

## Soft Tick Relapsing Fever — United States, 2012–2021

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### Abstract

Soft tick relapsing fever (STRF) (also known as tickborne relapsing fever) is a rare infection caused by certain *Borrelia* spirochetes and transmitted to humans by soft-bodied *Ornithodoros* ticks. In the United States, acquisition of STRF is commonly associated with exposure to rustic cabins, camping, and caves. Antibiotic treatment is highly effective for STRF, but without timely treatment, STRF can result in severe complications, including death. No nationally standardized case definition for STRF exists; however, the disease is reportable in 12 states. This report summarizes demographic and clinical information for STRF cases reported during 2012–2021 from states where STRF is reportable. During this period, 251 cases were identified in 11 states. The median annual case count was 24. Most patients with STRF (55%) were hospitalized; no fatalities were reported. The geographic distribution and seasonal pattern of STRF have remained relatively constant since the 1990s. Persons should avoid rodent-infested structures and rodent habitats, such as caves, in areas where STRF is endemic. STRF surveillance, prevention, and control efforts would benefit from a standardized case definition and increased awareness of the disease among the public and clinicians.

### Introduction

*Ornithodoros* ticks usually inhabit rodent nests and burrows. They can live for decades, and once infected with relapsing fever, *Borrelia* spp., can transmit the bacteria to humans throughout their lifetime through brief and painless bites that are often not detected. Soft tick relapsing fever (STRF) (also known as tickborne relapsing fever) is caused by infection with various *Borrelia* spp., each transmitted by a specific *Ornithodoros* species. STRF is endemic in certain areas in Africa, Asia, Europe, and the Americas. In the United States,

two *Borrelia* species, *Borrelia hermsii* and *Borrelia turicatae*, have been confirmed to cause STRF in humans. *B. hermsii*, spread by *Ornithodoros hermsi* ticks, is found in mountainous areas of western states at moderate to high elevations and is commonly associated with rustic, rodent-infested cabins. *B. turicatae*, spread by *Ornithodoros turicata*, is found in the south-central United States and is often associated with caves.

The clinical syndrome of STRF in humans includes high fever, which can be accompanied by headache, nausea, myalgias, and arthralgias. The initial illness typically lasts

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approximately 3 days; if untreated, febrile episodes can recur every 7–10 days for two or more cycles, because of the spirochetes' unique ability to repeatedly evade a host's immune system (1). Prompt treatment is important to prevent complications; effective antibiotics include doxycycline, beta-lactam antibiotics (e.g., penicillin or ceftriaxone), and azithromycin (2). Rare complications of STRF include neurologic and ocular disease, myocarditis, and acute respiratory distress syndrome (3). Infection during pregnancy can result in pregnancy loss, transplacental transmission, and neonatal death (4–6).

## Methods

In 2021, STRF was reportable in 12 states: Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Texas, Utah, Washington, and Wyoming.\* Seven of these states used a case definition during 2012–2021; definitions differed among states. This summary describes cases that were classified as confirmed, probable, or suspected,† as well as unclassified cases that met specific criteria.§ Trends in annual case counts were assessed using linear regression. This

\*STRF was not consistently reportable in all 12 states during 2012–2021. In Texas, STRF was removed from the reportable diseases list in 2016 and added back in 2021. In Wyoming, relapsing fevers became reportable in 2012.

† Cases were classified as confirmed, probable, or suspected according to each jurisdiction's case definition.

activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.¶

## Results

During 2012–2021, 251 cases were identified in 11 states. A median of 24 cases were reported from these states per year (range = 15 [2020] to 41 [2014]). No significant change in the number of cases was observed during this period ( $p = 0.21$ ). The median age of infected persons was 39 years (range = 2–92 years); 60% were male (Table 1). No infected persons were reported to be pregnant. Race and ethnicity data were available for 190 (76%) persons; among these, 93% were non-Hispanic White persons.

Reported case counts varied by state, with four states accounting for >75% of all cases (California [33%], Washington [18%], Colorado [14%], and Oregon [12%]). Other states

§ Unclassified cases from states that did not have a case definition in use were reviewed individually. These were included in this case summary if they had laboratory evidence of infection (defined as spirochetes detected on blood smear, relapsing fever *Borrelia* DNA detected by polymerase chain reaction, positive serologic testing for relapsing fever, or isolation of relapsing fever *Borrelia* spirochetes in culture) or if they had a clinical syndrome compatible with relapsing fever together with either exposure to soft tick habitat within 2–18 days of symptom onset or an epidemiologic link to a case with laboratory evidence of infection.

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

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**TABLE 1. Characteristics of patients with soft tick relapsing fever reported in U.S. states — United States, 2012–2021**

Characteristic	No. of cases (%)	No. of patients hospitalized/ No. with available hospitalization data (%)
<b>Total</b>	<b>251 (100)</b>	<b>115/211 (55)</b>
<b>Sex</b>		
Female	99 (39)	52/87 (60)
Male	151 (60)	63/123 (51)
Other or unknown	1 (<1)	0/1 (—)
<b>Age group, yrs</b>		
≤12	40 (16)	16/36 (44)
13–18	21 (8)	7/11 (64)
19–64	152 (61)	72/134 (54)
≥65	37 (15)	20/30 (67)
<b>Suspected exposure location</b>		
Texas*	12 (5)	6/12 (50)
Western United States†	217 (93)	104/187 (56)
International	4 (2)	2/2 (100)

\* The suspected etiology of soft tick relapsing fever for most patients with exposure in Texas is *Borrelia turicatae* based on known pathogen distribution.

† Includes Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, and Washington.

with reported cases included Arizona (9%), Texas (5%), Idaho (4%), Utah (3%), Montana (1%), Nevada (1%), and New Mexico (<1%). Among the 12 states with mandated reporting, no cases were reported in Wyoming. Among 232 (92%) cases with available data on state of residence and exposure, 33 (14%) occurred in out-of-state visitors; among the 210 (84%) cases for which county of the patient's exposure was available (Figure), 118 (56%) occurred in out-of-county visitors. Epidemiologic links to other cases were documented in 21% of cases; the largest outbreak (11 cases) occurred in Arizona in 2014 (7). Four (2%) cases were attributed to exposures occurring during international travel to Argentina, Canada, Jordan, and Tanzania.

Among 11 reported STRF cases with patient exposures in counties of lower elevations in central Texas, where infections are more likely to be caused by *B. turicatae*, cave exposures were documented in four. Among 217 cases with patient exposures in other western U.S. states, where infections are more likely to be caused by *B. hermsii*, a summer peak was observed, with 154 (71%) cases occurring during June–September. Notable exposures documented among 177 patients in these western states included visits to cabins (131, 74%) and camping (15, 8%).

Some clinical data were provided for 207 (82%) patients with reported STRF (Table 2). Fever was documented in 97% of cases; a median of two distinct febrile episodes (range = 1–9)\*\* was reported among febrile patients. Other commonly reported signs and symptoms included headache (63%), myalgias (59%), chills (54%), and nausea or vomiting (45%). Among

\*\* Relapses were defined as occurrences of fever separated by ≥3 days, although information on timing of fevers was incomplete for some patients.

## Summary

### What is already known about this topic?

Soft tick relapsing fever (STRF) is a rare but serious bacterial disease spread by *Ornithodoros* ticks. In the United States, acquisition of STRF is associated with rustic cabins, camping, and caves.

### What is added by this report?

During 2012–2021, a total of 251 STRF cases were identified in 11 of 12 states where infection is reportable; 55% of patients were hospitalized, and no deaths occurred. The geographic distribution and seasonal pattern of STRF have remained relatively constant since the 1990s.

### What are the implications for public health practice?

Persons should avoid rodent-infested structures and rodent habitats, such as caves, in areas where STRF is endemic. Improvements in surveillance, prevention, and diagnosis are needed to prevent STRF-associated morbidity and mortality.

211 patients for whom hospitalization data were available, 115 (55%) were hospitalized, including 44% of 36 children aged ≤12 years and 67% of 30 adults aged ≥65 years (Table 1). No deaths were reported.

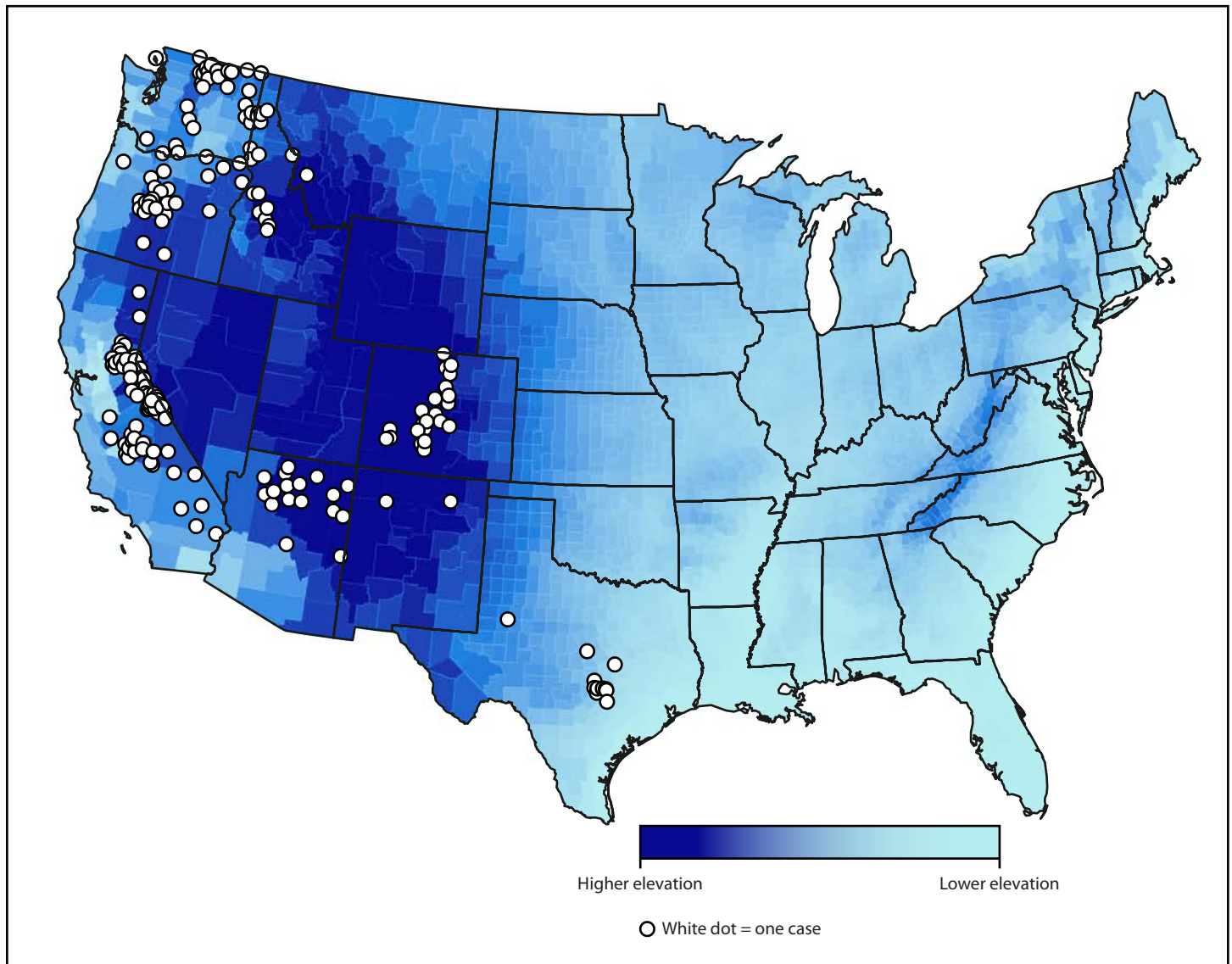
Laboratory test data were available for 221 (88%) patients; among these, spirochetes were identified by microscopy of peripheral blood smear in 130 (59%). In addition, relapsing fever *Borrelia* antibodies were detected by serologic testing in 91 (41%) patients, and relapsing fever *Borrelia* DNA was detected by polymerase chain reaction (PCR) testing in 33 (15%).<sup>††</sup> Relapsing fever spirochetes were cultured in four (2%) cases.

## Discussion

The geographic distribution and seasonal pattern of reported STRF have remained relatively constant since the 1990s (8). During 1990–2011, the median annual case count (20) (8) was slightly lower than that during 2012–2021 (24); however, the increase from 1990 to 2021 was not statistically significant ( $p = 0.84$ ). A large proportion of cases continue to occur in nonresident visitors to areas where the disease is endemic (such as vacationers to mountain cabins); cases in returned visitors who live in areas where STRF is not endemic or reportable would be more likely to be missed by clinicians and public health authorities. Though molecular diagnostic testing has become increasingly available in recent years, microscopic examination of peripheral blood smears remains an important diagnostic test; microscopy is most sensitive when performed

<sup>††</sup> Information on *Borrelia* species was not available, because most laboratory tests do not reliably distinguish between relapsing fever group *Borreliae* (e.g., between *B. hermsii* and *B. turicatae*).

FIGURE. Cases\* of soft tick relapsing fever (n = 210),† by county§ of exposure — United States, 2012–2021



\* The figure does not show exact location of cases because they were arbitrarily placed within the county of exposure.

† Data on county of exposure was not available for all 251 cases included in this report.

§ Mean elevation shown per county.

during febrile episodes because fever is associated with coincident high levels of spirochetemia.

### Limitations

The findings in this report are subject to at least four limitations. First, surveillance for STRF is likely hindered by underrecognition and underdiagnosis; some state health departments have also noted misdiagnosis of STRF as Lyme disease, given that antibodies to STRF-causing *Borrelia* spp. can cross-react with some serologic assays for Lyme disease. The emergence of hard tick relapsing fever (HTRF) caused by *Borrelia miyamotoi* has further complicated accurate diagnosis, particularly

in states where both STRF and HTRF might occur, because most serologic and PCR assays do not distinguish between these (9). Second, case ascertainment by state health departments is likely limited by underreporting, because states rely primarily on provider reporting.<sup>§§</sup> Third, case ascertainment is inconsistent across states because of differing or absent case definitions. STRF might also occur in states where it is not currently reportable; a very small number of cases have historically been reported from Oklahoma, Kansas, Ohio, and

<sup>§§</sup> Approximately one third of cases included in this summary (35%) were reported to state health departments through laboratory reporting compared with 58% reported by providers, and this proportion did not change over the 10-year period.

**TABLE 2. Documented signs and symptoms in patients with soft tick relapsing fever (n = 207) — United States, 2012–2021**

Sign or symptom	No. (%) <sup>*</sup> of patients
Fever (at least one episode)	201 (97)
Headache	130 (63)
Myalgias	123 (59)
Chills	112 (54)
Nausea/Vomiting	94 (45)
Sweats	65 (31)
Fatigue/Malaise	65 (31)
Anorexia	63 (30)
Arthralgias	43 (21)
Cough	28 (13)
Altered mental status	24 (12)
Thrombocytopenia	21 (10)
Rash	20 (10)
Photophobia	14 (7)
Neurologic or ocular symptoms <sup>†</sup>	10 (5)
Abdominal pain	9 (4)

\* Among persons with available clinical data; patients could have multiple signs or symptoms.

† Reported neurologic or ocular symptoms included uveitis, Bell's palsy, blurred vision, eye pain, and eye swelling.

the U.S. Virgin Islands (10). For these reasons, reported cases likely underestimate the true case count. Finally, information on clinical features and exposures was limited to what was obtained by health departments; these data are not collected in all case investigations.

### Implications for Public Health Practice

STRF often occurs in clusters because of common exposures; inhabitants and visitors to a soft tick–infested structure can become infected over multiple decades. Unrecognized or unreported cases are missed opportunities for intervention to prevent future exposures. To reduce STRF incidence in the United States, progress in surveillance, prevention, and disease recognition is needed. A regional standardized case definition has been developed by vectorborne disease epidemiologists in several states with endemic disease; broader adoption of this case definition would enhance STRF surveillance. In addition, residents and visitors to areas where STRF is endemic should be educated about how to prevent soft tick bites (most importantly, avoidance of rodent-infested structures and rodent habitats such as caves) and when to seek medical care. Owners of tick- or rodent-infested cabins should be made aware of recommendations for remediation of these structures.<sup>¶¶</sup> Clinicians should be aware of the clinical syndrome accompanying STRF, associated exposures, options for diagnostic testing, and

<sup>¶¶</sup> <https://www.cdc.gov/relapsing-fever/prevention/index.html#:~:text=%20=%20>

public health reporting requirements. Increased awareness of and access to molecular diagnostic testing for symptomatic patients with suspected STRF might improve recognition of cases at different stages of illness. Coordinated improvements in surveillance, prevention, and diagnosis have the potential to prevent morbidity and mortality from STRF in the United States in the next decade.

