U.S. Centers for Disease Control and Prevention
MMWR
Morbidity and Mortality Weekly Report
Weekly / Vol. 73 / No. 45
November 14, 2024

Nirsevimab Effectiveness Against Medically Attended Respiratory Syncytial Virus Illness and Hospitalization Among Alaska Native Children — Yukon-Kuskokwim Delta Region, Alaska, October 2023–June 2024

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Abstract

Respiratory syncytial virus (RSV) is a leading cause of hospitalization among young children. Historically, American Indian and Alaska Native (AI/AN) children have experienced high rates of RSV-associated hospitalization. In August 2023, a preventive monoclonal antibody (nirsevimab) was recommended for all infants aged <8 months (born during or entering their first RSV season) and for children aged 8–19 months (entering their second RSV season) who have increased risk for severe RSV illness, including all AI/AN children. This evaluation in Alaska's Yukon-Kuskokwim Delta region estimated nirsevimab effectiveness among AI/AN children in their first or second RSV seasons during 2023–2024. Among 472 children with medically attended acute respiratory illness (ARI), 48% overall had received nirsevimab ≥7 days earlier (median = 91 days before the ARI-related visit). For children in their first RSV season (292), nirsevimab effectiveness was 76% (95% CI = 42%–90%) against medically attended RSV illness and 89% (95% CI = 32%–98%) against RSV hospitalization. For children in their second RSV season (180), effectiveness against medically attended RSV illness was 88% (95% CI = 48%–97%). Nirsevimab is effective for preventing severe RSV illness among infants entering their first RSV season and children entering their second season with increased risk for severe RSV, including all AI/AN children.

Introduction

Respiratory syncytial virus (RSV) is a leading cause of hospitalization among young children (*1*). Historically, American Indian and Alaska Native (AI/AN) children have experienced high rates of RSV-associated hospitalization, with threefold to sevenfold higher rates in Alaska's Yukon-Kuskokwim Delta region than in other U.S. areas (*2*,*3*). In August 2023, CDC's Advisory Committee on Immunization Practices (ACIP) recommended a long-acting monoclonal antibody (nirsevimab) for all infants aged <8 months born during or entering their first RSV season and for children aged 8–19 months entering their second season who are at increased risk for severe RSV illness, including all AI/AN children (*4*). In clinical trials among children in their first RSV season, nirsevimab efficacy was 79% for preventing medically attended RSV-associated lower respiratory tract infection and 81% for preventing RSV-associated hospitalization through 150 days after receipt (*4*). In September 2023, ACIP recommended that all infants be protected against severe RSV either through maternal RSV vaccination during pregnancy or infant receipt of nirsevimab;

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a majority of infants do not need protection from both products (*5*). This evaluation in Alaska's Yukon-Kuskokwim Delta region provides the first real-world estimates of nirsevimab effectiveness among AI/AN children in their first and second RSV seasons.

Methods

Evaluation Site

The Yukon-Kuskokwim Delta region in southwestern Alaska includes approximately 27,000 persons (90% Alaska Native persons) living in the regional hub and 48 remote villages not connected by roads.* Yukon-Kuskokwim Health Corporation (YKHC), a tribal health organization, manages a regional hospital that performs RSV RNA testing and 46 village clinics that send swabs to the regional hospital for RNA testing. An estimated 1,591 children aged <20 months lived within the catchment area on October 1, 2023, the start of the RSV season† (*4*). YKHC administered nirsevimab to 756 (48%) children aged <20 months during October 16, 2023–April 30, 2024.§

Data Source and Inclusion Criteria

A deidentified database was developed that included demographic, clinical, laboratory testing, and immunization data from YKHC electronic health records and the state immunization information system.¶ Eligible children were aged <20 months on or born after October 1, 2023, living in the YKHC service area, and had a medically attended acute respiratory illness (ARI) visit at a YKHC facility during October 23, 2023–June 30, 2024. Medically attended ARI was defined as an outpatient visit or hospitalization with an ARI discharge diagnosis code** and RSV RNA testing of a respiratory specimen collected from 10 days before through 3 days after the visit. RSV tests were performed using Cepheid GeneXpert (multiplexed with SARS-CoV-2 and influenza A and B). After ARI visits within 30 days were combined, only the first occurring medically attended ARI was included for each child.†† Visits were excluded if the child 1) had received nirsevimab <7 days earlier, or had received >1 dose of nirsevimab on different dates, or 1 dose of palivizumab (a different preventive monoclonal antibody to prevent severe RSV); 2) had a mother

* https://data.census.gov/

† The first RSV case of the 2023–24 season in YKHC was identified on October 9, 2023.

§ Nirsevimab was first available in YKHC on October 16, 2023, and the period of administration was extended through April 30, 2024, in Alaska (https://health.alaska.gov/dph/Epi/Documents/phan/AKPHAN_20240319_RSVNextSteps.pdf). YKHC also provided RSV vaccine to 100 pregnant persons for the 2023–24 season.

¶ Current-season receipt of nirsevimab documented by state immunization information system or provider electronic health record.

** https://knowledgerepository.syndromicsurveillance.org/cdc-broad-acute-respiratory-dd-v1

†† In scenarios in which multiple tests or ARI medical visits had discordant RSV test results (e.g., negative result followed by a positive result or positive result followed by a negative result), the visits were counted as RSV test–positive visits.

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

Suggested citation: [Author names; first three, then et al., if more than six.] [Report title]. MMWR Morb Mortal Wkly Rep 2024;73:[inclusive page numbers].

who received RSV vaccine during pregnancy; 3) had received a negative RSV test result but had an RSV discharge code; or 4) was ineligible for nirsevimab.

Data Analysis

Nirsevimab effectiveness against medically attended ARI associated with RSV infection was evaluated using a test-negative design. Case-patients were those who had received a positive RSV test result. Control patients had received a negative RSV test result. Children were stratified by their RSV season based on their age on October 1, 2023 (first season included those aged <8 months or born after October 1, and second season included those aged 8–19 months). Odds ratios and 95% CIs were estimated using multivariable logistic regression analysis comparing receipt of nirsevimab among case- and control patients. Regression models were adjusted for age in months at medical visit, sex, calendar month, residence community type, and presence of one or more high-risk underlying condition.[§§] Effectiveness was calculated as (1 – adjusted odds ratio) × 100%. Sensitivity analyses were conducted excluding cases and controls in which SARS-CoV-2 or influenza virus was detected. Effectiveness was also determined by time since receipt and against hospitalization. Analyses were conducted using SAS (version 9.4; SAS Institute). This activity was reviewed by CDC, determined not to be research, and conducted consistent with applicable federal law and CDC policy.[¶¶] YKHC and the Alaska Native Tribal Health Consortium approved this project.

Results

Characteristics of Children Included in the Evaluation

Overall, 472 children had medically attended ARI visits (14% hospitalization, 70% emergency department, and 16% outpatient clinic) meeting inclusion and exclusion criteria, including 68 (14%) patients with positive RSV test results and 404 (86%) patients with negative RSV test results (Table 1). The percentage of positive RSV test results peaked during November 2023–January 2024 (Figure). The median age at the medical visit was 9 months (range = 0–27 months); 292 (62%) children were in their first RSV season, and 180 (38%) were in their second season. Overall, 98% of children were AI/AN, 73% lived in villages outside the regional hub, and 16% had at least one underlying condition increasing the risk for severe RSV illness; these characteristics differed for children in their first and second RSV seasons, with higher percentages of children in their first RSV season living outside the regional hub and having a high-risk underlying condition.[***]

Receipt of Nirsevimab

Overall, 48% of all children had received nirsevimab ≥7 days before the ARI medical visit; this percentage was lower among children in their second RSV season (37%) and among those living in the regional hub (35%) than among children in their first season (55%) and those living in other villages (53%). Overall, among patients with positive RSV test results, 10 (15%) had received nirsevimab; 217 (54%) patients with negative RSV test results had received nirsevimab.

Nirsevimab Effectiveness

Overall, nirsevimab effectiveness against medically attended RSV illness was 82% (Table 2). Among children in their first and second RSV seasons, effectiveness was 76% and 88%, respectively. Estimates were similar in sensitivity analyses excluding patients with specimens in which SARS-CoV-2 or influenza virus was detected (six with positive RSV test results and 86 with negative RSV test results) (Supplementary Table, https://stacks.cdc.gov/view/cdc/168888).

Among children who received nirsevimab overall, the median interval from receipt to ARI medical visit was 91 days (range = 7–255 days) (Table 2) (Supplementary Figure, https://stacks.cdc.gov/view/cdc/168889). Effectiveness against medically attended RSV illness was 90% at 7–89 days after nirsevimab receipt and 77% at 90–179 days after receipt.

Overall, 64 children were hospitalized for ARI, including 23 patients with positive RSV test results, three of whom received nirsevimab. Nirsevimab effectiveness against RSV-associated hospitalization was 93% among children overall and 89% among children in their first RSV season, who accounted for 49 (77%) hospitalizations. Because of small numbers, effectiveness against hospitalization was not estimated for the 15 children who were in their second RSV season.

Discussion

In this evaluation of 472 children with medically attended ARI in Alaska's Yukon-Kuskokwim Delta region, nirsevimab was 89% effective against RSV hospitalization among children in their first season and 76% and 88% effective against medically attended RSV illness among children in their first and second RSV seasons, respectively. Consistent with previous

[§§] High-risk underlying medical conditions were ascertained from the electronic health records, including chronic lung disease of prematurity, reactive airway disease, congenital heart disease, immunocompromise, cystic fibrosis, neuromuscular disease, congenital airway abnormalities that impair the ability to clear secretions, and prematurity.

[¶¶] 45 C.F.R. part 46.102(l), 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.

[***] Among children in their first season, 97% were AI/AN, 78% lived outside the regional hub, and 19% had underlying medical conditions. Among the children in their second season, 100% were AI/AN, 63% lived outside the regional hub, and 12% had underlying medical conditions. These differences in characteristics by the child's RSV season were all statistically significant ($p<0.05$).

TABLE 1. Characteristics of eligible children in their first or second respiratory syncytial virus season who had medically attended acute respiratory illness, by respiratory syncytial virus test result and receipt of nirsevimab*,† — Yukon-Kuskokwim Region, Alaska, October 23, 2023–June 30, 2024

Characteristic	Total no. (%)	RSV test result no. (column %)		Received nirsevimab no. (row %)	
		Positive	Negative	Yes	No
All children, no. (row %)	**472 (100)**	**68 (14)**	**404 (86)**	**227 (48)**	**245 (52)**
Child's RSV season (age at start of season, Oct 1, 2023)					
1st season (<8 mos)	**292 (62)**	39 (57)	253 (63)	161 (55)	131 (45)
2nd season (8–19 mos)	**180 (38)**	29 (43)	151 (37)	66 (37)	114 (63)
Age group at medical visit, mos					
0–5	**157 (33)**	22 (32)	135 (33)	92 (59)	65 (41)
6–11	**133 (28)**	16 (24)	117 (29)	64 (48)	69 (52)
12–17	**98 (21)**	18 (26)	80 (20)	44 (45)	54 (55)
18–23	**72 (15)**	10 (15)	62 (16)	24 (33)	48 (67)
24–27	**12 (3)**	2 (3)	10 (2)	3 (25)	9 (75)
Sex					
Female	**220 (47)**	30 (44)	190 (47)	107 (49)	113 (51)
Male	**252 (53)**	38 (56)	214 (53)	120 (48)	132 (52)
Race					
AI/AN	**464 (98)**	68 (100)	396 (98)	225 (48)	239 (52)
Other	**8 (2)**	0 (—)	8 (2)	2 (25)	6 (75)
Residence community type					
Hub town with regional hospital	**129 (27)**	28 (41)	101 (25)	45 (35)	84 (65)
Village	**343 (73)**	40 (59)	303 (75)	182 (53)	161 (47)
High-risk underlying condition§					
None	**396 (84)**	55 (81)	341 (84)	192 (48)	204 (52)
≥1	**76 (16)**	13 (19)	63 (16)	35 (46)	41 (54)
Hospitalization					
Yes	**64 (14)**	23 (34)	41 (10)	29 (45)	35 (55)
No	**408 (86)**	45 (66)	363 (90)	198 (49)	210 (51)

Abbreviations: AI/AN = American Indian or Alaska Native; ARI = acute respiratory illness; RSV = respiratory syncytial virus.

* Overall, 32 of 504 infants with ARI medical visits including receipt of RSV tests during the analysis period were excluded. Reasons for exclusion included being born to a mother who received RSV vaccination during pregnancy (14), receipt of nirsevimab <7 days before medical visit (nine), receipt of ≥1 dose of nirsevimab on different dates (five), ineligible for nirsevimab (non-Alaska Native in their second season without other risk factors) (two), receipt of palivizumab 124 days before the ARI visit (one), and receipt of a negative RSV test result but with an RSV discharge code (one).

† Receipt of nirsevimab documented by state immunization information system or provider electronic health record.

§ A subset of underlying medical conditions conferring higher risk for severe RSV illness was defined as chronic lung disease of prematurity (two); congenital heart disease (eight); immunocompromise (one); cystic fibrosis (zero); Down syndrome (two); neurologic, musculoskeletal conditions, or both (51); congenital airway abnormalities (one); reactive airway disease (17); or prematurity (nine); 10 children had one or more underlying conditions.

studies among infants in their first RSV season (*6*–*8*), this evaluation documents nirsevimab effectiveness in an AI/AN population known to be at increased risk for severe RSV illness (*2*,*3*) and at a longer median interval from nirsevimab receipt (91 days) (*8*). Some evidence of waning overall effectiveness was observed (90% at 7–89 days and 77% at 90–179 days after receipt), but 95% CIs were wide and overlapped. These real-world estimates support current recommendations for nirsevimab to prevent severe RSV among infants in their first and second RSV seasons (*4*,*5*).

