence increased among persons aged ≥ 20 years during 2023–2024 compared with 2010–2019.

Implications for Public Health Practice

Reemerging DENV serotypes and lowered population immunity could increase the risk for dengue-related hospitalizations in Puerto Rico. Hospitalization rates were higher among patients infected with DENV-2 and DENV-3, which could result in higher numbers of hospitalizations if these serotypes continue to predominate in Puerto Rico. Public health partners can increase health care system preparedness for dengue. For example, efforts to accelerate the development and licensing of dengue vaccines for all age groups could be an important prevention tool. Additional education for health care providers could also strengthen dengue responses. During 2023–2024, just over one third (36.4%) of pregnant persons with dengue were hospitalized, although all pregnant persons with suspected dengue should be hospitalized or under close observation because of the risk for progression to severe dengue. Finally, raising awareness among health care providers and the public about the changing epidemiology of dengue could facilitate early detection and prompt management of cases.

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Use of Additional Doses of 2024–2025 COVID-19 Vaccine for Adults Aged ≥ 65 Years and Persons Aged ≥ 6 Months with Moderate or Severe Immunocompromise: Recommendations of the Advisory Committee on Immunization Practices — United States, 2024

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Abstract

COVID-19 remains an important cause of morbidity and mortality, especially among adults aged ≥ 65 years and persons with moderate or severe immunocompromise; these persons are among those at highest risk for severe disease from COVID-19. On June 27, 2024, the Advisory Committee on Immunization Practices (ACIP) recommended 2024–2025 COVID-19 vaccination for all persons aged ≥ 6 months to target currently circulating strains of SARS-CoV-2 and provide additional protection against severe COVID-19. Because SARS-CoV-2 circulates year-round and immunity from vaccination wanes, on October 23, 2024, ACIP recommended a second 2024–2025 COVID-19 vaccine dose for all adults aged ≥ 65 years and for persons aged 6 months–64 years with moderate or severe immunocompromise, 6 months after their last dose of 2024–2025 COVID-19 vaccine (minimum interval = 2 months). Further, ACIP recommended that persons aged ≥ 6 months who are moderately or severely immunocompromised may receive additional doses of 2024–2025 COVID-19 vaccine (i.e., a total of ≥ 3 doses of 2024–2025 COVID-19 vaccine) based on shared clinical decision-making. Staying up to date with COVID-19 vaccination is recommended to decrease the risk for severe COVID-19, especially among adults aged ≥ 65 years and persons with moderate or severe immunocompromise.

Introduction

The overall risk for COVID-19–associated hospitalization and death has decreased in recent years, but COVID-19 continues to cause hundreds of deaths and thousands of hospitalizations in the United States each week (1). SARS-CoV-2 circulates year-round with infections and hospitalizations peaking in late summer and winter (2). COVID-19–associated hospitalization rates remain higher among adults aged ≥ 65 years compared with rates among younger adults. During October 2023–August 2024, 70% of COVID-19–associated hospitalizations were among adults aged ≥ 65 years (3). Further, COVID-19 death rates during January 1, 2023–September 30, 2024, were highest among

adults aged ≥ 75 years, followed by rates among adults aged 65–74 years (2). Adults aged ≥ 65 years are less likely to have infection-induced immunity to SARS-CoV-2 compared with adults aged 30–64 years (2). In addition, age-related immune system changes result in reduced ability to develop robust immunity after infection or vaccination (4,5). Thus, older adults are both more reliant on vaccination-related immunity and might require more frequent vaccination for protection against severe illness due to COVID-19. Approximately 6% of persons in the United States have an immunocompromising condition (6); however, 16% of persons hospitalized with COVID-19 during July 2023–May 2024 had an immunocompromising condition* (3). Persons with moderate or severe immunocompromise might not develop robust immunity after infection or vaccination.

Since June 2020, CDC’s Advisory Committee on Immunization Practices (ACIP) has convened 41 public meetings to review data and consider recommendations related to the use of COVID-19 vaccines (7). On June 27, 2024, ACIP recommended that all persons aged ≥ 6 months receive 2024–2025 COVID-19 vaccination to target currently circulating strains of SARS-CoV-2 and provide additional protection against severe COVID-19–associated illness and death (8). In August 2024, the Food and Drug Administration (FDA) approved and authorized the Omicron JN.1 lineage (JN.1 and KP.2 strains) 2024–2025 COVID-19 vaccines by Moderna and Pfizer-BioNTech (KP.2 strain) and Novavax (JN.1 strain) (9).

On October 23, 2024, ACIP voted to recommend that, in addition to previously recommended 2024–2025 COVID-19 vaccination, all adults aged ≥ 65 years and persons aged

* Immunocompromising conditions included AIDS or CD4 count < 200 ; complement deficiency; graft versus host disease; HIV infection; immunoglobulin deficiency; immunosuppressive therapy ≤ 12 months before admission; leukemia, lymphoma, solid organ malignancy, metastatic cancer, or multiple myeloma diagnosed ≤ 12 months of admission or currently in treatment; bone marrow transplant; steroid therapy (≤ 2 weeks before admission; excluding inhaled, intranasal steroids or intramuscular or intra-articular injection of steroids); solid organ transplant; or other conditions typically associated with immunocompromised status upon review.

6 months–64 years who are moderately or severely immunocompromised (including but not limited to active treatment for malignancy, hematologic malignancies associated with poor responses to COVID-19 vaccines regardless of treatment, solid organ transplant or islet transplant and taking immunosuppressive therapy, chimeric antigen receptor T-cell therapy, hematopoietic cell transplant within 2 years, moderate or severe primary immunodeficiency, advanced or untreated HIV infection, or certain immunosuppressive medications; more details are available at <https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html#immunocompromised>) should receive a second 2024–2025 COVID-19 vaccine dose. Further, ACIP voted to recommend that persons aged ≥ 6 months who are moderately or severely immunocompromised may receive additional doses of 2024–2025 COVID-19 vaccine (i.e., a total of ≥ 3 doses of 2024–2025 COVID-19 vaccine) based on shared clinical decision-making. This report summarizes these ACIP recommendations and the rationale, including evidence reviewed by the ACIP COVID-19 Vaccines Work Group (Work Group) and presented to ACIP.

Methods

In June 2024, ACIP evaluated published assessments of vaccine effectiveness (VE) and safety of previous COVID-19 vaccine formulations using the Grading of Recommendations, Assessment, Development and Evaluation[†] approach to guide the recommendations for use of 2024–2025 COVID-19 vaccine in persons aged ≥ 6 months (8). After the June 2024 ACIP meeting, the Evidence to Recommendations Framework (EtR)[§] was used to evaluate additional data, including VE, vaccine safety, and economic analyses, with a specific focus on information related to additional doses of 2024–2025 COVID-19 vaccine in older adults and persons with immunocompromising conditions.

Since July 2024, the Work Group met seven times to discuss the current policy questions: 1) whether adults aged ≥ 65 years should receive a second dose of 2024–2025 COVID-19 vaccine, and 2) whether persons aged ≥ 6 months with moderate or severe immunocompromise should receive ≥ 1 additional 2024–2025 COVID-19 vaccine doses. The Work Group reviewed evidence on COVID-19 disease surveillance and epidemiology; COVID-19 vaccination coverage, safety, and effectiveness; feasibility of implementation; and cost

effectiveness of COVID-19 vaccines (<https://www.cdc.gov/acip/evidence-to-recommendations/covid-19-2024-2025-additional-dose.html>).