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### References

- Barbour A. Relapsing fever [Chapter 16]. In: Goodman J, Dennis D, Sonenshine D, eds. Tick-borne diseases of humans. Washington, DC: ASM Press; 2005: 268–91.
- CDC. Tickborne diseases of the United States. Tickborne relapsing fever (TBRF). Washington, DC: US Department of Health and Human Services, CDC; 2022. <https://www.cdc.gov/ticks/tickbornediseases/tbrf.html>
- CDC. Acute respiratory distress syndrome in persons with tickborne relapsing fever—three states, 2004–2005. MMWR Morb Mortal Wkly Rep 2007;56:1073–6. PMID:17947965
- Melkert PW. Relapsing fever in pregnancy: analysis of high-risk factors. Br J Obstet Gynaecol 1988;95:1070–2. PMID:3191046 <https://doi.org/10.1111/j.1471-0528.1988.tb06516.x>
- Fuchs PC, Oyama AA. Neonatal relapsing fever due to transplacental transmission of Borrelia. JAMA 1969;208:690–2. PMID:5818572 <https://doi.org/10.1001/jama.1969.03160040098019>
- CDC. Tickborne relapsing fever in a mother and newborn child—Colorado, 2011. MMWR Morb Mortal Wkly Rep 2012;61:174–6. PMID:22419050
- Jones JM, Schumacher M, Peoples M, et al. Notes from the field: tickborne relapsing fever outbreak at an outdoor education camp—Arizona, 2014. MMWR Morb Mortal Wkly Rep 2015;64:651–2. PMID:26086637
- Forrester JD, Kjemtrup AM, Fritz CL, et al. Tickborne relapsing fever—United States, 1990–2011. MMWR Morb Mortal Wkly Rep 2015;64:58–60. PMID:25632952
- Rubio LA, Kjemtrup AM, Marx GE, et al. *Borrelia miyamotoi* infection in immunocompromised man, California, USA, 2021. Emerg Infect Dis 2023;29:1011–4. PMID:37081591 <https://doi.org/10.3201/eid2905.221638>
- Dworkin MS, Schwan TG, Anderson DE Jr, Borchardt SM. Tick-borne relapsing fever. Infect Dis Clin North Am 2008;22:449–68, viii. PMID:18755384 <https://doi.org/10.1016/j.idc.2008.03.006>

# Progress Toward Hepatitis B Control and Elimination of Mother-to-Child Transmission of Hepatitis B Virus — World Health Organization African Region, 2016–2021

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## Abstract

Chronic hepatitis B virus (HBV) infection is one of the leading causes of cirrhosis and liver cancer. In 2019, approximately 1.5 million persons newly acquired chronic HBV infection; among these, 990,000 (66%) were in the World Health Organization (WHO) African Region (AFR). Most chronic HBV infections are acquired through mother-to-child transmission (MTCT) or during early childhood, and approximately two thirds of these infections occur in AFR. In 2016, the World Health Assembly endorsed the goal of elimination of mother-to-child transmission (EMTCT) of HBV, documented by  $\geq 90\%$  coverage with both a timely hepatitis B vaccine (HepB) birth dose (HepB-BD) and 3 infant doses of HepB (HepB3), and  $\leq 0.1\%$  hepatitis B surface antigen (HBsAg) seroprevalence among children aged  $\leq 5$  years. In 2016, the WHO African Regional Committee endorsed targets for a 30% reduction in incidence ( $\leq 2\%$  HBsAg seroprevalence in children aged  $\leq 5$  years) and  $\geq 90\%$  HepB3 coverage by 2020. By 2021, all 47 countries in the region provided HepB3 to infants beginning at age 6 weeks, and 14 countries (30%) provided HepB-BD. By December 2021, 16 (34%) countries achieved  $\geq 90\%$  HepB3 coverage, and only two (4%) achieved  $\geq 90\%$  timely HepB-BD coverage. Eight countries (17%) conducted nationwide serosurveys among children born after the introduction of HepB to assess HBsAg seroprevalence: six countries had achieved  $\leq 2\%$  seroprevalence, but none had achieved  $\leq 0.1\%$  seroprevalence among children. The development of immunization recovery plans following the COVID-19 pandemic provides an opportunity to accelerate progress toward hepatitis B control and EMTCT, including introducing HepB-BD and increasing coverage with timely HepB-BD and HepB3 vaccination. Representative HBsAg serosurveys among children and a regional verification body for EMTCT of HBV will be needed to monitor progress.

## Introduction

In 2019, approximately 1.5 million persons newly acquired chronic hepatitis B virus (HBV) infection; among these, 990,000 (66%) were in the World Health Organization (WHO) African Region (AFR)\* (1). Because most chronic HBV infections are acquired through mother-to-child

transmission (MTCT) or during early childhood (2), WHO recommends that all newborns receive a dose of hepatitis B vaccine (HepB) within 24 hours of birth (hepatitis B vaccine birth dose [HepB-BD]) followed by 2 or 3 doses<sup>†</sup> of HepB during the first year of life (2). In 2016, the World Health Assembly endorsed the goal of eliminating viral hepatitis as a public health threat by 2030, including the elimination of mother-to-child transmission (EMTCT) of HBV, documented by demonstration of  $\geq 90\%$  coverage with both a timely<sup>§</sup> HepB-BD and 3 doses of HepB (HepB3), and  $\leq 0.1\%$  hepatitis B surface antigen (HBsAg)<sup>¶</sup> seroprevalence among children aged  $\leq 5$  years (3). In 2016, the WHO African Regional Committee endorsed two targets for hepatitis B control: 1) 30% reduction in incidence (equating to HBsAg prevalence of  $\leq 2\%$  in children aged  $\leq 5$  years), and 2)  $\geq 90\%$  HepB3 coverage by 2020. In 2021, AFR countries endorsed a call to develop strategies for elimination of MTCT of HBV, including increasing HepB-BD and HepB3 coverage and improving access to antenatal care and quality delivery services (4,5). This report describes progress made during 2016–2021 to achieve hepatitis B control and elimination of MTCT of HBV in AFR.

## Methods

Information on country immunization activities was obtained by review of administrative\*\* or official<sup>††</sup> HepB coverage data reported to WHO and UNICEF that generate annual country vaccination coverage estimates. To identify HBsAg seroprevalence surveys conducted in AFR, a MEDLINE literature review was conducted using the following search criteria (Afro country names), and (“hepatitis B” OR “HBV”) AND (2016/10/01:3000/12/31[Date - Publication]) AND (survey OR serosurvey OR serosurveillance OR seroepidemiology

\* The African Region, one of the six WHO regions, with a population of approximately 1.2 billion persons, includes 47 countries. <https://www.afro.who.int/countries>

<sup>†</sup> Depending on the country's immunization schedule.

<sup>§</sup> Administration of a dose within 24 hours of birth.

<sup>¶</sup> HBsAg seropositivity is an indicator of chronic HBV infection.

\*\* Administrative vaccination coverage data are derived from the country's immunization registry system. The coverage is calculated by dividing the total number of doses administered by the estimated target population for vaccination.

<sup>††</sup> Official vaccination coverage estimates are reported by national authorities based on administrative data, immunization coverage surveys, and reports.

OR prevalence OR seroprevalence). Population-based surveys including the Population based HIV Impact Assessment (PHIA) surveys and Demographic Health Survey (DHS) were also used. This activity was reviewed by CDC and was conducted with applicable federal laws and CDC policy.<sup>§§</sup>

## Results

### Immunization Activities

By 2014, all 47 countries in AFR had introduced HepB3 infant vaccination (Table 1). By December 2021, 14 (30%) countries provided HepB-BD, eight (57%) of which were in the West subregion.<sup>¶¶</sup> Although 10 countries had introduced HepB-BD before 2016, only four (Benin, Côte d'Ivoire, Equatorial Guinea, and Senegal) introduced HepB-BD during 2016–2021. During this period, regional HepB3 coverage ranged from 75% in 2019 to 71% in 2021. Eighteen (38%) countries reached  $\geq 90\%$  HepB3 coverage in 2016; this number peaked at 20 (43%) in 2018; by 2021, the number of countries with  $\geq 90\%$  HepB3 coverage had declined to 16 (34%); nine of these countries were in the East and South subregions. Regional HepB-BD coverage increased from 10% in 2016 to 17% in 2021. During 2016–2021, Algeria and Cabo Verde reached HepB-BD coverage of  $\geq 90\%$ , and Namibia and Senegal achieved  $\geq 50\%$  coverage.

### HBsAg Seroprevalence Surveys

Because most chronic HBV infections (particularly those among young children) are asymptomatic, the impact of hepatitis B vaccination is usually measured by HBsAg seroprevalence among children born after the introduction of HepB, usually those aged  $\leq 5$  years<sup>\*\*\*</sup> (3,6). During 2016–2021, HBsAg seroprevalence surveys among children were conducted at national or regional levels in eight (17%) countries. Among children of various age ranges surveyed in Ethiopia, Mauritania, Rwanda, Sierra Leone, Uganda, and Zambia, HBsAg seroprevalence was  $\leq 2\%$ . Prevalence among

children aged  $\leq 5$  years measured in the Democratic Republic of the Congo, Ethiopia, Mauritania, Nigeria, and Sierra Leone ranged from 0.7% (Mauritania) to 4.5% (Nigeria) (Table 2). No country achieved  $\leq 0.1\%$  HBsAg seroprevalence among children. Modeling studies estimated a HBsAg seroprevalence of 2.5% (95% CI = 1.7–4.0) among children aged  $\leq 5$  years in AFR, accounting for more than two thirds (4.3 million, approximately 69%) of all infected children worldwide (1).

HBsAg seroprevalence among women of reproductive age or pregnant women provides an estimate of the risk for MTCT of HBV. Data from population-based HBsAg surveys among women of reproductive age or from screening of pregnant women available from 11 countries showed HBsAg seroprevalences ranging from 1.2% (Rwanda) to 9.8% (Sierra Leone) (Table 2).

### Elimination of Mother-to-Child Transmission of HBV

By December 2021, although 21 (45%) AFR countries had developed a plan for EMTCT of HIV, syphilis, and HBV, only six countries<sup>†††</sup> reported having implemented the EMTCT guidelines for routine HBsAg testing of pregnant women, provision of antiviral medications to eligible (HBsAg-seropositive) women,<sup>§§§</sup> and administration of HepB-BD to newborns. As of December 2021,  $\geq 90\%$  of pregnant women in 29 (62%) AFR countries had at least one antenatal care visit (Table 3). Data from the most recent nationwide surveys showed that in 37 (79%) countries, approximately one half of women gave birth in health care facilities, and in 23 (49%) countries,  $\geq 80\%$  of women delivered in a health facility (Table 1). To acknowledge progress toward EMTCT of HBV in countries with high endemicity, WHO developed a certification mechanism for the path to elimination of MTCT of HBV, using three tiers (bronze, silver, and gold) indicating increasing levels of progress<sup>¶¶¶</sup> (6). Based on HepB immunization interventions in 2021, Botswana might be eligible for the bronze tier, three countries (Namibia, Sao Tome and Principe, and Senegal) might be eligible for the silver tier, and two countries (Algeria and Cabo Verde) might be eligible for the gold tier certification (Table 1) (Table 3).

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

<sup>¶¶</sup> AFR is organized into three functional subregions: Central subregion (Angola, Burundi, Cameroon, Central African Republic, Chad, Democratic Republic of the Congo, Equatorial Guinea, Gabon, Republic of the Congo, and Sao Tome and Principe); East and South subregion (Botswana, Comoros, Eritrea, Eswatini, Ethiopia, Kenya, Lesotho, Madagascar, Malawi, Mauritius, Mozambique, Namibia, Rwanda, Seychelles, South Africa, South Sudan, Uganda, United Republic of Tanzania, Zambia, and Zimbabwe) and West subregion (Algeria, Benin, Burkina Faso, Cabo Verde, Côte d'Ivoire, The Gambia, Ghana, Guinea, Guinea-Bissau, Liberia, Mali, Mauritania, Niger, Nigeria, Senegal, Sierra Leone, and Togo).

<sup>\*\*\*</sup> HBsAg seroprevalence can be measured among children aged 1 year, 5 years, or 1–5 years, according to existing country surveillance and data collection practices. For regions and countries with a long history of high hepatitis B vaccination coverage and those that already conduct school-based serosurveys, serosurveys might be conducted in children aged  $> 5$  years. <https://www.who.int/publications/i/item/9789240039360>

<sup>†††</sup> Angola, Cabo Verde, Equatorial Guinea, Mozambique, Namibia, and Sao Tome and Principe.

<sup>§§§</sup> Pregnant women who received positive HBsAg test results and had an HBV DNA  $\geq 5.3 \log_{10}$  IU/mL ( $\geq 200,000$  IU/mL) or received a positive HBsAg antigen test result are recommended by WHO to receive antiviral prophylaxis to prevent MTCT of HBV. <https://apps.who.int/iris/bitstream/handle/10665/333391/9789240002708-eng.pdf>

<sup>¶¶¶</sup> Bronze tier: 1)  $\geq 90\%$  HepB3 infant vaccination coverage, and 2) implementation of universal timely HepB-BD policy for  $\geq 2$  years. Silver tier: 1)  $\geq 90\%$  HepB3 infant vaccination coverage, 2)  $\geq 50\%$  universal timely HepB-BD coverage, and 3) availability of antenatal HBsAg testing in the public sector for  $\geq 2$  years. Gold tier: 1)  $\geq 90\%$  HepB3 infant vaccination coverage, 2)  $\geq 90\%$  universal timely HepB-BD coverage, and 3)  $> 30\%$  antenatal HBsAg testing coverage for  $\geq 2$  years. <https://www.who.int/publications/i/item/9789240039360>

**TABLE 1. Year of hepatitis B vaccine introduction, hepatitis B vaccination schedule and estimated coverage\* with the third vaccine dose, a timely administered hepatitis B vaccine birth dose,† and rates of institutional delivery, by country — World Health Organization African Region, 2016–2021**