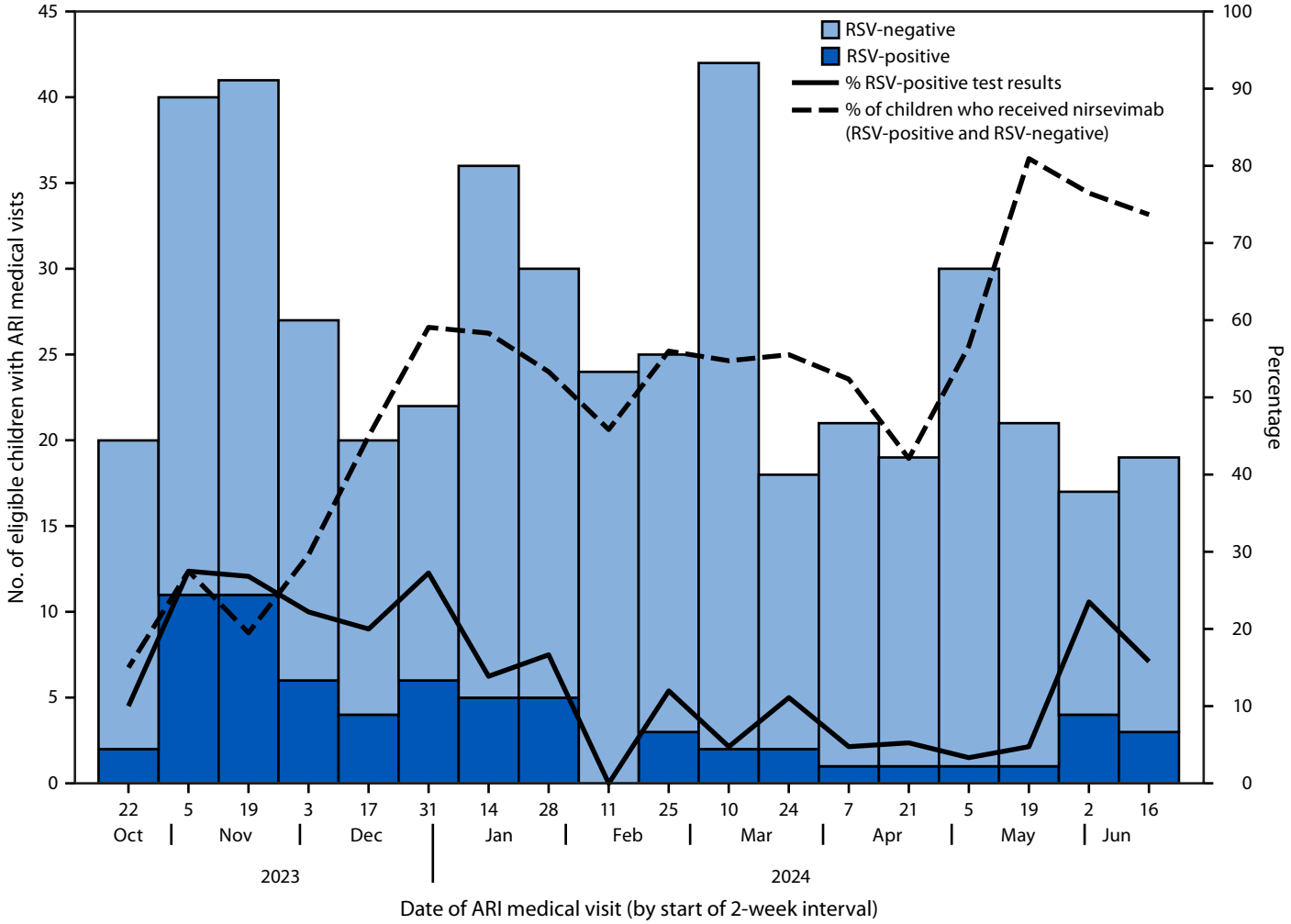
Compared with other U.S. data (*6*), a relatively high proportion of children aged <20 months in this evaluation (48%) received nirsevimab. In Alaska, all AI/AN children aged <8 months and aged 8–19 months in rural areas were prioritized to receive nirsevimab when shortages occurred during October 2023–January 2024.††† Compared with an average of 56 RSV-associated hospitalizations among children aged <2 years in the region during nine previous RSV seasons (C Desnoyers, YKHC, and S Bressler, Arctic Investigations Program, CDC, personal communication, October 2024),§§§ 28 RSV-associated hospitalizations occurred during the 2023–24 season (including five RSV hospitalizations that were excluded in the evaluation¶¶¶), and three occurred in children who received nirsevimab ≥7 days earlier. An adequate, timely

††† https://health.alaska.gov/dph/Epi/Documents/phan/AKPHAN_20231025_NirsevimabSupplyTable.pdf

§§§ From regional surveillance data, this statistic is the 9-year average of RSV hospitalizations among children aged <2 years during the 2013–2020 and 2021–2023 seasons (excluding 2020–21 during the COVID-19 pandemic, which had no cases).

¶¶¶ Another three RSV hospitalizations in the YKHC service area that occurred in children were excluded from the analysis: one child received nirsevimab <7 days before the ARI visit, one received palivizumab 124 days earlier, and one was ineligible for nirsevimab because the child was not AI/AN and was aged 8–19 months; another two RSV hospitalizations were excluded because the child's first ARI visit included in the evaluation period was >30 days earlier. None of these children received nirsevimab ≥7 days before the ARI visit.

FIGURE. Trends in number of eligible children in their first or second respiratory syncytial virus season who had medically attended acute respiratory illness, by respiratory syncytial virus test result, test positivity, and receipt of nirsevimab* — Yukon-Kuskokwim Region, Alaska, October 23, 2023–June 30, 2024



Abbreviations: ARI = acute respiratory illness; RSV = respiratory syncytial virus.

* Receipt of nirsevimab was calculated among eligible children with medically attended ARI medical visits and RSV-positive and RSV-negative test results. Receipt of nirsevimab was documented by state immunization information system or provider electronic health record.

nirsevimab supply and increased coverage might further reduce RSV hospitalizations during the 2024–25 season (*9*).

Limitations

The findings in this report are subject to at least five limitations. First, all RSV testing was clinician-directed, with inpatient and emergency visits accounting for the majority (84%) of included visits; possible exclusion of some children with milder illness could have affected estimated nirsevimab effectiveness. Second, low RSV incidence during the spring might have biased effectiveness estimates. Third, small numbers prevented estimation of effectiveness by time since receipt stratified by the child's RSV season and against hospitalization among children in their second RSV season. Fourth, nirsevimab dosage**** was not ascertained, preventing effectiveness estimation by dosage. Finally, this evaluation was conducted predominantly among AI/AN children in one region of Alaska, and findings might not be generalizable.

Implications for Public Health Practice

Nirsevimab was highly effective in preventing medically attended RSV illness and hospitalization among AI/AN children in Alaska's Yukon-Kuskokwim Delta region during their first and second RSV seasons. These findings support current

**** Nirsevimab dosage is determined by the child's age and weight. https://www.cdc.gov/vaccines/vpd/rsv/hcp/child.html

TABLE 2. Estimated nirsevimab effectiveness against medically attended respiratory syncytial virus illness and hospitalization, overall and by child's respiratory syncytial virus season — Yukon-Kuskokwim Region, Alaska, October 23, 2023–June 30, 2024

Outcome/RSV season (age at start of season, Oct 1, 2023)	Nirsevimab dosage pattern	No. of patients	No. (row %)		Median no. of days since dose (IQR)	Adjusted effectiveness, % (95% CI)*
			RSV-negative	RSV-positive		
Medically attended ARI						
Overall	No nirsevimab doses (Ref)	245	187 (76)	58 (24)	NA	Ref
	Nirsevimab dose ≥7 days earlier	227	217 (96)	10 (4)	91 (45–141)	82 (62–91)
	Nirsevimab dose 7–89 days earlier	111	108 (97)	3 (3)	45 (27–68)	90 (68–97)
	Nirsevimab dose 90–179 days earlier	82	78 (95)	4 (5)	122 (103–142)	77 (31–92)
1st season (<8 mos)	No nirsevimab doses (Ref)	131	100 (76)	31 (24)	NA	Ref
	Nirsevimab dose ≥7 days earlier	161	153 (95)	8 (5)	82 (41–136)	76 (42–90)
2nd season (8–19 mos)	No nirsevimab doses	114	87 (76)	27 (24)	NA	Ref
	Nirsevimab dose ≥7 days earlier	66	64 (97)	2 (3)	106 (67–159)	88 (48–97)
Hospitalization†						
Overall	No nirsevimab doses (Ref)	35	15 (43)	20 (57)	NA	Ref
	Nirsevimab dose ≥7 days earlier	29	26 (90)	3 (10)	71 (36–118)	93 (64–99)
1st season (<8 mos)	No nirsevimab doses (Ref)	27	10 (37)	17 (63)	NA	Ref
	Nirsevimab dose ≥7 days earlier	22	19 (86)	3 (14)	73 (36–142)	89 (32–98)

Abbreviations: NA = not applicable; Ref = referent group; RSV = respiratory syncytial virus.
* Effectiveness was calculated as (1 − adjusted odds ratio) × 100%. Odds ratios were calculated using multivariable logistic regression, adjusted by age in months at medical visit (continuous), sex, calendar month of medical visit, residence community type, and presence of a high-risk underlying condition.
† Effectiveness against hospitalization was not estimated for children in their second season because of small numbers (15).

Summary

What is already known about this topic?

To prevent severe respiratory syncytial virus (RSV) illness, nirsevimab is recommended for all infants aged <8 months (born during or entering their first RSV season) who are not protected through maternal vaccination and for children aged 8–19 months (entering their second season) who are at increased risk for severe RSV, including all American Indian and Alaska Native (AI/AN) children.

What is added by this report?

In Alaska's Yukon-Kuskokwim Delta, nirsevimab was 89% effective in preventing RSV-associated hospitalization for infants in their first RSV season and 76% and 88% effective against medically attended illness for children in their first and second seasons, respectively.

What are the implications for public health practice?

Nirsevimab can prevent severe RSV illness among AI/AN infants and children entering their first and second RSV seasons.

CDC recommendations for all infants in their first RSV season to either receive nirsevimab or be protected through maternal vaccination and for children entering their second season with increased risk for severe RSV illness, including all AI/AN children, to receive nirsevimab (*4*,*5*).

Acknowledgments

Community members of the Yukon-Kuskokwim Delta region and service providers of Yukon-Kuskokwim Health Corporation; Victoria Balta, Ian Blake, CDC.

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All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. James W. Keck reports grant support from the National Institutes of Health (NIH) for the Alaska Native Center for Health Research Project and for the Wastewater Assessment for Coronavirus in Kentucky: Implementing Enhanced Surveillance Technology; from the National Science Foundation for the Pandemic Environmental Surveillance Center for Assessing Pathogen Emergency Project; from NIH for the COVID-19 infection and diabetes incidence in Native American People project; from NIH for the Neqkiuryaraq – The Art of Preparing Food Project; from Greenwall Foundation for the developing stakeholder-engaged ethical guidance for public health wastewater surveillance project service; and as safety officer and chair of the Data Safety Monitoring Board for National Institute of Diabetes and Digestive and Kidney Diseases-funded study: Enhancing the Diabetes Prevention Program. No other potential conflicts of interest were disclosed.

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Underutilization of Influenza Antiviral Treatment Among Children and Adolescents at Higher Risk for Influenza-Associated Complications — United States, 2023–2024

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Abstract

Annually, tens of thousands of U.S. children and adolescents are hospitalized with seasonal influenza virus infection. Both influenza vaccination and early initiation of antiviral treatment can reduce complications of influenza. Using data from two U.S. influenza surveillance networks for children and adolescents aged <18 years with medically attended, laboratory-confirmed influenza for whom antiviral treatment is recommended, the percentage who received treatment was calculated. Trends in antiviral treatment of children and adolescents hospitalized with influenza from the 2017–18 to the 2023–2024 influenza seasons were also examined. Since 2017–18, when 70%–86% of hospitalized children and adolescents with influenza received antiviral treatment, the proportion receiving treatment notably declined. Among children and adolescents with influenza during the 2023–24 season, 52%–59% of those hospitalized received antiviral treatment. During the 2023–24 season, 31% of those at higher risk for influenza complications seen in the outpatient setting in one network were prescribed antiviral treatment. These findings demonstrate that influenza antiviral treatment is underutilized among children and adolescents who could benefit from treatment. All hospitalized children and adolescents, and those at higher risk for influenza complications in the outpatient setting, should receive antiviral treatment as soon as possible for suspected or confirmed influenza.

Introduction

Annually, seasonal influenza virus infections among children and adolescents in the United States are estimated to result in millions of medical visits, tens of thousands of hospitalizations, and hundreds of deaths.[†] Influenza hospitalization rates among children and adolescents are highest among those aged <1 year, and rates decrease with increasing age.[§] Influenza vaccination and early initiation of antiviral treatment can reduce the risk for influenza complications (*1*,*2*). Prompt antiviral treatment has also been associated with lower odds of intensive care unit (ICU) admission and death among hospitalized children and adolescents with influenza (*3*). Antiviral treatment is recommended as soon as possible, and treatment of any person with suspected or confirmed influenza who is hospitalized; has severe, complicated, or progressive illness; or is at higher risk for influenza complications should not await laboratory confirmation (*4*,*5*). In addition to persons with certain underlying medical conditions, children aged <5 years are considered to be at higher risk for influenza complications; the highest risk is among those aged <2 years (*5*).

During the 2022–23 influenza season, underutilization of antiviral treatment was observed among hospitalized children and adolescents with laboratory-confirmed influenza compared with its use during seasons before the COVID-19 pandemic (*6*). This report examines antiviral treatment patterns among children and adolescents with laboratory-confirmed influenza who were hospitalized and among those at higher risk for influenza complications within the outpatient setting during the 2023–24 influenza season.

Methods

Data Collection

Data were collected from two U.S. influenza surveillance networks,[¶] the Influenza Hospitalization Surveillance Network (FluSurv-NET) and the New Vaccine Surveillance Network (NVSN). For this analysis, patients were included from both networks during October 1, 2023–April 30, 2024.