Rationale and Evidence

Vaccine Effectiveness

ACIP reviewed CDC data on COVID-19 VE, including data on VE of the original monovalent, bivalent, and 2023–2024 COVID-19 vaccines in the populations of interest. COVID-19 vaccines have provided substantial protection for persons with and without immunocompromise, with generally lower VE in persons with immunocompromise than in those without (10). During the 2023–24 respiratory virus season, the 2023–2024 COVID-19 vaccines provided added benefit in a population with a high prevalence of immunity from previous immunization and infection. The 2023–2024 COVID-19 vaccines provided approximately 50% (95% CI = 44%–55%) additional protection against hospitalization initially and then waned to negligible additional protection by approximately 4–6 months after receipt of a 2023–2024 COVID-19 vaccine dose. Protection lasted longer against critical illness (i.e., intensive care unit admission and death). VE against critical illness started at 67% (95% CI = 55%–75%) and decreased to 40% (95% CI = 16%–58%) 4–6 months after the dose, with point estimates indicating additional waning of VE by 6–10 months after the dose (10).

Although waning patterns have varied season to season among persons with immunocompromise, an additional COVID-19 vaccine dose has consistently restored protection that has waned after previous doses in persons with and without immunocompromise. During September 2022–August 2023, no residual effectiveness of original monovalent vaccines against COVID-19–associated hospitalization was observed a median of >400 days after the last dose among persons with or without immunocompromise[¶]; receipt of a bivalent dose increased protection to 51% (95% CI = 25%–68%) among persons with immunocompromise and 52% (95% CI = 39%–61%) among persons without immunocompromise (11). During September 2023–August 2024, VE of a 2023–2024 COVID-19 vaccine dose among persons with immunocompromise was 36% (95% CI = 22%–48%) 7–59 days after vaccination and 1% (95% CI = –28% to 23%) 120–179 days after vaccination (9). In persons without immunocompromise, VE was 51% (95% CI = 45%–56%) 7–59 days after vaccination, waning to 15% (95% CI = 3%–26%) 120–179 days after vaccination (10).

[†] <https://www.cdc.gov/acip/evidence-based-recommendations/>

[§] Through the EtR, the Work Group reviewed data on the public health problem of COVID-19 among older adults and persons with immunocompromising conditions, as well as the benefits and harms, value to the target population, acceptability to key stakeholders, feasibility, societal resource use, and equity implications of additional doses of COVID-19 vaccines.

[¶] Effectiveness of original monovalent vaccine against COVID-19–associated hospitalization a median of >400 days after the last dose was 14% (95% CI = –9% to 33%) among persons with immunocompromise and 6% (95% CI = –7% to 17%) among persons without immunocompromise.

Safety

ACIP reviewed CDC data on COVID-19 vaccine safety with a focus on doses administered after the initial vaccination series. Robust safety surveillance of COVID-19 vaccines has demonstrated that serious adverse events are rare: anaphylactic reactions have been rarely reported after receipt of COVID-19 vaccines (12), and a rare risk for myocarditis and pericarditis has been observed after COVID-19 vaccination, predominantly among males aged 12–39 years (13). No increased risk for myocarditis or pericarditis was observed in adults aged ≥65 years after COVID-19 vaccination (13); whether the risk might be different in persons with immunocompromise is unknown.

COVID-19 vaccine doses are reactogenic (2). Compared with doses in the initial vaccination series, the rate of local and systemic reactions reported to V-safe, a voluntary smartphone-based U.S. safety surveillance system established by CDC to monitor health after COVID-19 vaccination, was lower after subsequent doses (14,15). Most vaccine recipients have mild reactions; however, during 2023–2024, ≥10% of COVID-19 vaccine recipients in V-safe reported health impact events during the 7 days after vaccination, such as being unable to complete daily activities (16). Reactogenicity observed in V-safe after a bivalent COVID-19 vaccine dose was milder and less frequent among older adults compared with adolescents and younger adults (17).

Economic Analyses

ACIP considered whether a second dose of 2024–2025 COVID-19 vaccine in persons aged ≥65 years and persons aged ≥6 months with moderate or severe immunocompromise is a reasonable and efficient allocation of resources. The societal incremental cost-effectiveness ratio (ICER) for an additional dose of COVID-19 vaccine in persons aged ≥65 years was \$356,534 per quality-adjusted life year saved for the base case estimate (18). ICER values were sensitive to seasonality-adjusted vaccine impact, probability of hospitalization, and vaccine cost. Estimates of ICER values that approximate cost effectiveness for those with higher risk for COVID-19–associated hospitalization, such as persons with underlying conditions, were more favorable (18). Data were not available specific to cost-effectiveness in persons with moderate or severe immunocompromise.

Updated Recommendations for 2024–2025 COVID-19 Vaccination for Persons Aged ≥65 Years

On October 23, 2024, ACIP recommended that all persons aged ≥65 years** receive a second dose of 2024–2025 COVID-19

vaccine (Table) 6 months^{††} (minimum interval = 2 months) after the last dose of 2024–2025 COVID-19 vaccine. If an adult aged ≥65 years is previously unvaccinated and receiving Novavax, 2 doses are recommended as an initial vaccination series and should be followed by a third dose of any age-appropriate 2024–2025 COVID-19 vaccine 6 months (minimum interval = 2 months) after the second dose.

Updated Recommendations for 2024–2025 COVID-19 Vaccination for Persons Aged ≥6 Months with Moderate or Severe Immunocompromise

On October 23, 2024, ACIP recommended that persons aged 6 months–64 years with moderate or severe immunocompromise^{§§} receive a second dose of 2024–2025 COVID-19 vaccine 6 months^{¶¶} after the last 2024–2025 COVID-19 vaccine dose (minimum interval = 2 months). For all persons with moderate or severe immunocompromise, ≥2 doses of 2024–2025 COVID-19 vaccine are recommended; 1 of the 2 recommended 2024–2025 COVID-19 vaccine doses may be a part of the initial vaccination series, and in this case, the remaining dose is recommended 6 months (minimum interval = 2 months) after completion of the initial vaccination series. ACIP also recommended that persons aged ≥6 months with moderate or severe immunocompromise may receive additional 2024–2025 COVID-19 vaccine doses (i.e., a total of ≥3 doses of 2024–2025 COVID-19 vaccine) based on shared clinical decision-making,^{***} which should be guided by the clinical judgment of a health care provider and personal preference and circumstances of the patient (18). Additional clinical considerations, including detailed schedules and tables by age and vaccination history for persons with and without moderate or severe immunocompromise, are available at <https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html>.

^{††} For adults aged ≥65 years, the recommended interval of the second dose is 6 months but can be as early as 2 months or later than 6 months after the first dose of 2024–2025 COVID-19 vaccine.

^{§§} ACIP voted (15 to zero) to recommend a second dose of 2024–2025 COVID-19 vaccine for persons aged 6 months–64 years with moderate or severe immunocompromise.

^{¶¶} For persons aged ≥6 months who are immunocompromised, the recommended interval of the second dose is 6 months but can be as early as 2 months or later than 6 months after the first dose of 2024–2025 COVID-19 vaccine.

^{***} ACIP voted (15 to zero) to recommend additional doses of 2024–2025 COVID-19 vaccine for persons aged ≥6 months with moderate or severe immunocompromise (minimum interval = 2 months) under shared clinical decision-making.

** ACIP voted (15 to zero) to recommend a second dose of 2024–2025 COVID-19 vaccine for persons aged ≥65 years.

TABLE. Routine 2024–2025 COVID-19 vaccination schedule for persons aged ≥65 years,* by COVID-19 vaccination history† — United States, October 2024

COVID-19 vaccination history before 2024–2025 vaccine	No. of 2024–2025 COVID-19 doses recommended	2024–2025 vaccination schedule
≥1 mRNA vaccine dose (Moderna or Pfizer-BioNTech) or ≥2 Novavax doses or ≥1 Janssen dose	2	2024–2025 dose 1 (Moderna, Novavax, or Pfizer-BioNTech): ≥8 wks after last dose 2024–2025 dose 2 (Moderna, Novavax, or Pfizer-BioNTech): 6 mos (minimum interval = 2 mos) after 2024–2025 dose 1
1 Novavax dose	2	2024–2025 dose 1 (Novavax): 3–8 wks after last dose [§] 2024–2025 dose 2 (Moderna, Novavax, or Pfizer-BioNTech): 6 mos (minimum interval = 2 mos) after 2024–2025 dose 1
Unvaccinated	2	2024–2025 dose 1 (Moderna or Pfizer-BioNTech): day 0 2024–2025 dose 2 (Moderna, Novavax, or Pfizer-BioNTech): 6 mos (minimum interval = 2 mos) after dose 1 or
	3	2024–2025 dose 1 (Novavax): day 0 2024–2025 dose 2 (Novavax): 3–8 wks after dose 1 [§] 2024–2025 dose 3 (Moderna, Novavax, or Pfizer-BioNTech): 6 mos (minimum interval = 2 mos) after dose 2

* Routine schedule applies to persons who are not moderately or severely immunocompromised. Additional clinical considerations, including detailed schedules and tables by age and vaccination history, are available at <https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html>.

