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Mortality Among Children Aged <5 Years Living with HIV Who Are Receiving Antiretroviral Treatment — U.S. President's Emergency Plan for AIDS Relief, 28 Supported Countries and Regions, October 2020–September 2022

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Abstract

Globally, children aged <5 years, including those living with HIV who are not receiving antiretroviral treatment (ART), experience disproportionately high mortality. Global mortality among children living with HIV aged <5 years receiving ART is not well described. This report compares mortality and related clinical measures among infants aged <1 year and children aged 1–4 years living with HIV with those among older persons aged 5–14, 15–49, and ≥50 years living with HIV receiving ART services at all clinical sites supported by the U.S. President's Emergency Plan for AIDS Relief. During October 2020–September 2022, an average of 11,980 infants aged <1 year and 105,510 children aged 1–4 years were receiving ART each quarter; among these infants and children receiving ART, 586 (4.9%) and 2,684 (2.5%), respectively, were reported to have died annually. These proportions of infants and children who died ranged from four to nine times higher in infants aged <1 year, and two to five times higher in children aged 1–4 years, than the proportions of older persons aged ≥5 years receiving ART. Compared with persons aged ≥5 years living with HIV, the proportions of children aged <5 years living with HIV who experienced interruptions in treatment were also higher, and the proportions who had a documented HIV viral load result or a suppressed viral load were lower. Prioritizing and optimizing HIV and general health services for children aged <5 years living with HIV receiving ART, including those recommended in the WHO STOP AIDS Package, might help address these disproportionately poorer outcomes.

Introduction

Globally, children aged <5 years living with HIV are less likely to receive a diagnosis of HIV and be linked to antiretroviral treatment (ART) than are older persons living with HIV, and are more likely to die, especially those who are not receiving ART (*1*). Disparities in mortality and other outcomes among children compared with older persons living with HIV after initiating ART are not as well described. Given the relatively high global

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mortality rates among children aged <5 years in general (*2*), those living with HIV receiving ART might experience excessively high mortality compared with older persons living with HIV receiving ART. This report compares mortality and other clinical measures among infants aged <1 year and children aged 1–4 years with those among persons aged ≥5 years living with HIV receiving ART services during October 2020–September 2022, at all clinical sites supported by the U.S. President's Emergency Plan for AIDS Relief (PEPFAR).

Methods

PEPFAR Monitoring, Evaluation, and Reporting data collected quarterly from all PEPFAR-supported treatment sites during October 2020–September 2022 were analyzed.* Indicators included the estimated number of persons living with HIV receiving ART,† mortality§ (i.e., reported to have died), interruption in treatment¶ (i.e., no clinical encounter during the 28 days after the last scheduled clinical contact), proxy viral load coverage** (i.e., documented viral load result during the previous 12 months among those assumed to be

* Sites from 25 PEPFAR-supported countries and three PEPFAR-supported regions were included in this analysis. The 25 countries include Angola, Botswana, Burundi, Cameroon, Côte d'Ivoire, Democratic Republic of the Congo, Dominican Republic, Eswatini, Ethiopia, Haiti, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, Rwanda, South Africa, South Sudan, Tanzania, Uganda, Ukraine, Vietnam, Zambia, and Zimbabwe. The three regions include Asia Region (Burma, India, Indonesia, Kazakhstan, Kyrgyzstan, Laos, Nepal, Papua New Guinea, Philippines, Tajikistan, and Thailand), West Africa Region (Benin, Burkina Faso, Ghana, Liberia, Mali, Senegal, Sierra Leone, and Togo), and Western Hemisphere Region (Barbados, Brazil, Colombia, El Salvador, Guatemala, Guyana, Honduras, Jamaica, Nicaragua, Panama, Peru, and Trinidad and Tobago).

† The estimated number of persons living with HIV receiving ART in the current quarterly reporting period equals the sum of the number of persons newly initiated on ART in the current quarterly reporting period and the number of persons receiving ART at the end of the previous quarterly reporting period.

§ Mortality is defined as having a reported death in the current quarterly reporting period.

¶ Interruption in treatment is defined as not having a clinical encounter for 28 days after the last scheduled appointment or expected clinical contact in the current quarterly reporting period. The proportions with treatment interruptions are calculated as the number of treatment interruptions in the current quarterly reporting period divided by the sum of those already receiving ART in the previous quarterly reporting period and those newly initiated on ART in the current quarterly reporting period.

** Viral load coverage is defined as having a documented viral load result within the previous 12 months among those assumed to be eligible for a viral load in the current quarterly reporting period. For calculating proxy viral load coverage, the numerator is the number of persons living with HIV receiving ART in the current quarterly reporting period reported to have a documented viral result during the previous 12 months, and the denominator is the number of persons with HIV receiving ART two quarters before the current quarterly reporting period. The term proxy is used because the numerator and denominator are determined from two distinct groups of persons living with HIV.

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eligible for a viral load test), and viral load suppression[††] (i.e., had a suppressed viral load result among those with a viral load result documented within the previous 12 months). Mortality was measured as the annual mean numbers and proportions of reported deaths among those receiving ART, and the other indicators are reported as quarterly mean numbers or proportions among those receiving ART[§§]; these measures were compared among children aged <5 years living with HIV receiving ART (stratified by age <1 and age 1–4 years to differentiate infants from other children aged <5 years) and older persons aged 5–14, 15–49, and ≥50 years living with HIV receiving ART. Crude mortality ratios (CMRs) were calculated comparing the proportions of reported deaths among these age groups. SAS (version 9.4; SAS Institute) was used to conduct all analyses. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.[¶¶]

[††] Viral load suppression is defined as having a suppressed viral load result (HIV RNA <1000 copies/mL) among those with a documented viral load result within the previous 12 months. For calculating proportion with viral load suppression, the numerator is number of persons living with HIV receiving ART in the current quarterly reporting period with a suppressed viral load result documented within the previous 12 months, and the denominator is number of persons with HIV receiving ART in the current quarterly reporting period reported to have a documented viral result during the previous 12 months.

[§§] To estimate annual mortality, an annual proportion with a reported death was calculated using quarterly reported data: the numerator is the sum of reported deaths from each of the four quarters, and the denominator is the mean of the estimated number of persons living with HIV receiving ART from each of the four quarters. The other measures (treatment interruption, proxy viral load coverage, and viral load suppression) could not be summarized as annual estimates because, unlike mortality, treatment could have been interrupted or viral load measures received multiple times during a 1- or 2-year period.

Results

Among all PEPFAR-supported sites, an average of 17.9 million persons living with HIV received ART each quarter, among whom 11,980 were aged <1 year, and 105,510 were aged 1–4 years during the 2-year analysis period. Among these ART recipients, 4.9% of those aged <1 year and 2.5% of those aged 1–4 years were reported to have died annually; among older age groups these prevalences were 0.5% (5–14 years), 0.7% (15–49 years), and 1.4% (≥50 years) (Table 1) (Figure). Proportions of reported deaths among infants aged <1 year were approximately four to nine times those among older age groups: CMR = 9.2, 7.2, and 3.6 among persons living with HIV aged 5–14 years, 15–49 years, and ≥50 years, respectively. Proportions among children aged 1–4 years were approximately

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

TABLE 1. Annual proportion of reported deaths and crude mortality ratios among persons living with HIV and receiving antiretroviral treatment — U.S. President's Emergency Plan for AIDS Relief, 28 supported countries and regions,* 2021–2022†

	2021			2022			2021 and 2022 (annual mean)§		
Characteristic	% Died	No. died	No. receiving ART	% Died	No. died	No. receiving ART	% Died	No. died	No. receiving ART
Age group, yrs									
<1	4.4	585	13,223	5.5	587	10,737	4.9	586	11,980
1–4	2.6	2,786	108,325	2.5	2,581	102,695	2.5	2,684	105,510
5–14	0.5	2,943	537,867	0.5	2,772	534,105	0.5	2,858	535,986
15–49	0.7	94,539	13,089,351	0.6	90,672	13,984,027	0.7	92,606	13,536,689
≥50	1.4	50,001	3,488,945	1.3	51,913	3,936,499	1.4	50,957	3,712,722
Total	**0.9**	**150,854**	**17,237,711**	**0.8**	**148,525**	**18,568,063**	**0.8**	**149,691**	**17,902,887**
Crude mortality ratios¶									
<1 vs. 5–14	8.1	—	—	10.5	—	—	9.2	—	—
<1 vs. 15–49	6.1	—	—	8.4	—	—	7.2	—	—
<1 vs. ≥50	3.1	—	—	4.1	—	—	3.6	—	—
1–4 vs. 5–14	4.7	—	—	4.8	—	—	4.8	—	—
1–4 vs. 15–49	3.6	—	—	3.9	—	—	3.7	—	—
1–4 vs. ≥50	1.8	—	—	1.9	—	—	1.9	—	—

Abbreviations: ART = antiretroviral therapy; PEPFAR = U.S. President's Emergency Plan for AIDS Relief.