*These senior authors contributed equally to this report.
[†] https://www.cdc.gov/flu-burden/php/data-vis/index.html

[§] https://gis.cdc.gov/grasp/FluView/FluHospRates.html
[¶] https://www.cdc.gov/fluview/overview/influenza-hospitalization-surveillance.html; https://www.cdc.gov/nvsn/php/about/index.html

FluSurv-NET is an active, population-based influenza hospitalization surveillance network that collects data on persons of all ages. A FluSurv-NET case was defined as a hospitalization of a person of any age residing in the surveillance catchment area with laboratory-confirmed influenza from a clinically ordered test.** Data were collected through review of medical records using a standardized case report form on an age-, site-, and month of admission–stratified random sample of cases from 12 sites.†† All sampled children and adolescents aged <18 years from FluSurv-NET were included in the analyses. Cases that were not sampled, cases missing influenza antiviral treatment data, cases of nosocomial influenza, and cases among pregnant persons were excluded.

NVSN is an active, population-based surveillance network that collects data from children and adolescents aged <18 years with acute respiratory illness (ARI) in outpatient (outpatient clinics, urgent care clinics, and emergency departments) and hospital settings at seven sites.§§ An NVSN case was defined as ARI¶¶ and laboratory-confirmed influenza*** from a clinically ordered test in a child or adolescent aged <18 years living in the catchment area. For NVSN, all hospitalized patients with laboratory-confirmed influenza were included, but in the outpatient setting, cases were only included if the patients were recommended to receive influenza antiviral treatment based on CDC guidance (age <5 years or having at least one underlying medical condition)††† (*5*). Data were collected through parent or guardian interviews with assent from the child (when applicable) and medical chart reviews. Cases with missing influenza antiviral treatment data were excluded.

Data Analysis

Influenza antiviral treatment was defined as documentation of prescription for or receipt of baloxavir, oseltamivir, peramivir, or zanamivir among persons in outpatient or inpatient hospital settings,§§§ respectively. Percentages of persons treated were calculated by dividing the number of persons treated with or prescribed antivirals by the number for whom receipt of antiviral treatment was recommended.¶¶¶ For historical context, the percentages of hospitalized children and adolescents with influenza who received antiviral treatment by age groups during October 1–April 30 from the 2017–18 through the 2022–23 seasons**** were calculated. For FluSurv-NET, unweighted counts and weighted percentages are presented to account for the complex survey design.

SAS software (version 9.4; SAS Institute) was used to conduct the analysis. FluSurv-NET and NVSN activities were reviewed by CDC, deemed not research, and were conducted consistent with applicable federal law and CDC policy.††††,§§§§

Results

Inpatient Influenza Antiviral Treatment Trends

During the 2017–18 season, the overall percentage of hospitalized patients aged <18 years with laboratory-confirmed influenza who were treated with antiviral medications was 70% in NVSN and 86% in FluSurv-NET (Figure). Since the 2019–20 season, the percentage of children and adolescents with influenza receiving treatment has declined and has remained lower than it was in seasons before the COVID-19 pandemic.

Characteristics of Children and Adolescents in FluSurv-NET and NVSN

During the 2023–24 influenza season, 573 influenza-associated outpatient visits and 283 influenza-associated hospitalizations in NVSN and 1,846 influenza-associated hospitalizations in FluSurv-NET were analyzed (Table 1).¶¶¶¶ Among children

** Defined as receipt of a positive test result from a viral culture, direct or indirect fluorescent antibody staining, rapid antigen test, molecular assay, or evidence of a positive influenza test result in a clinical note within 14 days before or during hospitalization.

†† Patients in FluSurv-NET lived in catchment area counties from the following states: California, Colorado, Connecticut, Georgia, Maryland, Michigan, Minnesota, New Mexico, New York, Oregon, Tennessee, and Utah.

§§ Vanderbilt University Medical Center, Nashville, Tennessee; University of Rochester School of Medicine and Dentistry-Medical Center/UR-Golisano Children's Hospital, Rochester, New York; Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; Texas Children's Hospital, Houston, Texas; Seattle Children's Hospital, Seattle, Washington; Children's Mercy Hospital, Kansas City, Missouri; Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania.

¶¶ ARI is defined as at least one of the following within 10 days of the medical encounter: fever, cough, earache, nasal congestion, runny nose, sore throat, wheezing, shortness of breath or rapid shallow breathing, apnea, apparent life-threatening event, or briefly resolved unexplained event.

*** Defined as receipt of a positive test result from a rapid antigen or polymerase chain reaction test or a molecular assay.

††† Asthma or reactive airway disease, chronic lung disease, cancer, organ transplant, chronic metabolic disease, blood disorders, cardiovascular disease, neurologic disorders, immunocompromised, renal disease, liver disease, or obesity among children and adolescents aged ≥2 years).

§§§ For FluSurv-NET, this could be up to 2 weeks before or at any time during hospitalization.

¶¶¶ Includes all persons with influenza who were hospitalized or, in the outpatient setting, those aged <5 years, or with illness in one of the following medical condition categories: asthma or reactive airway disease, chronic lung disease, cancer, organ transplant, chronic metabolic disease, blood disorders, cardiovascular disease, neurologic disorders, immunocompromised, renal disease, liver disease, or obesity (among children aged ≥2 years).

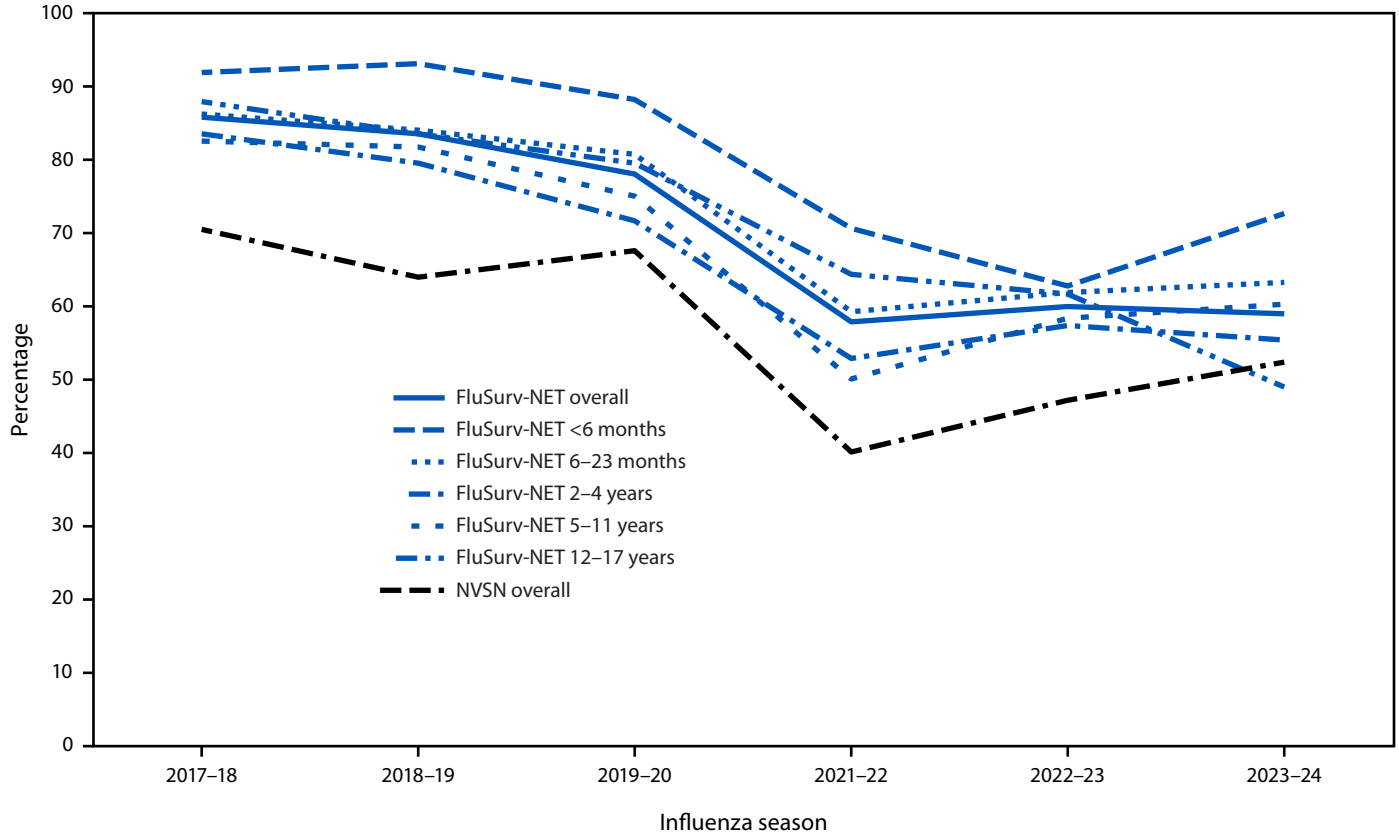
**** The 2020–21 influenza season was excluded because of minimal influenza activity.

†††† 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.

§§§§ FluSurv-NET and NVSN sites obtained human subjects and ethics approval from their respective state health departments, academic partners, or participating hospital institutional review boards.

¶¶¶¶ In FluSurv-NET, a total of 1,026 cases were excluded: 954 were not sampled, 14 sampled cases were missing antiviral use data, 50 sampled cases were considered nosocomial (positive influenza test result >3 days after hospital admission), and eight persons with sampled cases were pregnant.

FIGURE. Antiviral treatment among children and adolescents aged <18 years hospitalized with laboratory-confirmed influenza, overall and by age group — two multistate surveillance networks,* United States, 2017–18 to 2023–24 influenza seasons†,§



Abbreviations: FluSurv-NET = Influenza Hospitalization Surveillance Network; NVSN = New Vaccine Surveillance Network.

* Data presented overall for NVSN, and overall and by age groups for FluSurv-NET. Unless indicated, data included are from FluSurv-NET.

† Clinical data were available on sampled FluSurv-NET cases for persons admitted during October 1–April 30 each season. This includes 8,907 children and adolescents in total, with 1,827 from 2017–18; 1,797 from 2018–19; 1,864 from 2019–20; 337 from 2021–22; 1,236 from 2022–23; and 1,846 from 2023–24. The 2020–21 influenza season was excluded because of minimal influenza activity.

§ Clinical influenza-positive inpatient data were available from children and adolescents in NVSN admitted from October 1 through April 30 each season. This includes 1,175 children and adolescents in total, with 186 from 2017–18; 169 from 2018–19; 268 from 2019–20; 65 from 2021–22; 204 from 2022–23; and 283 from 2023–24. The 2020–21 influenza season was excluded because of minimal influenza activity.

and adolescents with influenza-associated hospitalizations in NVSN and FluSurv-NET, the largest percentages of patients were aged 5–11 years (42% and 39%, respectively) and were non-Hispanic White persons (36% and 33%, respectively). In the outpatient setting, most children with influenza (42%) were aged 2–4 years and most (43%) were non-Hispanic Black or African American persons. Within NVSN and FluSurv-NET, 58% and 47% of hospitalized children and adolescents with influenza, respectively, did not have any underlying medical condition. Asthma or reactive airway disease was a frequently observed medical condition across networks and settings (21% in NVSN and 26% in FluSurv-NET). Among the hospitalized children and adolescents, 16% (NVSN) and 19% (FluSurv-NET) were admitted to an ICU, and 7%–13% (NVSN) and 4%–7% (FluSurv-NET) received invasive or noninvasive mechanical ventilation.

Influenza Antiviral Treatment During the 2023–24 Season

In the outpatient setting, 31% of children and adolescents who were recommended to receive antiviral treatment were prescribed antivirals (Table 2). The percentage of prescriptions was highest among children aged <6 months (49%) and lowest among those aged 2–4 years (21%); all outpatient prescriptions were for oseltamivir (Supplementary Table, https://stacks.cdc.gov/view/cdc/168887).

Among children and adolescents hospitalized with influenza, 52% (NVSN) and 59% (FluSurv-NET) received antiviral treatment (Table 2). Antiviral treatment prevalence among hospitalized children and adolescents with influenza was highest among those aged <6 months (68% [NVSN]; 73% [FluSurv-NET]) and lowest among those aged 2–4 years in NVSN (43%) and 12–17 years in FluSurv-NET (49%). Nearly all treated patients received oseltamivir (99%) (Supplementary

TABLE 1. Characteristics of children and adolescents with medically attended laboratory-confirmed influenza, by setting — two multistate surveillance networks, United States, 2023–24 influenza season

Characteristic	Total unweighted no. (col. %*) NVSN Outpatient† n = 573	NVSN Inpatient n = 283	FluSurv-NET Inpatient N = 1,846
Age group			
<6 mos	37 (6)	22 (8)	175 (7)
6–23 mos	133 (23)	55 (19)	354 (17)
2–4 yrs	241 (42)	54 (19)	414 (22)
5–11 yrs	114 (20)	118 (42)	677 (39)
12–17 yrs	48 (8)	34 (12)	226 (15)
Sex			
Female	247 (43)	121 (43)	775 (44)
Male	326 (57)	162 (57)	1,071 (56)
Race and ethnicity§			
American Indian or Alaska Native	0 (—)	1 (0)	16 (1)
Asian or Pacific Islander	11 (2)	9 (3)	107 (5)
Black or African American	249 (43)	70 (25)	522 (31)
White	89 (16)	102 (36)	597 (33)
Hispanic or Latino	180 (31)	75(27)	498 (25)
Multiracial	32 (6)	20 (7)	24 (1)
Unknown	12 (2)	6 (2)	82 (4)
ARI at admission¶			
Yes	—	—	1,694 (92)
No	—	—	152 (8)
Underlying medical conditions			
Asthma or reactive airway disease	122 (21)	61 (21)	428 (26)
Blood disorders	17 (3)	14 (5)	89 (5)
Cardiovascular disease	14 (2)	16 (6)	129 (7)
Chronic lung disease	128 (22)	71 (25)	98 (6)
Chronic metabolic disease	11 (2)	9 (3)	76 (4)
Immunocompromised	3 (1)	6 (2)	83 (5)
Neurologic disorders	33 (6)	33 (12)	319 (20)
Prematurity (aged <24 mos)	11 (3)	10 (13)	95 (19)
No. of underlying medical condition categories**			
0	370 (65)	164 (58)	947 (47)
1	176 (31)	84 (30)	620 (36)
2	20 (3)	23 (8)	164 (12)
≥3	7 (1)	12 (4)	85 (5)
Hospital outcomes			
ICU admission	—	44 (16)	362 (19)
ECMO	—	2 (5)	7 (0)
Noninvasive mechanical ventilation††	—	16 (13)	125 (7)
Invasive mechanical ventilation	—	9 (7)	67 (4)
In-hospital death	—	0 (—)	14 (1)

Abbreviations: ARI = acute respiratory illness; ECMO = extracorporeal membrane oxygenation; FluSurv-NET = Influenza Hospitalization Surveillance Network; ICU = intensive care unit; NVSN = New Vaccine Surveillance Network.