Region, country	Year of introduction			HepB3 coverage, %						Timely HepB-BD coverage, %						Rates of institutional delivery, % (most recent source and year)
	HepB	HepBD	HepB Schedule	2016	2017	2018	2019	2020	2021	2016	2017	2018	2019	2020	2021	
<b>Central subregion</b>																
Angola	2006	2015	B, 2, 4, 6 mos	55	52	59	53	47	41	NR	NR	NR	NR	NR	NR	45.6 (DHS 2015–2016)
Burundi	2004	—	6, 10, 14 wks	94	91	90	93	93	94	NA	NA	NA	NA	NA	NA	83.9 (DHS 2016–2017)
Cameroon	2005	—	6, 10, 14 wks	75	74	67	67	69	69	NA	NA	NA	NA	NA	NA	67.0 (DHS 2018)
Central African Republic	2003	—	6, 10, 14 wks	42	42	42	42	42	42	NA	NA	NA	NA	NA	NA	58.3 (MICS 2018–2019)
Chad	2003	—	6, 10, 14 wks	41	41	46	50	52	58	NA	NA	NA	NA	NA	NA	27.2 (MICS 2019)
Congo	2003	—	8, 12, 16 wks	71	69	75	79	73	77	NA	NA	NA	NA	NA	NA	91.5 (MICS 2014–2015)
Democratic Republic of the Congo	2003	—	6, 10, 14 wks	70	71	71	73	70	65	NA	NA	NA	NA	NA	NA	81.5 (MICS 2017–2018)
Equatorial Guinea	2003	2018	B, 6, 10, 14 wks, 18 mos	53	53	53	53	53	53	NA	NA	NA	NR	NR	NR	67.3 (DHS 2011)
Gabon	2003	—	6, 10, 14 wks	75	75	70	70	63	75	NA	NA	NA	NA	NA	NA	90.2 (DHS 2012)
Sao Tome and Principe	2003	2010 <sup>§</sup>	B, 6, 10, 14 wks	96	95	95	95	96	97	NA	NA	NA	95	82	69	95.4 (MICS 2019)
<b>East and South subregion</b>																
Botswana	1994	1998	B, 2, 3, 4 mos	95	95	95	95	95	95	NR	NR	NR	NR	NR	NR	99.7 (Other NS 2015)
Comoros	2003	—	6, 10, 14 wks	91	91	91	91	87	85	NA	NA	NA	NA	NA	NA	76.1 (DHS–MICS 2012)
Eritrea	2002	—	6, 10, 14 wks	95	95	95	95	95	95	NA	NA	NA	NA	NA	NA	33.7 (Other NS 2010)
Eswatini	1996	—	6, 10, 14 wks	90	90	90	90	83	77	NA	NA	NA	NA	NA	NA	87.7 (MICS 2014)
Ethiopia	2007	—	6, 10, 14 wks	66	68	68	68	71	65	NA	NA	NA	NA	NA	NA	47.5 (DHS (Mini) 2019)
Kenya	2001	—	6, 10, 14 wks	89	82	92	91	91	91	NA	NA	NA	NA	NA	NA	61.2 (DHS 2014)
Lesotho	2003	—	6, 10, 14 wks	87	87	87	87	87	87	NA	NA	NA	NA	NA	NA	89.4 (MICS 2018)
Madagascar	2002	—	6, 10, 14 wks	68	65	65	68	66	55	NA	NA	NA	NA	NA	NA	38.7 (MICS 2018)
Malawi	2002	—	6, 10, 14 wks	84	88	92	95	90	93	NA	NA	NA	NA	NA	NA	96.7 (MICS 2019–2020)
Mauritius	1996	1996 <sup>§</sup>	R, <sup>¶</sup> 6, 10, 14 wks, 18 mos	72	96	97	97	93	92	NA	NA	NA	NA	NA	NA	98.4 (MoH 2003)
Mozambique	2001	—	6, 10, 14 wks	88	88	88	88	79	61	NA	NA	NA	NA	NA	NA	54.8 (DHS 2011)
Namibia	2009	2014	B, 6, 10, 14 wks	85	88	89	87	93	93	85	81	76	81	86	86	87.4 (DHS 2013)
Rwanda	2002	—	6, 10, 14 wks	98	98	97	98	91	88	NA	NA	NA	NA	NA	NA	93.1 (DHS 2019–2020)
Seychelles	1996	—	3, 4, 5 mos	96	97	99	99	97	94	NA	NA	NA	NA	NA	NA	NR
South Africa	1995	—	6, 10, 14 wks, 18 mos	85	84	82	85	84	86	NA	NA	NA	NA	NA	NA	95.9 (DHS 2016)
South Sudan	2014	—	6, 10, 14 wks	45	47	49	49	49	49	NA	NA	NA	NA	NA	NA	11.5 (SHHS 2010)
Uganda	2002	—	6, 10, 14 wks	93	94	93	93	89	91	NA	NA	NA	NA	NA	NA	73.4 (DHS 2016)
Tanzania	2002	—	6, 10, 14 wks	92	90	89	89	86	81	NA	NA	NA	NA	NA	NA	62.6 (DHS 2015–2016)
Zambia	2005	—	6, 10, 14 wks	95	94	90	88	84	91	NA	NA	NA	NA	NA	NA	83.8 (DHS 2018–2019)
Zimbabwe	1994	—	6, 10, 14 wks	90	89	89	90	86	86	NA	NA	NA	NA	NA	NA	85.5 (MICS 2019)
<b>West subregion</b>																
Algeria	2001	2001	B, 2, 4, 12 mos	91	91	91	91	91	91	99	99	99	99	99	99	98.6 (MICS 2018–2019)
Benin	2002	2020	B, 6, 10, 14 wks	76	76	76	76	72	76	NA	NA	NA	NA	21	71	83.9 (DHS 2017–2018)
Burkina Faso	2006	—	8, 12, 16 wks	91	91	91	91	91	91	NA	NA	NA	NA	NA	NA	82.2 (Other NS 2015)
Cabo Verde	2002	2002	B, 2, 4, 6, 18 mos	96	97	99	97	94	94	96	96	97	96	96	96	97.0 (IDSR 2018)**
Côte d'Ivoire	2003	2019	B, 6, 10, 14 wks	87	83	84	81	75	76	NA	NA	NA	9	62	66	69.8 (MICS 2016)
The Gambia	1995	1999	B, 2, 3, 4 mos	95	92	93	88	86	82	NR	NR	NR	NR	NR	25	83.7 (DHS 2019–2020)
Ghana	2002	—	6, 10, 14 wks	93	99	97	97	94	98	NA	NA	NA	NA	NA	NA	77.9 (MICS 2017–2018)
Guinea	2006	—	6, 10, 14 wks	47	45	47	47	47	47	NA	NA	NA	NA	NA	NA	52.6 (DHS 2018)
Guinea-Bissau	2008	—	6, 10, 14 wks	85	79	82	78	74	67	NA	NA	NA	NA	NA	NA	50.4 (MICS 2018–2019)
Liberia	2008	—	6, 10, 14 wks	73	80	80	70	65	66	NA	NA	NA	NA	NA	NA	79.8 (DHS 2019–2020)
Mali	2002	—	6, 10, 14 wks	76	77	77	77	70	77	NA	NA	NA	NA	NA	NA	66.8 (DHS 2018)
Mauritania	2005	2013	B, 6, 10, 14 wks	74	76	77	80	72	68	NR	NR	NR	NR	NR	NR	69.3 (MICS 2015)
Niger	2008	—	6, 10, 14 wks	80	85	79	81	81	82	NA	NA	NA	NA	NA	NA	44.3 (ENAFEME 2021)**
Nigeria	2004	2004	B, 6, 10, 14 wks	53	55	55	56	56	56	30	30	41	52	52	52	39.4 (DHS 2018)
Senegal	2004	2016	B, 6, 10, 14 wks	93	93	92	96	92	86	62	76	81	85	86	78	80.3 (DHS 2019)
Sierra Leone	2007	—	6, 10, 14 wks	84	90	93	95	91	92	NA	NA	NA	NA	NA	NA	83.4 (DHS 2019)
Togo	2008	—	6, 10, 14 wks	82	83	81	84	82	83	NA	NA	NA	NA	NA	NA	80.0 (MICS 2017)
<b>African Region</b>		—	—	73	74	74	75	73	71	10	10	12	15	16	17	—

See table footnotes on the next page.



**TABLE 1. (Continued) Year of hepatitis B vaccine introduction, hepatitis B vaccination schedule and estimated coverage\* with the third vaccine dose, a timely administered hepatitis B vaccine birth dose,† and rates of institutional delivery, by country — World Health Organization African Region, 2016–2021**

**Abbreviations:** B = birth; DHS = demographic health survey; ENAFEME = Enquête Nationale sur la Fécondité et la Mortalité des Enfants de Moins de 5 Ans; HepB = hepatitis B vaccine; HepB-BD = birth dose of monovalent hepatitis B vaccine; HepB3 = third dose of hepatitis B-containing vaccine; IDSR = integrated disease surveillance and response; MICS = multiple indicator cluster survey; MoH = Ministry of Health; NR = not reported; NS = national survey; R = restricted HepB-BD; SHHS = South Sudan Household Health Survey.

\* WHO-UNICEF Estimates of National Immunization Coverage. <https://immunizationdata.who.int/pages/coverage/HEPB.html>

† Timely receipt of HepB-BD is defined as administration of a dose of HepB within 24 hours of birth.

§ During 2010 to 2018: HepB-BD was selectively given to newborns of mothers who have received a positive for hepatitis B surface antigen test result; in 2019, the country switched to universal HepB-BD vaccination of all newborns.

¶ Restricted HepB-BD given only to children born to mothers with hepatitis B.

\*\* Preliminary data.

**TABLE 2. Hepatitis B virus surface antigen seroprevalence based on population-based serosurveys among children and women of reproductive age or pregnant women during antenatal screening in selected countries — World Health Organization African Region, 2016–2021**

Survey group, Country	Year of most recent data (source)	Geographic area	Age group	No. of persons tested	HBsAg prevalence, % (95% CI)
<b>Children born after HepB introduction</b>					
Democratic Republic of the Congo*	2013–2014 (DHS)	Nationwide	0–5 yrs	277	2.20 (0.3–4.1)
Ethiopia†	2017–2018 (PHIA)	Nationwide (Urban)	0–14 yrs§	4,729	1.48 (NR)
			5–9 yrs	539	3.34 (NR)
			10–14 yrs	655	3.05 (NR)
Mauritania¶	2019–2021 (DHS)	Nationwide	1–4 yrs	2,642	0.70 (NR)
			5–9 yrs	3,447	0.40 (NR)
			10–14 yrs	2,939	2.40 (NR)
Nigeria**	2018 (NAIS)	Nationwide	2–4 yrs	2,968	4.50 (3.6–5.6)
			5–9 yrs	3,620	6.60 (5.5–7.9)
			2–9 yrs	6,588	5.80 (5.0–6.6)
Rwanda††	2018–2019 (PHIA)	Nationwide	10–14 yrs	869	0.00 (NR)
Sierra Leone§§	2018 (Household-based survey)	3 of 5 provinces	4–30 mos	1,889	1.30 (0.8–2.0)
			5–9 yrs	2,025	1.60 (1.1–2.3)
Uganda¶¶	2016–2017 (PHIA)	Nationwide	0–14 yrs	10,345	0.60 (NR)
Zambia***	2016 (PHIA)	Nationwide	0–14 yrs†††	8,015	1.30 (NR)
<b>Women of reproductive age</b>					
Burkina Faso§§§	2010–2011 (DHS)	Nationwide	15–49 yrs	8,056	7.80 (7.1–8.6)
Cameroon¶¶¶	2017–2018 (PHIA)	Nationwide	15–49 yrs	1,058	6.00 (NR)
Democratic Republic of the Congo*	2013–2014 (DHS)	Nationwide	15–59 yrs	368	3.80 (NR)
Kenya****	2018–2019 (PHIA)	Nationwide	15–49 yrs	1,652	2.70 (NR)
Mauritania¶	2019–2021 (DHS)	Nationwide	15–49 yrs	4,420	6.40 (NR)
Nigeria**	2018 (NAIS)	Nationwide	15–49 yrs	8,682	6.10 (5.1–7.0)
Rwanda††	2018–2019 (PHIA)	Nationwide	15–49 yrs	1,813	1.20 (NR)
Sierra Leone§§	2018 (Household based survey)	3 of 5 provinces	15–49 yrs	1,776	9.80 (8.1–11.7)
Tanzania††††	2016–2017 (PHIA)	Nationwide	15–49 yrs	615	3.70 (NR)
Uganda¶¶¶	2016–2017 (PHIA)	Nationwide	15–49 yrs	14,716	3.10 (NR)
Zambia***	2016 (PHIA)	Nationwide	15–59 yrs	10,973	4.10 (NR)
<b>Antenatal screening of pregnant women</b>					
Nigeria§§§§	2019 (ANC screening in HIV facilities)	Nationwide (34 of 36 states)	NA	200,473	3.94 (NR)

**Abbreviations:** ANC = antenatal care; DHS = demographic and health survey; HBsAg = hepatitis B virus surface antigen; HepB = hepatitis B vaccine; HIV = human immunodeficiency virus; NA = not applicable; NAIS = Nigeria HIV/AIDS Indicator and Impact Survey; NR = not reported; PHIA = population-based HIV impact assessment survey.

\* <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6609197/pdf/tpmd180883.pdf>

† <https://onlinelibrary.wiley.com/doi/full/10.1111/hiv.13457>

§ Includes children aged 11–13 years born before HepB introduction.

¶ <https://dhsprogram.com/pubs/pdf/FR373/FR373.pdf>

\*\* [https://global-hepatitis.com/wp-content/uploads/2023/04/GHS2023-Abstract-Book-ONLINE\\_4.pdf?utm\\_source=mobile+app&utm\\_medium=link&utm\\_campaign=abstract-book](https://global-hepatitis.com/wp-content/uploads/2023/04/GHS2023-Abstract-Book-ONLINE_4.pdf?utm_source=mobile+app&utm_medium=link&utm_campaign=abstract-book) (abstract no. 047)

†† [https://phia.icap.columbia.edu/wp-content/uploads/2020/11/RPHIA-Final-Report\\_Web.pdf](https://phia.icap.columbia.edu/wp-content/uploads/2020/11/RPHIA-Final-Report_Web.pdf)

§§ <https://www.sciencedirect.com/science/article/pii/S0264410X22003607>

¶¶ [https://phia.icap.columbia.edu/wp-content/uploads/2020/02/UPHIA\\_Final\\_Report\\_Revise\\_07.11.2019\\_Final\\_for-web.pdf](https://phia.icap.columbia.edu/wp-content/uploads/2020/02/UPHIA_Final_Report_Revise_07.11.2019_Final_for-web.pdf)

\*\*\* [https://phia.icap.columbia.edu/wp-content/uploads/2019/03/ZAMPHIA-Final-Report\\_\\_2.26.19.pdf](https://phia.icap.columbia.edu/wp-content/uploads/2019/03/ZAMPHIA-Final-Report__2.26.19.pdf)

††† Includes children aged 11–14 years born before the introduction of HepB vaccine.

§§§ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6239015/>

¶¶¶ [https://phia.icap.columbia.edu/wp-content/uploads/2021/09/53059-CAMPHIA-Report\\_EN\\_WEB\\_August1.pdf](https://phia.icap.columbia.edu/wp-content/uploads/2021/09/53059-CAMPHIA-Report_EN_WEB_August1.pdf)

\*\*\*\* <https://phia.icap.columbia.edu/kenya-final-report-2018/>

†††† [https://phia.icap.columbia.edu/wp-content/uploads/2020/02/FINAL\\_THIS-2016-2017\\_Final-Report\\_\\_06.21.19\\_for-web\\_TS.pdf](https://phia.icap.columbia.edu/wp-content/uploads/2020/02/FINAL_THIS-2016-2017_Final-Report__06.21.19_for-web_TS.pdf)

§§§§ <https://pubmed.ncbi.nlm.nih.gov/34387113/>

**TABLE 3. Policies and interventions to prevent mother-to-child transmission of hepatitis B and tier eligibility\* for the path to elimination of mother-to-child transmission of hepatitis B virus — World Health Organization African Region, 2021**

Policies and interventions	No. (%) of countries with policy or intervention present or not present	
	Present	Not present
National strategic plan for viral hepatitis <sup>†</sup>	21 (45)	26 (55)
National plan for triple elimination of HIV, syphilis, and hepatitis B <sup>§</sup>	21 (45)	26 (55)
National guidelines for antenatal HBsAg testing and maternal treatment <sup>†,¶</sup>	17 (36)	30 (64)
ANC1 coverage $\geq 90\%$ <sup>**</sup> , <sup>††</sup>	29 (62)	16 (34)
HepB-BD coverage $\geq 90\%$ <sup>§§</sup>	2 (4)	45 (96)
HepB-BD coverage $\geq 50\%$ <sup>§§</sup>	6 (13)	41 (87)
HepB3 coverage $\geq 90\%$ <sup>§§</sup>	16 (34)	31 (66)
Eligibility for bronze tier for path to elimination of MTCT of HBV <sup>*,§§</sup>	1 (2)	—
Eligibility for silver tier for path to elimination of MTCT of HBV <sup>*,§§</sup>	3 (6)	—
Eligibility for gold tier for path to elimination of MTCT of HBV <sup>*,§§</sup>	2 (4)	—

**Abbreviations:** ANC1 = at least 1 antenatal care visit; HBsAg = hepatitis B surface antigen; HBV = hepatitis B virus; HepB-BD = birth dose of monovalent hepatitis B vaccine; HepB3 = three doses of a hepatitis B containing vaccine; MTCT = mother-to-child transmission; WHO = World Health Organization.

\* Eligibility for tier certification on the path to elimination of mother-to-child transmission of hepatitis B is based on immunization interventions. Bronze tier: 1)  $\geq 90\%$  coverage of HepB3 infant vaccination, and 2) implementation of universal timely HepB-BD policy. Silver tier:  $\geq 90\%$  coverage of HepB3 infant vaccination, 2)  $\geq 50\%$  coverage of universal timely HepB-BD, and 3) Availability of antenatal HBsAg testing in the public sector. Gold tier: 1)  $\geq 90\%$  coverage of HepB3 infant vaccination, 2)  $\geq 90\%$  coverage of universal timely HepB-BD, and 3)  $>30\%$  coverage of antenatal HBsAg testing. Indicators for each tier should be achieved for at least 2 years. <https://www.who.int/publications/i/item/9789240039360>

<sup>†</sup> <https://www.afro.who.int/publications/viral-hepatitis-scorecard-2021-african-region>

<sup>§</sup> All 21 priority countries reported by WHO regional office: Angola, Botswana, Burundi, Cameroun, Chad, Côte-d'Ivoire, Democratic Republic of the Congo, Eswatini, Ethiopia, Ghana, Kenya, Lesotho, Malawi, Mozambique, Namibia, Nigeria, Uganda, South Africa, Tanzania, Zambia, Zimbabwe.

<sup>¶</sup> Included in national testing and treatment guidelines.

<sup>\*\*</sup> <https://data.unicef.org/resources/dataset/maternal-newborn-health/>

<sup>††</sup> Data are not available for two (4%) countries (Mauritius and Seychelles).