* Sites from 25 PEPFAR-supported countries and three PEPFAR-supported regions were included in this analysis. The 25 countries include Angola, Botswana, Burundi, Cameroon, Côte d'Ivoire, Democratic Republic of the Congo, Dominican Republic, Eswatini, Ethiopia, Haiti, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, Rwanda, South Africa, South Sudan, Tanzania, Uganda, Ukraine, Vietnam, Zambia, and Zimbabwe. The three regions include Asia Region (Burma, India, Indonesia, Kazakhstan, Kyrgyzstan, Laos, Nepal, Papua New Guinea, Philippines, Tajikistan, and Thailand), West Africa Region (Benin, Burkina Faso, Ghana, Liberia, Mali, Senegal, Sierra Leone, and Togo), and Western Hemisphere Region (Barbados, Brazil, Colombia, El Salvador, Guatemala, Guyana, Honduras, Jamaica, Nicaragua, Panama, Peru, and Trinidad and Tobago).

† 2021–2022 represents fiscal years, which start in the previous October (e.g., October 2021–September 2022 represents 2022).

§ Proportions of reported deaths were calculated for fiscal years 2021 and 2022 by summing the reported number of deaths across the four quarters and dividing by the mean number of persons living with HIV receiving ART estimated from each of the four quarters. The number of persons living with HIV receiving ART estimated from each quarter equals the number of persons reported to be newly initiated on ART in the current quarterly reporting period plus the number reported to be receiving ART at the end of the previous quarterly reporting period.

¶ Crude mortality ratios are ratios of proportions of reported deaths for each age group among persons living with HIV receiving ART who are aged <1 or 1–4 years and those who are aged 5–14, 15–49, and ≥50 years.

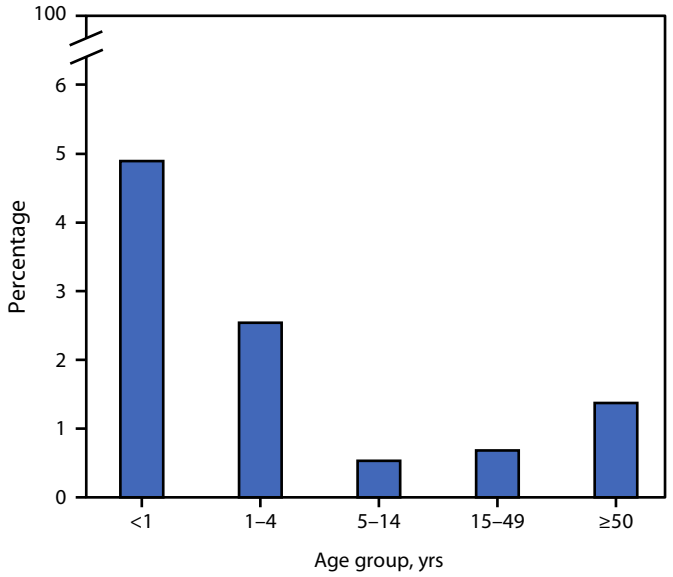
two to five times those among older age groups: CMR = 4.8, 3.7, and 1.9 among those aged 5–14 years, 15–49 years, and ≥50 years, respectively (Table 1). Interruptions in treatment were also more prevalent among children aged <5 years living with HIV than among persons within older age groups (<1 year and 1–4 years, 4%; 5–14 years, 2%; 15–49 years, 3%; and ≥50 years, 2%) living with HIV receiving ART; proportions were lower for proxy viral load coverage (<1 year: not reported***; 1–4 years, 66%; 5–14 years, 82%; 15–49 years, 77%; and ≥50 years, 83%), and for viral load suppression (<1 year, 78%; 1–4 years, 73%; 5–14 years, 85%; 15–49 years, 94%; and ≥50 years, 96%) (Table 2).

Discussion

Among approximately 18 million persons living with HIV receiving ART through PEPFAR during October 2020–September 2022, prevalences of reported death were higher among children aged <5 years than among persons in older age groups, consistent with previously published findings (*3*). The additional finding that interruptions in treatment were also more common among children aged <5 years living with HIV might suggest that mortality is disproportionately underreported in this age group, because patients with interruptions in treatment or who are lost to follow-up might have died (*3*).

Among persons living with HIV receiving ART, several factors might explain the disparities in mortality among children aged <5 years compared with older persons. First, many children aged <5 years with HIV are severely immunosuppressed and at high risk for poor outcomes when they receive an HIV diagnosis and initiate ART (*4*). WHO considers all children aged <5 years living with HIV who are not clinically stable receiving ART to have advanced disease (*4*); in contrast, persons aged ≥5 years living with HIV are considered to have advanced disease only if they have a WHO stage 3 or 4 illness††† or a CD4 count <200 cells/mm^3 (*4*). Second, these findings demonstrate that children aged <5 years receiving ART have lower rates of viral load suppression along with higher rates of mortality, and viral nonsuppression is a well-described risk factor for death among children living with HIV (*5*). Finally, general mortality for persons aged <5 years, regardless of HIV status, remains high in many low-resource settings, including those where PEPFAR supports HIV programs (*2*). Factors that influence mortality in all children aged <5 years likely also influence mortality in children aged <5 years living with HIV in these settings. For example, one study from western Kenya identified common and overlapping immediate causes of

FIGURE. Annual percentage of reported deaths* among persons living with HIV and receiving antiretroviral treatment — U.S. President's Emergency Plan for AIDS Relief, 28 supported countries and regions,† 2021–2022§



Abbreviations: ART = antiretroviral therapy; PEPFAR = U.S. President's Emergency Plan for AIDS Relief.

* Percentage of reported deaths was calculated for fiscal years 2021 and 2022 by summing the reported number of deaths across the four quarters and dividing by the mean number of persons living with HIV receiving ART estimated from each of the four quarters. The number of persons living with HIV receiving ART estimated from each quarter equals the number of persons living with HIV reported to be newly initiated on ART in the current quarterly reporting period plus the number reported to be receiving ART at the end of the previous quarterly reporting period.

† Sites from 25 PEPFAR-supported countries and three PEPFAR-supported regions were included in this analysis. The 25 countries include Angola, Botswana, Burundi, Cameroon, Côte d'Ivoire, Democratic Republic of the Congo, Dominican Republic, Eswatini, Ethiopia, Haiti, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, Rwanda, South Africa, South Sudan, Tanzania, Uganda, Ukraine, Vietnam, Zambia, and Zimbabwe. The three regions include Asia Region (Burma, India, Indonesia, Kazakhstan, Kyrgyzstan, Laos, Nepal, Papua New Guinea, Philippines, Tajikistan, and Thailand), West Africa Region (Benin, Burkina Faso, Ghana, Liberia, Mali, Senegal, Sierra Leone, and Togo), and Western Hemisphere Region (Barbados, Brazil, Colombia, El Salvador, Guatemala, Guyana, Honduras, Jamaica, Nicaragua, Panama, Peru, and Trinidad and Tobago).

§ 2021–2022 represents fiscal years, which start in the previous October (e.g., October 2021–September 2022 represents 2022).

*** PEPFAR Monitoring, Evaluation, and Reporting data underestimate proxy viral load coverage for children aged <1 year living with HIV, and it has not been included in this analysis. The numerator for proxy viral load coverage in infants aged <1 year only records those diagnosed and placed on treatment before age 6 months who received a viral load in their first year of life. The numerator excludes infants linked to ART later (aged ≥6 months) who are not eligible for a viral load until their second year of life.

††† Persons living with HIV are assigned a WHO-defined clinical stage between 1 and 4 based on the presence of different clinical conditions; an increase in staging likely represents a clinical worsening or progression of illness in a person living with HIV. Clinical staging criteria differ for adults and adolescents aged ≥15 years and children and adolescents aged <15 years. Notable conditions in stage 3 include pulmonary or lymph node tuberculosis, and unexplained hematologic abnormalities, fever, diarrhea, or moderate malnutrition, among other conditions. Notable conditions in stage 4 include unexplained severe malnutrition, pneumocystis jirovecii pneumonia, central nervous system complications and infections, and HIV-related malignancies, among other conditions (https://iris.who.int/bitstream/handle/10665/208825/9789241549684_eng.pdf?sequence=1 (Annex 10).

TABLE 2. Interruptions in treatment, proxy viral load coverage, and viral load suppression among persons living with HIV receiving antiretroviral treatment — U.S. President's Emergency Plan for AIDS Relief, 28 supported countries and regions,* 2021–2022†,§

Characteristic	%	Numerator	Denominator
Interruptions in treatment¶			
Age group, yrs			
<1	4.2	509	11,980
1–4	4.0	4,224	105,510
5–14	2.4	12,735	535,986
15–49	3.0	406,565	13,536,689
≥50	2.0	74,721	3,712,722
Proxy viral load coverage**			
Age group, yrs			
<1††	NA	NA	NA
1–4	66.0	65,742	99,639
5–14	81.9	431,988	527,392
15–49	76.7	9,836,384	12,831,401
≥50	82.9	2,940,808	3,546,420
Viral load suppression§§			
Age group, yrs			
<1	78.4	2,687	3,427
1–4	73.2	48,106	65,742
5–14	85.0	367,312	431,988
15–49	94.3	9,279,763	9,836,384
≥50	96.3	2,830,747	2,940,808

Abbreviations: ART = antiretroviral therapy; NA = not applicable; PEPFAR = U.S. President's Emergency Plan for AIDS Relief.