* Weighted percentages are calculated using sampling weights for FluSurv-NET.

† Including outpatient clinics, urgent care clinics, and emergency departments. Only children and adolescents recommended to receive antiviral medication in the outpatient setting are included (specifically those aged <5 years or any child or adolescent with illness in one of the following medical condition categories: asthma or reactive airway disease, chronic lung disease, cancer, organ transplant, chronic metabolic disease, blood disorders, cardiovascular disease, neurologic disorders, immunocompromised, renal disease, liver disease, or obesity [among children aged ≥2 years]).

§ Persons of Hispanic or Latino (Hispanic) origin might be of any race but are categorized as Hispanic; all racial groups are non-Hispanic.

¶ For FluSurv-NET, ARI includes any of the following: fever, cough, nasal congestion, chest congestion, sore throat, hemoptysis, wheezing, apnea, cyanosis, difficulty breathing, nasal flaring, grunting, retractions, stridor, or shortness of breath. ARI at admission is part of the inclusion criteria for NVSN.

** Calculated as the number of conditions across categories including asthma or reactive airway disease, chronic lung disease, cancer, organ transplant, chronic metabolic disease, blood disorders, cardiovascular disease, neurologic disorders, immunocompromised, renal disease, liver disease, obesity (among children and adolescents aged ≥2 years), and prematurity (among those aged <24 months).

†† Bilevel positive airway pressure or continuous positive airway pressure.

Table, https://stacks.cdc.gov/view/cdc/168887); most (68% [NVSN]; 60% [FluSurv-NET]) received treatment on the day of admission, and 29% (NVSN) and 34% (FluSurv-NET) were not treated until ≥1 day after admission.

In both outpatient and inpatient settings, the percentage of children and adolescents who received antiviral treatment for laboratory-confirmed influenza rose with an increasing number of underlying medical conditions, from 28% of those with no underlying conditions to 57% among those with three or more (outpatient) and, among hospitalized patients, from 45% to 75% (NVSN), respectively, and from 55% to 77% (FluSurv-NET), respectively (Table 2). The percentage of patients with underlying medical conditions who received antiviral treatment varied by condition, network, and setting. Among those with asthma or reactive airway disease (a frequent comorbidity between networks and settings), 34% of those in outpatient settings were prescribed antivirals, and 64% (NVSN) and 62% (FluSurv-NET) of those who were hospitalized received antiviral treatment.

In children and adolescents who were hospitalized, a higher proportion of those admitted to an ICU received antiviral treatment (84% [NVSN]; 82% [FluSurv-NET]); 81% of those admitted were treated on the day of or after ICU admission. Among those who received noninvasive or invasive ventilation, 89%–94% in NVSN and 82% in FluSurv-NET received antiviral treatment.

Discussion

Seasonal influenza causes substantial disease among children and adolescents in the United States each year, and annual influenza vaccination is recommended for all persons aged ≥6 months, including those who are pregnant (to protect themselves and their infants aged <6 months through passive transplacentally transferred antibodies) (*7*). Antiviral treatment

TABLE 2. Number and percentage of children and adolescents with medically attended, laboratory-confirmed influenza who received antiviral treatment, by setting — two multistate surveillance networks, United States, 2023–24 influenza season

Characteristic	Receipt of antiviral treatment, no./No. (%)*		
	NVSN		FluSurv-NET
	Outpatient†	Inpatient	Inpatient
Overall	**177/573 (31)**	**148/283 (52)**	**1,136/1,846 (59)**
Age group			
<6 mos	18/37 (49)	15/22 (68)	132/175 (73)
6–23 mos	51/133 (38)	26/55 (47)	223/354 (63)
2–4 yrs	51/241 (21)	23/54 (43)	244/414 (55)
5–11 yrs	39/114 (35)	64/118 (54)	401/677 (60)
12–17 yrs	19/48 (40)	20/34 (59)	136/226 (49)
Sex			
Female	66/247 (27)	64/121 (53)	484/775 (59)
Male	111/326 (33)	84/162 (52)	352/1,071 (60)
Race and ethnicity§			
American Indian or Alaska Native	0 (—)	1/1 (100)	9/16 (53)
Asian or Pacific Islander	6/11 (54)	2/9 (22)	64/107 (58)
Black or African American	61/249 (25)	31/70 (44)	326/522 (59)
White	34/89 (38)	59/102 (58)	354/597 (54)
Hispanic or Latino	69/180 (38)	43/75 (57)	320/498 (66)
Multiracial	6/32 (19)	11/20 (55)	16/24 (50)
Unknown	1/12 (8)	1/6 (17)	47/82 (84)
High-risk category			
Aged <5 years	101/362 (28)	27/65 (42)	351/584 (57)
High-risk condition¶	57/162 (35)	43/92 (47)	358/540 (61)
Aged <5 years and high-risk condition	19/79 (39)	57/87 (65)	248/359 (66)
No additional high-risk factors	—	21/39 (54)	179/363 (51)
Underlying medical conditions			
Asthma or reactive airway disease	41/122 (34)	39/61 (64)	280/428 (62)
Blood disorders	5/17 (29)	7/14 (50)	74/89 (83)
Cardiovascular disease	7/14 (50)	13/16 (81)	102/129 (75)
Chronic lung disease	45/128 (35)	46/71 (65)	82/98 (75)
Chronic metabolic disease	8/11 (73)	5/9 (56)	54/76 (62)
Immunocompromised	2/3 (67)	3/6 (50)	61/83 (72)
Neurologic disorders	13/33 (39)	21/33 (64)	208/319 (59)
Prematurity (aged <24 mos)	5/11 (45)	4/10 (40)	73/95 (74)
No. of underlying medical conditions**			
0	104/370 (28)	73/164 (45)	530/947 (55)
1	59/176 (34)	51/84 (61)	394/620 (60)
2	10/20 (50)	15/23 (65)	144/194 (66)
≥3	4/7 (57)	9/12 (75)	68/85 (77)
Hospital outcomes			
ICU admission	—	37/44 (84)	301/362 (82)
ECMO	—	2/2 (100)	6/7 (86)
Noninvasive mechanical ventilation††	—	15/16 (94)	115/125 (82)
Invasive mechanical ventilation	—	8/9 (89)	58/67 (82)
In-hospital death	—	0 (—)	12/14 (86)

Abbreviations: ECMO = extracorporeal membrane oxygenation; FluSurv-NET = Influenza Hospitalization Surveillance Network; ICU = intensive care unit; NVSN = New Vaccine Surveillance Network.

* Weighted percentages calculated using sampling weights for FluSurv-NET.

† Including outpatient clinics, urgent care clinics, and emergency departments. Only children and adolescents recommended to receive antiviral medication in the outpatient setting are included (specifically those aged <5 years or any child or adolescent with an illness in one of the following medical condition categories: asthma or reactive airway disease, chronic lung disease, cancer, organ transplant, chronic metabolic disease, blood disorders, cardiovascular disease, neurologic disorders, immunocompromised, renal disease, liver disease, or obesity [among children and adolescents aged ≥2 years]).

§ Persons of Hispanic or Latino (Hispanic) origin might be of any race but are categorized as Hispanic; all racial groups are non-Hispanic.

¶ Includes the following medical condition categories: asthma or reactive airway disease, chronic lung disease, cancer, organ transplant, chronic metabolic disease, blood disorders, cardiovascular disease, neurologic disorders, immunocompromised, renal disease, liver disease, obesity (among children aged ≥2 years), and prematurity (among those aged <24 months).

** Calculated as the number of conditions across categories including asthma or reactive airway disease, chronic lung disease, cancer, organ transplant, chronic metabolic disease, blood disorders, cardiovascular disease, neurologic disorders, immunocompromised, renal disease, liver disease, obesity (among children and adolescents aged ≥2 years), and prematurity (among those aged <24 months).

†† Bilevel positive airway pressure or continuous positive airway pressure.

is an important adjunct to reduce the risk for influenza complications. Among patients with confirmed or suspected influenza, initiation of antiviral treatment is recommended as soon as possible for outpatients at higher risk for influenza complications and for all hospitalized patients (*4*,*5*). The percentage of children and adolescents with influenza-associated hospitalization who received antiviral treatment remained relatively stable from the 2017–18 season to the 2019–20 season, and subsequently decreased sharply during the COVID-19 pandemic. Although antiviral treatment has stabilized during the past two seasons, the percentages of patients treated have remained suboptimal and have not returned to prepandemic levels. During the 2023–24 influenza season, approximately one half (41%–48%) of children and adolescents with an influenza-associated hospitalization and approximately two thirds (69%) of those with an influenza-associated outpatient visit did not receive recommended antiviral treatment, highlighting missed opportunities to reduce the risk for influenza complications. This decrease in use of influenza antiviral treatment underscores the importance of increasing awareness among pediatric health care professionals about current recommendations for antiviral treatment.

Antiviral treatment is associated with improved outcomes for children and adolescents with influenza, including in-hospital survival (*2*,*3*,*8*). Antiviral treatment initiation shortly after influenza symptom onset provides more clinical benefit than does later treatment initiation (*2*,*3*). Among children and adolescents who are hospitalized or who are at higher risk for influenza-associated complications, there is no restriction

Summary

What is already known about this topic?

Tens of thousands of children and adolescents are hospitalized each year in the United States with influenza. Both vaccination and antiviral treatment can reduce the risk for influenza complications.

What is added by this report?

Data from two national influenza surveillance networks indicate that antiviral treatment of hospitalized children and adolescents with influenza has declined from 70%– 86% during the 2017–18 season to <60% in 2023–24. Only 30% of children and adolescents at higher risk for influenza complications were prescribed antivirals during outpatient visits.

What are the implications for public health practice?

All hospitalized children and adolescents and those at higher risk for influenza complications seen in outpatient settings with suspected influenza should receive antivirals as soon as possible to reduce the risk for influenza complications.

on the timing of initiation of antiviral treatment, although starting as early as possible is recommended. Despite these recommendations, concerns about the timing of antiviral treatment relative to symptom onset and waiting for influenza test results have been noted as reasons for not prescribing antivirals among infants in the outpatient setting (*9*). Understanding of the reasons for nontreatment among hospitalized children and adolescents with influenza is limited, but some reasons might include concerns about adverse events (*10*). Increasing access to timely care, identifying potential barriers to antiviral treatment in the hospital setting, and increasing provider education concerning the benefits of timely treatment might lead to increases in antiviral treatment of persons who are recommended to receive it.

Limitations

The findings in this report are subject to at least three limitations. First, FluSurv-NET and NVSN catchment areas do not cover the entire U.S. population; characteristics of children and adolescents with medically attended and laboratory-confirmed influenza infection might not be generalizable throughout the United States. Second, antiviral treatment before hospitalization might be recorded incompletely because patients might have received treatment in the outpatient setting. Finally, the calculation of antiviral treatment timing might be imprecise because only dates and not time of admission and treatment initiation were collected.

Implications for Public Health Practice

Annual influenza vaccination provides important protection against influenza and associated complications. Among patients with confirmed or suspected influenza who are at higher risk for complications, early initiation of antiviral treatment is recommended to further reduce the risk for complications. The decrease in influenza antiviral use among children and adolescents with laboratory-confirmed influenza since the COVID-19 pandemic is concerning. Health care providers are reminded that children and adolescents with suspected or confirmed influenza who are hospitalized or have higher risk for influenza complications should receive prompt antiviral treatment.