† COVID-19 vaccination history refers to all doses of COVID-19 vaccine from any manufacturer received before the availability of the 2024–2025 COVID-19 vaccines and includes original, bivalent, and 2023–2024 COVID-19 vaccines.

§ If ≥8 weeks have elapsed since receipt of the first dose of Novavax, any 2024–2025 COVID-19 vaccine (i.e., Moderna, Novavax, or Pfizer-BioNTech) may be administered.

Implementation Considerations

These recommendations were based on persistent SARS-CoV-2 circulation throughout the year, higher risk for severe illness attributable to COVID-19 in adults aged ≥65 years and persons with moderate or severe immunocompromise, protection anticipated from the updated vaccines against JN.1 and other closely related circulating SARS-CoV-2 variants, the expected waning of COVID-19 VE, and additional implementation considerations, including facilitating clear communication and equitable access to vaccination (2). The available data indicate that persons aged ≥65 years and those with moderate or severe immunocompromise should receive 2 doses of 2024–2025 COVID-19 vaccine, at an interval of 6 months, to enhance protection throughout the year. However, although the recommended interval between these doses is 6 months, the minimum interval of 2 months allows for flexibility of vaccine administration when accounting for individual risk and circumstances.

Persons aged ≥6 months with moderate or severe immunocompromise may receive additional 2024–2025 COVID-19 vaccine doses based on shared clinical decision-making. Vaccine recommendations using shared clinical decision-making are individually based and guided by a discussion between the health care provider and the patient or their parent or guardian (19). Although shared clinical decision-making recommendations can be difficult to implement (20), this recommendation allows persons with moderate or severe immunocompromise to time additional doses of COVID-19 vaccine around

immunosuppressive treatments, after which recipients might be at increased risk of severe COVID-19, or around travel and other life events, during which they might have increased risk of exposure to SARS-CoV-2 (2).

Persons can self-attest to their moderately or severely immunocompromised status and receive COVID-19 vaccine doses wherever vaccines are offered. Vaccinators should not deny COVID-19 vaccination to a person because of a lack of documentation of their immunocompromised status. A description of immunocompromising conditions and considerations is available at <https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html#immunocompromised>.

Reporting Vaccine Adverse Events

Adverse events after vaccination should be reported to the Vaccine Adverse Event Reporting System (VAERS). For licensed COVID-19 vaccines administered to persons aged ≥12 years, reporting is encouraged for any clinically significant adverse event, even when a causal association between the vaccine and the event is uncertain, as well as for vaccine administration errors. For COVID-19 vaccines given under Emergency Use Authorization,^{†††} vaccination providers are required to report certain adverse events to VAERS. Additional information is available at <https://vaers.hhs.gov> or by telephone at 1-800-822-7967.

^{†††} 2024–2025 COVID-19 vaccines under FDA Emergency Use Authorization are Moderna and Pfizer-BioNTech for use among persons aged 6 months–11 years and Novavax for use among persons aged ≥12 years.

Summary**What is already known about this topic?**

The Advisory Committee on Immunization Practices (ACIP) recommends 2024–2025 COVID-19 vaccination for all persons aged ≥ 6 months.

What is added by this report?

In October 2024, ACIP recommended that all persons aged ≥ 65 years and persons aged 6 months–64 years with moderate or severe immunocompromise receive a second 2024–2025 COVID-19 vaccine dose 6 months after their last dose. Further, ACIP recommended that persons aged ≥ 6 months with moderate or severe immunocompromise may receive additional doses based on shared clinical decision-making.

What are the implications for public health practice?

Adults aged ≥ 65 years should receive 2 doses of 2024–2025 COVID-19 vaccine, and persons aged ≥ 6 months with moderate or severe immunocompromise should receive ≥ 2 doses to protect against severe COVID-19.

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New Dosing Interval and Schedule for the Bexsero MenB-4C Vaccine: Updated Recommendations of the Advisory Committee on Immunization Practices — United States, October 2024

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Abstract

Two meningococcal serogroup B vaccines are licensed for use in the United States. In August 2024, the Food and Drug Administration (FDA) changed the label for the meningococcal serogroup B MenB-4C vaccine (Bexsero) from a 2-dose schedule (intervals of 0 and ≥ 1 month) to a 2-dose schedule (0 and 6 months) and added a 3-dose schedule (0, 1–2, and 6 months), based on new immunogenicity data. On October 24, 2024, the Advisory Committee on Immunization Practices (ACIP) voted to update its recommendations for the MenB-4C dosing interval and schedule to align with the new FDA label. ACIP recommends extending the interval for the 2-dose series of MenB-4C from 0 and ≥ 1 month to 0 and 6 months for healthy adolescents and young adults aged 16–23 years based on shared clinical decision-making and has added a recommendation for a 3-dose series with doses administered at 0, 1–2, and 6 months for persons aged ≥ 10 years at increased risk. The updated ACIP recommendations for MenB-4C align with existing ACIP recommendations for the other FDA-licensed meningococcal serogroup B vaccine, MenB-FHbp (Trumenba).

Introduction

Vaccination against serogroup B meningococcal disease is recommended by the Advisory Committee on Immunization Practices (ACIP) for adolescents and young adults aged 16–23 years, based on shared clinical decision-making (<https://www.cdc.gov/vaccines/hcp/admin/downloads/ISD-job-aid-SCDM-mening-b-shared-clinical-decision-making.pdf>); and for persons aged ≥ 10 years who are at increased risk for serogroup B meningococcal disease (i.e., persons with anatomic or functional asplenia, complement component deficiencies, or complement inhibitor use; microbiologists routinely exposed to *Neisseria meningitidis* isolates; and persons at increased risk during an outbreak). Shared clinical decision-making recommendations are intended to be flexible and are guided by a decision-making process between the health care provider and the patient or the patient's parent or guardian. Considerations for shared clinical decision-making for vaccine administration might include the serious nature of meningococcal infections, the low number of serogroup B meningococcal disease

cases, the estimated relatively short duration of protection from MenB vaccines (antibody waning within 1–2 years after completion of the primary series), and the increased risk among college students, especially those who are freshmen, attend a 4-year university, live in on-campus housing, or participate in sororities and fraternities. Two serogroup B meningococcal vaccines (MenB-FHbp [Trumenba, Pfizer, Inc.] and MenB-4C [Bexsero, GSK]) and one serogroup ABCWY pentavalent meningococcal (MenABCWY) vaccine (MenACWY-TT/MenB-FHbp [Penbraya, Pfizer Inc.]) are currently licensed for use in persons aged 10–25 years in the United States (1,2). Primary series MenB vaccination in persons aged ≥ 26 years and booster vaccination in persons at increased risk for meningococcal disease are not licensed in the United States and are considered off-label ACIP recommendations.