* Sites from 25 PEPFAR-supported countries and three PEPFAR-supported regions were included in this analysis. The 25 countries include Angola, Botswana, Burundi, Cameroon, Côte d'Ivoire, Democratic Republic of the Congo, Dominican Republic, Eswatini, Ethiopia, Haiti, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, Rwanda, South Africa, South Sudan, Tanzania, Uganda, Ukraine, Vietnam, Zambia, and Zimbabwe. The three regions include Asia Region (Burma, India, Indonesia, Kazakhstan, Kyrgyzstan, Laos, Nepal, Papua New Guinea, Philippines, Tajikistan, and Thailand), West Africa Region (Benin, Burkina Faso, Ghana, Liberia, Mali, Senegal, Sierra Leone, and Togo), and Western Hemisphere Region (Barbados, Brazil, Colombia, El Salvador, Guatemala, Guyana, Honduras, Jamaica, Nicaragua, Panama, Peru, and Trinidad and Tobago).

TABLE 2. (*Continued*) Interruptions in treatment, proxy viral load coverage, and viral load suppression among persons living with HIV receiving antiretroviral treatment — U.S. President's Emergency Plan for AIDS Relief, 28 supported countries and regions,* 2021–2022†,§

† 2021–2022 represents fiscal years, which start in the previous October (e.g., October 2021–September 2022 represents 2022).

§ The other measures (treatment interruption, proxy viral load coverage, and viral load suppression) could not be summarized as annual estimates because, unlike mortality, treatment could have been interrupted or viral load measures received multiple times during a 1- or 2-year period. Therefore, trying to create annual estimates of these quarterly collected and reported measures would likely lead to overestimates of the actual measures because of duplication.

¶ Interruption in treatment is defined as not having a clinical encounter for 28 days after the last scheduled appointment or expected clinical contact. The proportions with treatment interruptions are calculated as the number of treatment interruptions in the current quarterly reporting period divided by the sum of those already receiving ART in the previous quarterly reporting period and those newly initiated on ART in the current quarterly reporting period.

** Proxy viral load coverage is defined as having a documented viral load result within the previous 12 months among those assumed to be eligible for a viral load in the current quarterly reporting period. For calculating proxy viral load coverage, the numerator is number of persons living with HIV receiving ART in the current quarterly reporting period reported to have a documented viral result during the previous 12 months, and the denominator is the number of persons receiving ART two quarters before the current quarterly reporting period. The term proxy is used because the numerator and denominator are determined from two different populations of persons.

†† PEPFAR Monitoring, Evaluation, and Reporting data underestimate proxy viral load coverage for infants aged <1 year living with HIV, and it has not been included in this analysis. The numerator for proxy viral load coverage in infants aged <1 year only records those with diagnoses and placed on treatment before age 6 months who received a viral load in their first year of life. The numerator excludes infants linked to ART later (aged ≥6 months) who are not eligible for a viral load until their second year of life.

§§ Viral load suppression is defined as having a suppressed viral load result (HIV RNA <1,000 copies/mL) among those with a documented viral load result within the previous 12 months. For calculating the proportion of persons living with HIV receiving ART with suppression, the numerator is the number of persons living with HIV receiving ART in the current quarterly reporting period with a suppressed viral load result documented within the previous 12 months, and the denominator is number of persons receiving ART in the current quarterly reporting period reported to have a documented viral result during the previous 12 months.

death among children aged <5 years with HIV and uninfected children, including pneumonia, malnutrition, and malaria (*6*). Measures to enhance data collected at the individual level and explore causes and circumstances of death among children aged <5 years living with HIV receiving ART might help guide programs and policies aimed at preventing these deaths.

Limitations

The findings in this report are subject to at least three limitations. First, treatment interruption and mortality estimates from PEPFAR Monitoring, Evaluation, and Reporting data are likely underreported, underestimating the actual number of deaths and interruptions in treatment among ART recipients served by PEPFAR. Second, underreporting and inconsistencies in reporting death and treatment interruption between PEPFAR-supported sites vary, which might bias or confound the findings of this analysis (i.e., site-level factors that influence completeness or consistency in reporting might also influence outcomes among children or older persons living with HIV).§§§ Finally, these findings might not be generalizable to children living with HIV served in non–PEPFAR-supported sites.

Implications for Public Health Practice

Prioritizing and optimizing HIV and general health services for children aged <5 years living with HIV receiving ART might help address the disproportionately poorer outcomes they experience. Global efforts to help prevent pediatric HIV

§§§ Outcomes, including CMRs among persons living with HIV of different age groups, were reviewed and compared from sites that reported data on treatment loss, including treatment interruption and death, regularly (i.e., sites that reported at least one treatment loss each quarter during the 2-year period) and persons living with HIV from sites that did not report data on treatment loss regularly. The indicator that records treatment loss includes deaths, treatment interruption, transferred out, or refused or stopped treatment. CMRs were similar and substantially high in these two samples.

Summary

What is already known about this topic?

Globally, children aged <5 years, including children living with HIV who are not receiving antiretroviral treatment (ART), experience disproportionately high mortality.

What is added by this report?

Compared with older persons living with HIV receiving ART served by the U.S. President's Emergency Plan for AIDS Relief during October 2020–September 2022, a higher proportion of children aged <5 years receiving ART died or had interrupted treatment, and a lower proportion had a suppressed HIV viral load.

What are the implications for public health practice?

Prioritizing and optimizing HIV and general health services for children aged <5 years living with HIV receiving ART, including those recommended in the WHO STOP AIDS Package, might help address these disproportionately poorer outcomes.

infections and optimize the entire pediatric HIV clinical cascade have intensified, including the multilateral Global Alliance to End AIDS in Children by 2030 (*7*) and the PEPFAR Accelerating Progress in Pediatrics and Prevention of Mother to Child Transmission initiative (*8*). Strategies aimed at optimizing HIV care for children living with HIV include 1) diagnosing children as early as possible, and linking them to optimized ART (especially dolutegravir-based regimens); 2) ensuring that these children continue in effective HIV care and treatment through family-centered, differentiated service delivery models (*9*); and 3) comprehensively preventing, identifying, and managing advanced HIV disease and its complications, including tuberculosis and severe acute malnutrition, according to the WHO STOP AIDS Package (*4*). Ensuring that children aged <5 years living with HIV also receive timely general pediatric services, including immunizations, micronutrient supplementation, and antimalarial treatment can also improve their health and might reduce mortality attributable to common pediatric causes of death. Enrolling children at high risk living with HIV into community-based support programs such as PEPFAR's Orphan and Vulnerable Children program gives them access to more comprehensive services, including family-based case management and socioeconomic support, additional services that can augment the care these children receive and help them and their caregivers thrive (*8*,*10*). These strategies, as highlighted in PEPFAR's 2023 country and regional operational planning guidance¶¶¶ (*8*), have the potential to prevent death, reduce the inequities experienced by children aged <5 years living with HIV, and contribute to the global measures to end AIDS among children by 2030.

¶¶¶ COP/ROP 2023 guidance contains a new section of recommendations entitled "Ending Preventable Deaths in Young Children Living with HIV."

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SARS-CoV-2 Epidemiology and COVID-19 mRNA Vaccine Effectiveness Among Infants and Children Aged 6 Months–4 Years — New Vaccine Surveillance Network, United States, July 2022–September 2023

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Abstract

SARS-CoV-2 infection in young children is often mild or asymptomatic; however, some children are at risk for severe disease. Data describing the protective effectiveness of COVID-19 mRNA vaccines against COVID-19–associated emergency department (ED) visits and hospitalization in this population are limited. Data from the New Vaccine Surveillance Network, a prospective population-based surveillance system, were used to estimate vaccine effectiveness using a test-negative, case-control design and describe the epidemiology of SARS-CoV-2 in infants and children aged 6 months–4 years during July 1, 2022–September 30, 2023. Among 7,434 children included, 5% received a positive SARS-CoV-2 test result, and 95% received a negative test result; 86% were unvaccinated, 4% had received 1 dose of any vaccine product, and 10% had received ≥2 doses. When compared with receipt of no vaccines among children, receipt of ≥2 COVID-19 mRNA vaccine doses was 40% effective (95% CI = 8%–60%) in preventing ED visits and hospitalization. These findings support existing recommendations for COVID-19 vaccination of young children to reduce COVID-19–associated ED visits and hospitalization.