Acknowledgments

Charisse Cummings, Angelle Naquin, Devi Sundaresan, Influenza Division, National Center for Immunization and Respiratory Diseases, CDC; Monet Tosch-Berneburg, Leanne Kehoe, Kirsten Lacombe, Bonnie Strelitz, Seattle Children's Research Institute; Amanda Carter, Ryan Chatelain, Melanie Crossland, Andrea George, Emma Mendez-Edwards, Kristen Olsen, Andrea Price, Isabella Reyes, Holly Staten, Ashley Swain, Hafsa Zahid, Salt Lake County Health Department; Vasanthi Avadhanula, Pedro A. Piedra, Texas Children's Hospital and Baylor College of Medicine; Samar Alsabah, Justin Amarin, James Antoon, James Chappell, Annika Conlee, Katie Dyer, Emma Claire Gauthier, Haya Hayek, Gail Hughett, Karen Leib, Tiffanie Markus, Terri McMinn, Nida Mohammad, Jillian Myers, Danielle Ndi, Claudia Guevara Pulido, Collin Ragsdale, Laura Short, Andrew Spieker, Adriana Blanco Vasquez, MaKale Washington, Vanderbilt University Medical Center; Monika Johnson, Sophia Kainaroi, Samar Musa, UPMC Children's Hospital of Pittsburgh; Julie Freshwater, Denise Ingabire-Smith, Ann Salvator, Eli Shiltz, Ohio Department of Health; Heidi Arth, Eva Caudill, Miranda Howard, Caymden Hughes, Marilyn Rice, Chelsea Rohlfs, Cincinnati Children's Hospital Medical Center; Christina S. Albertin, Sophrena Bushey, Wende Fregoe, Maria Gaitan, Erin Licherdell, Christine Long, University of Rochester School of Medicine and Dentistry; Aleah Abdellatif, Grant Barney, Kerianne Engesser, Fiona Keating, Adam Rowe, New York State Department of Health; Yomei Shaw, Chad Smelser, Daniel M. Sosin, New Mexico Department of Health; Molly Bleecker, Nancy Eisenberg, Sarah Lathrop, Francesca Pacheco, Yadira Salazar-Sanchez, New Mexico Emerging Infections Program; Caroline McCahon, CDC Foundation, New Mexico Department of Health; Dinah Dosdos, Mary Moffatt, Gina Weddle, Children's Mercy Hospital; Anna Chon, Karissa Helvig, Alli Johnson, Cynthia Kenyon, Minnesota Department of Health; Amber Brewer, Jim Collins, Justin Henderson, Shannon Johnson, Lauren Leegwater, Liz McCormick, Genevieve Palazzolo, Libby Reeg, Sarah Rojewski, Michigan Department of Health and Human Services; David Blythe, Alicia Brooks, Michael Girard, Rachel Park, Maryland Department of Health; Emily Bacon, Meghann Cantey, Rayna Ceaser, Alyssa Clausen, Trisha Deshmuhk, Emily Fawcett, Sydney Hagley-Alexander, Sabrina Hendrick, Johanna Hernandez, Asmith Joseph, Annabel Patterson, Allison Roebling, MaCayla Servais, Chandler Surell, Emma Grace Turner, Hope Wilson, Emory University School of Medicine, Georgia Emerging Infections Program, Georgia Department of Public Health, Atlanta Veterans Affairs Medical Center; Maria Correa, Julia Desiato, Daewi Kim, Amber Maslar,

Adam Misiorski, Connecticut Emerging Infections Program, Yale School of Public Health; Sharon Emmerling, Breanna Kawasaki, Madelyn Lensing, Sarah McLafferty, Jordan Surgnier, Millen Tsegaye, Colorado Department of Public Health and Environment; Brenna Hall, Joelle Nadle, Monica Napoles, Jeremy Roland, Gretchen Rothrock, California Emerging Infections Program.

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All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Janet A. Englund reports institutional support from AstraZeneca, Pfizer, Moderna, and GlaxoSmithKline; receipt of consulting fees from AstraZeneca, GlaxoSmithKline, Merck, Meissa Vaccines, Moderna, Pfizer, and Sanofi Pasteur; and receipt of honoraria from Pfizer. Natasha B. Halasa reports institutional support from Merck, and receipt of an honorarium from CSL Seqirus for service on an advisory board. Sue Kim reports grants from the Michigan Department of Health and Human Services. Ruth Lynfield reports receipt of a fee for serving as an Associate Editor for the American Academy of Pediatrics Redbook, which was then donated to the Minnesota Department of Health. Leila C. Sahni reports travel support from the Gates Foundation. Elizabeth P. Schlaudecker reports institutional support from Pfizer; receipt of an honorarium from Sanofi Pasteur for service on an advisory board; and travel support for meeting attendance from the World Society for Pediatric Infectious Diseases, the European Society for Paediatric Infectious Diseases, and Pediatric Infectious Diseases Society; uncompensated membership of a National Institutes of Health Data Safety Monitoring Board; and membership on the board of the World Society for Pediatric Infectious Diseases. Jennifer E. Schuster reports institutional support from the National Institutes of Health, the Food and Drug Administration and the State of Missouri; receipt of a consulting fee from the Association of Professionals in Infection Control and Epidemiology and a speaking honorarium from the Missouri Chapter of the American Academy of Pediatrics; membership on the Association of American medical Colleges advisory board. Rangaraj Selvarangan reports institutional support from Abbot, Cepheid, Biomerieux, Hologic, BioRad, Qiagen, Diasorin, and Merck; receipt of payment from GlaxoSmithKline, Baebies Biomerieux and Abbot; and travel support from Biomerieux and Hologic. Mary A. Staat reports institutional support from the National Institutes of Health, Cepheid, and Merck; royalties from UpToDate; and consulting fees from Merck. Dawud Ujamaa reports consulting fees from Goldbelt, Inc. Geoffrey A. Weinberg reports institutional support from the New York State Department of Health; consulting fees from the New York State Department of Health, Inhalon Biopharma, and ReViral; honorarium from Merck; and participation on an Emory University Data Safety Monitoring Board. No other potential conflicts of interest were disclosed.

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Pediatric Rash Illness Outbreak with Initial Positive Measles Immunoglobulin M Antibody Test Results — American Samoa, March–July 2023

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Abstract

On April 24, 2023, the American Samoa Department of Health (ASDoH) declared a public health emergency amid concern about a possible measles outbreak given low 2-dose vaccination coverage at the time. ASDoH had received two positive measles immunoglobulin (Ig) M test results after Flag Day festivities 1 week earlier from vaccinated children. ASDoH performed active case finding, took actions to mitigate transmission, and requested technical assistance from CDC. ASDoH implemented a vaccination campaign to improve suboptimal coverage. Confirmatory molecular testing of specimens from these initial persons under investigation (PUIs) was not possible, but subsequent testing of specimens from additional PUIs by Hawaii State Laboratories Division and CDC ruled out measles. In settings with low measles prevalence, measles antibody testing results have low positive predictive value and can lead to difficulties with interpreting results. Testing for additional pathogens revealed a variety of viruses known to cause common childhood viral exanthems. Both molecular and serologic testing should be performed for all suspected measles cases. To decrease the probability of false-positive IgM results, testing should be reserved for cases that meet the Council of State and Territorial Epidemiologists measles case definition, especially those in persons with no evidence of immunity and with a history of recent international travel. In addition, maintaining high measles vaccination coverage can prevent future outbreaks.

Investigation and Results

Identification of Two Persons Who Received Positive Measles Immunoglobulin M Antibody Test Results

On March 23, 2023, an afebrile child aged 8 years who had received 2 doses of measles, mumps, and rubella (MMR) vaccine[†] was evaluated in American Samoa, a remote unincorporated U.S. territory in the southern hemisphere (population approximately 50,000) (Figure) for a 3-day history of generalized pruritic rash. Nearly 20 days later, another afebrile child aged 4 years who also had received 2 doses of MMR vaccine was evaluated for a rash. Both children received a positive measles immunoglobulin (Ig) M test result from a commercial laboratory in California. The American Samoa Department of Health (ASDoH) received these results after Flag Day[§] festivities, an island-wide event with large gatherings that occurred on April 17. Once a positive measles IgM test result was received, concern was raised that community measles transmission was already occurring.

In 2019, a large measles outbreak involving multiple Pacific Island countries occurred, including cases in American Samoa. High morbidity and mortality occurred in neighboring island country Samoa where vaccination coverage was low; nearly 6,000 measles cases and >80 measles-associated deaths occurred (*1*). Low 2-dose MMR vaccination coverage estimates (72%) among children aged 6 years in American Samoa in January 2023 (CDC, unpublished data, 2023) raised concern among health authorities about the potential for another large measles outbreak. Since 2019, the 21 Pacific Island Countries and Areas (PICs) of which American Samoa is a part, interrupted endemic measles transmission and were on track to achieve measles elimination (*2*).

Declaration of Public Health Emergency

On April 24, 2023, 1 week after Flag Day, a public health emergency was declared in American Samoa. The ASDoH closed schools and child care centers, initiated a territory-wide MMR vaccination campaign, implemented travel restrictions, conducted active case finding, and requested technical assistance from CDC. This activity was reviewed by CDC, deemed not research, and was conducted consistent with applicable federal law and CDC policy.[¶]

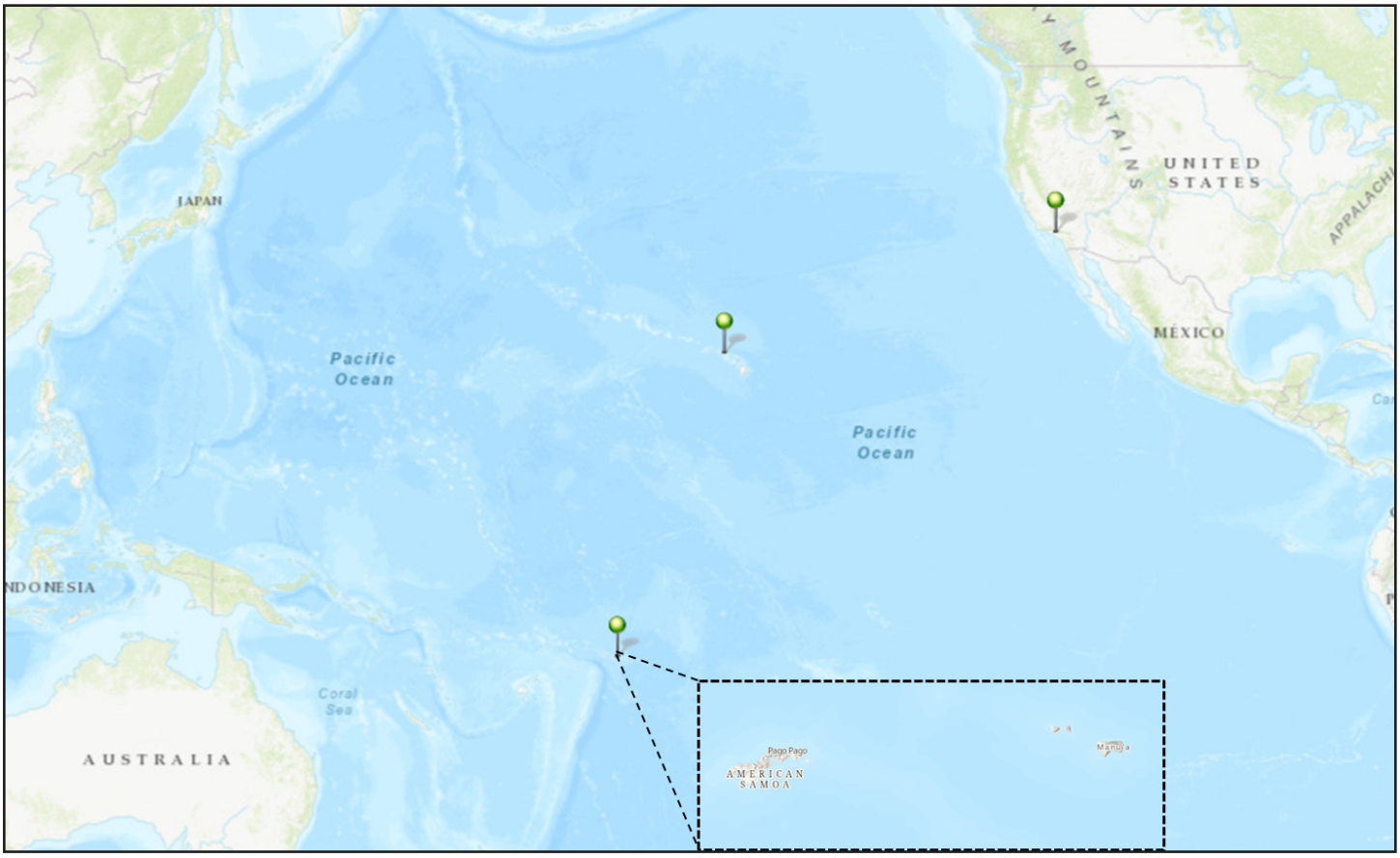
[*] These authors contributed equally to this report.

[†] Per the U.S. routine MMR vaccination schedule, children are usually considered fully vaccinated against measles after receipt of 2 MMR vaccine doses at ages 12–15 months and 4–6 years. https://www.cdc.gov/vaccines/vpd/mmr/public/index.html

[§] The American flag was officially raised in American Samoa for the first time on April 17, 1900, and Flag Day is celebrated each year on April 17 in commemoration of this historic event.

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

FIGURE. Geographic locations where non-CDC laboratory testing was performed for measles during a pediatric rash illness outbreak — American Samoa, California, and Hawaii, March–July 2023



Identification of Persons Under Investigation

During March–July 2023, ASDoH evaluated 86 persons for measles (persons under investigation [PUIs]), including the two pediatric index patients. The median PUI age was 5.9 years, and 95% were aged <13 years (Table 1). Among all PUIs, illness among more than one half (51; 59%) did not meet the Council of State and Territorial Epidemiologists (CSTE) measles clinical case definition**; however, clinical suspicion of measles based on the characteristics and distribution of rash prompted laboratory testing for these children. Among the 35 children whose illness did meet the CSTE clinical case definition, 31 (86%) had received ≥1 MMR vaccine dose and 18 (all aged 1–12 years) had received 2 doses.

Laboratory Investigation

During the public health emergency, no validated molecular or serologic assays for measles were available in American Samoa, which resulted in the need for logistically challenging off-island testing. Off-island testing is affected by long travel times and limited flights from the island that delay receipt of specimens by laboratories. Nasopharyngeal (NP) swabs or throat swabs, the preferred specimen for detection of measles viral RNA, were not collected from the two initial PUIs, and therefore real-time reverse transcription-polymerase chain reaction (RT-PCR) testing was not performed. However, 62 specimens from PUIs identified later in the investigation were sent to the Hawaii State Laboratories Division for measles real-time RT-PCR testing. Among the 62 NP swabs and 52 serum samples sent to Hawaii, 37 (60%) NP swabs and 42 (81%) serum samples were forwarded to CDC for further testing, including 1) measles virus genotype A (MeVA) real-time RT-PCR to detect measles vaccine virus; 2) measles and rubella serology, including IgM and IgG; 3) IgG avidity testing for measles and rubella; and 4) measles plaque reduction neutralization (PRN) to determine baseline immunity and differentiate recent infection from vaccination. The CDC IgM capture enzyme immunoassay used for measles IgM testing has been found to be more sensitive and specific than indirect enzyme immunoassays (*3*). IgG avidity testing was performed

** A generalized maculopapular rash with fever and at least one of the following: cough, coryza, or conjunctivitis. https://ndc.services.cdc.gov/case-definitions/measles-2013/

to measure the overall strength of antigen-antibody binding to help distinguish recent from remote infection, and PRN is a functional assay that measures neutralizing antibodies. To identify additional pathogens, CDC performed enterovirus and parechovirus real-time RT-PCR and typing, pan-herpesvirus PCR, pan-erythrovirus PCR, agnostic metagenomic next-generation sequencing (NGS), and viral-enriched NGS on deidentified specimens.