ACIP recommends MenB-FHbp vaccine as a 2-dose series (at intervals of 0 and 6 months) for adolescents and young adults and a 3-dose series (at 0, 1–2, and 6 months) for those at increased risk. Previously, ACIP recommended MenB-4C vaccine as a 2-dose series (at 0 and ≥ 1 month) for adolescents and young adults and those at increased risk, consistent with FDA licensure (1). In August 2024, FDA changed the label for MenB-4C from a 2-dose schedule (0 and ≥ 1 month) to a 2-dose schedule (0 and 6 months) and added a 3-dose schedule (0, 1–2, and 6 months) (3). These changes were prompted by new immunogenicity data and were not due to safety concerns (4). This report summarizes evidence considered for the MenB-4C dosing interval and schedule changes and provides clinical guidance for the use of MenB vaccines. This report only updates recommendations for the dosing interval and schedule for MenB-4C; other previously published meningococcal vaccination guidance remains unchanged (1,2).

Methods

Data Source and Assessment of Immunogenicity

During August–October 2024, the ACIP Meningococcal Vaccines Work Group (Work Group) held bimonthly conference calls to review meningococcal disease epidemiology and evidence regarding the dosing interval and schedule for MenB-4C in persons for whom MenB vaccination is recommended. The Evidence to Recommendations framework

was used to guide deliberations; the Work Group considered the importance of meningococcal disease as a public health problem, benefits and harms, values of the target population, acceptability, resource use, equity, and feasibility (5). The Work Group and ACIP reviewed comparative data on the immunogenicity and safety of MenB-4C when administered using different dosing intervals and schedules. Data from five clinical trials (four published and one unpublished) are included in the updated package insert; data from three trials (two published and one unpublished) were considered in the assessment of immunogenicity.

Summary of Evidence

Immunogenicity

The percentage of participants achieving seroresponse was compared across four antigen indicator strains using an assay measuring serum bactericidal activity with an exogenous source of human complement (human serum bactericidal activity [hSBA]). Seroresponse was defined as a postvaccination hSBA titer at least fourfold the limit of detection (LOD) or at least the lower limit of quantitation (LLOQ), whichever is greater, for participants with prevaccination hSBA titer less than LOD, a postvaccination hSBA titer at least fourfold the LLOQ for participants with prevaccination hSBA titer at least meeting LOD and less than LLOQ, and a postvaccination hSBA at least fourfold the prevaccination hSBA titer for participants with prevaccination hSBA titer at least meeting LLOQ. Immunogenicity data were based on 1,803 persons aged 10–25 years who received at least 1 dose of MenB-4C; approximately 30% of vaccine recipients were from the United States. The proportion of persons achieving seroresponse to four antigen indicator strains ranged from 54%–97% after dose 2 of a 0-, 2-, and 6-month schedule to 57%–95% and 57%–99% after dose 2 of a 0- and 6-month schedule and dose 3 of a 0-, 2-, and 6-month schedule, respectively (3,4) (Table).

Safety

MenB-4C safety data have been reported previously (1). The most common solicited adverse reactions after receipt of MenB-4C were pain at the injection site ($\geq 87\%$ of recipients), fatigue ($\geq 45\%$), and headache ($\geq 37\%$). Adverse reactions occurred with similar frequency after both doses in the 0- and 6-month schedule and each dose in the 0-, 2-, and 6-month schedule (3,4).

Evidence to Recommendations Framework Domains

An extended interval between doses might be associated with reduced series completion and might disproportionately affect some populations. During 2022, among adolescents initiating

MenB vaccination who were not eligible for the Vaccines for Children (VFC) program,* 49.6% of MenB-4C recipients and 35.5% of MenB-FHbp recipients completed their series by age 17 years. Among those initiating MenB vaccination who were eligible for the VFC program, 51.4% and 16.2% completed their MenB-4C and MenB-FHbp series, respectively, by age 17 years. Among commercially insured adolescents in the Merative MarketScan Commercial Claims and Encounters database,† 67% and 60% of those initiating vaccination completed their MenB-4C and MenB-FHbp series, respectively, by age 19 years during 2017–2023; series completion by age 19 years could not be assessed for the VFC-eligible population because this population was not ascertained in the database. The Work Group deliberations included potential detrimental effects on equity with extended dosing intervals and favorable effects regarding feasibility associated with harmonization of MenB-4C and MenB-FHbp recommendations (4).

ACIP Recommendations

These recommendations apply to use of the 2- and 3-dose schedules of MenB-4C and supersede previous ACIP recommendations for use of MenB-4C published in 2020 (1). Recommendations regarding use of MenB-FHbp and MenACWY-TT/MenB-FHbp, as well as recommendations for booster doses, are unchanged (1,2).

Adolescents and Young Adults Aged 16–23 Years (Shared Clinical Decision-Making Recommendation)

ACIP recommends that MenB-4C be administered to healthy adolescents and young adults aged 16–23 years as a 2-dose series at 0 and 6 months for the prevention of serogroup B meningococcal disease, based on shared clinical decision-making (Box). Shared clinical decision-making recommendations are not recommended for everyone in an age or risk group but are individually based and guided by a decision process between the health care provider and the patient or the patient's parent or guardian.

Persons Aged ≥ 10 Years at Increased Risk for Serogroup B Meningococcal Disease

ACIP recommends that MenB-4C be administered as a 3-dose series at 0, 1–2, and 6 months to persons aged ≥ 10 years who are at increased risk for serogroup B meningococcal disease (i.e., persons with anatomic or functional splenia,

*VFC provides vaccines at no cost to children and adolescents aged ≤ 18 years who are uninsured, underinsured, Medicaid-eligible, or American Indian or Alaska Native. <https://www.cdc.gov/vaccines-for-children/about/index.html>

† <https://www.merative.com/content/dam/merative/documents/brief/marketscan-explainer-general.pdf>

TABLE. Number and percentage of persons aged 10–25 years achieving seroresponse to antigen indicator strains* 1 month after receipt of dose 2 (0- and 6-month schedule), and doses 2 and 3 (0-, 2-, and 6-month schedule) of MenB-4C (Bexsero) vaccine (N = 1,803) — United States, Australia, Canada, Czechia, Estonia, Finland, and Turkey, 2020–2022

Antigen indicator strain*	0- and 6-mo schedule		0-, 2-, and 6-mo schedule			
	Dose 2		Dose 2		Dose 3	
	No.	% (95% CI)	No.	% (95% CI)	No.	% (95% CI)
fHbp	699	78 (74–81)	739	67 (64–71)	679	81 (78–84)
NadA	700	95 (93–97)	738	97 (95–98)	679	99 (98–99)
NHBA	704	69 (66–72)	739	58 (55–62)	685	67 (63–70)
OMV	664	57 (53–61)	724	54 (50–57)	637	57 (53–60)

Abbreviations: fHbp = factor H binding protein; NadA = neisserial adhesin A; NHBA = neisserial heparin binding antigen; OMV = outer membrane vesicle.

* Bacterial antigenic strains for which immune response was assessed.

complement component deficiencies, or complement inhibitor use; microbiologists routinely exposed to *N. meningitidis* isolates; and persons at increased risk during an outbreak).

CDC Guidance for Use

Interchangeability of Vaccine Products

Two manufacturers provide three MenB vaccine products (1,2) that are licensed and available for use in the United States. MenB vaccines from different manufacturers are not interchangeable; all doses in a series, as well as booster doses, should be from the same manufacturer. If doses from both manufacturers have been administered to the same patient, the patient should receive a complete series of either manufacturer's product without counting doses of the other manufacturer as valid. The next dose of the selected manufacturer should be administered no sooner than the recommended interval after the previous dose from the same manufacturer and ≥ 4 weeks after the most recent dose (from either manufacturer) was administered (1).

Dosing Interval and Schedule

There is no recommendation to administer additional doses to persons vaccinated with MenB-4C before October 24, 2024, using a 0- and 1-month dosing schedule. Persons who have completed a MenB vaccine primary series and who remain or become at increased risk for invasive meningococcal disease are recommended to receive booster vaccination. Booster doses need to be from the same manufacturer used for doses in the primary series.