<sup>§§</sup> World Health Organization-UNICEF estimates. <https://immunizationdata.who.int/pages/coverage/HEPB.html>

## Discussion

All 47 AFR countries have had HepB in their infant immunization schedule since 2014, and 16 (34%) have achieved  $\geq 90\%$  HepB3 coverage for  $\geq 2$  years, including four countries that documented  $<2\%$  HBsAg seroprevalence in children, consistent with hepatitis B control. The COVID-19 pandemic led to disruptions in immunization services,<sup>\*\*\*\*</sup> resulting in fewer AFR countries attaining  $\geq 90\%$  HepB3 coverage, declining from a peak of 20 (43%) in 2018 to 16 (34%) in 2021. Strategies to recover and strengthen immunization programs

<sup>\*\*\*\*</sup> [https://www.who.int/publications/i/item/WHO-2019-nCoV-EHS\\_continuity-survey-2022.1](https://www.who.int/publications/i/item/WHO-2019-nCoV-EHS_continuity-survey-2022.1)

## Summary

### What is already known about this topic?

In 2019, the World Health Organization African Region (AFR) accounted for 66% of all new chronic hepatitis B virus (HBV) infections. Chronic HBV infection is the leading causes of cirrhosis and liver cancer.

### What is added by this report?

By 2021, all 47 AFR countries provided 3 doses of hepatitis B vaccine (HepB3) to infants, and 14 (30%) provided a birth dose (HepB-BD). By December 2021, 16 (34%) countries achieved  $\geq 90\%$  HepB3 coverage; two (4%) achieved  $\geq 90\%$  timely HepB-BD coverage. Four countries achieved hepatitis B control; none achieved elimination of mother-to-child transmission (EMTCT).

### What are the implications for public health practice?

Introduction of HepB-BD, improving HepB3 and HepB-BD coverage, and monitoring implementation of EMTCT interventions are essential to accelerating progress toward hepatitis B control and EMTCT in AFR.

such as catch-up vaccination campaigns, could help ensure that all eligible children who missed HepB vaccination receive the recommended doses (7).

Fewer than one third (30%, 14) of countries had introduced HepB-BD by 2021, and just two countries achieved  $\geq 90\%$  HepB-BD coverage. Scaling up HepB-BD introduction and coverage is critical to eliminating MTCT of HBV and preventing subsequent liver disease and associated mortality. During 2016–2021, four countries in AFR introduced HepB-BD which, in addition to increasing HepB-BD coverage in two of these countries (Nigeria and Senegal), resulted in an increase in regional HepB-BD coverage from 10% to 17%. However, in 2021, almost 33 million newborns in AFR did not receive timely HepB-BD. (Table 1) Based on modeled estimates, maintaining current HepB3 coverage and increasing HepB-BD coverage to  $\geq 90\%$  in all countries in the region could avert 554,318 HBV-related deaths among 2020–2030 birth cohorts (8). Among the 33 countries that did not have HepB-BD as part of their routine immunization schedules in 2021, two (Burkina Faso and Uganda) introduced it in 2022. Among the remaining 31 countries,<sup>††††</sup> 13<sup>§§§§</sup> plan to introduce HepB-BD by 2025.<sup>¶¶¶¶</sup> However, achieving the regional target

<sup>††††</sup> Burundi, Cameroon, Central African Republic, Chad, Comoros, Democratic Republic of the Congo, Eritrea, Eswatini, Ethiopia, Gabon, Ghana, Guinea, Guinea-Bissau, Kenya, Lesotho, Liberia, Madagascar, Malawi, Mali, Mozambique, Niger, Republic of the Congo, Rwanda, Seychelles, Sierra Leone, South Africa, South Sudan, Togo, United Republic of Tanzania, Zambia, and Zimbabwe.

<sup>§§§§</sup> Burundi, Cameroon, Comoros, Eritrea, Ghana, Lesotho, Madagascar, Niger, Seychelle, Sierra Leone, South Africa, Togo, and Zimbabwe.

<sup>¶¶¶¶</sup> Obtained from workshop reports on National Immunization Plan; meetings were held during September–October 2022.

of 35 countries by 2025 (5) would require six to seven countries to introduce HepB-BD each year. Following introduction, delivery in health facilities by skilled workers was shown to be significantly correlated with timely HepB-BD administration (9). Promoting and enabling delivery in health facilities, training health care workers, and integrating HepB-BD vaccination into newborn care, are essential to increasing timely HepB-BD coverage in AFR.

In addition to providing timely HepB-BD and HepB3, the identification of pregnant women with HBV infection and provision of antiviral medications for those who are eligible for treatment would further advance EMTCT of HBV (9,10). However, as of 2021, only 17 (36%) AFR countries had national policies for antenatal HBsAg testing and treatment, and nationally representative serosurveys in AFR were uncommon. HBsAg seroprevalence surveys would help document progress and guide policy decisions regarding hepatitis B control and elimination in the region.

### Limitations

The findings in this report are subject to at least two limitations. First, HepB-BD coverage data were not consistently reported by five countries,\*\*\*\*\* which might have resulted in the underestimation of overall HepB-BD regional coverage. Second, assessment of hepatitis B control and EMTCT is challenging in countries that have introduced HepB-BD and achieved high coverage with HepB3, because nationally representative seroprevalence surveys to estimate the prevalence of HBV infection among children are lacking in those countries.

### Implications for Public Health Practice

Establishing a regional verification mechanism for hepatitis B control and EMTCT of HBV could elevate the profile of elimination initiatives in AFR. Scaling up the introduction of HepB-BD and strategies to increase timely HepB-BD and HepB3 coverage would accelerate the reduction of preventable hepatitis B–associated morbidity and mortality and progress toward 2030 hepatitis B elimination goals.

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### References

1. World Health Organization. Global progress report on HIV, viral hepatitis, and sexually transmitted infections, 2021. Accountability for the global health sector strategies 2016–2021: actions for impact. Web annex 1: key data at a glance. Geneva, Switzerland: World Health Organization; 2021. <http://apps.who.int/iris/bitstream/handle/10665/342808/9789240030985-eng.pdf>
2. World Health Organization. Hepatitis B vaccines: WHO position paper – July 2017. *Wkly Epidemiol Rec* 2017;92:369–92. PMID:28685564
3. World Health Organization. Global HIV, Hepatitis and STIs programmes: global health sector strategies 2022–2030. Geneva, Switzerland: World Health Organization; 2022. <https://www.who.int/teams/global-hiv-hepatitis-and-stis-programmes/strategies/global-health-sector-strategies>
4. Regional Office for Africa. Prevention, care and treatment of viral hepatitis in the African Region: framework for action, 2016–2020. Brazzaville, Republic of the Congo: World Health Organization, Regional Office for Africa; 2017. <https://www.afro.who.int/publications/prevention-care-and-treatment-viral-hepatitis-african-region-framework-action-2016>
5. Regional Committee for Africa, 71. Framework for an integrated multisectoral response to TB, HIV, STIs and hepatitis in the WHO African Region 2021–2030: report of the secretariat. Brazzaville, Republic of the Congo: World Health Organization, Regional Office for Africa; 2021. <https://apps.who.int/iris/handle/10665/345321>
6. World Health Organization. Global guidance on criteria and processes for validation: elimination of mother-to-child transmission of HIV, syphilis, and hepatitis B virus. Geneva, Switzerland: World Health Organization; 2021. <https://www.who.int/initiatives/triple-elimination-initiative-of-mother-to-child-transmission-of-hiv-syphilis-and-hepatitis-b/validation>
7. World Health Organization. Guiding principles for recovering, building resiliency, and strengthening of immunization in 2022 and beyond. Geneva, Switzerland: World Health Organization; 2002. <https://apps.who.int/iris/bitstream/handle/10665/364944/9789240052772-eng.pdf>
8. de Villiers MJ, Nayagam S, Hallett TB. The impact of the timely birth dose vaccine on the global elimination of hepatitis B. *Nat Commun* 2021;12:6223. PMID:34711822 <https://doi.org/10.1038/s41467-021-26475-6>
9. Allison RD, Patel MK, Tohme RA. Hepatitis B vaccine birth dose coverage correlates worldwide with rates of institutional deliveries and skilled attendance at birth. *Vaccine* 2017;35:4094–8. PMID:28668571 <https://doi.org/10.1016/j.vaccine.2017.06.051>
10. Spearman CW, Afihene M, Ally R, et al.; Gastroenterology and Hepatology Association of sub-Saharan Africa (GHASSA). Hepatitis B in sub-Saharan Africa: strategies to achieve the 2030 elimination targets. *Lancet Gastroenterol Hepatol* 2017;2:900–9. PMID:29132759 [https://doi.org/10.1016/S2468-1253\(17\)30295-9](https://doi.org/10.1016/S2468-1253(17)30295-9)

## Arthritis Among Children and Adolescents Aged <18 Years — United States, 2017–2021

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### Abstract

Arthritis affects persons of all ages, including younger adults, adolescents, and children; however, recent arthritis prevalence estimates among children and adolescents aged <18 years are not available. Previous prevalence estimates among U.S. children and adolescents aged <18 years ranged from 21 to 403 per 100,000 population depending upon the case definition used. CDC analyzed aggregated 2017–2021 National Survey of Children’s Health data to estimate the national prevalence of parent-reported arthritis diagnosed among children and adolescents aged <18 years. An estimated 220,000 (95% CI = 187,000–260,000) U.S. children and adolescents aged <18 years (305 per 100,000) had diagnosed arthritis. Arthritis prevalence among non-Hispanic Black or African American children and adolescents was twice that of non-Hispanic White children and adolescents. Co-occurring conditions, including depression, anxiety, overweight, physical inactivity, and food insecurity were associated with higher prevalences of arthritis. These findings highlight that children and adolescents should be prioritized for arthritis prevention and treatments by identifying risk factors for arthritis, developing self-management interventions to improve arthritis, physical activity or weight control, and screening and linking to mental health services. Health systems and payors can take steps to ensure equitable access to therapies (e.g., physical therapies and medications).

### Introduction

Previous estimates of the number of arthritis cases and prevalence among U.S. children and adolescents aged <18 years range from 13,400 (21 per 100,000 population) in one 1978 study using a very narrow definition of juvenile arthritis (1) to 294,000 (403 per 100,000) during 2001–2004 using a much broader definition of pediatric arthritis and other rheumatologic conditions (2). Although children and adolescents can receive diagnoses of many types of arthritis, the most common are acquired autoinflammatory diseases\* that are associated with joint pain, swelling, stiffness, physical disability, and

activity limitation that often persist into adulthood; depression and anxiety often co-occur with arthritis among children and adolescents (3,4,5). The National Survey of Children’s Health (NSCH) is an annual household survey conducted by the U.S. Census Bureau designed and funded by the Health Resources and Services Administration’s Maternal and Child Health Bureau. It is the largest national- and state-level survey of U.S. children’s health and uses a national address-based sample for online or mail collection of data from parents.† NSCH asks parents about the physical and emotional health, well-being, and related factors of one randomly selected§,¶ child or adolescent aged <18 years from their household.

### Methods

The overall NSCH response rates during 2017, 2018, 2019, 2020, and 2021 were 37.4%, 43.1%, 42.4%, 42.4%, and 40.3%, respectively. Diagnosed arthritis was defined as parents answering “yes” to the single question, “Has a doctor or other health care provider ever told you that this child has arthritis?” These analyses included combined 2017–2021 public use deidentified data from parents who answered the question about arthritis for the selected child or adolescent, resulting in a study population of 173,406 children and adolescents aged <18 years.

Annualized, unadjusted prevalence estimates of arthritis (cases per 100,000 U.S. children and adolescents) were generated overall and by selected characteristics of the child or adolescent (e.g., demographic characteristics; depression, anxiety, or overweight; physical inactivity; and having health insurance or a place for preventive care) and characteristics of the household (e.g., parents’ highest educational attainment, whether smoking occurs in the household, and presence of food insecurity). All estimates presented were weighted to be nationally representative of the U.S. population of children and adolescents living in households.\*\*,†† Differences in subgroups were tested against a reference group using a t-test with an a priori  $\alpha$ -level of 0.05. Analyses accounted for the complex survey design and were conducted using SAS-callable SUDAAN (version 11.0.1; RTI International). This activity was reviewed

\*The seven most common autoinflammatory arthritis types among children and adolescents include 1) oligoarticular juvenile idiopathic arthritis, 2) polyarticular juvenile idiopathic arthritis–rheumatoid factor negative, 3) polyarticular juvenile idiopathic arthritis–rheumatoid factor positive, 4) enthesitis-related juvenile idiopathic arthritis, 5) psoriatic juvenile idiopathic arthritis, 6) systemic juvenile idiopathic arthritis, and 7) undifferentiated arthritis.

† Respondent relationship to the child was defined as biologic or adoptive parent, stepparent, grandparent, foster parent, other relative, other nonrelative, or missing response.

§ <https://www.census.gov/programs-surveys/nsch.html>

¶ <https://mchb.hrsa.gov/data-research/national-survey-childrens-health>

by CDC and conducted consistent with applicable federal law and CDC policy.<sup>§§</sup>

## Results

During 2017–2021, an estimated 220,000 U.S. children and adolescents aged <18 years had arthritis, equating to a prevalence of 305 per 100,000 U.S. children and adolescents (Table). Arthritis prevalence increased with age, from 77 per 100,000 among children aged <6 years to 592 among those aged 12–17 years. Prevalence was higher among non-Hispanic Black or African American (Black) children and adolescents (571 per 100,000) than among non-Hispanic White (White) children and adolescents (260). Among children and adolescents with reported co-occurring conditions, prevalence was highest among those with diagnosed depression (1,980), a heart condition (1,900), or anxiety (1,310), as well as among those who had overweight (1,040). Among children and adolescents ≥6 years, arthritis prevalence was higher among those who were physically inactive (791) than those who were active 1–3 days (409), 4–6 days (282) or everyday (331). The prevalence was also higher among children and adolescents in households with food insecurity (905) or smoking (560) compared with that among children living in households without these characteristics (267 and 260, respectively). In addition, the prevalence of arthritis decreased as the level of parental educational attainment increased (534 per 100,000 among those whose parent had less than a high school education compared with 199 per 100,000 among children and adolescents with a parent with at least a 4-year college degree).

## Discussion

This report found that during 2017–2021, an estimated 220,000 U.S. children and adolescents had an arthritis diagnosis, and prevalence was highest among those aged 12–17 years. Previous U.S. population estimates of arthritis among children and adolescents ranged from 13,400 to 294,000 cases, and prevalences of 21 to 403 per 100,000 population (1,2). The

wide range of estimates in these studies is likely attributable to a combination of factors including the relative rarity of arthritis among children and adolescents, advances in early detection and differential diagnosis of arthritis, differences in terminology and arthritis case definitions, and variations in data sources, sampling, collection, and weighting methodologies (1,2,5). Whereas the current study used parent-reported health care provider diagnosis of arthritis as the case definition, previous studies (1,2) have used medical billing codes to ascertain arthritis and rheumatologic conditions among children and adolescents.

Although arthritis can affect children and adolescents of all races and ethnicities, this study identified racial and ethnic disparities. Arthritis prevalence among Black children and adolescents was twice that among those who were White. Further, prevalence of arthritis was inversely related to the highest level of parental education attained. These disparities highlight the importance of addressing social determinants of health because the impacts on health and well-being can be seen as early as childhood.

Similar to other studies, the results of this analysis determined that arthritis prevalence was high among children and adolescents with anxiety and depression. A 2019 systematic review of depression and anxiety in patients with juvenile idiopathic arthritis (4) found higher prevalences of symptoms of depression and anxiety among juvenile idiopathic arthritis patients and their family members than among children and adolescents without juvenile idiopathic arthritis. This review also identified a need for further data on the effect of treatment of mental health symptoms on disease outcomes among children and adolescents with juvenile idiopathic arthritis. Further, the systematic review found that children and adolescents with arthritis who were experiencing anxiety and depression also had a poorer quality of life, underscoring the need to address mental health among children and adolescents with arthritis and their families (4). The U.S. Preventive Services Task Force recommends screening all persons aged 8–18 years for anxiety,<sup>¶¶</sup> and those aged 12–18 years for major depressive disorder.<sup>\*\*\*</sup> The rationale for routine screening is to identify youths without an anxiety diagnosis who might benefit from effective treatment for anxiety disorders.