All NP swabs tested at the Hawaii State Laboratories Division for measles using real-time RT-PCR were negative, with the exception of one from a recently vaccinated child (Table 2); based on MeVA testing, this result was consistent with measles vaccination 11 days before specimen collection. Measles IgM capture assay and IgG results were positive for four PUIs, which could indicate a recent or acute measles infection or recent measles vaccination. Two of the four PUIs with positive IgM capture and IgG test results also had high IgG avidity test results and low plaque reduction neutralization titers, suggesting false-positive IgM results (recent measles infection would elicit a high neutralizing antibody titer). One specimen from a PUI without reported MMR vaccination was also rubella IgM-positive and had low avidity for both measles and rubella, suggesting recent vaccination. ASDoH later confirmed an MMR dose 1 month before rash onset in their immunization registry. One IgM capture–positive specimen was not tested further. Thirty-two (87%) of 37 NP specimens tested at CDC were positive for any virus, including 19 (53%) for parvovirus B19. Other viruses (e.g., rhinovirus [12], human herpesvirus 6 [five], influenza B [five], respiratory syncytial virus [one], and SARS-CoV-2 [two]) were also identified. Among 14 (44%) of 32 specimens that yielded a positive virus test result, more than one pathogen was identified.

TABLE 1. Characteristics of persons under investigation for measles during a public health response, by age group — American Samoa, March–July 2023

Characteristic	No. (col. %)					
		Age group, yrs				
	Total* N = 86	<1 n = 8	1–6 n = 43	7–12 n = 31	13–17 n = 3	≥18 n = 1
Rash†	**71 (83)**	6 (75)	36 (84)	26 (84)	2 (67)	1 (100)
Rash plus fever†	**45 (52)**	4 (50)	26 (60)	14 (45)	1 (33)	0 (—)
MCC met, all†	**35 (41)**	3 (38)	24 (56)	8 (26)	0 (—)	0 (—)
MCC met, no MMR received§	**4 (5)**	3 (38)	1 (2)	0 (—)	0 (—)	0 (—)
MCC met, ≥1 MMR dose received¶	**31 (36)**	0 (—)	23 (53)	8 (26)	0 (—)	0 (—)
MCC met, ≥2 MMR doses received¶	**18 (21)**	0 (—)	10 (23)	8 (26)	0 (—)	0 (—)

Abbreviations: MCC = measles clinical criteria; MMR = measles, mumps, and rubella vaccine.

* During March 23–July 25, 2023, a total of 86 persons were investigated for measles. One child who was evaluated twice with different symptoms during this period was included based on symptoms reported at the first clinical encounter.

† Council of State and Territorial Epidemiologists measles clinical criteria included rash and fever and at least one of the following: coryza, cough, or conjunctivitis (https://ndc.services.cdc.gov/case-definitions/measles-2013/). Three patients did not have electronic medical record notes, and information regarding cough was missing. Fever included subjective reports from parents and patients as well as measured temperatures during the health care encounter. Characteristics of rash and sequence of symptom occurrence was variable (i.e., some rashes were described as pruritic, or distribution of rash was not consistently described as generalized with spread from face down to the rest of the body).

§ No MMR vaccine dose was documented, or MMR vaccine was documented as having been given on or after April 25, 2023, after declaration of the public health emergency on April 24, 2023.

¶ MMR vaccine doses were included if administered on or before April 24, 2023. Doses administered to children aged <12 months were included.

Public Health Response

The public health emergency ended on June 8, 2023. To improve communication between response team members in American Samoa, including laboratorians, clinicians, and epidemiologists, a table-top exercise was facilitated. Continuing medical education lectures were offered to clinicians to review measles diagnostic criteria and appropriate testing. Initial efforts to create a measles response manual and an improved case-based surveillance system are ongoing. Establishment of a syndromic surveillance system at ASDoH, including data from the Lyndon B. Johnson Tropical Medical Center, the only hospital on the island, and other health care facilities in the region, were already in development before this investigation and continued opportunities were explored through the National Syndromic Surveillance Program. Efforts to support laboratory capacity building were also explored and ongoing at ASDoH. These efforts include providing a measles serological IgM capture enzyme-linked immunosorbent assay to increase assay specificity, laboratory training and test validation panels, and continued assistance to bring molecular testing online.

Discussion

The receipt of two positive measles IgM test results by fully vaccinated children with rash illnesses whose clinical signs and symptoms did not meet the CSTE clinical case definition for measles resulted in declaration of a public health emergency in American Samoa. A widespread measles outbreak with high morbidity and mortality on a neighboring island 4 years earlier, coupled with suboptimal measles vaccination coverage and recent large public gatherings, raised concern about the possibility of a large outbreak and prompted these public health actions.

In a person who has not received measles vaccine, signs and symptoms of disease are typically 3–5 days of fever along with cough, coryza, or conjunctivitis, followed by a generalized, descending, maculopapular rash. The differential diagnosis includes Fifth Disease (caused by parvovirus B19), hand-foot-and-mouth disease (most commonly caused by coxsackievirus, an enterovirus), roseola or exanthem subitum (caused by

TABLE 2. Laboratory test results of persons under investigation for measles during public health response, by age group — American Samoa, March–July 2023

Laboratory test	No. of positive test results/Total no. (%), by age group, yrs					
	<1	1–6	7–12	13–17	≥18	All
Measles real-time RT-PCR*	0/7 (—)	1/28 (4)	0/25 (—)	0/1 (—)	0/1 (—)	**1/62 (2)**
Measles virus genotype A, RT-qPCR (MEVA)†	—§	1/1 (100)	—	—	—	**1/1 (100)**
CDC measles IgM¶	0/1 (—)	3/18 (17)	1/20 (5)	0/2 (—)	0/1 (—)	**4/42 (10)**
CDC measles IgG¶	0/1 (—)	16/18 (89)	20/20 (100)	2/2 (100)	1/1 (100)	**39/42 (93)**
CDC rubella IgM¶	0/1 (—)	3/18 (17)	2/20 (10)	0/2 (—)	0/1 (—)	**5/42 (12)**
CDC rubella IgG¶	0/1 (—)	17/18 (94)	19/20 (95)	2/2 (100)	1/1 (100)	**39/42 (93)**
Enterovirus and parechrovirus real-time RT-PCR**	4/6 (67)	3/15 (20)	3/15 (20)	—	0/1 (—)	**10/37 (27)**
Deidentified specimen testing††						
Virus testing total§§ (any virus)	NA	NA	NA	NA	NA	**32/37 (87)**
Codetection	NA	NA	NA	NA	NA	**14/32 (44)**
Human parvovirus B19¶¶	NA	NA	NA	NA	NA	**19/36 (53)**
Rhinovirus	NA	NA	NA	NA	NA	**12/37 (32)**
Influenza¶¶	NA	NA	NA	NA	NA	**5/33 (15)**
HHV-6	NA	NA	NA	NA	NA	**5/33 (15)**
HHV-7	NA	NA	NA	NA	NA	**3/33 (9)**
SARS-CoV-2	NA	NA	NA	NA	NA	**2/33 (6)**
RSV	NA	NA	NA	NA	NA	**1/33 (3)**

Abbreviations: CLIA = Clinical Laboratory Improvement Amendments; IgG = immunoglobulin G; IgM = immunoglobulin M; HHV-6 = human herpesvirus 6, HHV-7= human herpesvirus 7; MeVA = measles virus genotype A; NA = not applicable; PCR = polymerase chain reaction; PUI = person under investigation; RSV = respiratory syncytial virus; RT-PCR = reverse transcription–polymerase chain reaction.

* One child aged 7–12 years was evaluated twice, and two specimens were collected. Specimens were not collected for all PUIs. As a result, test results are not available for one PUI aged <1 year, 15 aged 1–6 years, seven aged 7–12 years, and two aged 13–17 years.

† Measles vaccine strain was detected in the only positive measles real-time RT-PCR specimen from a PUI vaccinated against measles 11 days before specimen collection.

§ Dashes indicate that there were no specimens tested in that age range.

¶ Specimens that were positive for both IgM and IgG for measles or rubella were further evaluated with measles and rubella IgG avidity and measles plaque reduction neutralization testing.

** Positive enterovirus and parechrovirus RT-PCR specimens were further evaluated, and all were determined to be rhinovirus types.

†† Specimens were deidentified before non-CLIA testing, and results cannot be age stratified.

§§ Summary of viruses that were identified from enterovirus and parechrovirus typing, pan-herpesvirus PCR, pan-erythrovirus PCR, and next generation sequencing including pan-viral enrichment and metagenomics sequencing methods. Multiple viruses were detected in 14 specimens.

¶¶ One specimen was depleted after enterovirus and parechrovirus typing, and three specimens were depleted after pan-erythrovirus PCR testing.

human herpesvirus 6), human herpesvirus 7, rubella and other viral exanthems.

CDC recommends that health care providers collect NP or throat swabs for molecular and peripheral blood for serologic testing for all suspected cases of measles (i.e., cases of febrile rash illness).†† Serologic assays are important for ascertaining immunity to measles as well identification of actual cases, including those that occur in vaccinated persons (*4,5*). However, as countries achieve or approach elimination status, the positive predictive value of IgM testing for measles (i.e., the likelihood that a positive test indicates the presence of disease) decreases in low incidence settings and increases the risk for false-positive results (*6*). In addition, sensitivity and specificity of measles IgM assays can vary because of cross-reactivity to pathogens associated with common childhood viral exanthems, with parvovirus B19 particularly implicated in some assays,§§ thereby creating the potential for false-positive results in areas with high measles vaccination coverage and low disease incidence (*7*).

Some persons experience signs and symptoms associated with measles, including rash, after measles vaccination, and RT-PCR as well as IgM and IgG and serologic testing cannot distinguish vaccine-associated rash from measles illness; measles vaccine strain viral RNA has been detected months after vaccination (*8*). CDC's MeVA testing can distinguish vaccine-associated rash illness from infection with wild measles virus because it detects only measles vaccines strains. In a suspected outbreak setting, MeVA testing can distinguish vaccine reactions from actual measles cases even as vaccination campaigns are ongoing (*9*).

In some cases, additional serologic assays can also be used to further classify cases. For example, IgG avidity assays can be performed on IgG-positive specimens to aid in distinguishing recent immunity (resulting in low avidity) from immunity that developed in the past (resulting in high avidity). PRN is considered the benchmark serologic assay to determine the presence of measles neutralizing antibodies (*10*).

Specimens from the initial PUIs in this investigation were unavailable for further laboratory testing. Clinical and

†† https://www.cdc.gov/measles/hcp/clinical-overview/?CDC_AAref_Val=https://www.cdc.gov/measles/hcp/index.html

§§ In addition, cross reactivity with another similar virus or rheumatoid factor can cause false-positive IgM test results.

Summary

What is already known about this topic?

In settings with low measles prevalence, measles immunoglobulin (Ig) M antibody testing results have low positive predictive value and can result in difficulties with interpreting results.

What is added by this report?

In 2023, the occurrence of positive measles IgM test results for two vaccinated children in American Samoa led to suspicion of a measles outbreak and resulted in declaration of a public health emergency and a mass vaccination campaign to improve coverage. Additional testing from these two children was not possible. Review of medical records and additional laboratory testing of subsequent persons under investigation confirmed alternative viral etiologies.

What are the implications for public health practice?

Confirmation of measles cases relies on a combination of clinical, serologic and molecular laboratory, and vaccination data. High measles vaccination coverage can prevent outbreaks.

laboratory findings, including reference test findings from 84 other PUIs, suggest that rash illnesses might have been caused by other viral pathogens, including parvovirus B-19, which can cross-react with measles IgM testing. As countries approach measles elimination, enhancing local capacity for molecular and serologic diagnostic testing is critical to rapidly discriminating between actual measles cases, vaccine-associated rash illness, and cases in previously vaccinated persons so that recommended public health measures can be implemented.

After this investigation, improvements at ASDoH in partnership with the Lyndon B. Johnson Tropical Medical Center in case-based and syndromic surveillance and laboratory serologic and molecular capacity are in progress in American Samoa. These efforts will support future public health outbreak response efforts for measles and might serve as a model for other Pacific Islands. Physicians should be cautious about ordering and interpreting measles IgM testing when a patient's clinical features do not meet the CSTE measles case definition, especially in settings where measles prevalence is low, patients have documentation of measles immunity, and there is no history of recent international travel. In settings of low vaccination coverage, physicians and public health authorities should take appropriate infection control and mitigation measures while awaiting confirmatory test results. Achieving and maintaining high coverage with measles-containing vaccine through routine vaccination programs is critical to preventing measles outbreaks and achieving measles elimination.

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Acknowledgments

Saipale Fuimaono, Elisapeta Ponausuia, Faiese Roby, Aigaeiva Sesega, Margaret Sesepasara, Jacqueline Solaita, Osania Tausaga, American Samoa Department of Health; Raydel Anderson, Kevin R. Clarke, Silvia D. Dimitrova, LiJuan Hao, Michael H. Kinzer, Hannah L. Kirking, Lakshmi Malapati, Claire M. Midgley, M. Steven Oberste, Edward Ramos, CDC; Ana Jane M. Bontia, Amor Gonzales, Akapusi Ledua, Lyndon B. Johnson Tropical Medical Center, American Samoa; Roger Evans, Varja Grabovac, Shafiqul Hossain, World Health Organization.

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All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Annette Fa'alevao Ilimaleota reports travel support from the Pacific Island Health Officers Association and the World Health Organization and an uncompensated leadership role in the U.S.-Affiliated Pacific Islands Serology Technicians Program Collaboration and Service Integration as the Coordinator for American Samoa. No other potential conflicts of interest were disclosed.