When administering the 2-dose series (e.g., for healthy adolescents) of MenB-4C (Bexsero) or MenB-FHbp (Trumenba), the 2 doses should be separated by 6 months. If the second dose is administered < 6 months after the first dose, a third dose should be administered ≥ 4 months after the second dose. A second dose administered at an interval > 6 months after the first dose is valid and does not need to be repeated (1).

BOX. MenB-4C vaccination recommendations* — Advisory Committee on Immunization Practices, United States, 2024

Adolescents and young adults aged 16–23 years (shared clinical decision-making recommendation)

- MenB-4C is recommended for healthy adolescents and young adults aged 16–23 years.
- Administer as a 2-dose series at intervals of 0 and 6 months, based on shared clinical decision-making.
- All doses in a series, in addition to booster doses, should be from the same manufacturer.

Persons aged ≥ 10 years at increased risk for serogroup B meningococcal disease

- MenB-4C is recommended for persons aged ≥ 10 years who are at increased risk for serogroup B meningococcal disease:
 - Persons with anatomic or functional asplenia
 - Persons with complement component deficiencies
 - Persons using a complement inhibitor
 - Microbiologists routinely exposed to *Neisseria meningitidis* isolates
 - Persons at increased risk during an outbreak
- Administer MenB-4C as a 3-dose series at 0, 1–2, and 6 months.
- All doses in a series, in addition to booster doses, should be from the same manufacturer.

* <https://www.fda.gov/media/90996/download>

When administering the 3-dose series (e.g., for persons aged ≥ 10 years at increased risk for MenB infection) of MenB-4C (Bexsero) or MenB-FHbp (Trumenba), a third dose is not needed if the second dose was administered ≥ 6 months after the first dose. If the third dose is administered < 4 months after the second dose, the dose should be repeated ≥ 4 months after the last dose, unless the third dose was administered ≥ 6 months after the first dose (1,3,6).

Summary**What is already known about this topic?**

Meningococcal disease is a life-threatening invasive infection caused by *Neisseria meningitidis*. MenB-4C (Bexsero, GSK), one of two licensed meningococcal serogroup B vaccines, protects against serogroup B *N. meningitidis* and is licensed for persons aged 10–25 years.

What is added by this report?

On October 24, 2024, the Advisory Committee on Immunization Practices (ACIP) updated its recommendations for MenB-4C to align the dosing interval and schedule with the new Food and Drug Administration (FDA) label and harmonize with recommendations for MenB-FHbp (Trumenba, Pfizer, Inc.) vaccine. ACIP now recommends MenB-4C as a 2-dose series with doses administered at intervals of 0 and 6 months for healthy adolescents and young adults aged 16–23 years based on shared clinical decision-making and as a 3-dose series with doses administered at 0, 1–2, and 6 months for persons aged ≥10 years at increased risk.

What are the implications for public health practice?

The new MenB-4C dosing interval and schedule improves immune protection. ACIP recommendations for the MenB-4C dosing interval and schedule are now aligned with the updated FDA label and are harmonized with ACIP recommendations for use of MenB-FHbp.

Persons receiving a MenB vaccine based on shared clinical decision-making who desire more rapid protection against serogroup B (e.g., students initiating vaccination <6 months before college entry) may receive the 3-dose series (0, 1–2, and 6 months) to optimize rapid protection. This guidance applies to both MenB-4C and MenB-FHbp. When deciding timing of vaccination, providers may consider that VFC program eligibility ends at age 19 years.

Persons Taking Complement Inhibitors

Persons on complement inhibitor therapy likely remain at substantially increased risk for meningococcal disease, even if they are fully vaccinated or taking antimicrobial prophylaxis. Although evidence suggests that vaccination might not adequately prevent meningococcal infections among persons with certain complement deficiencies or those using a complement inhibitor, these persons should continue to be vaccinated according to recommendations because of the potential for benefit among persons at high risk for infection (1).

Persons not up to date with meningococcal vaccinations for whom urgent complement inhibitor therapy is indicated should be provided antimicrobial prophylaxis (1,3). Few data are available to guide decision-making regarding the optimal duration of antimicrobial prophylaxis; therefore, the duration of prophylaxis should be determined based on clinical

judgment. Providers could consider treating patients with antimicrobial prophylaxis for the duration of complement inhibitor treatment.

Reporting of Vaccine Adverse Events

Adverse events after vaccination should be reported to the Vaccine Adverse Event Reporting System. Reporting is encouraged for any clinically significant adverse event, even when a causal association between the vaccine and the event is uncertain, as well as for vaccination errors. Additional information is available at <https://vaers.hhs.gov> or by telephone at 1-800-822-7967.

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Progress Toward Poliomyelitis Eradication — Afghanistan, January 2023–September 2024

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Abstract

Since the Global Polio Eradication Initiative began in 1988, wild poliovirus (WPV) types 2 and 3 have been eradicated, and annual polio case numbers have decreased by >99.9%. WPV type 1 (WPV1) transmission remains endemic in Afghanistan and Pakistan, two countries that share a 1,600-mile (2,600-km) border. This report describes immunization and surveillance activities and progress toward polio eradication in Afghanistan during January 2023–September 2024. As of November 1, Afghanistan reported 23 WPV1 cases in 2024, with onset during January–September 30, 2024. During the 3 previous years, 12 WPV1 cases were reported, including six during 2023. In August 2021, the Taliban took control nationwide and allowed increased geographic access for poliovirus vaccination campaigns. Multiple challenges have affected polio eradication activities in Afghanistan, including mandated repatriation of approximately 1 million Afghans by Pakistan beginning in late 2023, the ongoing humanitarian crisis that limits international agency effectiveness, polio program constraints imposed by authorities, and increased restrictions on female participation in vaccination activities. House-to-house vaccination coverage reached 90%–98% of children during June–July 2024. Beginning in 2021, authorities had progressively lifted restrictions on house-to-house campaigns, but abruptly reverted to national restrictions in September 2024. Both nationwide house-to-house activities and strengthening of the routine childhood immunization program would help ensure that every vulnerable child is vaccinated and provide a pathway to polio eradication in Afghanistan.

Introduction

After the Global Polio Eradication Initiative (GPEI) was launched in 1988, wild poliovirus (WPV) type 2 and type 3 were eradicated, and the annual incidence of poliomyelitis decreased by >99.9%; however, WPV type 1 (WPV1) transmission remains endemic in Afghanistan and neighboring Pakistan (1,2). In 2016, the global synchronized switch from use of trivalent oral polio vaccine (tOPV) (containing Sabin strain types 1, 2, and 3) to use of 3 doses of bivalent OPV (bOPV) (containing Sabin types 1 and 3) and introduction of ≥1 dose of inactivated poliovirus vaccine (IPV) (containing types 1, 2, and 3 antigens) occurred in the routine childhood immunization

schedule (3). During 2021, Afghanistan introduced a second dose of IPV into the routine immunization schedule (3).

Afghanistan is administratively divided into eight regions, 34 provinces, and 400 districts. Since the Taliban takeover in 2021, the humanitarian crisis has worsened, and several challenges continue: further economic stagnation, food insecurity, poor water and sanitation systems, limited access to health care, and increased social restrictions on women (4,5). This ongoing crisis was further compounded when approximately 1 million Afghans were forced to return from Pakistan during October 2023 to early 2024 (6). Competing needs (e.g., water and sanitation, nutrition, and food security) can result in lower community prioritization of vaccination. The polio program partners implemented several integrated strategies to help address some of these needs.

During 2022–July 2024, Afghanistan progressively moved toward the global standard of nationwide house-to-house (door-to-door) vaccination campaigns. The house-to-house modality is a more effective means of reaching every child when compared with temporary fixed vaccination sites (fixed post with multiple posts serving a narrow population area, or fixed sites at mosques, a single post serving a wide population area) that require caregivers to bring their children to these locations.