The current study also found associations between arthritis and food insecurity as well as overweight and physical inactivity. Children and adolescents with special health care needs who are also experiencing food insecurity have been found to

\*\* The National Survey of Children's Health is weighted to be representative of the U.S. population of noninstitutionalized persons aged ≤17 years. <https://www.census.gov/content/dam/Census/programs-surveys/nsch/tech-documentation/methodology/2017-NSCH-Methodology-Report.pdf>; <https://www2.census.gov/programs-surveys/nsch/technical-documentation/methodology/2018-NSCH-Methodology-Report.pdf>; <https://www2.census.gov/programs-surveys/nsch/technical-documentation/methodology/2019-NSCH-Methodology-Report.pdf>; <https://www2.census.gov/programs-surveys/nsch/technical-documentation/methodology/2020-NSCH-Methodology-Report.pdf>; and <https://www2.census.gov/programs-surveys/nsch/technical-documentation/methodology/2021-NSCH-Methodology-Report.pdf>

†† <https://www2.census.gov/programs-surveys/nsch/technical-documentation/methodology/NSCH-Guide-to-Multi-Year-Estimates.pdf>

§§ 45 C.F.R. part 46.102(1)(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.

¶¶ <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/screening-anxiety-children-adolescents>

\*\*\* <https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/screening-depression-suicide-risk-children-adolescents>

TABLE. Characteristics of parent-reported\* diagnosed arthritis† among children and adolescents aged &lt;18 years — National Survey of Children's Health, United States, 2017–2021

Characteristic	No. of respondents <sup>§</sup>	No. of children and adolescents with arthritis <sup>§</sup>	Weighted no. with arthritis <sup>¶</sup>	Prevalence** (95% CI)
<b>Overall (2017–2021)</b>	<b>173,406</b>	<b>568</b>	<b>220,000</b>	<b>305 (259–360)</b>
<b>Survey year</b>				
2017 <sup>††</sup>	21,373	79	275,000	379 (257–558)
2018	30,132	108	193,000	267 (183–389)
2019	29,144	105	203,000	280 (199–395)
2020	42,321	136	200,000	279 (211–368)
2021	50,436	140	231,000	321 (215–478)
<b>Characteristic of the child or adolescent</b>				
<b>Sex</b>				
Male <sup>††</sup>	90,016	237	102,000	276 (213–359)
Female	83,390	331	118,000	335 (272–414)
<b>Age group, yrs</b>				
0–5	55,304	38	18,000	77 (31–191) <sup>§§</sup>
6–11	51,516	127	56,000	231 (169–317) <sup>¶¶</sup>
12–17 <sup>††</sup>	66,586	403	146,000	592 (491–713) <sup>¶¶</sup>
<b>Race***</b>				
American Indian or Alaska Native	1,586	9	3,000	235 (92–598) <sup>§§</sup>
Black or African American	12,150	55	57,000	571 (389–839) <sup>¶¶</sup>
Asian or Native Hawaiian or other Pacific Islander	10,428	19	11,000	234 (99–552) <sup>§§</sup>
White <sup>††</sup>	133,494	434	125,000	260 (215–314)
Multiple races	14,364	47	22,000	339 (185–620) <sup>§§</sup>
<b>Hispanic or Latino***</b>				
No <sup>††</sup>	151,330	501	200,000	370 (310–443)
Yes	22,076	67	21,000	114 (79–164) <sup>¶¶</sup>
<b>Depression<sup>†††</sup></b>				
No <sup>††</sup>	163,976	431	159,000	230 (191–277)
Yes	8,985	131	58,000	1,980 (1,380–2,830) <sup>¶¶</sup>
<b>Anxiety<sup>§§§</sup></b>				
No <sup>**</sup>	153,924	362	138,000	209 (170–257)
Yes	18,977	202	82,000	1,310 (991–1,730) <sup>¶¶</sup>
<b>Heart condition<sup>¶¶¶</sup></b>				
No <sup>††</sup>	168,780	520	187,000	265 (224–313)
Yes	4,399	46	31,000	1,900 (1,080–3,320) <sup>¶¶</sup>
<b>Overweight<sup>****</sup></b>				
No <sup>††</sup>	141,530	396	115,000	218 (179–265)
Yes	9,879	89	48,000	1,040 (705–1,540) <sup>¶¶</sup>
<b>Physically active, no. of days per wk<sup>††††</sup></b>				
0 <sup>††</sup>	11,457	99	40,000	791 (521–1,200)
1–3	46,158	199	81,000	409 (317–529) <sup>¶¶</sup>
4–6	34,534	138	36,000	282 (214–371) <sup>¶¶</sup>
Every day	24,581	81	34,000	331 (221–495) <sup>¶¶</sup>
<b>Has place for routine preventive care<sup>§§§§</sup></b>				
No	10,752	34	35,000	528 (297–939) <sup>§§</sup>
Yes <sup>††</sup>	161,556	524	178,000	273 (232–322)
<b>Has health insurance<sup>¶¶¶¶</sup></b>				
No	7,034	26	16,000	343 (152–775) <sup>§§</sup>
Yes <sup>††</sup>	165,692	539	204,000	304 (257–359)
<b>Characteristic of parent or household</b>				
<b>Parents' highest educational level attained<sup>*****</sup></b>				
Less than high school	4,369	25	36,000	534 (296–962) <sup>††</sup>
High school (including GED, vocational, trade, or business school)	22,550	112	54,000	390 (268–565)
Some college or associate degree	39,150	152	58,000	378 (282–507)
4-yr college degree or higher <sup>††</sup>	107,337	279	72,000	199 (166–239) <sup>¶¶</sup>
<b>Household food insecurity<sup>†††††</sup></b>				
No <sup>††</sup>	163,891	495	178,000	267 (225–318)
Yes	5,611	57	33,000	905 (530–1,540) <sup>¶¶</sup>
<b>Home owned<sup>†††††</sup></b>				
No	28,496	122	54,000	332 (240–459)
Yes <sup>††</sup>	123,537	367	111,000	269 (217–333)

See table footnotes on the next page.

TABLE. (Continued) Characteristics of parent-reported\* diagnosed arthritis<sup>†</sup> among children and adolescents aged <18 years — National Survey of Children's Health, United States 2017–2021

Characteristic	No. of respondents <sup>§</sup>	No. of children and adolescents with arthritis <sup>§</sup>	Weighted no. with arthritis <sup>¶</sup>	Prevalence** (95% CI)
<b>Smoking in household<sup>¶¶¶¶</sup></b>				
No <sup>††</sup>	146,963	447	157,000	260 (218–310)
Yes	22,986	106	56,000	560 (370–846) <sup>¶¶</sup>

**Abbreviation:** GED = general educational development certificate.

\* Respondent relationship to the child was defined as biologic or adoptive parent, stepparent, grandparent, foster parent, other relative, other nonrelative, or missing response.

<sup>†</sup> Diagnosed arthritis was defined by answering “yes” to the question “Has a doctor or other health care provider ever told you that this child has arthritis?” The analyses excluded respondents who did not respond to the question: 216 (1.05%) during 2017, 398 (1.32%) during 2018, 289 (0.98%) during 2019, 456 (1.07%) during 2020, and 456 (0.90%) during 2021.

<sup>§</sup> Categories might not sum to the respondent total because of missing responses for some characteristics.

<sup>¶</sup> Weighted estimates generalize to state and national resident populations. <https://www.census.gov/content/dam/Census/programs-surveys/nsch/technical-documentation/methodology/2017-NSCH-Methodology-Report.pdf>; <https://www2.census.gov/programs-surveys/nsch/technical-documentation/methodology/2018-NSCH-Methodology-Report.pdf>; <https://www2.census.gov/programs-surveys/nsch/technical-documentation/methodology/2019-NSCH-Methodology-Report.pdf>; <https://www2.census.gov/programs-surveys/nsch/technical-documentation/methodology/2020-NSCH-Methodology-Report.pdf>; and <https://www2.census.gov/programs-surveys/nsch/technical-documentation/methodology/2021-NSCH-Methodology-Report.pdf>

\*\* Cases per 100,000 U.S. children and adolescents aged <18 years.

<sup>††</sup> Referent group for subgroup comparisons of arthritis prevalence.

<sup>§§</sup> Estimate might be unreliable. The absolute CI width is >20%, or the relative CI width is >120% (1.2 times the estimate).

<sup>¶¶</sup> T-tests were used to determine statistically significant differences in arthritis prevalence for subgroups defined by selected characteristics; differences with  $p \leq 0.05$  were considered statistically significant.

<sup>\*\*\*</sup> Race was recoded from responses to the question, “What is this child’s race?” and included American Indian or Alaska Native, Black or African American, Asian or Native Hawaiian or other Pacific Islander, White, and two or more races. The 2017 and 2018 surveys included a response for “Some other race only,” which are coded as missing. Persons of Hispanic or Latino (Hispanic) origin might be of any race but are categorized as Hispanic; all racial groups are non-Hispanic. Asian and Native Hawaiian or other Pacific Islander were combined to make one racial group.

<sup>†††</sup> Depression was defined by answering “yes” to the question, “Has a doctor or other health care provider ever told you that this child has depression?”

<sup>§§§</sup> Anxiety was defined by answering “yes” to the question, “Has a doctor or other health care provider ever told you that this child has anxiety?”

<sup>¶¶¶</sup> Heart condition was defined by answering “yes” to the question, “Has a doctor or other health care provider ever told you that this child has a heart condition?”

<sup>\*\*\*\*</sup> Overweight was defined by answering yes to the question, “Has a doctor or other health care provider ever told you that this child is overweight?” The 2017 survey did not include this question.

<sup>††††</sup> Physical activity was not asked of children aged  $\leq 5$  years old, and was determined by the question, “During the past week, on how many days did this child exercise, play a sport, or participate in physical activity for at least 60 minutes?”

<sup>§§§§</sup> Place for routine preventive care was defined by answering “yes” to the question, “Is there a place this child usually goes when he or she needs routine preventive care, such as physical examination or well-child checkups?” Starting in 2020, the survey changed pronoun language from “he or she” to “they.”

<sup>¶¶¶¶</sup> Health insurance was determined by answering “yes” to the question, “Is this child currently covered by any kind of health insurance or health coverage plan?”

<sup>\*\*\*\*\*</sup> Parents’ highest level of education attained: less than high school (i.e., 8th grade or less or 9th–12th grade, no diploma); high school (e.g., high school graduate or GED obtained or completed a vocational, trade, or business school program); some college or associate degree (e.g., some college credit, but no degree or associate degree [Associate of Arts or Associate of Science]); 4-year college degree or higher (e.g., bachelor’s degree [Bachelor of Arts or Bachelor of Science]; master’s degree [Master of Art, Master of Science, Master of Social Work, or Master of Business Administration]; doctorate [Doctor of Philosophy or Doctor of Education]; professional degree [Doctor of Medicine, Doctor of Dental Surgery, Doctor of Veterinary Medicine, or Juris Doctorate]).

<sup>†††††</sup> Household food insecurity was defined by answering “Sometimes we could not afford enough to eat” or “often we could not afford enough to eat” to the question “Which of these statements best describes your household’s ability to afford the food you need during the past 12 months?”

<sup>§§§§§</sup> Home owned was defined by answering “yes” to either, “Is this house, apartment, or mobile home owned by you or someone in this household with a mortgage or loan?” or “Is this house, apartment, or mobile home owned by you or someone in this household free and clear (without a mortgage or loan)?” The 2017 survey did not collect data on homeownership.

<sup>¶¶¶¶¶</sup> Smoking in household was defined by answering “yes” to the question, “Does anyone living in your household use cigarettes, cigars, or pipe tobacco?” or “Does anyone smoke inside your home?”

have increased prevalences of various negative health outcomes, including overweight or obesity (6). A healthy, age-appropriate diet is strongly recommended as a treatment strategy for children and adolescents with arthritis (7). However, more research on physical activity and weight management interventions for children and adolescents with arthritis is needed.

Arthritis therapy guidelines for children and adolescents include pharmacologic and nonpharmacologic interventions and treatments (7–9). Pharmacologic treatments include antirheumatic drugs, which help preserve joints by blocking or slowing inflammation, and nonsteroidal antiinflammatory drugs to treat stiffness, pain, and fever (8,9). The 2021 American College of Rheumatology guideline for the treatment of juvenile idiopathic arthritis recommends nonpharmacologic

interventions including physical and occupational therapy to improve range of motion, muscle strength, endurance, functional deficits, and activities of daily living (7). Although this American College of Rheumatology guideline does not make specific physical activity recommendations, the 2018 Physical Activity Guidelines for Americans<sup>†††</sup> recommend that, for optimal health and fitness, children and adolescents aged 6–17 years should engage in 60 minutes of daily moderate-to-vigorous physical activity. Physically active children and adolescents experience improved cognition and fitness, stronger bones and muscles, have lower percentages of body fat, and lower risk for depression

<sup>†††</sup> [https://health.gov/sites/default/files/2019-09/Physical\\_Activity\\_Guidelines\\_2nd\\_edition.pdf](https://health.gov/sites/default/files/2019-09/Physical_Activity_Guidelines_2nd_edition.pdf)

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

Arthritis affects persons of all ages; little is known about arthritis prevalence among children and adolescents aged <18 years.

**What is added by this report?**

Approximately 220,000 children and adolescents had arthritis during 2017–2021. Prevalence increased with age and was highest among those aged 12–17 years, non-Hispanic Black or African American children and adolescents, children and adolescents with anxiety or depression, those who were physically inactive, had overweight or a heart condition, or lived in a food-insecure or smoking household.

**What are the implications for public health practice?**

Self-management interventions, physical activity or weight control, screening and linking to mental health services, and equitable access to therapies might improve arthritis outcomes in children and adolescents.

compared with inactive children and adolescents. Although preventing some types of arthritis among children and adolescents is challenging, early diagnosis and prompt treatment might prevent permanent joint damage, improve health outcomes, reduce health disparities, and maintain quality of life (10).

**Limitations**

The findings in this report are subject to at least five limitations. First, because of the cross-sectional nature of this survey, causality among selected characteristics and arthritis prevalence cannot be inferred. Second, parent-reported arthritis diagnoses cannot be validated by medical records. Third, recall and social desirability biases or lack of knowledge about arthritis or other health conditions might result in misclassification. Fourth, because of the rarity of arthritis among children and adolescents, estimates for all subgroups might not be stable or precise, as evidenced by the wide CIs. Finally, the single survey question about an arthritis diagnosis does not provide the opportunity to estimate the prevalence of or distinguish among arthritis subtypes and does not assess undiagnosed arthritis cases.

**Implications for Public Health Practice**

This study combined data across 5 years resulting in a large sample size, providing stable prevalence estimates of arthritis among U.S. children and adolescents with the most recently available data and filling a gap in nationally representative, population-based estimates of arthritis among children and adolescents. The findings from this report highlight children and adolescents to prioritize for arthritis prevention and treatment by identifying risk factors for arthritis among children and adolescents, developing self-management interventions to improve childhood

arthritis, physical activity or weight control, and screening and linking children and adolescents to needed mental health services. Addressing social determinants of health and systemic factors that might contribute to disparities in arthritis prevalence needs to be prioritized. Health systems and payors can take steps to ensure equitable access to therapies (e.g., physical therapies and medications).