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Progress Toward Measles Elimination — Worldwide, 2000–2023

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Abstract

Measles vaccination effectively prevents measles, a highly contagious disease that can cause severe complications and death and requires high population immunity to interrupt transmission. This report describes measles elimination progress during 2000–2023. During 2000–2023, an estimated 60.3 million measles deaths were averted by vaccination. However, despite commitment from all six World Health Organization regions to eliminate measles, no region has successfully achieved and maintained measles elimination as of the end of 2023. During the COVID-19 pandemic, estimated global coverage with the first dose of measles-containing vaccine (MCV1) declined to 81%, the lowest level since 2008. MCV1 coverage improved to 83% in 2022 but was unchanged in 2023. From 2022 to 2023, estimated measles cases increased 20% worldwide, from 8,645,000 to 10,341,000; the number of countries experiencing large or disruptive outbreaks increased from 36 to 57. Estimated measles deaths decreased 8%, from 116,800 in 2022 to 107,500 in 2023, primarily because an increased number of cases occurred in countries with lower risk for death. The stagnation in MCV1 coverage means millions of children remain unprotected, leading to increases in cases and outbreaks. Coverage with measles-containing vaccine (MCV) is lower, and measles incidence is higher, in low-income countries and countries experiencing fragile, conflict-affected, and vulnerable settings, which exacerbate inequities. Urgent and targeted efforts are needed to ensure that all children receive 2 MCV doses and that surveillance is strengthened to hasten progress toward measles elimination.

Introduction

Measles is a highly contagious disease that can cause severe complications and death (*1*). Measles vaccination is highly effective at preventing measles and, during the past 50 years, has saved an estimated 94 million lives (*2*). Although all countries in the six World Health Organization (WHO) regions have committed to eliminating measles,* no region has both achieved and sustained measles elimination as of the end of 2023. The Immunization Agenda 2030 (IA2030) includes measles elimination as a core indicator of impact of immunization programs, highlighting the importance of rigorous measles surveillance systems to identify immunity gaps and achieving equitable 95% coverage with 2 timely doses of measles-containing vaccine (MCV) to close these gaps (*3*). Measles infections act as a tracer of the health system's capacity to deliver essential vaccines during childhood. This report updates a previous report (*4*) and describes progress toward measles elimination during 2000–2023.

Methods

Immunization and Surveillance Data Collection and Analysis

Each year, countries report data on vaccinations delivered through routine immunization services, supplementary immunization activities (SIAs),† and outbreak response activities to WHO and UNICEF through the Joint Reporting Form (JRF). WHO and UNICEF estimate coverage with first and second MCV doses (MCV1 and MCV2, respectively) delivered through routine immunization services§ for all countries. Countries report the number of annual incident measles

* Measles elimination is defined as the absence of endemic measles virus transmission in a region or other defined geographic area for ≥12 months in the presence of a high-quality surveillance system that meets the targets of key performance indicators. Independent regional commissions verify a country's elimination status.

† Measles SIAs are generally conducted using two target age ranges: 1) an initial catch-up SIA targets children aged 9 months–14 years, with the aim of eliminating susceptibility to measles in the general population, and 2) periodic follow-up SIAs are conducted nationwide every 2–4 years and target all children aged 9–59 months to eliminate any measles susceptibility that has accumulated in recent birth cohorts because of low MCV coverage and to protect the estimated 2%–5% of children who did not respond to MCV1. Countries can provide additional data to WHO, and data are updated retrospectively. https://immunizationdata.who.int/ (Accessed August 29, 2024).

§ Calculated for MCV1, among children aged 1 year or, if MCV1 is given at age ≥1 year, among children aged 24 months. Calculated for MCV2 among children at the recommended age for the administration of MCV2, according to the national immunization schedule. Estimates are generated using annual administrative coverage data (the number of vaccine doses administered divided by the estimated target population), national coverage estimates, and vaccination coverage surveys. https://www.who.int/teams/immunization-vaccines-and-biologicals/immunization-analysis-and-insights/global-monitoring/immunization-coverage/who-unicef-estimates-of-national-immunization-coverage; https://immunizationdata.who.int/ (Accessed July 19, 2024).

¶ A discarded measles case is defined as a suspected case that has been investigated and determined to be neither measles nor rubella by using either 1) laboratory testing in a proficient laboratory or 2) epidemiologic linkage to a laboratory-confirmed outbreak of a communicable disease that is not measles or rubella. The discarded case rate is a measure of the sensitivity of measles surveillance; the target is two or more discarded cases per 100,000 population. https://immunizationdata.who.int/ (Accessed July 23, 2024).

cases through JRF and monthly discarded cases[¶] to WHO. Vaccination coverage, reported measles incidence,[**] and discarded case rates are calculated using population estimates from the 2024 United Nations Population Division update.[††] Countries' vaccination and reported case data are categorized by income group[§§]; presence of fragile, conflict-affected, and vulnerable (FCV) settings[¶¶]; and presence of large or disruptive outbreaks (20 or more cases per 1 million population over 12 months). Laboratory data are generated by the Global Measles and Rubella Laboratory Network (GMRLN), which consists of 762 laboratories supporting measles and rubella surveillance by confirming cases through quality-controlled laboratory testing and performing genotyping of circulating measles viruses (*5*).

Modeling Estimates

Because routine surveillance data typically underestimate measles cases, measles cases and deaths were estimated using a previously described model updated with 2023 measles and United Nations population estimates[***] (*6*). Data on case fatality rates from a publicly available statistical package (measlesCFR)[†††] were used in the model to calculate estimates of measles mortality based on previously published methodology (*7*). These activities were reviewed by CDC, deemed not research, and were conducted consistent with applicable federal law and CDC policy.[§§§]

Results

Immunization Activities

During 2000–2019, estimated MCV1 coverage increased worldwide from 71% to 86%, then declined to 81% in 2021 during the COVID-19 pandemic, increased to 83% in 2022, and remained unchanged in 2023 (Table 1). Coverage in all regions declined during 2019–2021 and only increased during 2022–2023 in the African Region (AFR), Region of the Americas (AMR), and European Region (EUR). No region regained its 2019 MCV1 coverage levels. In 2023, MCV1 coverage was 64% in low-income countries, 86% in middle-income countries, and 94% in high-income countries; it was 67% and 89% in countries with and without FCV settings, respectively (Supplementary Table 1, https://stacks.cdc.gov/view/cdc/168892). During 2023, MCV1 coverage in the 104 countries affected by at least one large or disruptive measles outbreak during 2019–2023 was 80% compared with 91% in nonaffected countries.

In 2023, 22.2 million children did not receive MCV1 through routine immunization services, an increase of 472,000 (2%) compared with 2022, but a 2.1 million (9%) decrease compared with 2021. The 10 countries with the highest number of infants who did not receive MCV1 were in AFR (four countries), Eastern Mediterranean Region (EMR) (four), and South-East Asia Region (SEAR) (two), representing 57% of all children worldwide who did not receive MCV1.

During 2000–2019, estimated MCV2 coverage increased from 17% to 71%, primarily owing to MCV2 introductions. However, the increase in MCV2 coverage stalled during 2020–2021 amid the COVID-19 pandemic, then increased to 73% in 2022 and 74% in 2023. The number of countries offering MCV2 increased by 101%, from 95 (49%) of 194 countries in 2000 to 190 (98%) in 2023, including two additions in 2023. Approximately 112 million persons received MCV through SIAs in 37 countries in 2023, and another 9.4 million during measles outbreak response activities in 14 countries.

Surveillance Performance and Reported Measles Incidence

Among the 149 (77%) countries reporting discarded cases in 2023, the measles surveillance sensitivity indicator target of two or more discarded cases per 100,000 population was achieved by 86 (58%) countries, compared with 74 (51%) of 145 countries in 2022. In 2023, GMRLN received 436,421 specimens for measles testing compared with 274,270 in 2022.

** To calculate incidence, only the countries reporting data are included in the numerator and denominator. Countries do not provide WHO with their reasons for not reporting measles cases. https://immunizationdata.who.int/global/wiise-detail-page/measles-reported-cases-and-incidence (Accessed July 23, 2024).

†† https://population.un.org/wpp/Download/Standard/MostUsed/

§§ https://datahelpdesk.worldbank.org/knowledgebase/articles/906519-world-bank-country-and-lending-groups

¶¶ FCV settings is a broad term describing a range of situations including humanitarian crises, protracted emergencies, and armed conflicts. https://www.who.int/teams/integrated-health-services/quality-of-care/quality-of-care-in-fragile-conflict-affected-and-vulnerable-settings; https://gho.unocha.org/

*** State-space model of unobserved measles incidence during 2000–2023 generated using the following data from all WHO countries: 1) total annual reported measles cases; 2) annual MCV1 coverage from WHO and UNICEF estimates of national immunization coverage (WUENIC); 3) annual MCV2 coverage from WUENIC; 4) annual SIAs, with coverage and age targets (subnational SIAs are discounted by the proportion of the total population targeted); 5) total annual population size; 6) total annual births; and 7) list of all countries and years for which reporting was enhanced.

††† The measlesCFR model (https://github.com/Measles-Case-Fatality-Ratio-Estimation/measlesCFR) fitted the reported case fatality ratios from a systematic review as a function of the following covariates: 1) gross domestic product per capita, 2) HIV prevalence, 3) maternal education, 4) MCV1 coverage, 5) proportion urban, 6) total fertility rate, 7) mortality rate among children aged <5 years, 8) prevalence of vitamin A deficiency, 9) war and terrorism mortality rate, 10) wasting (weight-for-height ≥1 standard deviation below the reference median) prevalence (https://www.healthdata.org/research-analysis/diseases-injuries-risks/factsheets/2021-child-wasting-level-4-risk), and 11) measles incidence. Annual measles incidence for each country and year was based on this fitted state-space model. High-income countries were excluded from this analysis.

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

TABLE 1. Estimates of regional immunization coverage with the first and second doses of measles-containing vaccine administered through routine immunization services, reported measles cases, and reported measles incidence, by World Health Organization region — worldwide, 2000–2023

WHO region/Year (no. of countries in the region)*	Percentage				No. of reported measles cases[¶] (% of total cases)	Measles incidence[¶,**,††]
	MCV1 coverage[†]	Countries with ≥95% MCV1 coverage[§]	MCV2 coverage[†]	Reporting countries with fewer than five measles cases per 1 million population[¶,**]		
Total (all regions)						
2000 (191)	**71**	**28**	**17**	**33**	**853,479 (100.0)**	**144.6**
2016 (194)	**85**	**42**	**67**	**65**	**132,490 (100.0)**	**18.0**
2019 (194)	**86**	**44**	**71**	**44**	**873,373 (100.0)**	**118.8**
2020 (194)	**83**	**30**	**71**	**58**	**159,073 (100.0)**	**21.2**
2021 (194)	**81**	**30**	**71**	**68**	**123,171 (100.0)**	**16.4**
2022 (194)	**83**	**34**	**73**	**61**	**205,173 (100.0)**	**28.0**
2023 (194)	**83**	**35**	**74**	**47**	**663,795 (100.0)**	**91.0**
African						
2000 (46)	53	2	5	6	**520,102 (60.9)**	821.3
2016 (47)	68	15	22	49	**36,269 (27.4)**	35.9
2019 (47)	71	13	33	34	**618,595 (70.8)**	551.8
2020 (47)	69	6	39	30	**115,369 (72.5)**	104.8
2021 (47)	67	4	40	34	**88,789 (72.1)**	80.8
2022 (47)	68	11	44	23	**97,230 (47.4)**	80.5
2023 (47)	70	11	49	13	**424,433 (63.9)**	342.9
Americas						
2000 (35)	93	40	65	89	**1,754 (0.2)**	2.1
2016 (35)	92	46	80	97	**97 (0.1)**	0.1
2019 (35)	87	43	72	89	**21,971 (2.5)**	32.6
2020 (35)	86	20	73	97	**9,996 (6.3)**	9.8
2021 (35)	85	17	77	97	**682 (0.6)**	0.7
2022 (35)	84	17	76	91	**47 (—)**	0.1
2023 (35)	85	14	75	86	**14 (—)**	0
Eastern Mediterranean						
2000 (21)	70	29	27	14	**38,592 (4.5)**	85.8
2016 (21)	81	57	73	57	**6,275 (4.7)**	9.3
2019 (21)	82	48	75	38	**18,458 (2.1)**	26.0
2020 (21)	82	38	75	48	**6,769 (4.3)**	10.1
2021 (21)	80	43	75	52	**26,089 (21.2)**	39.2
2022 (21)	80	52	75	38	**56,401 (27.5)**	80.9
2023 (21)	79	57	73	19	**92,761 (14.0)**	122.8
European						
2000 (52)	91	45	47	38	**37,421 (4.4)**	49.8
2016 (53)	93	49	88	77	**4,440 (3.4)**	5.2
2019 (53)	96	60	92	30	**106,481 (12.2)**	115.0
2020 (53)	94	43	91	74	**10,945 (6.9)**	13.4
2021 (53)	95	47	91	94	**99 (0.1)**	0.1
2022 (53)	94	51	91	92	**852 (0.4)**	0.9
2023 (53)	95	55	91	64	**55,589 (8.4)**	74.7
South-East Asia						
2000 (10)	63	18	3	0	**78,558 (9.2)**	50.3
2016 (11)	89	55	75	27	**27,530 (20.8)**	14.0
2019 (11)	94	64	83	27	**29,389 (3.4)**	14.7
2020 (11)	88	45	80	45	**9,389 (5.9)**	4.8
2021 (11)	87	45	79	55	**6,448 (5.2)**	3.3
2022 (11)	94	45	86	64	**49,201 (24.0)**	23.6
2023 (11)	91	36	85	36	**85,368 (12.9)**	40.7
Western Pacific						
2000 (27)	85	30	2	26	**177,052 (20.7)**	105.6
2016 (27)	96	52	93	48	**57,879 (43.7)**	30.8
2019 (27)	96	59	93	41	**78,479 (9.0)**	40.9
2020 (27)	95	44	93	37	**6,605 (4.2)**	3.4
2021 (27)	92	41	91	56	**1,064 (0.9)**	0.6
2022 (27)	93	44	92	44	**1,442 (0.7)**	0.8
2023 (27)	92	44	90	52	**5,630 (0.9)**	3.1

See table footnotes on the next page.