Methods

Data Sources

Data were provided by the Afghanistan National Emergency Operation Center, the World Health Organization (WHO), and UNICEF, including data obtained from acute flaccid paralysis (AFP) surveillance, environmental surveillance (ES), and supplementary immunization activity (SIA)* effectiveness measures. GPEI monitors the sensitivity of case detection and investigation through two AFP surveillance performance indicators: detection of two or more nonpolio AFP (NPAFP)[†] cases per 100,000 children aged ≤15 years per year at subnational

*SIAs are immunization activities that supplement the routine immunization program and generally target children aged <5 years for OPV, regardless of their vaccination history. Countries with ongoing polio circulation conduct multiple SIA activities.

[†]NPAFP cases are discarded as polio cases because they do not have laboratory or other documentation of poliovirus as the cause of paralysis. The expected background NPAFP rate is two or more cases per 100,000 children aged <15 years per year, the WHO standard performance indicator target for sufficiently sensitive surveillance to detect a case of polio.

administrative levels and adequate stool specimen[§] collection for ≥80% of AFP cases. ES in Afghanistan consists of poliovirus testing of systematically collected sewage samples within all eight regions: in 2023 at 38 sites in 21 districts located in 16 provinces and in 2024, expanded to 43 sites located in 24 districts in 18 provinces.

WHO and UNICEF annually estimate national routine immunization coverage using recent surveys and other data (7). SIA effectiveness measures include administrative coverage from data collected during the campaign (doses administered during the campaign divided by the estimated target population) and point estimates of postcampaign monitoring surveys. Administrative data are less reliable but more widely available than are survey data. Postcampaign surveys are conducted by independent, trained personnel who select households by purposive sampling, and monitor finger-marking of children (performed by SIA teams upon OPV administration) as evidence of recent SIA vaccination; the proportions of children who are finger-marked among children in the surveyed households in the target age group are reviewed and analyzed.

Data Analysis

Vaccination activities, coverage data, and performance indicators were reviewed and tabulated by region and by vaccination modality. AFP and ES data, characteristics of patients with laboratory-confirmed poliomyelitis, and genomic sequence analysis of poliovirus isolates were reviewed and described. Vaccine dose histories reported by caregivers and collected during AFP investigations were reviewed and analyzed among children with confirmed WPV1 cases.

Genomic sequencing analysis of the region coding the VP1 capsid protein of all poliovirus isolates provides critical detail on transmission of genetic lineages and surveillance quality. Genomic analysis was carried out by a WHO regional reference laboratory for poliomyelitis. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.[¶]

Results

Immunization Activities

In 2023, WHO/UNICEF estimated national 3-dose coverage with bOPV among children aged 1 year in Afghanistan was 68%, compared with 56% and 61% in 2021 and 2022,

[§] An adequate stool specimen refers to the quantity and quality required to detect poliovirus and is defined as two stool specimens of sufficient quality for laboratory analysis, collected ≥24 hours apart and ≤14 days of paralysis onset, and arriving at a WHO-accredited laboratory in good condition (<8 grams, reverse cold chain maintained, without leakage or desiccation, and with proper documentation).

[¶] 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.

respectively; estimated 2-dose IPV coverage was 45%, compared with 30% in 2021 and 43% in 2022. During 2023, the polio program implemented 13 bOPV SIAs targeting children aged <5 years: three national immunization days (NIDs), five subnational immunization days (SNIDs), and five case-response campaigns. Three SIAs focused on the provinces in the East Region and targeted an expanded age group (children aged <10 years). Reported NID administrative coverage ranged from 77% to 98%; SNID coverage ranged from 88% to 97%, and case-response campaigns coverage ranged from 81% to 120% (coverage >100% can occur if the target population is highly underestimated or if vaccine doses are administered to children not in the target age group or area).

During January–July 2024, the polio program implemented two NIDs and three SNIDs; four SIAs were synchronized with neighboring Pakistan. Administrative bOPV coverage during the January–May 2024 SIA ranged from 88% to 97%. In June 2024, authorities announced nationwide house-to-house access for the first time in approximately 7 years. Before nationwide access, house-to-house vaccination was carried out in 72%–85% of districts, with an increase to 96%–99% of districts during June and July, which is close to full house-to-house access. After progressively improved campaign access and quality were achieved, in September 2024 authorities abruptly reversed from allowing nationwide house-to-house access to mandating only fixed-post modality.

In 2023, postcampaign monitoring survey coverage ranged from 73% to 85% in the South Region, 80% to 87% in the Northeast, and 90% to 100% in all other regions. Large differences in coverage were noted by delivery modality: coverage among children ranged from 68% to 75% at fixed posts, 68% to 81% at mosques, and 90% to 97% among those reached through house-to-house vaccination. In 2024, SIA coverage determined by postcampaign monitoring surveys increased to 91%–99% in all regions compared with coverage in 2023, except in the South Region, where coverage ranged from 19% to 77% before June when only fixed-site vaccination was approved; during June and July, when house-to-house vaccination was permitted, SIA coverage in the South Region ranged from 89% to 91%. As in 2023, large coverage differences by vaccine administration modality were again noted in 2024, with 73%–85% fixed-post coverage compared with 90%–98% house-to-house coverage. OPV was also administered to persons of all ages entering through two main border crossings with Pakistan: Torkham (East Region) and Friendship Gate (South Region). During January 2023–September 2024, approximately 1.7 million persons were vaccinated. To further improve SIAs and surveillance, both Afghanistan and Pakistan conducted cross-border meetings to enhance coordination, discuss findings, and plan synchronized campaigns.

Poliovirus Surveillance

AFP Surveillance. In 2023, the AFP surveillance system included a network of 1,932 active surveillance sites,** 3,251 passive reporting sites,†† and 49,870 community-based reporting volunteers; this network expanded in 2024 to 2,078 active sites, 3,315 passive sites, and 50,409 reporting volunteers. The NPAFP rate in 2023 was 26 per 100,000 children aged <15 years (regional range = 17.0–39.1), and stool specimen adequacy was 94% (regional range = 90.7%–97.0%) (Table). During January–September 2024, the annualized NPAFP rate was 23.7 per 100,000 persons aged <15 years (regional range = 15.2–36.8), and stool adequacy was 95% (regional range = 91.8%–98.0%).

Environmental Surveillance. In 2023, WPV1 was detected in 62 ES samples from eight provinces in four regions: East (Nangarhar [42] and Kunar [five]), South (Kandahar [eight], Zabul [two], Helmand [one], and Uruzgan [one]), Central (Kabul [two]), and North (Balkh [one]). During January–September 2024, 85 WPV1 ES detections were reported in 10 provinces in five regions: South (Kandahar [35], Helmand [22], and Uruzgan [two]), East (Nangarhar [13], Laghman [three], and Kunar [one]), Southeast (Paktya [one] and Ghazni [one]), Central (Kabul [five]), and West (Hirat [two]).

** Active AFP surveillance involves proactively seeking (weekly or biweekly), reporting, and investigating cases. Active systems tend to be more accurate and comprehensive, although they are more time-consuming than are passive systems.

†† Passive AFP surveillance relies on reporting by providers or other persons; passive AFP is less time-consuming and expensive but tends to be less accurate because of inherent underreporting. Reporting typically occurs monthly.

Epidemiology of Poliovirus Cases

During 2021–2022, six WPV1 cases were reported, from the Southeast and Northeast regions. Six total WPV1 cases were reported during 2023, all from Nangarhar province in the East Region (five reported cases during January–June 2023 and one during July–December) (Figure 1) (Figure 2). In 2023, the mean age at onset of paralysis was 79 months (6 years, 7 months) (range = 30–144 months). Caregiver histories indicated that these children had received >7 OPV doses through SIAs and a median of 3 doses through routine immunization (range = 1–3 doses).