Introduction

SARS-CoV-2 infection in young children and adolescents commonly manifests as a mild or asymptomatic illness; however, some children are at risk for severe disease, including those with certain chronic conditions (*1*,*2*). COVID-19 mRNA vaccines were recommended for children aged ≥5 years in November 2021, and for infants and children aged 6 months–4 years in June 2022, with further authorizations for bivalent mRNA vaccines during December 2022–April 2023 (*3*). Vaccination coverage in this population remains markedly lower than that in the adult population, and complete primary series COVID-19 mRNA vaccination coverage in young children has been approximately 5% nationwide since January 2023.† As such, vaccine effectiveness (VE) estimates in infants and children aged 6 months–4 years are limited (*4*,*5*). Despite low coverage in this age group, COVID-19–associated hospitalization rates among infants and children aged 6 months–4 years has remained low.§ This analysis assessed the effectiveness of COVID-19 mRNA vaccines in protecting against COVID-19–associated emergency department (ED) visits and hospitalization during the first year of authorization of vaccination for infants and children aged 6 months–4 years, a period when several Omicron sublineages were circulating.¶

Methods

Data Collection

The New Vaccine Surveillance Network (NVSN) conducts population-based, prospective surveillance for acute respiratory illness (ARI) in children at seven pediatric medical centers.** During July 1, 2022–September 30, 2023, infants and children aged 6 months–4 years hospitalized or seeking care in EDs for ARI were eligible for enrollment.†† Demographic, clinical, and vaccination data were systematically collected through parent or guardian interview and medical chart abstraction. Respiratory specimens were collected and tested for SARS-CoV-2 and seven other respiratory viruses§§ using real-time reverse transcription–polymerase chain reaction. COVID-19 vaccination status was ascertained through state

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† https://covid.cdc.gov/covid-data-tracker/#vaccination-demographics-trends

§ https://www.cdc.gov/coronavirus/2019-ncov/covidnetdashboard/de/powerbi/dashboard.html

¶ https://www.cdc.gov/museum/timeline/covid19.html#Mid-2022

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†† ARI is defined as one or more of the following symptoms occurring for <14 days before enrollment encounter: fever, cough, earache, nasal congestion, runny nose, sore throat, vomiting after coughing, wheezing, shortness of breath, rapid or shallow breathing, apnea, apparent life-threatening event, or brief resolved unexplained event.

§§ All children received testing for the following viruses: SARS-CoV-2, rhinovirus/enterovirus, respiratory syncytial virus, human metapneumovirus, enterovirus-D68, parainfluenza viruses, human coronaviruses, and influenza viruses.

immunization information systems and verified, if necessary, by reviewing health care provider records.¶¶

Data Analysis

COVID-19 VE to prevent COVID-19–associated ED visits and hospitalization among children with ARI was estimated using a test-negative, case-control design. Case-patients were children with ARI and who received a positive SARS-CoV-2 test result. Control-patients were children with ARI and who received a negative SARS-CoV-2 test result. Children were included in the analysis if they had a verified vaccination status including 1) zero doses of any COVID-19 vaccine product (unvaccinated), 2) 1 dose of any COVID-19 vaccine product (1 dose only), or 3) ≥2 doses of any COVID-19 vaccine product (≥2 doses). Children were excluded if they met NVSN exclusion criteria,*** were enrolled <14 days after receipt of a vaccine dose, received an inconclusive SARS-CoV-2 test result, were missing COVID-19 vaccination data, or if receipt of vaccination was unverified. Pearson's chi-square tests were used to compare demographic and clinical characteristics among case- and control-patients and by vaccination status. VE was estimated using logistic regression models, comparing the odds of receipt of 1 or ≥2 vaccine doses with those with no COVID-19 vaccination between case- and control-patients. Regression models controlled for race, age, calendar time (week of enrollment), and enrollment site. VE was calculated as (1 – adjusted odds ratio) x 100%; estimates with nonoverlapping 95% CIs were considered statistically significant. SAS (version 9.4; SAS Institute) was used to conduct all analyses. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.†††

Results

Differences Between Case-Patients and Control-Patients

During July 1, 2022–September 30, 2023, among 7,434 infants and children aged 6 months–4 years with ARI enrolled in ED or hospital settings, 387 (5.0%) received a positive SARS-CoV-2 test result, and 7,047 (95.0%) received a negative test result (Table 1). Case-patients were significantly younger than were control-patients (median age 15 months versus 22 months, respectively). There was no difference in median length of stay (2 days), sex, race and ethnicity, insurance status, history of prematurity, or underlying medical conditions between case- and control-patients. Case-patients were less likely to receive supplemental oxygen and high-flow nasal cannula respiratory support than were control-patients; however, there was no difference between case- and control-patients in the proportion who received mechanical ventilation or were admitted to an intensive care unit. Two case-patients (0.5%) were intubated, none received extracorporeal membrane oxygenation, and none died, compared with 69 (1.0%), three (0.9%), and three (0.1%) control-patients, respectively. Other respiratory viruses were detected in 140 (36.2%) case-patients; rhinoviruses/enteroviruses (RV/EV) accounted for one half of these detections, and respiratory syncytial virus accounted for 21.4%. Among control-patients, RV/EV and respiratory syncytial virus also accounted for the majority of detections and were detected in 36.7% and 17.1% of control-patients, respectively.

Sociodemographic Characteristics by Vaccination Coverage Status

During this period, 86.0% of infants and children aged 6 months–4 years with ARI had not received any COVID-19 vaccine doses; 2-dose vaccination coverage varied significantly geographically, from 3.9% to 27.9% across NVSN sites. Children receiving ≥2 COVID-19 vaccine doses were more likely to be 1) from Seattle (27.9%), 2) non-Hispanic White (White) or non-Hispanic other race (37.6%), and 3) have private insurance (25.3%). Overall, 2-dose vaccination coverage was 19.0% among White children and 2.5% among non-Hispanic Black or African American (Black) children. Children who had received ≥2 COVID-19 vaccine doses were older (median age = 27 months) than unvaccinated children (median age = 21 months).

Weekly SARS-CoV-2 detections peaked once during August 31–September 6, 2022, (21) and again during August 27–September 2, 2023 (13) (Figure). Cumulative coverage with ≥2 COVID-19 vaccine doses was 10.4% and with 1 dose was 3.8%.

Vaccine Effectiveness

When compared with no receipt of COVID-19 vaccination among children, the estimated VE of ≥2 COVID-19 mRNA vaccine doses was 40% (95% CI = 8%–60%) for preventing COVID-19–associated ED visits and hospitalization, with a median interval since receipt of last vaccine dose of 93 days

¶¶ Primary care provider record verification was required after the expiration of the public health emergency in sites without mandatory reporting of COVID-19 vaccines to state immunization information systems.

*** 1) age ≥18 years, 2) residence outside surveillance area, 3) admitted patient not enrolled or specimen collected ≤48 hours of hospital admission, 4) fever and neutropenia (absolute neutrophil count <500), 5) newborn who never left the hospital, 6) transferred from another hospital admission of >48 hours, 7) known nonrespiratory cause for admission, 8) duration of illness lasting >10 days, or 9) previous encounter <10 days before hospital admission at the same level or higher level of care and not enrolled.

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

TABLE 1. Characteristics of infants and children* aged 6 months–4 years enrolled in vaccine effectiveness study, by SARS-CoV-2 test result and COVID-19 vaccination status (N = 7,434) — New Vaccine Surveillance Network, United States, July 2022–September 2023