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**References**

- Gewanter HL, Roghmann KJ, Baum J. The prevalence of juvenile arthritis. *Arthritis Rheum* 1983;26:599–603. PMID:6847723 <https://doi.org/10.1002/art.1780260504>
- Sacks JJ, Helmick CG, Luo YH, Ilowite NT, Bowyer S. Prevalence of and annual ambulatory health care visits for pediatric arthritis and other rheumatologic conditions in the United States in 2001–2004. *Arthritis Rheum* 2007;57:1439–45. PMID:18050185 <https://doi.org/10.1002/art.23087>
- Simon TA, Harikrishnan GP, Kawabata H, Singhal S, Brunner HI, Lovell DJ. Prevalence of co-existing autoimmune disease in juvenile idiopathic arthritis: a cross-sectional study. *Pediatr Rheumatol Online J* 2020;18:43. PMID:32503658 <https://doi.org/10.1186/s12969-020-00426-9>
- Fair DC, Rodriguez M, Knight AM, Rubinstein TB. Depression and anxiety in patients with juvenile idiopathic arthritis: current insights and impact on quality of life, a systematic review. *Open Access Rheumatol* 2019;11:237–52. PMID:31807093 <https://doi.org/10.2147/OARRR.S174408>
- Helmick CG, Felson DT, Lawrence RC, et al.; National Arthritis Data Workgroup. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States: part I. *Arthritis Rheum* 2008;58:15–25. PMID:18163481 <https://doi.org/10.1002/art.23177>
- Khanjehani A, Pawcio S. Household food insecurity and childhood obesity/overweight among children with special healthcare needs: results from a nationally representative sample of 10–17 years old U.S. children. *Pediatr Obes* 2023;18:e13015. PMID:36825692 <https://doi.org/10.1111/ijpo.13015>
- Onel KB, Horton DB, Lovell DJ, et al. 2021 American College of Rheumatology guideline for the treatment of juvenile idiopathic arthritis: recommendations for nonpharmacologic therapies, medication monitoring, immunizations, and imaging. *Arthritis Care Res (Hoboken)* 2022;74:505–20. PMID:35233989 <https://doi.org/10.1002/acr.24839>
- Ringold S, Angeles-Han ST, Beukelman T, et al. 2019 American College of Rheumatology/Arthritis Foundation guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for non-systemic polyarthritis, sacroiliitis, and enthesitis. *Arthritis Rheumatol* 2019;71:846–63. PMID:31021537 <https://doi.org/10.1002/art.40884>
- Onel KB, Horton DB, Lovell DJ, et al. 2021 American College of Rheumatology guideline for the treatment of juvenile idiopathic arthritis: therapeutic approaches for oligoarthritis, temporomandibular joint arthritis, and systemic juvenile idiopathic arthritis. *Arthritis Care Res (Hoboken)* 2022;74:521–37. PMID:35233986 <https://doi.org/10.1002/acr.24853>
- Marzan KA, Shaham B. Early juvenile idiopathic arthritis. *Rheum Dis Clin North Am* 2012;38:355–72. PMID:22819089 <https://doi.org/10.1016/j.rdc.2012.04.006>



# Use of Respiratory Syncytial Virus Vaccines in Older Adults: Recommendations of the Advisory Committee on Immunization Practices — United States, 2023

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## Abstract

Respiratory syncytial virus (RSV) is a cause of severe respiratory illness in older adults. In May 2023, the Food and Drug Administration approved the first vaccines for prevention of RSV-associated lower respiratory tract disease in adults aged  $\geq 60$  years. Since May 2022, the Advisory Committee on Immunization Practices (ACIP) Respiratory Syncytial Virus Vaccines Adult Work Group met at least monthly to review available evidence regarding the safety, immunogenicity, and efficacy of these vaccines among adults aged  $\geq 60$  years. On June 21, 2023, ACIP voted to recommend that adults aged  $\geq 60$  years may receive a single dose of an RSV vaccine, using shared clinical decision-making. This report summarizes the body of evidence considered for this recommendation and provides clinical guidance for the use of RSV vaccines in adults aged  $\geq 60$  years. RSV vaccines have demonstrated moderate to high efficacy in preventing RSV-associated lower respiratory tract disease and have the potential to prevent substantial morbidity and mortality among older adults; postmarketing surveillance will direct future guidance.

## Introduction

In the United States, respiratory syncytial virus (RSV) causes seasonal epidemics of respiratory illness. Although the COVID-19 pandemic interrupted seasonal RSV circulation, the timing and number of incident cases of the 2022–23 fall and winter epidemic suggested a likely gradual return to pre-pandemic seasonality (1).

Each season, RSV causes substantial morbidity and mortality in older adults, including lower respiratory tract disease (LRTD), hospitalization, and death. Incidence estimates vary widely and are affected by undertesting and potentially low sensitivity of standard diagnostic testing among adults (2–5). Most adult RSV disease cases occur among older adults with an estimated 60,000–160,000 hospitalizations and 6,000–10,000 deaths annually among adults aged  $\geq 65$  years (5–10).

Adults with certain medical conditions, including chronic obstructive pulmonary disease, asthma, congestive heart failure, coronary artery disease, cerebrovascular disease, diabetes mellitus, and chronic kidney disease, are at increased risk for RSV-associated hospitalization (11–13), as are residents of

long-term care facilities (14), and persons who are frail\* or of advanced age (incidence of RSV-associated hospitalization among adults increases with age, with the highest rates among those aged  $\geq 75$  years) (6,15). RSV can also cause severe disease in persons with compromised immunity, including recipients of hematopoietic stem cell transplantation and patients taking immunosuppressive medications (e.g., for solid organ transplantation, cancer treatment, or other conditions) (16,17).

In May 2023, the Food and Drug Administration (FDA) approved the first vaccines for prevention of RSV-associated LRTD in adults aged  $\geq 60$  years. RSVPreF3 (Arexvy, GSK) is a 1-dose (0.5 mL) adjuvanted (AS01E) recombinant stabilized pre-fusion F protein (preF) vaccine (18). RSVpreF (Abrysvo, Pfizer) is a 1-dose (0.5 mL) recombinant stabilized preF vaccine (19).

## Methods

Since May 2022, CDC's Advisory Committee on Immunization Practices (ACIP) RSV Vaccines Adult Work Group (Work Group) met at least monthly to review available evidence regarding the safety, immunogenicity, and efficacy of the GSK and Pfizer RSV vaccines among adults aged  $\geq 60$  years. A systematic review of published and unpublished evidence of the efficacy and safety of these vaccines among persons aged  $\geq 60$  years was conducted. The body of evidence consisted of one phase 3 randomized controlled trial and one combined phase 1 and 2 (phase 1/2) randomized controlled trial for each vaccine. The Work Group used the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach to independently determine the certainty of evidence for outcomes related to each vaccine, rated on a scale of high to very low certainty.<sup>†</sup> In evaluating safety, the

\*Frailty is a multidimensional geriatric syndrome and reflects a state of increased vulnerability to adverse health outcomes. Although there is no consensus definition, one frequently used tool is the Fried frailty phenotype in which frailty is defined as a clinical syndrome with three or more of the following signs or symptoms: unintentional weight loss (10 lbs [4.5 kg] in the past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity.

<sup>†</sup>GRADE tables are available online for both the GSK RSV vaccine (<https://www.cdc.gov/vaccines/acip/recs/grade/GSK-Adjuvanted-RSVPreF3-adults.html>) and the Pfizer RSV vaccine (<https://www.cdc.gov/vaccines/acip/recs/grade/Pfizer-Bivalent-RSVpreF-adults.html>). For the GSK RSV vaccine, the efficacy estimates presented differ slightly from efficacy estimates included in the GRADE tables because the manufacturer used a different method from CDC to calculate vaccine efficacy. Estimates in this report are those of the manufacturer, and estimates in the GRADE tables are those calculated by CDC.

Work Group defined inflammatory neurologic events as cases of Guillain-Barré syndrome (GBS), chronic inflammatory demyelinating polyneuropathy, and acute central nervous system inflammation (e.g., transverse myelitis or acute disseminated encephalomyelitis [ADEM]) occurring within 42 days after vaccination. The Work Group then employed the Evidence to Recommendation Framework to guide its deliberations on recommendation for RSV vaccination, reviewing data on the public health problem, benefits and harms, value to the target population, acceptability to key stakeholders, feasibility, resource use, and equity.<sup>§</sup> Work Group conclusions regarding evidence for the use of RSV vaccines among adults aged ≥60 years were presented to ACIP at public meetings on February 23 and June 21, 2023 (10,15).

## Vaccine Efficacy and Safety

### GSK Vaccine

Evaluated efficacy evidence for the GSK RSV vaccine consisted of data from one ongoing randomized, double-blind, placebo-controlled phase 3 clinical trial conducted in 17 countries and including 24,973 immunocompetent participants aged ≥60 years randomized 1:1 to receive 1 dose of vaccine (intervention group, 120 μg preF protein with AS01E adjuvant) or saline placebo (control group) (20). Efficacy findings were based on analyses of data collected during May 2021–March 2023, which included two complete RSV seasons for Northern Hemisphere participants and one complete RSV season for Southern Hemisphere participants. Efficacy analyses for season one spanned May 2021–April 2022, while efficacy analyses for season two spanned August 2022–March 2023; exact study-defined season dates were site-dependent. Mean time from vaccination to end of efficacy follow-up across both seasons was approximately 15 months per participant.

The efficacy of 1 dose of the GSK vaccine in preventing symptomatic, laboratory-confirmed RSV-associated LRTD<sup>†</sup> was 82.6% (96.95% CI = 57.9%–94.1%) during the first RSV season and 56.1% (95% CI = 28.2%–74.4%) during the second season (Table 1).\*\* Efficacy of 1 dose over two

**TABLE 1. Efficacy of 1 dose of GSK respiratory syncytial virus RSVpreF3 vaccine against respiratory syncytial virus–associated disease among adults aged ≥60 years — multiple countries, 2021–2023**

Efficacy evaluation period	Vaccine efficacy against outcome*	
	RSV-associated LRTD <sup>†</sup>	RSV-associated medically attended LRTD <sup>§</sup>
Season 1 <sup>¶</sup>	82.6 (57.9–94.1)**	87.5 (58.9–97.6) <sup>††</sup>
Season 2 <sup>§§</sup>	56.1 (28.2–74.4) <sup>††</sup>	— <sup>¶¶</sup>
Combined seasons 1 and 2 (interim) <sup>***</sup>	74.5 (60.0–84.5) <sup>†††</sup>	77.5 (57.9–89.0) <sup>††</sup>

**Abbreviations:** LRTD = lower respiratory tract disease; RSV = respiratory syncytial virus.

\* Manufacturer-calculated efficacy. Includes events >14 days after injection and person-time available from the manufacturer's pivotal phase 3 trial. Estimates adjusted for participant age and region.

<sup>†</sup> LRTD defined as two or more lower respiratory symptoms (new or increased sputum, cough, and dyspnea) or signs (new or increased wheezing, crackles or rhonchi detected during chest auscultation, respiratory rate ≥20 respirations per minute, low or decreased oxygen saturation [ $<95\%$  or  $\leq 90\%$  if baseline was  $<95\%$ ] and need for oxygen supplementation) for ≥24 hours, including one or more lower respiratory signs, or three or more lower respiratory symptoms for ≥24 hours.

<sup>§</sup> Medically attended RSV-associated LRTD defined as LRTD plus attention at one or more inpatient or outpatient health care service. Estimates were not included in per-protocol assessments.

<sup>¶</sup> Season 1 vaccine efficacy estimates reflect efficacy against first events occurring during the first complete RSV season for Northern Hemisphere participants and a partial first RSV season for Southern Hemisphere participants (May 2021–April 2022; exact study-defined season dates were site-dependent).

\*\* 96.95% CI; the CI for primary trial endpoint was adjusted for multiplicity.

<sup>††</sup> 95% CI.

<sup>§§</sup> Season 2 vaccine efficacy estimates reflect efficacy against first events occurring during the second complete Northern Hemisphere RSV season for Northern Hemisphere participants (August 2022–March 2023; exact study-defined season dates were site-dependent). In addition to Northern Hemisphere participants, Southern Hemisphere participants were also included in these analyses, but this time span reflects an interseason period with low RSV incidence in the Southern Hemisphere.

<sup>¶¶</sup> Interim analysis underpowered to estimate efficacy.

<sup>\*\*\*</sup> Combined season 1 and 2 (interim) vaccine efficacy estimates reflect efficacy against first events occurring any time during Season 1 or Season 2. The mean time from start to end of efficacy surveillance was approximately 15 months per participant.

<sup>†††</sup> 97.5% CI; the CI for primary trial endpoint was adjusted for multiplicity.

seasons was 74.5% (97.5% CI = 60.0%–84.5%) in preventing RSV-associated LRTD and 77.5% (95% CI = 57.9%–89.0%) in preventing medically attended RSV-associated LRTD.<sup>††</sup> The study was not powered to estimate efficacy against hospitalization (intervention group = one event; control group = five events), severe

<sup>§</sup> Evidence to Recommendation documents are available for the GSK vaccine (<https://www.cdc.gov/vaccines/acip/recs/grade/GSK-Adjuvanted-RSVPreF3-adults-etr.html>) and Pfizer RSV vaccines (<https://www.cdc.gov/vaccines/acip/recs/grade/Pfizer-Bivalent-RSVpreF-adults-etr.html>).

<sup>†</sup> RSV-associated LRTD (RSVpreF3 trial): two or more lower respiratory symptoms (new or increased sputum, cough, and dyspnea) or signs (new or increased wheezing, crackles or rhonchi detected during chest auscultation, respiratory rate ≥20 respirations per minute, low or decreased oxygen saturation, and need for oxygen supplementation) for ≥24 hours (including one or more lower respiratory signs) or three or more lower respiratory symptoms for ≥24 hours.

\*\* Manufacturer-calculated efficacy. Includes events >14 days after injection and person-time available from the manufacturer's pivotal phase 3 trial. Estimates are adjusted for participant age and region.

<sup>††</sup> Medically attended RSV-associated LRTD (RSVpreF3 trial): LRTD plus attendance at one or more inpatient or outpatient health care service. Estimates not included in per-protocol assessments.

<sup>§§</sup> Persons with severe RSV illness requiring respiratory support (RSVpreF3 trial): RSV-associated illness requiring oxygen supplementation, positive airway pressure, or other types of mechanical ventilation. If participant was already receiving any of these, significant change or adaptation was considered.

<sup>¶¶</sup> The limited number of hospitalizations, severe RSV illnesses, and deaths observed in the trial might have been partially due to limited enrollment of persons at highest risk for RSV disease including those who were frail, of advanced age, and those living in long-term care facilities and the exclusion of persons with immune compromise. The 2021–22 RSV season was also disrupted by the COVID-19 pandemic, and RSV incidence was lower than expected based on prepandemic surveillance studies.

RSV illness requiring respiratory support (intervention group = one event; control group = five events),<sup>§§</sup> or death (no events).<sup>¶¶</sup>

Evidence regarding safety of the GSK vaccine consisted of data from two randomized, double-blind, placebo-controlled clinical trials, including the same ongoing phase 3 trial (20) and a phase 1/2 trial with 201 participants aged ≥60 years who received either the vaccine formulation used in phase 3 or placebo (21). Across both clinical trials, severe reactogenicity events (grade 3 solicited local or systemic reactions recorded during days 0–4 [phase 3 trial] and days 0–7 [phase 1/2 trial] after vaccination) occurred in 3.8% of the intervention group participants, compared with 0.9% of the control group participants (pooled relative risk [RR] = 4.10; 95% CI = 1.99–8.45) (Table 2). The frequency of serious adverse events (SAEs)<sup>\*\*\*</sup> across both trials was similar in the intervention (4.4%) and control (4.3%) groups (pooled RR = 1.02; 95% CI = 0.91–1.15). A higher number of participants in the intervention group than in the control group reported atrial fibrillation as an unsolicited event within the 30 days after injection (intervention = 10 events [0.1%]; control = four events [ $<0.1\%$ ]), eight of which were SAEs [intervention = seven; control = one]; three of the SAEs corresponded to new onset atrial fibrillation (intervention = two; control = one) (22).

Across all GSK vaccine clinical trials in older adults, inflammatory neurologic events were reported in three of 17,922 participants within 42 days after receipt of the GSK vaccine (23). All three events occurred in trials excluded from GRADE because of lack of an unvaccinated comparator arm. The reported cases included one case of GBS in a participant aged 78 years from Japan with symptom onset 9 days postvaccination in an open-label phase 3 clinical trial and two cases of ADEM among participants in a randomized phase 3 coadministration study (15,22). The two ADEM cases were reported in participants aged 71 years from the same site in South Africa after concomitant receipt of the GSK vaccine and standard dose seasonal influenza vaccine; symptom onset occurred 7 and 22 days postvaccination, and one case was fatal. In both ADEM cases, the diagnosis was based on symptoms and clinical findings only; diagnostic testing (including brain imaging, cerebrospinal fluid testing, and nerve conduction studies) was not performed, leading to uncertainty in the diagnoses. The investigator in the fatal case later revised the diagnosis from ADEM to hypoglycemia and dementia (15,22).

\*\*\* Serious adverse events were defined as any untoward medical occurrence that resulted in death, was life threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent disability or incapacity, or was a congenital anomaly or birth defect.

**TABLE 2. Safety\* of 1 dose of GSK respiratory syncytial virus RSVPreF3 vaccine in adults aged ≥60 years — multiple countries, 2021–2023**

Safety event	Risk for event		
	RSVPreF3 recipients no./No. (%) <sup>†</sup>	Placebo recipients no./No. (%) <sup>§</sup>	Relative risk (95% CI) <sup>¶</sup>
Serious AE <sup>**</sup>	549/12,570 (4.4)	540/12,604 (4.3)	1.02 (0.91–1.15)
Severe reactogenicity events <sup>††</sup>	37/979 (3.8)	9/976 (0.9)	4.10 (1.99–8.45)
Inflammatory neurologic events <sup>§§</sup>	3 events in trials without placebo recipients <sup>¶¶</sup>	— <sup>¶¶</sup>	— <sup>¶¶</sup>

**Abbreviations:** AE = adverse event; GBS = Guillain-Barré syndrome.

\* Includes serious adverse events and severe reactogenicity events observed in GSK's pivotal phase 3 trial (<https://pubmed.ncbi.nlm.nih.gov/36791160/>) and phase 1/2 trial (<https://pubmed.ncbi.nlm.nih.gov/35904987/>). Inflammatory events include those observed across all GSK clinical trials, including an open-label study (<https://clinicaltrials.gov/ct2/show/NCT04732871>) and a coadministration study (<https://clinicaltrials.gov/ct2/show/NCT04841577>). Additional data provided by GSK.