During January–September 2024 (as of November 1), 23 WPV1 cases were reported in Afghanistan, representing approximately four times the number of cases during all of 2023, and the highest number in four years (Figure 1). Cases in 2024 were reported from five provinces in two regions: East (Nuristan [one] and Kunar [one]) and South (Kandahar [14], Helmand [six], and Uruzgan [one]). The mean patient age was 39 months (3 years, 3 months) (range = 8–120 months). Among the 23 WPV1 patients, three had never received an OPV dose through routine immunization or SIAs. Seventeen children received OPV through SIAs (average = 8 doses; range = 2–20), and 17 received OPV through routine immunization (average = 3 doses; range = 1–5).

Genomic Sequence Analysis of Poliovirus Isolates

Genomic sequence analysis revealed two WPV1 genetic clusters (groups of isolates sharing ≥95% identity) during July 2023–September 2024. A majority of WPV1 isolates, including

TABLE. Acute flaccid paralysis surveillance performance indicators, reported cases of wild poliovirus type 1, and number of environmental specimens with detection of wild poliovirus type 1, by region and period — Afghanistan, January 2023–September 2024*

Region	AFP surveillance performance indicators						No. of WPV1 cases reported				No. of ES samples with WPV1 detected†			
	No. of AFP cases		NPAFP rate [§]		% with adequate stool specimens [¶]		2023		2024		2023		2024	
	2023	2024	2023	2024**	2023	2024	Jan–Jun	Jul–Dec	Jan–Jun	Jul–Sep	Jan–Jun	Jul–Dec	Jan–Jun	Jul–Sep
All	5,856	4,080	26.0	23.7	94.0	94.6	5	1	11	12	32	30	55	30
Badakhshan	113	98	17.0	19.3	96.5	98.0	0	0	0	0	0	0	0	0
Central	1,144	597	22.3	15.2	97.0	97.8	0	0	0	0	0	2	1	4
East	885	638	39.1	36.8	93.6	94.4	5	1	2	0	30	17	14	3
North	482	341	17.3	16.3	90.7	92.4	0	0	0	0	1	0	0	0
Northeast	569	413	22.5	21.3	95.4	95.7	0	0	0	0	0	0	0	0
South	1,298	999	33.3	33.5	91.1	91.8	0	0	9	12	1	11	36	23
Southeast	566	366	25.2	21.3	94.3	95.9	0	0	0	0	0	0	2	0
West	799	628	26.5	26.8	95.0	95.7	0	0	0	0	0	0	2	0

Abbreviations: AFP = acute flaccid paralysis; ES = environmental surveillance; NPAFP = nonpolio acute flaccid paralysis; WPV1 = wild poliovirus type 1.

* Data as of October 14, 2024.

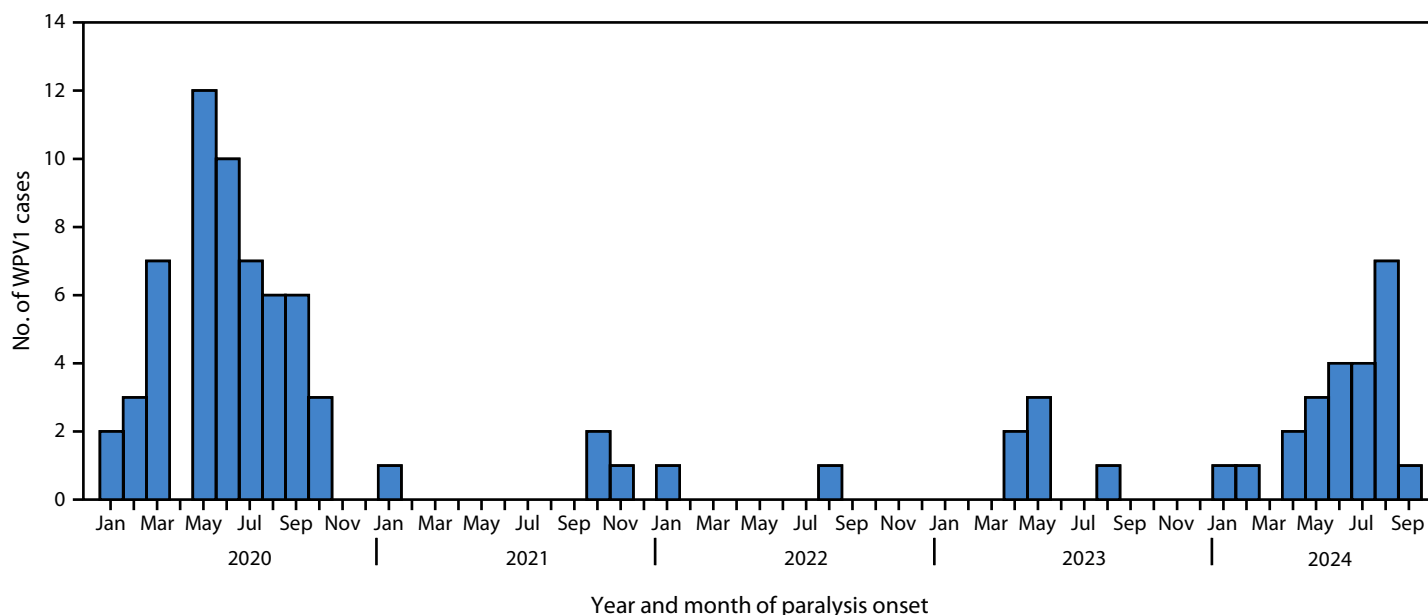
† Total number of ES samples by period, January 2023–September 2024.

§ Cases per 100,000 persons aged <15 years. The surveillance performance indicator target for countries with poliovirus circulation is two or more NPAFP cases per 100,000 persons aged <15 years per year.

¶ Percentage of cases with adequate stool specimen. An adequate stool specimen refers to the quantity and quality required to detect poliovirus and is defined as two stool specimens of sufficient quality for laboratory analysis, collected ≥24 hours apart and within 14 days of paralysis onset, and arriving at a WHO-accredited laboratory in good condition (<8 grams, reverse cold chain maintained, without leakage or desiccation, and with proper documentation).

** Annualized based on AFP surveillance data through September 2024.

FIGURE 1. Number of wild poliovirus type 1 cases, by month of paralysis onset (N = 91) — Afghanistan, January 2020–September 2024*



Abbreviation: WPV1 = wild poliovirus type 1.

* As of September 30, 2024.

those from all AFP cases, were part of cluster YB3A4A, found exclusively in the East Region in 2023. Detection of YB3A4A lineages along the southern corridor, including Kandahar and Helmand provinces, occurred in 2024. All isolates from AFP cases were genetically linked to other sequences within Afghanistan, apart from one isolate from an August 2024 case in Kandahar province linked to a Pakistan isolate. Isolates from three ES detections were part of cluster YB3A4B, with a single detection in a sample collected in March 2024 from Hirat province (West Region) and were linked to both Afghanistan and Pakistan isolates. The first ES isolate in the South Region in 2024 was linked to transmission in the East Region in 2023.