Characteristic	Overall (column %) N = 7,434	SARS-CoV-2 test result (column %)			Vaccination status (row %)			
		Positive (case-patients) n = 387	Negative (control-patients) n = 7,047	p-value†	Unvaccinated n = 6,377	1 dose only n = 281	≥2 doses n = 776	p-value†,§
Highest level of care								
ED	**4,026 (54.2)**	247 (63.8)	3,779 (53.6)	<0.001	3,557 (88.4)	127 (3.2)	342 (8.5)	<0.001
Inpatient	**3,408 (45.8)**	140 (36.2)	3,268 (46.4)		2,820 (82.7)	154 (4.5)	434 (12.7)	
Study site								
Cincinnati, Ohio	**1,328 (17.9)**	55 (14.2)	1,273 (18.1)	0.013	1,251 (94.2)	19 (1.4)	58 (4.4)	<0.001
Houston, Texas	**1,048 (14.1)**	67 (17.3)	981 (13.9)		943 (90.0)	32 (3.1)	73 (7.0)	
Kansas City, Missouri	**845 (11.4)**	39 (10.1)	806 (11.4)		792 (93.7)	20 (2.4)	33 (3.9)	
Nashville, Tennessee	**1,121 (15.1)**	56 (14.5)	1,065 (15.1)		1,004 (89.6)	43 (3.8)	74 (6.6)	
Pittsburgh, Pennsylvania	**1,239 (16.7)**	50 (12.9)	1,189 (16.9)		1,066 (86.0)	44 (3.6)	129 (10.4)	
Rochester, New York	**570 (7.7)**	37 (9.6)	533 (7.6)		499 (87.5)	20 (3.5)	51 (8.9)	
Seattle, Washington	**1,283 (17.3)**	83 (21.4)	1,200 (17.0)		822 (64.1)	103 (8.0)	358 (27.9)	
Age, mos								
Median (IQR)	**22 (12.0–37.0)**	15 (9.0–29.0)	22 (13.0–38.0)	<0.001	21 (12.0–37.0)	25 (13.0–38.0)	27 (17.0–40.5)	<0.001
6–11	**1,640 (22.1)**	146 (37.7)	1,494 (21.2)	<0.001	1,536 (93.7)	54 (3.3)	50 (3.0)	<0.001
12–23	**2,329 (31.3)**	122 (31.5)	2,207 (31.3)		1,970 (84.6)	80 (3.4)	279 (12.0)	
24–59	**3,465 (46.6)**	119 (30.7)	3,346 (47.5)		2,871 (82.9)	147 (4.2)	447 (12.9)	
Sex								
Female	**3,214 (43.2)**	170 (43.9)	3,044 (43.2)	0.777	2,765 (86.0)	125 (3.9)	324 (10.1)	0.394
Male	**4,220 (56.8)**	217 (56.1)	4,003 (56.8)		3,612 (85.6)	156 (3.7)	452 (10.7)	
Race and ethnicity								
Black or African American, NH	**2,277 (30.6)**	98 (25.3)	2,179 (30.9)	0.055	2,169 (95.3)	50 (2.2)	58 (2.5)	<0.001
White, NH	**2,218 (29.8)**	127 (32.8)	2,091 (29.7)		1,707 (77.0)	90 (4.1)	421 (19.0)	
Hispanic or Latino	**1,938 (26.1)**	112 (28.9)	1,826 (25.9)		1,741 (89.8)	73 (3.8)	124 (6.4)	
Other, NH	**857 (11.5)**	47 (12.1)	810 (11.5)		638 (74.4)	60 (7.0)	159 (18.6)	
Unknown	**144 (1.9)**	3 (0.8)	141 (2.0)		122 (84.7)	8 (5.6)	14 (9.7)	
Insurance status								
Private	**2,085 (28.0)**	106 (27.4)	1,979 (28.1)	0.645	1,426 (68.4)	132 (6.3)	527 (25.3)	<0.001
Public	**4,726 (63.6)**	254 (65.6)	4,472 (63.5)		4,394 (93.0)	126 (2.7)	206 (4.4)	
Public and private	**130 (1.7)**	6 (1.6)	124 (1.8)		107 (82.3)	8 (6.2)	15 (11.5)	
Self-pay (none)	**227 (3.1)**	7 (1.8)	220 (3.1)		213 (93.8)	6 (2.6)	8 (3.5)	
Unknown	**266 (3.6)**	14 (3.6)	252 (3.6)		237 (89.1)	9 (3.4)	20 (7.5)	
Median no. of days since last vaccine dose (IQR)	**86 (46.0–160.0)**	76 (31.0–171.0)	86 (47.0–160.0)	0.021	NA	71 (31.0–128.0)	93 (51.0–171.5)	0.083
Prematurity¶	**781 (20.1)**	44 (17.0)	737 (20.3)	0.194	705 (90.3)	20 (2.6)	56 (7.2)	0.206
Underlying conditions								
One or more**	**1,916 (26.4)**	104 (27.5)	1,812 (26.3)	0.608	1,576 (82.3)	90 (4.7)	250 (13.0)	<0.001
Cardiovascular condition††	**336 (4.6)**	27 (7.1)	309 (4.5)	0.017	282 (83.9)	12 (3.6)	42 (12.5)	0.261
Immunocompromised§§	**101 (1.4)**	12 (3.2)	89 (1.3)	0.002	90 (89.1)	3 (3.0)	8 (7.9)	0.359
Neurologic condition¶¶	**373 (5.1)**	25 (6.6)	348 (5.1)	0.181	321 (86.1)	16 (4.3)	36 (9.7)	0.550
Respiratory condition***	**1,101 (15.2)**	40 (10.6)	1,061 (15.4)	0.011	880 (79.9)	53 (4.8)	168 (15.3)	<0.001
Other condition	**674 (26.7)**	32 (23.9)	642 (26.8)	0.456	560 (83.1)	30 (4.5)	84 (12.5)	0.750
Respiratory support								
Supplemental oxygen	**2,206 (55.4)**	63 (29.3)	2,143 (56.8)	<0.001	1,816 (82.3)	99 (4.5)	291 (13.2)	<0.001
Nasal cannula or blowby	**1,025 (77.3)**	32 (88.9)	993 (77.0)	0.092	803 (78.3)	46 (4.5)	176 (17.2)	0.050
High-flow nasal cannula	**472 (35.6)**	4 (11.4)	468 (36.2)	0.002	396 (83.9)	23 (4.9)	53 (11.2)	<0.001
CPAP or BiPAP therapy	**138 (10.5)**	4 (11.1)	134 (10.4)	0.896	115 (83.3)	4 (2.9)	19 (13.8)	0.382
Intubation	**71 (1.0)**	2 (0.5)	69 (1.0)	0.363	62 (87.3)	4 (5.6)	5 (7.0)	0.347
ECMO†††	**3 (0.9)**	0 (—)	3 (0.9)	0.789	3 (100.0)	0 (—)	0 (—)	0.488

See table footnotes the next page.

(IQR = 51–172 days) (Table 2). VE of 1 mRNA COVID-19 vaccine dose for preventing COVID-19–associated ED visits and hospitalization was 31% (95% CI = –27% to 62%), although the 95% CI included the null value.

Discussion

In this analysis of 7,434 infants and children aged 6 months–4 years with ARI in NVSN, 86.0% had not received any COVID-19 vaccine doses, and clear geographic, age, and racial differences in vaccination coverage were observed:

TABLE 1. (*Continued*) Characteristics of infants and children* aged 6 months–4 years enrolled in vaccine effectiveness study, by SARS-CoV-2 test result and COVID-19 vaccination status (N = 7,434) — New Vaccine Surveillance Network, United States, July 2022–September 2023

Characteristic	Overall (column %) N = 7,434	SARS-CoV-2 test result (column %)			Vaccination status (row %)			
		Positive (case-patients) n = 387	Negative (control-patients) n = 7,047	p-value†	Unvaccinated n = 6,377	1 dose only n = 281	≥2 doses n = 776	p-value†,§
Received intensive care†††	**347 (17.0)**	8 (10.5)	339 (17.2)	0.126	289 (83.3)	12 (3.5)	46 (13.3)	0.271
Length of stay, days†††								
Median (IQR)	**2 (1.0–3.0)**	2 (1.0–3.0)	2 (1.0–3.0)	0.350	2 (1.0–3.0)	2 (1.0–3.0)	1 (1.0–3.0)	0.748
0–1	**1,005 (49.2)**	34 (44.7)	971 (49.4)	0.281	787 (78.3)	53 (5.3)	165 (16.4)	0.058
2	**475 (23.3)**	23 (30.3)	452 (23.0)		398 (83.8)	21 (4.4)	56 (11.8)	
3–4	**330 (16.2)**	14 (18.4)	316 (16.1)		260 (78.8)	15 (4.5)	55 (16.7)	
≥5	**232 (11.4)**	5 (6.6)	227 (11.5)		195 (84.1)	7 (3.0)	30 (12.9)	
Death	**3 (0.1)**	0 (—)	3 (0.1)	0.641	2 (66.7)	1 (33.3)	0 (—)	0.692
Viral detections§§§								
One or more viruses	**5,560 (74.8)**	387 (100.0)	5,173 (73.4)	<0.001	4,701 (84.6)	222 (4.0)	637 (11.5)	<0.001
RV/EV	**2,720 (36.6)**	70 (18.1)	2,650 (37.6)	<0.001	2,266 (83.3)	115 (4.2)	339 (12.5)	<0.001
RSV	**1,236 (16.6)**	30 (7.8)	1,206 (17.1)	<0.001	1,043 (84.4)	57 (4.6)	136 (11.0)	0.642
Adenovirus	**795 (10.7)**	17 (4.4)	778 (11.0)	<0.001	656 (82.5)	43 (5.4)	96 (12.1)	0.161
PIV	**747 (10.0)**	15 (3.9)	732 (10.4)	<0.001	647 (86.6)	21 (2.8)	79 (10.6)	0.461
HMPV	**534 (7.2)**	14 (3.6)	520 (7.4)	0.023	451 (84.5)	21 (3.9)	62 (11.6)	0.480
EV-D68	**277 (3.7)**	9 (2.3)	268 (3.8)	<0.001	246 (88.8)	9 (3.2)	22 (7.9)	0.451
HCoV	**188 (2.5)**	7 (1.8)	181 (2.6)	0.508	143 (76.1)	10 (5.3)	35 (18.6)	0.001
Influenza	**157 (2.1)**	4 (1.0)	153 (2.2)	0.033	143 (91.1)	4 (2.5)	10 (6.4)	0.098
SARS-CoV-2 codetection¶¶¶	**140 (1.9)**	140 (36.2)	NA	—	126 (90.0)	3 (2.1)	11 (7.9)	0.284
RV/EV¶¶¶	**70 (50.0)**	70 (50.0)			62 (88.6)	3 (4.3)	5 (7.1)	0.811
RSV¶¶¶	**30 (21.4)**	30 (21.4)			28 (93.3)	0 (—)	2 (6.7)	0.756
Adenovirus¶¶¶	**17 (12.1)**	17 (12.1)			17 (100.0)	0 (—)	0 (—)	0.405
PIV¶¶¶	**15 (10.7)**	15 (10.7)			12 (80.0)	0 (—)	3 (20.0)	0.189
HMPV¶¶¶	**14 (10.0)**	14 (10.0)			13 (92.9)	0 (—)	1 (7.1)	0.948
EV-D68¶¶¶	**9 (6.4)**	9 (6.4)			8 (88.9)	0 (—)	1 (11.1)	0.429
HCoV¶¶¶	**7 (5.0)**	7 (5.0)			6 (85.7)	0 (—)	1 (14.3)	0.793
Influenza¶¶¶	**4 (2.9)**	4 (2.9)			4 (100.0)	0 (—)	0 (—)	0.575

Abbreviations: BiPAP = bilevel positive airway pressure; CPAP = continuous positive airway pressure; ECMO = extracorporeal membrane oxygenation; ED = emergency department; EV-D68 = enterovirus D68; HCoV = human coronaviruses; HMPV = human metapneumovirus; NA = not applicable; NH = non-Hispanic; PIV = parainfluenza viruses 1–4; RSV = respiratory syncytial virus; RV/EV = rhinovirus/enterovirus.