<sup>†</sup> Represents number of events and percentage of all participants experiencing events observed among RSVPreF3 vaccine recipients across all included trials for each outcome.

<sup>§</sup> Represents number of events and percentage of all participants experiencing events observed among placebo recipients across all included trials for each outcome.

<sup>¶</sup> Pooled relative risk for events in all included trials for each outcome.

<sup>\*\*</sup> Serious AEs were defined as any untoward medical occurrence (during 6 months after injection in the phase 3 trial and 60 days after injection in the phase 1/2 trial) that resulted in death, was life threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent disability or incapacity, or was a congenital anomaly or birth defect.

<sup>††</sup> Severe reactogenicity events were defined as grade 3–solicited local reaction (injection site pain, redness and swelling) or systemic reactions (fatigue, fever, headache, gastrointestinal symptoms [nausea, vomiting, diarrhea, or abdominal pain], arthralgia, myalgia, and shivering) recorded during days 0–4 after vaccination in the phase 3 trial and days 0–7 after vaccination in the phase 1/2 trial. For injection site redness and swelling, grade 3 corresponded to a diameter  $>3.9"$  ( $>100$  mm). For fever, grade 3 corresponded to a temperature  $>102.2^{\circ}\text{F}$  ( $>39^{\circ}\text{C}$ ). For all other reactions, grade 3 corresponded to reactions that prevented normal, everyday activities. Grade 4 events were not defined in these trials.

<sup>§§</sup> Defined by the Advisory Committee on Immunization Practices Respiratory Syncytial Virus Vaccines Adult Work Group as GBS (including GBS variants), chronic inflammatory demyelinating polyneuropathy, or acute central nervous system inflammation (e.g., transverse myelitis or acute disseminated encephalomyelitis) occurring  $\leq 42$  days after vaccination.

<sup>¶¶</sup> No inflammatory neurologic events were reported in either the phase 3 or phase 1/2 trials. However, across all RSVPreF3 trials inflammatory neurologic events were reported in three of 17,922 adults vaccinated with RSVPreF3. Events included one case of GBS in an open-label phase 3 clinical trial and two cases of acute disseminated encephalomyelitis among participants in a randomized phase 3 study of coadministration of RSVPreF3 and standard dose seasonal influenza vaccine. Relative risk could not be calculated because neither trial had a placebo-controlled comparator group.

### Pfizer Vaccine

Evaluated efficacy evidence for the Pfizer vaccine consisted of data from one ongoing, randomized, double-blind, placebo-controlled phase 3 clinical trial conducted in seven countries and including 36,862 immunocompetent participants aged ≥60 years randomized 1:1 to receive 1 dose of vaccine (intervention group, 120  $\mu\text{g}$  preF protein) or placebo containing the same buffer ingredients as the vaccine but without active

components (control group) (24). Efficacy findings were based on analyses of data collected during August 2021–January 2023, which included one complete RSV season for Northern and Southern Hemisphere participants and a partial second season for Northern Hemisphere participants only. Efficacy analyses for season one spanned August 2021–October 2022, while efficacy analyses for season two spanned July 2022–January 2023; exact study-defined season dates were site-dependent. Mean follow-up time from vaccination to end of efficacy follow-up across both seasons, including a gap in RSV surveillance between the first and second RSV seasons, was approximately 12 months per participant.

Efficacy of 1 dose of the Pfizer vaccine in preventing symptomatic, laboratory-confirmed RSV-associated LRTD<sup>†††</sup> was 88.9% (95% CI = 53.6%–98.7%) during the first RSV season and 78.6% (95% CI = 23.2%–96.1%) during the partial second season (Table 3).<sup>§§§</sup> Efficacy of a single dose over two seasons was 84.4% (95% CI = 59.6%–95.2%) in preventing RSV-associated LRTD and 81.0% (95% CI = 43.5%–95.2%) in preventing medically attended RSV-associated LRTD.<sup>¶¶¶</sup> The study was not powered to estimate efficacy against hospitalization (intervention group = one event; control group = three events), severe RSV illness requiring respiratory support (intervention group = one event; control group = one event),<sup>\*\*\*\*</sup> or death (no events).<sup>††††</sup>

Evidence regarding safety of the Pfizer vaccine consisted of data from two randomized, double-blind, placebo-controlled clinical trials, including the same ongoing phase 3 trial (24), and a phase 1/2 trial with 91 participants aged ≥65 years who received either the vaccine formulation used in phase 3 or placebo (25). Across both clinical trials, severe reactogenicity events (grade 3 or higher local or systemic reactions recorded during days 0–7 after vaccination) occurred in 1.0% of the intervention group participants, compared with 0.7% of the

**TABLE 3. Efficacy of 1 dose of Pfizer respiratory syncytial virus RSVpreF vaccine against respiratory syncytial virus–associated disease among adults aged ≥60 years — multiple countries, 2021–2023**

Efficacy evaluation period	Vaccine efficacy against outcome, % (95% CI)*	
	RSV-associated LRTD <sup>†</sup>	RSV-associated medically attended LRTD <sup>§</sup>
Season 1 <sup>¶</sup>	88.9 (53.6–98.7)	84.6 (32.0–98.3)
Season 2 (interim)**	78.6 (23.2–96.1)	— <sup>††</sup>
Combined seasons 1 and 2 (interim) <sup>§§</sup>	84.4 (59.6–95.2)	81.0 (43.5–95.2)

**Abbreviations:** LRTD = lower respiratory tract disease; LRTI = lower respiratory tract illness; RSV = respiratory syncytial virus.

\* Manufacturer-calculated efficacy. Includes events >14 days after injection and person-time available from the manufacturer's pivotal phase 3 trial. Estimates are unadjusted.

<sup>†</sup> The RSVpreF trial had two co-primary endpoints, defined as RSV LRTI with two or more lower respiratory signs or symptoms lasting >1 day, and RSV LRTI with three or more lower respiratory signs or symptoms lasting >1 day. Lower respiratory signs and symptoms included new or worsened cough, sputum production, wheezing, shortness of breath, and tachypnea. For RSVpreF estimates in this report, LRTD refers to the RSVpreF trial endpoint of RSV LRTI with three or more lower respiratory signs or symptoms.

<sup>§</sup> Medically attended RSV-associated LRTD was defined as LRTD prompting any health care visit (any outpatient or inpatient visit such as hospitalization, emergency department visit, urgent care visit, home health care services, primary care physician office visit, pulmonologist office visit, specialist office visit, other visit, or telehealth contact). Estimates were not included in per-protocol assessments.

<sup>¶</sup> Season 1 vaccine efficacy estimates reflect efficacy against first events occurring during the first complete RSV season for Northern and Southern Hemisphere participants (August 2021–October 2022; exact study-defined season dates were site-dependent).

\*\* Season 2 (interim) vaccine efficacy estimates reflect efficacy against first events occurring during the second complete RSV season for Northern Hemisphere participants only (through January 2023; Southern Hemisphere data not yet available).

<sup>††</sup> Interim analysis underpowered to estimate efficacy.

<sup>§§</sup> Combined season 1 and 2 (interim) vaccine efficacy estimates reflect efficacy against first events occurring any time during season 1 or season 2. The mean time from start to end of efficacy surveillance was approximately 12 months per participant.

control group participants (pooled RR = 1.43; 95% CI = 0.85–2.39) (Table 4). The frequency of SAEs across both trials was similar in the intervention (4.3%) and control (4.1%) groups (pooled RR = 1.04; 95% CI = 0.94–1.15). A higher number of participants in the intervention group than in the control group reported atrial fibrillation as an unsolicited event within the 30 days after injection (intervention = 10 events [ $<0.1\%$ ]; control = four events [ $<0.1\%$ ], of which seven were SAEs [intervention = four; control = three]). Among participants who reported atrial fibrillation, a medical history of atrial fibrillation was reported by six of 10 Pfizer vaccine recipients and two of four placebo recipients (26).

Across all Pfizer vaccine clinical trials among older adults, inflammatory neurologic events were reported in three of 20,255 participants within 42 days after receipt of the vaccine (15,26,27). The events included GBS in a participant aged 66 years from the United States with symptom onset 14 days postvaccination; Miller Fisher syndrome (a GBS variant) in

<sup>†††</sup> RSV-associated LRTD (RSVpreF trial): the trial had two co-primary endpoints, defined as RSV lower respiratory tract illness (LRTI) with two or more lower respiratory signs or three or more lower respiratory symptoms (including new or worsened cough, sputum production, wheezing, shortness of breath, and tachypnea) lasting >1 day. For RSVpreF estimates in this report, LRTD refers to the RSVpreF trial endpoint of LRTI with three or more signs or symptoms.

<sup>§§§</sup> Manufacturer-calculated efficacy. Includes events occurring >14 days after injection and person-time available from the manufacturer's pivotal phase 3 trial. Estimates are not adjusted.

<sup>¶¶¶</sup> Medically attended RSV-associated LRTD (RSVpreF trial): LRTD prompting any health care visit. Estimates not included in per-protocol assessments.

<sup>\*\*\*\*</sup> Severe RSV illness requiring respiratory support (RSVpreF trial): RSV-associated acute respiratory illness with new or increased oxygen supplementation or mechanical ventilation.

<sup>††††</sup> The limited number of hospitalizations, severe RSV illnesses, and deaths observed in the trial might have been partially due to limited enrollment of persons at highest risk for RSV disease including those who were frail, of advanced age, and those living in long-term care facilities and the exclusion of persons with immune compromise. The 2021–22 RSV season was also disrupted by the COVID-19 pandemic, and RSV incidence was lower than expected based on pre-pandemic surveillance studies.

**TABLE 4. Safety\* of 1 dose of Pfizer respiratory syncytial virus RSVpreF vaccine in adults aged ≥60 years — multiple countries, 2021–2023**

Safety event	Risk for event		
	RSVpreF recipients no./No. (%) <sup>†</sup>	Placebo recipients no./No. (%) <sup>§</sup>	Relative risk (95% CI) <sup>¶</sup>
Serious AE**	792/18619 (4.3%)	749/18334 (4.1%)	1.04 (0.94–1.15)
Severe reactogenicity events <sup>††</sup>	36/3673 (1.0%)	24/3491 (0.7%)	1.43 (0.85–2.39)
Inflammatory neurologic events <sup>§§</sup>	3/18622 (—) <sup>¶¶</sup>	0/18335 (—)	— <sup>¶¶</sup>

**Abbreviations:** AE = adverse events; GBS = Guillain-Barré syndrome.

\* Safety events observed in Pfizer's pivotal phase 3 trial (<https://pubmed.ncbi.nlm.nih.gov/37018468/>) and phase 1/2 trial (<https://pubmed.ncbi.nlm.nih.gov/34932102/>). There were no additional inflammatory neurologic events observed in any Pfizer clinical trials other than the two trials included. Additional data provided by Pfizer.

<sup>†</sup> Represents number of events and percent of all participants experiencing events observed among RSVpreF vaccine recipients across phase 3 and phase 1/2 trials.

<sup>§</sup> Represents number of events and percent of all participants experiencing events observed among placebo recipients across phase 3 and phase 1/2 trials.

<sup>¶</sup> Pooled relative risk for events in phase 3 and phase 1/2 trials.

\*\* Serious AEs were defined as any untoward medical occurrence (during all available follow-up time [safety follow-up through February 2023] after injection in the phase 3 trial and 60 days for the phase 1/2 trial) that resulted in death, was life threatening, required inpatient hospitalization or prolongation of existing hospitalization, resulted in persistent disability or incapacity, or was a congenital anomaly or birth defect.

<sup>††</sup> Severe reactogenicity events were defined as grade 3 or higher local reaction (injection site pain, redness and swelling) or systemic reaction (fever, fatigue or tiredness, headache, nausea, muscle pain, joint pain, vomiting, diarrhea, and other systemic event) recorded during days 0–7 after vaccination. For injection site redness and swelling, grade 3 corresponded to a diameter >3.9" (>100 mm) from e-diary or severe grade from adverse event case report form. For fever, grade 3 corresponded to a temperature >102°F (>38.9°C) from e-diary or severe grade from adverse event case report form. For all other reactions, grade 3 corresponded to reactions that prevented normal, everyday activities. Grade 4 event corresponded only to a fever >104°F (>40°C).

<sup>§§</sup> Defined by the Advisory Committee on Immunization Practices Work Group as GBS (including GBS variants), chronic inflammatory demyelinating polyneuropathy, or acute central nervous system inflammation (e.g., transverse myelitis or acute disseminated encephalomyelitis) occurring ≤42 days after vaccination.

<sup>¶¶</sup> Across all RSVpreF clinical trials, including trials other than the phase 3 and phase 1/2 trials summarized in this table, inflammatory neurologic events were reported in three of 20,255 adults ≤42 days after vaccination with RSVpreF (all in the phase 3 trial). The events included GBS, Miller Fisher syndrome (a GBS variant), and undifferentiated motor-sensory axonal polyneuropathy. Relative risk could not be calculated because no events were observed in the placebo-controlled comparator group.

a participant aged 66 years from Japan with symptom onset 10 days postvaccination; and undifferentiated motor-sensory axonal polyneuropathy with worsening of preexisting symptoms 21 days postvaccination in a participant aged 68 years from Argentina (15,26,27).

## Rationale for Recommendations

Vaccination with a single dose of the GSK or Pfizer RSV vaccines demonstrated moderate to high efficacy in preventing symptomatic RSV-associated LRTD over two consecutive RSV seasons among adults aged ≥60 years. Although trials

were underpowered to estimate efficacy against RSV-associated hospitalization and death, prevention of LRTD, including medically attended LRTD, suggests that vaccination might prevent considerable morbidity from RSV disease among adults aged ≥60 years.

Although both vaccines were generally well-tolerated with an acceptable safety profile, six cases of inflammatory neurologic events (including GBS, ADEM, and others) were reported after RSV vaccination in clinical trials. Whether these events occurred due to chance, or whether RSV vaccination increases the risk for inflammatory neurologic events is currently unknown. Until additional evidence becomes available from postmarketing surveillance clarifying the existence of any potential risk, RSV vaccination in older adults should be targeted to those who are at highest risk for severe RSV disease and therefore most likely to benefit from vaccination. The recommendation for shared clinical decision-making is intended to allow flexibility for providers and patients to consider individual risk for RSV disease, while taking into account patient preferences.

## Recommendations for Use of RSV Vaccines in Older Adults

On June 21, 2023, ACIP recommended that adults aged ≥60 years may receive a single dose of RSV vaccine, using shared clinical decision-making.<sup>§§§§</sup>

### Clinical Guidance

#### Shared Clinical Decision-Making for Adults Aged ≥60 years.

Unlike routine and risk-based vaccine recommendations, recommendations based on shared clinical decision-making do not target all persons in a particular age group or an identifiable risk group. For RSV vaccination, the decision to vaccinate a patient should be based on a discussion between the health care provider and the patient, which might be guided by the patient's risk for disease and their characteristics, values, and preferences; the provider's clinical discretion; and the characteristics of the vaccine.

As part of this discussion, providers and patients should consider the patient's risk for severe RSV-associated disease. Epidemiologic evidence indicates that persons aged ≥60 years who are at highest risk for severe RSV disease and who might be most likely to benefit from vaccination include those with

<sup>§§§§</sup> Votes: 1) Adults aged 60–64 years may receive a single dose of RSV vaccine, using shared clinical decision-making (13–0 vote in favor, one abstention), and 2) Adults aged ≥65 years may receive a single dose of RSV vaccine, using shared clinical decision-making (nine to five in favor). Several ACIP members who voted no for shared clinical decision-making in adults aged ≥65 years were in favor of a routine recommendation for all persons in this age group. <https://www.cdc.gov/media/releases/2023/s0629-rsv.html>

chronic medical conditions such as lung diseases, including chronic obstructive pulmonary disease and asthma; cardiovascular diseases such as congestive heart failure and coronary artery disease; moderate or severe immune compromise (either attributable to a medical condition or receipt of immunosuppressive medications or treatment)<sup>\*\*\*\*</sup>; diabetes mellitus; neurologic or neuromuscular conditions; kidney disorders, liver disorders, and hematologic disorders; persons who are frail; persons of advanced age; and persons with other underlying conditions or factors that the provider determines might increase the risk for severe RSV-associated respiratory disease (Box). Adults aged  $\geq 60$  years who are residents of nursing homes and other long-term care facilities are also at risk for severe RSV disease. It should be noted that the numbers of persons enrolled in the trials who were frail, were of advanced age, and lived in long-term care facilities were limited, and persons with compromised immunity were excluded (some of whom might have an attenuated immune response to RSV vaccination). However, adults aged  $\geq 60$  years in these populations may receive vaccination using shared clinical decision-making given the potential for benefit.