Among the 23 AFP WPV1 case isolates identified during January–September 2024, one isolate (from a case detected in Kandahar) was >1.5% divergent from its closest genetic match, the orphan virus threshold,^{§§} and four others, including two from Kandahar, one from Nuristan, and one from Helmand, were >1.1% (but ≤1.5%) divergent. Five ES isolates exceeded the orphan virus threshold, including one from Nangarhar in 2023 and four in 2024, from Kandahar (two), Kabul (one), and Paktya (one). Fourteen other ES isolates, from Helmand (one), Kabul (two), Kandahar (eight), Laghman (one), and Nangarhar (two) were >1.1% divergent from their closest

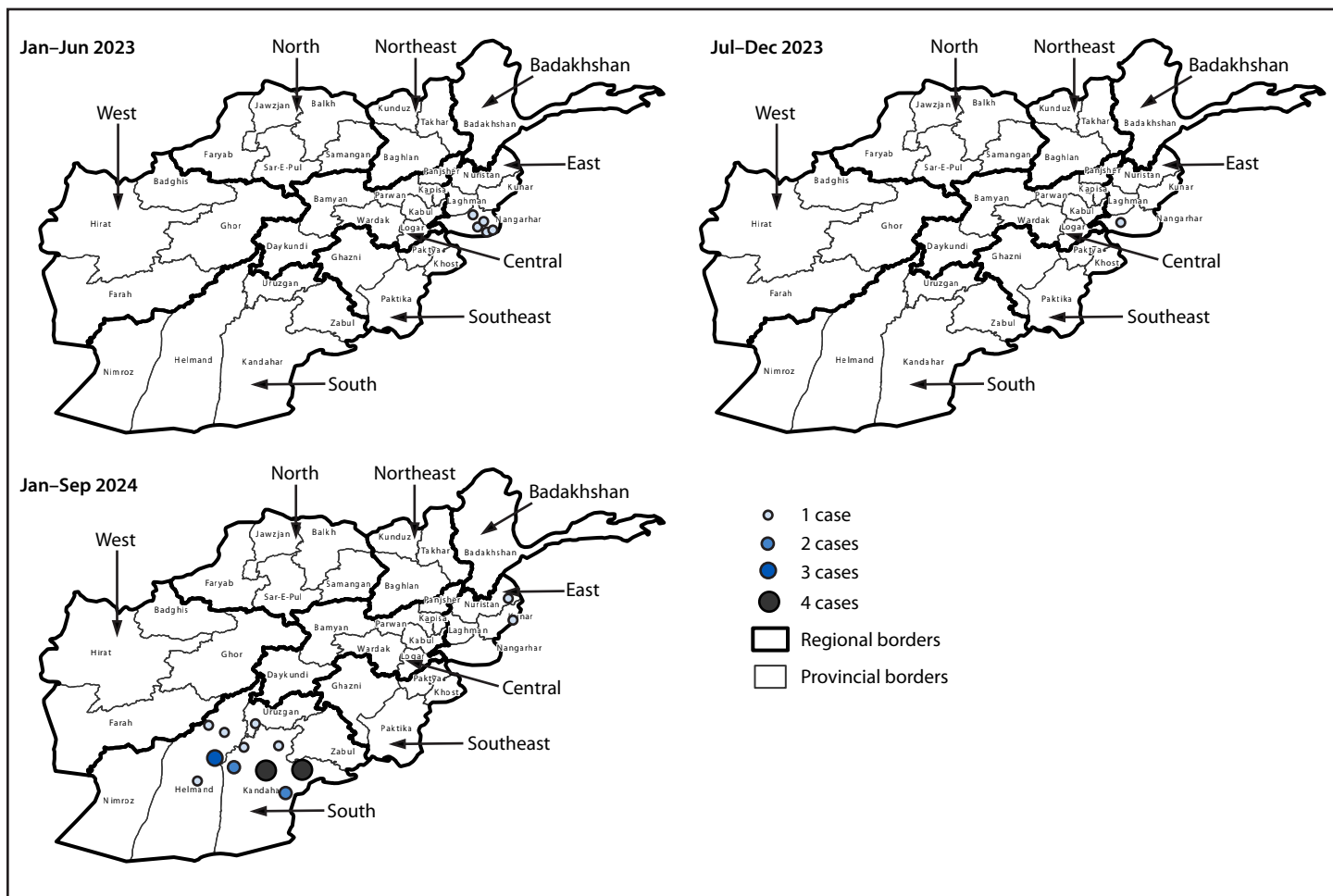
genetic match. The above six orphan viruses (1 AFP, 5 ES) and 18 isolates >1.1% divergent (4 AFP, 14 ES) from their closest genetic match identified during this reporting period indicate a considerable proportion of undetected cases and therefore substantial gaps in surveillance.

Discussion

During a 2-year period, 2021–2022, Afghanistan reported six WPV1 cases, followed by six cases in 2023. In response to five WPV1 cases reported during the first half of 2023 from Afghanistan's Nangarhar province, an intense SIA calendar was implemented in the East Region. One of the six 2023 cases was reported in Nangarhar later in 2023. During October 2023–early 2024, approximately 1 million Afghans were forced to return from Pakistan, 44% of whom settled in the South Region, mostly in Kandahar province, and 26% in the East Region, mostly in Nangarhar province. These two provinces, which reported the majority of polio cases during 2023–2024, had been historical WPV1 reservoirs in Afghanistan (8). Despite achieving AFP surveillance performance indicators thresholds, genomic sequencing analyses depicting orphan viruses and others with marked divergence from closest known genetic relatives highlight limitations in the sensitivity of surveillance and likely indicate undetected cases in undervaccinated children. Compared with polio cases in 2023 (9), patients in 2024 were younger at onset of paralysis and had received fewer vaccine doses; three 2024 WPV cases

^{§§} Orphan viruses are >1.5% divergent from their closest genetic match (i.e., <98.5% identity) and can indicate a gap in poliovirus surveillance. The Global Polio Laboratory Network bases its findings on analysis of the genetic divergences of the 906-nucleotide VP1 capsid protein coding region of poliovirus isolates.

FIGURE 2. Reported cases of polio caused by wild poliovirus type 1 (N = 29), by region, province, and period — Afghanistan, January 2023–September 2024



were in children who had never received an OPV dose through routine immunization or SIAs.

In Afghanistan, women are allowed to enter homes to vaccinate young children, whereas men who are not close relatives are not. Despite incrementally increased numbers of female workers in the polio program in Afghanistan during the period up to 2021, progressively tighter restrictions on women’s rights and freedom of movement have limited their engagement in polio eradication activities, both as polio workers and as caregivers seeking vaccines for their children outside the home.

In early 2024, the Afghanistan polio program instituted several initiatives that provided desired commodities for hard-to-reach children and strengthened humanitarian organizations’ community engagement in polio eradication activities. After authorities announced nationwide house-to-house access, 99% of children were vaccinated through this modality during June and July SIAs, and vaccination coverage improved in all areas; however, authorities unexpectedly reversed their decision

in August. The polio program postponed the September SIA to strategize on how to optimize fixed-site campaign quality. Administrative data and postcampaign–monitoring survey data consistently indicate that SIA coverage achieved through non–house-to-house modalities is unacceptably low. This finding is especially relevant for the South Region, the current epicenter of transmission, where reaching children has always been challenging.

Limitations

The findings of this report are subject to at least two limitations. First, population figures and campaign target estimates have been based on outdated detailed community vaccination plans, some from 2017. The large influx of returnees from Pakistan during 2023–2024 exacerbated uncertainties in population estimates. Second, caregiver histories of doses administered might be inaccurate because of poor recall among caregivers and reporting bias among investigators.

Summary**What is already known about this topic?**

Wild poliovirus (WPV) type 1 (WPV1) circulation continues in Afghanistan as well as in neighboring Pakistan, the two remaining countries with ongoing endemic WPV transmission.

What is added by this report?

During 2024 (through September 30), Afghanistan reported 23 WPV1 cases, the highest number in 4 years. Poliovirus vaccination campaign coverage improved markedly with house-to-house vaccination; however, local authorities have reinstated restrictions on house-to-house vaccine administration.

What are the implications for public health practice?

New challenges continue to affect progress toward polio eradication in Afghanistan. Both nationwide house-to-house vaccination campaigns and strengthened routine childhood immunization are needed to reach every vulnerable child with vaccines in Afghanistan and provide additional pathways toward stopping transmission.

Implications for Public Health Practice

Data indicate that house-to-house vaccination is the most effective campaign modality. The current approach by authorities in Afghanistan to limit SIA implementation to modalities other than house-to-house jeopardizes eradication. Interrupting transmission in the South Region reservoir will require further strengthening of coordination between the Afghanistan and Pakistan polio programs. To ensure that every vulnerable child is reached with vaccine, nationwide house-to-house activities are necessary, as is strengthening the routine childhood immunization program to provide a pathway to global polio eradication.

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