* Restricted to children enrolled in inpatient and ED clinical settings.

† p-value refers to results of Pearson's chi-square comparison.

§ p-value measuring difference between unvaccinated children and children receiving ≥2 vaccine doses.

¶ Gestational age <37 weeks, restricted to infants and children aged <2 years.

** Underlying medical conditions include congenital heart malformation or other heart condition, transplant recipient, cancer, sickle cell anemia, cerebral palsy, seizure disorder or other neurologic or neuromuscular disorder, asthma, reactive airway disease, cystic fibrosis, bronchopulmonary dysplasia, chronic lung disease of prematurity or other chronic lung condition, kidney disease, Down syndrome or other genetic or metabolic disorder, blood disorders, liver disease, diabetes, chronic endocrine condition, chronic gastrointestinal disease, and other developmental disabilities.

†† Congenital heart malformation or other heart condition.

§§ Immune condition, transplant recipient (peripheral blood stem cells, bone marrow, cord blood, or organ), cancer, and sickle cell anemia.

¶¶ Cerebral palsy, seizure disorder, or other neurologic or neuromuscular disorder.

*** Asthma, reactive airway disease, cystic fibrosis, bronchopulmonary dysplasia, chronic lung disease of prematurity, or other chronic lung condition.

††† Among hospitalized children only.

§§§ Among all children.

¶¶¶ Among children who received a positive SARS-CoV-2 test result only.

≥2-dose coverage in Seattle was approximately 2–6 times that of other NVSN sites, which is consistent with high vaccination coverage in this region for other routine childhood vaccines.§§§ Compared with White children, Black children were approximately seven times less likely and Hispanic or Latino children were approximately three times less likely to have received ≥2 doses of COVID-19 vaccine, underscoring the continued need to promote access and address vaccine hesitancy (*6*).

Among young children with medically attended ARI, SARS-CoV-2 detections were low, with just 5% of children receiving a positive SARS-CoV-2 test result. Co-detections of other respiratory viruses were present in approximately one third of children who received positive SARS-CoV-2 test results. Systematic testing for multiple respiratory viruses is a strength of NVSN and provides essential information on co-detections that is not possible from isolated SARS-CoV-2 testing. It might be important to account for coinfections in future

§§§ https://www.cdc.gov/vaccines/imz-managers/coverage/childvaxview/interactive-reports/index.html

FIGURE. SARS-CoV-2 test results and COVID-19 vaccination coverage among infants and children aged 6 months–4 years evaluated in the emergency department or hospitalized with acute respiratory illness, by week (N = 7,434) — New Vaccine Surveillance Network, United States, July 2022–September 2023

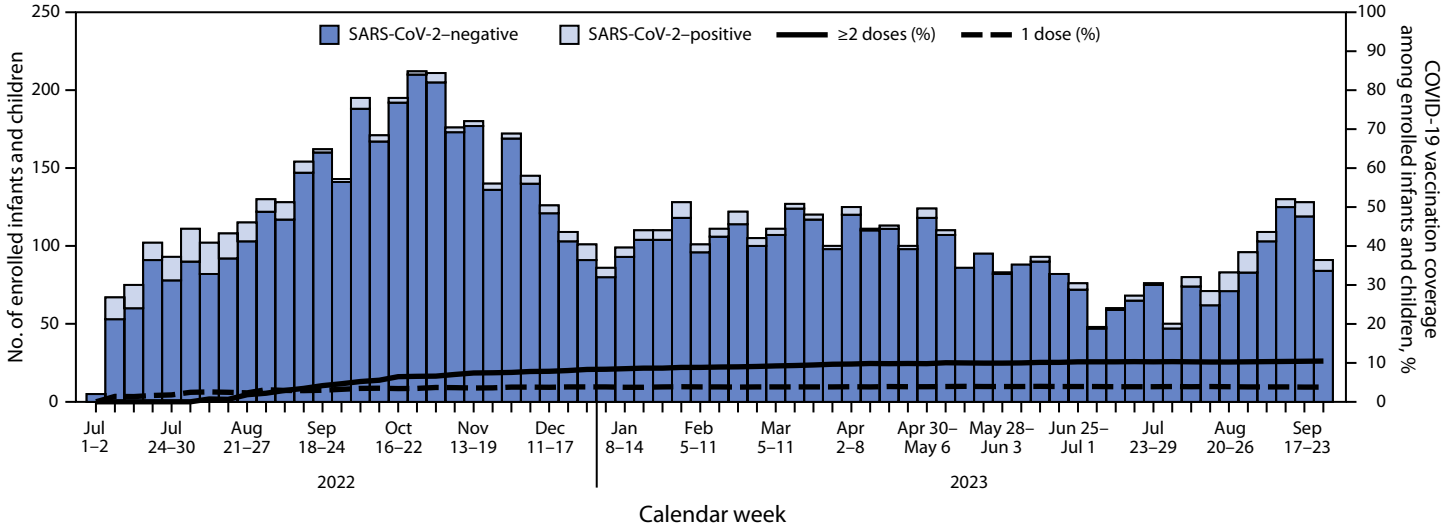

TABLE 2. COVID-19 vaccine effectiveness among infants and children aged 6 months–4 years evaluated in the emergency department or hospitalized with acute respiratory illness (N = 7,434) — New Vaccine Surveillance Network, United States, July 2022–September 2023*

Vaccination status	No. (%) Case-patients (positive SARS-CoV-2 test result) n = 387	No. (%) Control patients (negative SARS-CoV-2 test result) n = 7,047	Median no. of days since last dose (IQR)	Adjusted VE,† % (95% CI)
Unvaccinated	348 (90)	6,029 (85)	NA	—
Vaccinated	39 (10)	1,018 (15)	Not calculated	Not calculated
1 dose only	12 (3)	269 (4)	71 (31 to 128)	31 (–27 to 62)
≥2 doses	27 (7)	749 (11)	93 (51 to 172)	40 (8 to 60)§

Abbreviations: NA = not applicable; VE = vaccine effectiveness.

* Some estimates are imprecise, which might be because of a relatively small number of persons in each level of vaccination or case-patient status. This imprecision indicates 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 appropriate interpretation.

† VE was estimated by comparing odds of being vaccinated with 1 dose or ≥2 doses among case-patients to the odds of being vaccinated with 1 dose or ≥2 doses among control patients. Calculated as VE = 100 x (1 – odds ratio). Regression models adjusted for race, age, calendar time (week of enrollment), and enrollment site.

§ $p<0.05$.

VE estimates, particularly as more vaccines are introduced for respiratory viruses that could bias pediatric VE estimates.

Receipt of ≥2 COVID-19 mRNA vaccine doses was 40% effective in preventing COVID-19–associated ED visits and hospitalization. Despite low vaccination coverage and the circulation of several Omicron subvariants, COVID-19–associated ED visits and hospitalization among children with ARI enrolled in NVSN were rare, suggesting most children in this age group experience mild illness from these subvariants or have immune protection from previous SARS-CoV-2 exposure (*7*). These findings indicate that COVID-19 mRNA vaccines are protective and are consistent with other VE estimates for this age group, ranging from 29% for 2-dose Moderna coverage to 43% for 3-dose Pfizer-BioNTech coverage (*5*); however, low vaccination coverage and low incidence of medically attended COVID-19 limit precision in these VE estimates.

Limitations

The findings in this report are subject to at least five limitations. First, seroprevalence of infection-induced SARS-CoV-2 antibodies in children and adolescents has increased over time, which might affect VE estimates and assessment of severe outcomes, as more children have immunity from previous SARS-CoV-2 infection (*8*). Second, low vaccination coverage might indicate that vaccinated children are systematically different from unvaccinated children. For example, children with underlying medical conditions might be more likely to be vaccinated and, because of their underlying conditions,

Summary

What is already known about this topic?

SARS-CoV-2 infection in young children is often mild or asymptomatic; however, some children are at risk for severe disease. In June 2022, original monovalent COVID-19 mRNA vaccines were recommended for infants and children aged 6 months–4 years.

What is added by this report?

Among vaccine-eligible children aged <5 years hospitalized or seeking care in emergency departments for acute respiratory illness during July 2022–September 2023, 86% had not received any COVID-19 vaccine. Despite low vaccination coverage, only 5% of children received a positive SARS-CoV-2 test result. Receipt of ≥2 COVID-19 mRNA vaccine doses was 40% effective (95% CI = 8%–60%) in preventing emergency department visits and hospitalization.

What are the implications for public health practice?