TABLE 1. (*Continued*) Estimates of regional immunization coverage with the first and second doses of measles-containing vaccine administered through routine immunization services, reported measles cases, and reported measles incidence, by World Health Organization region — worldwide, 2000–2023

Abbreviations: MCV1 = first dose of measles-containing vaccine; MCV2 = second dose of measles-containing vaccine; WHO = World Health Organization.
* All countries that are United Nations members can become members of WHO by accepting its constitution. Other countries can be admitted as members when their application has been approved by a simple majority vote of the World Health Assembly. https://www.who.int/countries
† https://immunizationdata.who.int/ (Accessed July 19, 2024).
§ Denominator is the number of WHO member countries.
¶ https://immunizationdata.who.int/ (Accessed July 23, 2024).
** Population data from United Nations Department of Economic and Social Affairs, Population Division, 2024. Any country not reporting measles cases for that year was removed from the numerator and denominator when calculating incidence.
†† Cases per 1 million population.

During 2023, the number of reported measles cases (663,795) increased 224% compared with cases during 2022 (205,173 cases), corresponding to a 225% increase in incidence from 28 to 91 cases per 1 million population (Table 1). In 2023, measles incidence in low-income countries was 583 per million compared with 37 and 26 per million in middle- and high-income countries, respectively. In 2023, measles incidence in countries with FCV settings was 362 cases per million, more than 10 times that in non-FCV countries (34 per million).

In 2023, large or disruptive measles outbreaks occurred in 57 countries in five WHO regions, an increase of 58% compared with 36 countries in four regions in 2022. Among the 57 outbreaks in 2023, 27 (47%) occurred in countries in AFR, 13 (23%) in EMR, 10 (18%) in EUR, four (7%) in SEAR, and three (5%) in the Western Pacific Region (WPR) (Supplementary Table 2, https://stacks.cdc.gov/view/cdc/168893).

Reported Measles Genotypes

The number of measles genotypes reported by GMRLN has decreased, from nine in 2013 to two since 2021. In 2023, a total of 3,373 sequences from 74 countries were reported, among which 2,503 (74%) were genotype D8, and 870 (26%) were genotype B3; among 1,588 reported sequences from 48 countries in 2022, 848 (53%) were genotype D8, and 740 (47%) were genotype B3.

Measles Cases and Mortality Estimates

On the basis of the updated model, the estimated number of measles cases decreased 72%, from 36,940,000 in 2000 to 10,341,000 in 2023; the estimated annual number of measles deaths decreased 87%, from 800,000 in 2000 to 107,500 in 2023 (Table 2). The estimated number of cases increased by 20%, and deaths decreased by 8% in 2023 compared with an estimated 8,645,000 cases and an estimated 116,800 deaths in 2022. During 2000–2023, compared with no vaccination, measles vaccination prevented an estimated 60.3 million deaths globally (Figure).

Regional Verification of Measles Elimination

By the end of 2023, 82 (42%) countries had been verified to have achieved or maintained measles elimination, but no WHO region had achieved and sustained elimination, and no AFR country had yet been verified to have eliminated measles (Supplementary Table 3, https://stacks.cdc.gov/view/cdc/168894). After AMR achieved verification of measles elimination in 2016, endemic transmission was reestablished in Brazil and Venezuela; elimination was reverified in Venezuela in 2023. In November 2024, Brazil was reverified based on 2023 data, and AMR is once again free from endemic measles.

Discussion

Globally, MCV coverage stagnated during 2022–2023, and no region has regained pre–COVID-19 pandemic MCV1 coverage levels. AFR experienced improvements in MCV1 and MCV2 coverage in 2022–2023; however, the number of unvaccinated children will increase if coverage stagnates and cannot outpace a rapidly growing population. Given worldwide stagnant, suboptimal routine MCV1 coverage, SIAs in selected countries provide opportunities to reach children who missed routine MCV (*8*,*9*).

Measles surveillance performance has shown signs of improvement, with increasing numbers of countries achieving the target discarded case rate and increasing numbers of specimens being submitted to GMRLN for routine testing and sequencing in 2023 compared with other recent years. Improvements in the discarded case rate can be due to improved surveillance performance; however, an increase in testing in outbreak settings also contributes.

From 2022 to 2023, more countries experienced large or disruptive outbreaks, with EUR, EMR, SEAR, and WPR experiencing more large or disruptive outbreaks. The distribution of measles outbreaks across more countries, including countries where children are less likely to die from measles than in AFR countries, which had a similar number of large or disruptive outbreaks during 2022–2023, resulted in a small decrease in estimated global measles deaths in 2023 compared with 2022, despite the increased number of measles cases. Vaccination coverage is lowest, and measles incidence the highest in low-income

TABLE 2. Estimated number of measles cases and deaths,* by World Health Organization region — worldwide, 2000 and 2023

WHO region/Year (no. of countries in the region)†	Estimated no. (95% CI)		Change from 2000 to 2023	
	Measles cases	Measles deaths	% Estimated reduction in measles mortality	Cumulative no. of measles deaths averted by vaccination
Total (all regions)				
2000 (191)	**36,939,956 (26,084,165–51,808,643)**	**800,062 (530,300–1,140,188)**	**87**	**60,322,106**
2023 (194)	**10,341,059 (6,050,433–16,839,675)**	**107,482 (60,910–170,246)**		
African				
2000 (46)	11,475,194 (5,796,070–17,162,334)	361,694 (192,573–536,143)	79	20,959,652
2023 (47)	4,801,946 (2,708,283–7,804,959)	75,942 (42,703–120,893)		
Americas				
2000 (35)	8,770 (4,385–35,080)	3	96	6,217,493
2023 (35)	375 (188–1,500)	1§		
Eastern Mediterranean				
2000 (21)	4,440,048 (2,856,258–8,230,961)	141,059 (98,351–236,713)	89	9,543,661
2023 (21)	1,382,323 (516,020–2,436,395)	15,280 (5,280–28,088)		
European				
2000 (52)	768,811 (485,144–1,447,060)	3,397 (2,310–5,670)	93	1,492,203
2023 (53)	306,375 (141,791–993,945)	222 (89–621)		
South-East Asia				
2000 (10)	14,609,126 (12,106,256–17,667,700)	265,859 (214,349–327,839)	94	17,093,757
2023 (11)	2,905,680 (2,508,418–3,403,522)	14,691 (12,457–17,514)		
Western Pacific				
2000 (27)	5,638,007 (4,836,053–7,265,509)	28,049 (22,715–33,812)	95	5,015,340
2023 (27)	944,360 (175,733–2,199,353)	1,347 (380–3,129)		

Abbreviation: WHO = World Health Organization.

* The measles mortality model used to generate estimated measles cases and deaths is rerun each year using the new and revised annual WHO/UNICEF estimates of national immunization coverage data, as well as updated surveillance data.

† All countries that are United Nations members can become members of WHO by accepting its constitution. Other countries can be admitted as members when their application has been approved by a simple majority vote of the World Health Assembly. https://www.who.int/countries

§ Estimated measles mortality rounded to 1.

countries and in countries affected by FCV settings. These types of inequities hinder measles elimination (*10*).

Limitations

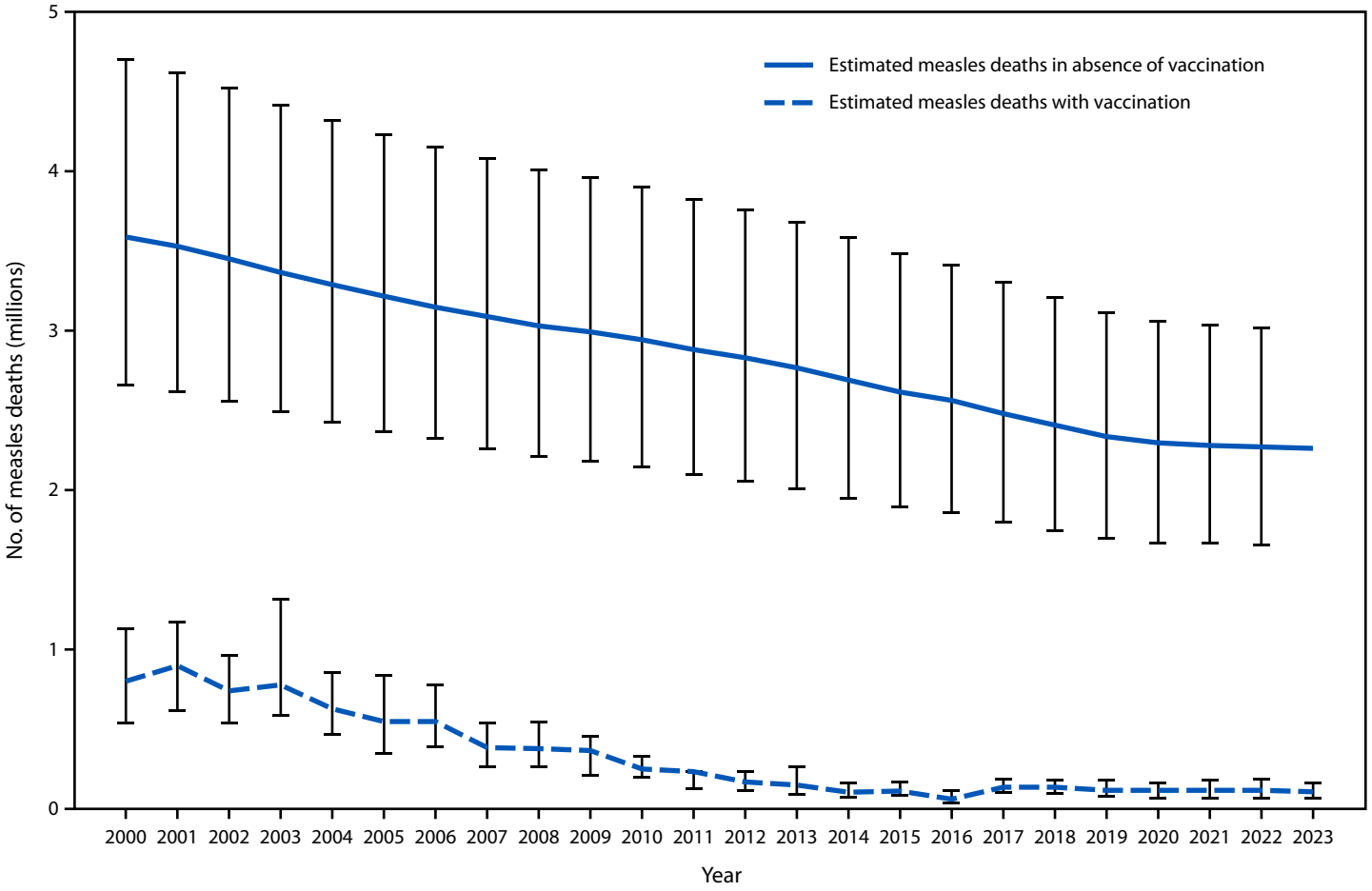
The findings in this report are subject to at least three limitations. First, vaccination coverage and reported cases are subject to variable data quality and potentially inaccurate estimations. Second, not all countries provide adequate SIA and outbreak response data; therefore, reported MCV doses administered might be underestimated. Finally, the modeled estimates are dependent on data input and are updated annually for the current and previous years, which can introduce uncertainty and slight differences over time; however, the estimates are within expectations given the CIs.

Implications for Public Health Practice

The Measles and Rubella Strategic Framework (*1*), aligning with IA2030, outlines strategies countries can use to improve measles surveillance, increase routine immunization to achieve ≥95% coverage with 2 MCV doses, and strengthen outbreak preparedness and response. Activities such as the Big Catch-Up¶¶¶ and follow-up campaigns are designed to help close immunity gaps that developed during the COVID-19 pandemic. During the previous 50 years, vaccination has made

¶¶¶ https://www.who.int/publications/i/item/9789240075511

FIGURE. Estimated number of annual measles deaths with measles vaccination and in the absence of measles vaccination — worldwide, 2000–2023*,†



* With 95% CIs indicated by error bars.
† Deaths prevented by vaccination are estimated by the area between estimated deaths with vaccination and those without vaccination. A cumulative total of 60.3 million deaths were estimated to have been prevented by measles vaccination during 2000–2023.

Summary

What is already known about this topic?

Measles vaccination is effective at preventing measles, a highly contagious disease that can cause severe complications and death and requires high population immunity to interrupt transmission.

What is added by this report?

During 2000–2023, measles vaccination saved an estimated 60 million lives. From 2022 to 2023, coverage with the first dose of measles-containing vaccine (MCV) remained at 83%, estimated measles cases increased 20%, and the number of countries affected by large or disruptive outbreaks increased from 36 to 57. Coverage was lower and measles incidence was higher in low-income countries and countries with fragile, conflict-affected, and vulnerable settings.

What are the implications for public health practice?

Progress toward eliminating measles will require strengthened surveillance and urgent and targeted improvements in coverage to reach all children with 2 MCV doses.

the greatest health intervention contribution to mortality reduction, with measles vaccination contributing the most benefit (*2*). Although estimated measles deaths have decreased substantially over time and AMR has now eliminated measles, an estimated 107,500 persons died globally from this vaccine-preventable disease in 2023. Countries and global partners working together is essential to accelerate efforts to reach and sustain measles elimination.

Acknowledgments

Allison Portnoy, Department of Global Health, Boston University School of Public Health; Alyssa Sbarra, Johns Hopkins Bloomberg School of Public Health; country surveillance and immunization program staff members.

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All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. Matt Ferrari reports institutional support from the World Health Organization, Gavi, the Vaccine Alliance, and the Bill and Melinda Gates Foundation; grants or contracts from Gavi, the Vaccine Alliance, the Bill and Melinda Gates Foundation, and the National Science Foundation; and travel support from the World Health Organization, the Bill and Melinda Gates Foundation, and Imperial College. No other potential conflicts of interest were disclosed.

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ISSN: 0149-2195 (Print)