These findings support existing recommendations for COVID-19 vaccination of young children to reduce COVID-19–associated emergency department visits and hospitalization.

more likely to be hospitalized or to need respiratory support, which could bias the observed VE. Third, NVSN data might be subject to enrollment biases that might vary by site, such as number of enrollment days per week and availability of interpreters for non-English speakers. Fourth, low vaccination coverage and disease incidence limit the precision of the point estimates and were too low to analyze data by time since dose or to stratify by setting or product. Finally, Moderna vaccine is administered as a 2-dose primary series whereas Pfizer-BioNTech requires 3 doses, and receipt of ≥2 doses might underestimate the protection afforded by the complete 3-dose Pfizer-BioNTech primary series.

Implications for Public Health Practice

Limited data are available on the impact of COVID-19 vaccination among infants and children aged 6 months–4 years to help guide vaccination policies. Data from this study are consistent with those from other studies of COVID-19 mRNA VE among young children and might assist medical providers when counseling parents of young children about COVID-19 vaccination (*4*,*5*). The findings in this report support the recommendation for COVID-19 vaccination for all children aged ≥6 months and highlight the importance of completion of a primary series for young children (*3*).

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Notes from the Field

Firearm Suicide Rates, by Race and Ethnicity — United States, 2019–2022

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Suicide, including firearm suicide, remains a substantial public health concern in the United States. During the previous 2 decades, overall suicide rates and firearm suicide rates have risen by approximately one third, approaching 50,000 overall suicides during 2022, including approximately 27,000 firearm suicides (*1*). Firearm suicides account for approximately one half of all suicides, and this proportion has been increasing (*2*,*3*). This analysis includes national firearm suicide data from 2019 through the end of 2022, categorized by race and ethnicity, presented both annually and by month (or quarterly) to track subannual changes.

Investigation and Outcomes

National Vital Statistics System mortality data for 2019–2021 (final) and 2022 (provisional), stratified by race and ethnicity, were obtained from CDC WONDER* (*1*). Corresponding population estimates were obtained from the U.S. Census Bureau.† Annual and monthly crude rates were calculated by race and ethnicity, with all rates expressed per 100,000 person-years. Because subannual data for non-Hispanic American Indian or Alaska Native (AI/AN) persons involve small monthly counts, these data are presented by quarter. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.§

The annual U.S. firearm suicide rate increased approximately 11% from 7.3 per 100,000 during 2019 to 8.1 during 2022 (Table), the highest documented level since at least 1968 (the earliest year for which data are available in CDC WONDER).

Firearm suicide rates increased in all racial and ethnic groups from 2019 through 2022, but the magnitude of increase differed among groups (Supplementary Figure; https://stacks.cdc.gov/view/cdc/135612). For example, whereas non-Hispanic White persons experienced the highest overall rate (11.1 during 2022), this rate represented a 9% increase from 10.2 during 2019. The largest rate increase (66%) occurred among AI/AN persons, among whom the firearm suicide rate increased from 6.4 during 2019 to 10.6 during 2022. During 2022, rates were lower among non-Hispanic Black or African American and Hispanic or Latino persons (5.3 and 3.3, respectively); rates in these groups increased 42% and 28%, respectively, from 2019 through 2022. The lowest firearm suicide rates were among non-Hispanic Asian or Pacific Islander¶ persons, increasing 10%, from 1.7 during 2019 to 1.9 during 2022.

Preliminary Conclusions and Analysis

Firearm suicide rates increased in all racial and ethnic groups from 2019 through 2022. Multiple social and structural factors likely contributed to these increases. The large increase in the AI/AN rate might reflect systematic inequities, such as in mental health care access or unemployment, worsened by the COVID-19 pandemic (*4*); the pandemic might also have exacerbated known risk factors related to social isolation, relationship stressors, and substance use, broadly affecting observed trends (*5*).

The persistent upward trend in firearm suicide rates since 2020 across all racial and ethnic groups, coupled with the unprecedented high rates during 2022, highlight the need for continued prevention efforts. Public health organizations can facilitate collaborative cross-sector efforts to implement comprehensive, evidence-based prevention strategies, which are detailed in CDC's Suicide Prevention Resource for Action.** Potential approaches to reducing firearm suicides include promoting secure firearm storage and counseling mental health and social services providers on access to lethal means. Other strategies to reduce suicide risk include fostering positive social connections, identifying and supporting persons at risk, and addressing underlying inequities in economic security and housing. For persons who are struggling or in crisis, help is available through the 988 Suicide and Crisis Lifeline (available at https://www.988lifeline.org/ or by texting or calling 988).

* Persons within some racial and ethnic groups, particularly AI/AN persons, might be undercounted because of misclassification. https://www.cdc.gov/nchs/data/series/sr_02/sr02_172.pdf; https://www.cdc.gov/nchs/data/nvsr/nvsr70/NVSR70-12.pdf

† Monthly population estimates, by age, sex, race, and Hispanic origin, April 1, 2010–July 1, 2020; NC-EST2020-ALLDATA were used for January 2019–March 2020 estimates (https://www.census.gov/programs-surveys/popest/technical-documentation/research/evaluation-estimates/2020-evaluation-estimates/2010s-national-detail.html). Monthly population estimates by age, sex, race, and Hispanic origin, April 1, 2020–July 1, 2022, with short-term projections to December 2023; NC-EST2022-ALLDATA were used for April 2020–December 2022 estimates (https://www.census.gov/data/tables/time-series/demo/popest/2020s-national-detail.html) (Accessed June 29, 2023).

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

¶ Data for non-Hispanic Asian and non-Hispanic Native Hawaiian or other Pacific Islander persons were combined to form a single non-Hispanic Asian or Pacific Islander reporting category.

** https://www.cdc.gov/suicide/resources/prevention.html

TABLE. Annual firearm suicide rates and counts, by race and ethnicity — United States, 2019–2022

Race and ethnicity*	Rate† (no.)			
	2019	2020	2021	2022
AI/AN, NH	6.4 (154)	9.3 (225)	10.0 (241)	10.6 (256)
A/PI, NH	1.7 (337)	1.7 (343)	1.9 (379)	1.9 (395)
Black or African American, NH	3.8 (1,546)	4.3 (1,784)	5.2 (2,165)	5.3 (2,237)
White, NH	10.2 (20,090)	10.0 (19,851)	10.8 (21,197)	11.1 (21,726)
Hispanic or Latino	2.5 (1,534)	2.9 (1,790)	3.3 (2,037)	3.3 (2,073)
Overall§	**7.3 (23,941)**	**7.3 (24,292)**	**7.9 (26,328)**	**8.1 (27,024)**

Sources: CDC WONDER; U.S. Census Bureau (NC-EST2020-ALLDATA; NC-EST2022-ALLDATA).
Abbreviations: AI/AN = American Indian or Alaska Native; A/PI = Asian or Pacific Islander; NH = non-Hispanic.
* Persons within some racial and ethnic groups, particularly AI/AN persons, might be undercounted because of misclassification. https://www.cdc.gov/nchs/data/series/sr_02/sr02_172.pdf; https://www.cdc.gov/nchs/data/nvsr/nvsr70/NVSR70-12.pdf
† Crude rates represent the number of firearm suicides per 100,000 person-years.
§ Rates and numbers for the "Overall" category include the non-Hispanic multiple-race population grouping, not shown separately in the table.

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Notes from the Field

The National Wastewater Surveillance System's Centers of Excellence Contributions to Public Health Action During the Respiratory Virus Season — Four U.S. Jurisdictions, 2022–23

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Wastewater surveillance (WWS), the systematic detection of infectious agents in wastewater, provided a valuable tool for monitoring SARS-CoV-2 circulation during the COVID-19 pandemic; surveillance has expanded from 20 to 53 jurisdictions across the United States, with increasing capacity to test for more respiratory pathogens (*1*,*2*). This report highlights the use of wastewater data by the four National Wastewater Surveillance System's (NWSS) Centers of Excellence (California; Colorado; Houston, Texas; and Wisconsin) to guide public health action during the 2022–23 respiratory disease season. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.*

Implementation and Action

Four CDC-funded NWSS Centers of Excellence were established during 2021–22. During 2022–23, wastewater sampling covered a large proportion of the sites' populations: 94% (Houston, Texas), 67% (California), 65% (Colorado), and 50% (Wisconsin). Implementation and data usage varied by locality (Box).

Public Health Actions at the Local Level

Colorado. To help guide local public health action in Colorado, three Denver sewersheds, covering 1.2 million residents, submitted biweekly wastewater samples. Retrospective analyses indicated that WWS detected enterovirus D68 (EV-D68) ≤1 month before syndromic and clinical laboratory signals. This finding led public health officials in Colorado to implement wastewater testing for EV-D68 as part of the enterovirus surveillance model to provide an early warning system for health care surge planning during respiratory virus season.

Houston. This metropolitan area WWS included 122 sampling sites covering 2.17 million residents. Sampling and testing for SARS-CoV-2, influenza virus, and respiratory syncytial virus (RSV) from 48 manholes associated with selected schools provided data to support strategically deployed school vaccination clinics (1,058 COVID-19 and influenza vaccine doses administered), empowered staff members in 48 schools to implement respiratory disease prevention strategies through school reports, and increased public awareness through a dashboard, which recorded approximately 350,000 views as of 2023. Recently, alert notifications were launched (698 registered users are associated with 46 schools) to inform users about identification of surges in respiratory viruses.†

Public Health Actions at the State Level

California. In California, WWS supports local health department decision-making, and has been used to provide tailored metrics and messaging to communities, providers, and health care systems to improve awareness and preparedness. Activities included daily to weekly sampling of 98 sewersheds to detect SARS-CoV-2 variants, RSV, and influenza virus in 41 counties, covering approximately 26 million residents; results are communicated via dashboards and weekly reports.

Wisconsin. Wisconsin performed daily to weekly sampling for SARS-CoV-2 at 43 sampling sites covering approximately 2.93 million residents. As of 2023, WWS data were shared on a public dashboard with alert notifications (>250,000 views), a genomic sequencing dashboard (>6,000 views), and weekly reports to local health departments and water treatment utility companies. Wisconsin's genomic sequencing dashboard has become an important tool for identifying and monitoring SARS-CoV-2 variants in wastewater, in some cases identifying variants (e.g., BA.5 and XBB) before detection through clinical surveillance (e.g., case reports and hospitalizations).

* 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.

† Centers of Excellence dashboard links. Houston (https://covidwwtp.spatialstudieslab.org, https://www.houstonhealth.org/services/wastewater), Colorado (https://cdphe.colorado.gov/covid-19/wastewater-trends, https://cdphe.maps.arcgis.com/apps/dashboards/d79cf93c3938470ca4bcc4823328946b), California (https://www.cdph.ca.gov/Programs/CID/DCDC/Pages/COVID-19/CalSuWers-Dashboard.aspx), and Wisconsin (https://www.dhs.wisconsin.gov/covid-19/wastewater.htm, https://dataportal.slh.wisc.edu/sc2-ww-dashboard).

Twenty sites covering approximately 2.48 million residents, were sampled for influenza viruses and RSV, and data were monitored on an internal dashboard. Wastewater concentrations for these viruses were highly correlated with emergency department visits in Wisconsin during 2022–23 (*3*), forming the basis for continued monitoring through the 2023–24 respiratory disease season.

Preliminary Conclusions and Actions

NWSS Centers of Excellence have reported correlation between WWS data and clinical surveillance with WWS allowing localized, timely coverage, and in some situations, valuable lead time notification. In Wisconsin, WWS detected increases in influenza and RSV weeks before increases in related emergency department visits were observed (*3*–*5*). NWSS data, together with clinical surveillance data, have guided jurisdictional partner decisions regarding allocation of resources, deployment of vaccination clinics, updating clinical guidance, and sending respiratory disease notifications and alerts when trends exceed baseline thresholds. NWSS Centers of Excellence have developed public-facing and internal pathogen data dashboards that provide metrics for public health partners and the communities they serve. During the 2022–23 respiratory disease season, NWSS Centers of Excellence translated WWS data into real-time public health action for multiple respiratory pathogens, highlighting the contribution of WWS in monitoring disease circulation and helping guide public health response.

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BOX. Examples of implemented public health actions related to respiratory viruses — National Wastewater Surveillance System's Centers of Excellence, four U.S. jurisdictions, 2022–23

Local level

Colorado (Denver metro)

- Biweekly sampling for EV-D68 in the Denver metro area to guide and collaborate with health system and pediatric providers during 2022–23 respiratory season
- Biweekly sampling of three sewersheds in Denver, covering 1.2 million residents
- Three statewide alerts to guide hospitals and providers about increases in cases to plan surge staffing and resource allocation as a result of the EV-D68 syndromic surveillance alarm
- Wastewater testing performed retrospectively and showed an increasing trend 1 month before the syndromic surveillance alarm; wastewater testing is now part of the EV-D68 multimodal surveillance model

Houston

- Weekly wastewater monitoring for SARS-CoV-2, influenza, and RSV in K–12 schools to detect outbreaks during 2022–23 school year
- Weekly sampling of 122 sampling sites (39 wastewater treatment plants, 14 lift stations, and 69 manholes) covering 2.17 million residents
- Forty-eight manholes sampled from 48 schools serving approximately 34,000 students (1.6% of total National Wastewater Surveillance System sewershed and 18.6% of the city's school population)
- Data shared on public dashboard (>362,000 views) and 27 reports to schools
- Data provided for vaccine clinic deployment that administered 1,058 COVID-19 and influenza vaccine doses to 992 students as of May 2023

State level

California

- Daily to weekly sampling of 98 sewersheds to estimate SARS-CoV-2 variants, RSV, and influenza disease activity in 41 counties (67% of residents [26 million persons] within sampled sewersheds) during 2022–23 respiratory disease season
- Messaging to local public health and the public, including through weekly summary reports and dashboards
- Local public health messaging to health care providers and the community for awareness and to support recommendations (e.g., vaccines and masking) including through media, press reports, and dashboards

Wisconsin

- Weekly or biweekly monitoring for SARS-CoV-2 and variants at wastewater treatment facilities
  - Forty-three sampling sites covering 2.93 million residents
  - Data shared on public dashboards with alert notification (>250,000 views), genomic sequencing dashboard (>6,000 views), and weekly stakeholder reports
- Weekly or biweekly monitoring for influenza A and B and RSV at wastewater treatment facilities
  - Twenty sampling sites covering 2.48 million residents
  - Internal monitoring dashboard; public dashboard and weekly stakeholder reports in development

Abbreviations: EV = enterovirus; RSV = respiratory syncytial virus.

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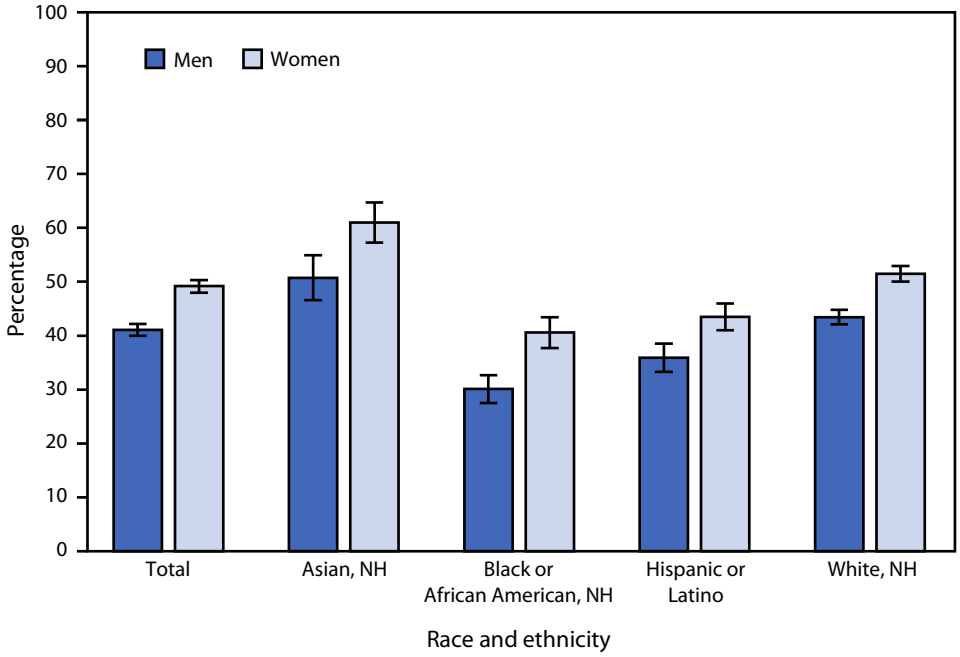
QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

Age-Adjusted Percentage* of Adults Aged ≥18 Years Who Received an Influenza Vaccination During the Past 12 Months,† by Sex and Race and Ethnicity§ — National Health Interview Survey, United States, 2022



Abbreviation: NH = non-Hispanic.

* Age-adjusted percentages are based on the 2000 U.S. Census Bureau standard population, using age groups 18–44, 45–64, 65–74, and ≥75 years, with 95% CIs indicated by error bars.

† Estimates are based on a sample of the civilian, noninstitutionalized U.S. population and are derived from a response to the question, "There are two types of flu vaccinations. One is a shot, and the other is a spray, mist, or drop in the nose. During the past 12 months, have you had a flu vaccination?"

§ Adults categorized as non-Hispanic White (White), non-Hispanic Asian (Asian), and non-Hispanic Black or African American (Black) indicated one race only; respondents had the option to select more than one race. Hispanic or Latino (Hispanic) respondents might be of any race or combination of races; all race groups are non-Hispanic. Total includes all adults, including other race groups not shown separately.

In 2022, among persons aged ≥18 years, women were more likely than were men (49.2% versus 41.1%) to have received an influenza vaccination during the past 12 months. Women were more likely than were men to have received an influenza vaccination among Asian (61.0% versus 50.7%), Black (40.6% versus 30.1%), Hispanic (43.5% versus 35.9%), and White (51.5% versus 43.4%) adults. Among men, Black adults were the least likely to have received an influenza vaccination during the past 12 months compared with Asian, Hispanic, and White adults. Among women, Black and Hispanic adults were less likely to have received an influenza vaccination during the past 12 months than were Asian and White adults.

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/flu/

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