### RSV Vaccination Timing

RSV vaccination is currently approved and recommended for administration as a single dose; sufficient evidence does not exist at this time to determine the need for revaccination. Optimally, vaccination should occur before the onset of the RSV season; however, typical RSV seasonality was disrupted by the COVID-19 pandemic and has not returned to pre-pandemic patterns. For the 2023–24 season, clinicians should offer RSV vaccination to adults aged  $\geq 60$  years using shared clinical decision-making as early as vaccine supply becomes available and should continue to offer vaccination to eligible adults who remain unvaccinated.

### Vaccine Administration, Including Coadministration with Other Vaccines

Coadministration of RSV vaccines with other adult vaccines during the same visit is acceptable.<sup>\*\*\*\*\*</sup> Available data on immunogenicity of coadministration of RSV vaccines and other vaccines are currently limited. Coadministration of RSV and seasonal influenza vaccines met noninferiority criteria for immunogenicity with the exception of the FluA/Darwin H3N2 strain when the GSK RSV vaccine was coadministered

<sup>\*\*\*\*</sup> <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-who-are-immunocompromised.html>

<sup>\*\*\*\*\*</sup> When administering more than one vaccine at the same clinical visit, providers should separate injection sites by at least 1 inch if possible and consider administering vaccines that are associated with an enhanced local reaction in separate limbs.

### BOX. Underlying medical conditions and other factors associated with increased risk for severe RSV disease

#### Chronic underlying medical conditions associated with increased risk

- Lung disease (such as chronic obstructive pulmonary disease and asthma)
- Cardiovascular diseases (such as congestive heart failure and coronary artery disease)
- Moderate or severe immune compromise\*
- Diabetes mellitus
- Neurologic or neuromuscular conditions
- Kidney disorders
- Liver disorders
- Hematologic disorders
- Other underlying conditions that a health care provider determines might increase the risk for severe respiratory disease

#### Other factors associated with increased risk

- Frailty<sup>†</sup>
- Advanced age<sup>§</sup>
- Residence in a nursing home or other long-term care facility
- Other underlying factors that a health care provider determines might increase the risk for severe respiratory disease

**Abbreviation:** RSV = respiratory syncytial virus.

\* A list of potentially immune compromising conditions is available at <https://www.cdc.gov/coronavirus/2019-ncov/need-extra-precautions/people-who-are-immunocompromised.html>.

<sup>†</sup> Frailty is a multidimensional geriatric syndrome and reflects a state of increased vulnerability to adverse health outcomes. Although there is no consensus definition, one frequently used tool is the Fried frailty phenotype in which frailty is defined as a clinical syndrome with three or more of the following symptoms present: unintentional weight loss (10 lbs in past year), self-reported exhaustion, weakness (grip strength), slow walking speed, and low physical activity.

<sup>§</sup> Among adults aged  $\geq 60$  years, RSV incidence increases with advancing age. Although age may be considered in determining an older adult patient's risk for severe RSV-associated disease, there is no specific age threshold at which RSV vaccination is more strongly recommended within the age group of adults aged  $\geq 60$  years.

with adjuvanted quadrivalent inactivated influenza vaccine (28,29). RSV and influenza antibody titers were somewhat lower with coadministration; however, the clinical significance of this is unknown.

Administering RSV vaccine with one or more other vaccines at the same visit might increase local or systemic reactogenicity. Data are only available for coadministration of RSV and influenza vaccines, and evidence is mixed regarding increased reactogenicity. Data are lacking on the safety of coadministration with other vaccines that might be recommended for persons

in this age group, such as COVID-19 vaccines; pneumococcal vaccines; adult tetanus, diphtheria, and pertussis vaccines; and the recombinant zoster vaccine (the recombinant zoster vaccine and GSK's RSV vaccine contains the same adjuvant). When deciding whether to coadminister other vaccines with an RSV vaccine, providers should consider whether the patient is up to date with currently recommended vaccines, the feasibility of the patient returning for additional vaccine doses, risk for acquiring vaccine-preventable disease, vaccine reactogenicity profiles, and patient preferences. Postlicensure efficacy and safety monitoring of coadministered RSV vaccines with other vaccines will further direct guidance.

### Precautions and Contraindications

As with all vaccines, RSV vaccination should be delayed for persons experiencing moderate or severe acute illness with or without fever (precaution). RSV vaccines are contraindicated for and should not be administered to persons with a history of severe allergic reaction, such as anaphylaxis, to any component of the vaccine (30,31).

### Reporting of Vaccine Adverse Events

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

### Future Research and Monitoring Priorities

CDC will monitor adverse events, including cases of GBS, ADEM, and other inflammatory neurologic events after RSV vaccination through VAERS and the Vaccine Safety Datalink (<https://www.cdc.gov/vaccinesafety/ensuringsafety/monitoring/vsd/index.html>). CDC will also prioritize estimating vaccine effectiveness against RSV-associated hospitalization. These data will be evaluated by CDC and ACIP as soon as they are available.

According to FDA postmarketing requirements and commitments, GSK will conduct a study evaluating risk for GBS, ADEM, and atrial fibrillation after vaccination with RSVPreF3 (18). Pfizer will conduct two studies, one evaluating risk for GBS and a second evaluating risk for atrial fibrillation after vaccination with RSVpreF (19). Pfizer will also evaluate the safety and immunogenicity of a second RSVpreF dose in a subset of participants in the main phase 3 trial; GSK will evaluate safety, immunogenicity, and efficacy of RSVPreF3 revaccination as part of its main phase 3 trial.

### Summary

#### What is already known about this topic?

Respiratory syncytial virus (RSV) causes substantial morbidity and mortality in older adults. In May 2023, the Food and Drug Administration approved the first two vaccines for prevention of RSV lower respiratory tract disease (LRTD) for use in adults aged  $\geq 60$  years.

#### What is added by this report?

For both vaccine products, vaccination with a single RSV vaccine dose demonstrated moderate to high efficacy in preventing symptomatic RSV-associated LRTD among adults aged  $\geq 60$  years. On June 21, 2023, the Advisory Committee on Immunization Practices recommended that persons aged  $\geq 60$  years may receive a single dose of RSV vaccine, using shared clinical decision-making.

#### What are the implications for public health practice?

RSV vaccination might prevent substantial morbidity in older adults at risk for severe RSV disease; postmarketing surveillance for safety and effectiveness will direct future guidance.

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## References

1. Hamid S, Winn A, Parikh R, et al. Seasonality of respiratory syncytial virus—United States, 2017–2023. *MMWR Morb Mortal Wkly Rep* 2023;72:355–61. PMID:37022977 <https://doi.org/10.15585/mmwr.mm7214a1>
2. Zhang Y, Sakthivel SK, Bramley A, et al. Serology enhances molecular diagnosis of respiratory virus infections other than influenza in children and adults hospitalized with community-acquired pneumonia. *J Clin Microbiol* 2016;55:79–89. PMID:27795341 <https://doi.org/10.1128/JCM.01701-16>
3. Onwuchekwa C, Moreo LM, Menon S, et al. Underascertainment of respiratory syncytial virus infection in adults due to diagnostic testing limitations: a systematic literature review and meta-analysis. *J Infect Dis* 2023;228:173–84. PMID:36661222 <https://doi.org/10.1093/infdis/jiad012>
4. Ramirez J, Carrico R, Wilde A, et al. Diagnosis of respiratory syncytial virus in adults substantially increases when adding sputum, saliva, and serology testing to nasopharyngeal swab RT-PCR. *Infect Dis Ther* 2023;12:1593–603. PMID:37148463 <https://doi.org/10.1007/s40121-023-00805-1>
5. McLaughlin JM, Khan F, Begier E, Swerdlow DL, Jodar L, Falsey AR. Rates of medically attended RSV among US adults: a systematic review and meta-analysis. *Open Forum Infect Dis* 2022;9:ofac300. PMID:35873302 <https://doi.org/10.1093/ofid/ofac300>
6. Zheng Z, Warren JL, Shapiro ED, Pitzer VE, Weinberger DM. Estimated incidence of respiratory hospitalizations attributable to RSV infections across age and socioeconomic groups. *Pneumonia* 2022;14:6. PMID:36280891 <https://doi.org/10.1186/s41479-022-00098-x>
7. Thompson WW, Shay DK, Weintraub E, et al. Mortality associated with influenza and respiratory syncytial virus in the United States. *JAMA* 2003;289:179–86. PMID:12517228 <https://doi.org/10.1001/jama.289.2.179>
8. Matias G, Taylor R, Haguinet F, Schuck-Paim C, Lustig R, Shinde V. Estimates of mortality attributable to influenza and RSV in the United States during 1997–2009 by influenza type or subtype, age, cause of death, and risk status. *Influenza Other Respir Viruses* 2014;8:507–15. PMID:24975705 <https://doi.org/10.1111/irv.12258>
9. Hansen CL, Chaves SS, Demont C, Viboud C. Mortality associated with influenza and respiratory syncytial virus in the US, 1999–2018. *JAMA Netw Open* 2022;5:e220527. PMID:35226079 <https://doi.org/10.1001/jamanetworkopen.2022.0527>
10. Melgar M. Evidence to recommendation framework: respiratory syncytial virus (RSV) in adults [Presentation slides]. Presented at the Advisory Committee on Immunization Practices meeting, Atlanta, GA; February 23, 2023. <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-02/slides-02-23/RSV-Adults-04-Melgar-508.pdf>
11. Branche AR, Saiman L, Walsh EE, et al. Incidence of respiratory syncytial virus infection among hospitalized adults, 2017–2020. *Clin Infect Dis* 2022;74:1004–11. PMID:34244735 <https://doi.org/10.1093/cid/ciab595>
12. Wyffels V, Kariburyo F, Gavart S, Fleischhackl R, Yuce H. A real-world analysis of patient characteristics and predictors of hospitalization among US Medicare beneficiaries with respiratory syncytial virus infection. *Adv Ther* 2020;37:1203–17. PMID:32026380 <https://doi.org/10.1007/s12325-020-01230-3>
13. Kujawski SA, Whitaker M, Ritchey MD, et al. Rates of respiratory syncytial virus (RSV)-associated hospitalization among adults with congestive heart failure—United States, 2015–2017. *PLoS One* 2022;17:e0264890. PMID:35263382 <https://doi.org/10.1371/journal.pone.0264890>
14. Childs A, Zullo AR, Joyce NR, et al. The burden of respiratory infections among older adults in long-term care: a systematic review. *BMC Geriatr* 2019;19:210. PMID:31382895 <https://doi.org/10.1186/s12877-019-1236-6>
15. Melgar M. Updated Evidence to Recommendation Framework: respiratory syncytial virus (RSV) in adults [Presentation slides]. Presented at the Advisory Committee on Immunization Practices meeting, Atlanta, GA; June 21, 2023. <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/06-RSV-Adults-Melgar-508.pdf>
16. Nam HH, Ison MG. Respiratory syncytial virus infection in adults. *BMJ* 2019;366:l5021. PMID:31506273 <https://doi.org/10.1136/bmj.l5021>
17. Waghmare A, Campbell AP, Xie H, et al. Respiratory syncytial virus lower respiratory disease in hematopoietic cell transplant recipients: viral RNA detection in blood, antiviral treatment, and clinical outcomes. *Clin Infect Dis* 2013;57:1731–41. PMID:24065324 <https://doi.org/10.1093/cid/cit639>
18. Kaslow DC. Approval letter: Arexvy. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2023. <https://www.fda.gov/media/167806/download>
19. Kaslow DC. Approval letter: Abrysvo. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2023. <https://www.fda.gov/media/168890/download>
20. Papi A, Ison MG, Langley JM, et al.; ARESVi-006 Study Group. Respiratory syncytial virus prefusion F protein vaccine in older adults. *N Engl J Med* 2023;388:595–608. PMID:36791160 <https://doi.org/10.1056/NEJMoa2209604>
21. Leroux-Roels I, Davis MG, Steenackers K, et al. Safety and immunogenicity of a respiratory syncytial virus prefusion F (RSVPreF3) candidate vaccine in older adults: phase 1/2 randomized clinical trial. *J Infect Dis* 2023;227:761–72. PMID:35904987 <https://doi.org/10.1093/infdis/jiac327>
22. Food and Drug Administration, Vaccines and Related Biological Products Advisory Committee. FDA briefing document: respiratory syncytial virus vaccine recombinant, adjuvanted (proposed trade name: Arexvy). Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2023. <https://www.fda.gov/media/165622/download>



23. GSK. GSK data on file, presentation to ACIP Work Group for RSV in Adults, listing of number of participants by clinical trial. London, United Kingdom; June 2023.
24. Walsh EE, Pérez Marc G, Zareba AM, et al.; RENOIR Clinical Trial Group. Efficacy and safety of a bivalent RSV prefusion F vaccine in older adults. *N Engl J Med* 2023;388:1465–77. PMID:37018468 <https://doi.org/10.1056/NEJMoa2213836>
25. Falsey AR, Walsh EE, Scott DA, et al. Phase 1/2 randomized study of the immunogenicity, safety, and tolerability of a respiratory syncytial virus prefusion F Vaccine in adults with concomitant inactivated influenza vaccine. *J Infect Dis* 2022;225:2056–66. PMID:34931667 <https://doi.org/10.1093/infdis/jiab611>
26. Food and Drug Administration, Vaccines and Related Biological Products Advisory Committee. FDA briefing document: respiratory syncytial virus Vaccine (proposed trade name: Abrysvo). Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2023. <https://www.fda.gov/media/165623/download>
27. Pfizer. Pfizer data on file, tables provided to ACIP Work Group for RSV in Adults, listing of number of participants by clinical trial. New York, NY; June 2023.
28. Friedland L. GSK's RSVPreF3 OA vaccine (AREXVY) [Presentation slides]. Presented at the Advisory Committee on Immunization Practices meeting, Atlanta, GA; June 21, 2023. <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/03-RSV-Adults-Friedland-508.pdf>
29. Gurtman S. RSVpreF older adults clinical development program updates [Presentation slides]. Presented at the Advisory Committee on Immunization Practices meeting, Atlanta, GA; June 21, 2023. <https://www.cdc.gov/vaccines/acip/meetings/downloads/slides-2023-06-21-23/02-RSV-Adults-Gurtman-508.pdf>
30. Food and Drug Administration. Arexvy [package insert]. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2023. <https://www.fda.gov/media/167805/download>
31. Food and Drug Administration. Abrysvo [package insert]. Silver Spring, MD: US Department of Health and Human Services, Food and Drug Administration; 2023. <https://www.fda.gov/media/168889/download>

## Notes from the Field

### Autism Spectrum Disorder Among Children with Laboratory Evidence of Prenatal Zika Virus Exposure — Puerto Rico, 2023

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Infection during pregnancy with Zika virus, a mosquito-borne flavivirus, can cause birth defects and neurodevelopmental abnormalities (1). Autism spectrum disorder (ASD) is a neurodevelopmental disability characterized by social and communication impairment and restricted or repetitive patterns of behavior or interests (2); possible associations between antenatal exposure to a limited number of viruses and ASD have been observed (2). The U.S. Zika Pregnancy and Infant Registry (USZPIR)\* monitors children born during January 1, 2016–March 31, 2018, to women with laboratory evidence of Zika virus infection during pregnancy. This report used data from USZPIR and the Puerto Rico Autism Registry† to estimate the prevalence of ASD diagnoses among children with possible prenatal Zika virus exposure and to describe prenatal characteristics and other outcomes by ASD diagnosis status. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.§

#### Investigation and Outcomes

In Puerto Rico, any child who fails a standardized autism-specific screening, regardless of Zika virus exposure, receives a standardized evaluation at Puerto Rico Children with Special Health Care Needs Pediatric Program and Autism Centers‡ to confirm an ASD diagnosis by *Diagnostic and Statistical Manual for Mental Disorders, Fifth Edition*\*\* criteria. Those who meet ASD criteria are included in the Puerto Rico Autism Registry.

Among 3,122 children reported to USZPIR in Puerto Rico, 109 (3.5%) had received an ASD diagnosis (Table). When analysis was restricted to 1,968 (63.0%) children who received a social-emotional or ASD-specific screener†† at age ≥18 months, 105 (5.3%) received an ASD diagnosis. No statistically significant differences were identified in the proportions of children with differing evidence of Zika virus

exposure,§§ maternal symptoms,¶¶ pregnancy trimester of exposure,\*\*\* or Zika-associated birth defects between those with and without an ASD diagnosis. A higher percentage of children with an ASD diagnosis were male compared with those without an ASD diagnosis.

Among the 109 children with an ASD diagnosis, most required substantial or very substantial support in social communication (79.8%) and restricted, repetitive behaviors (77.0%). The median age at ASD diagnosis was 39 months (range = 19–73 months), and 33 (30.3%) children with an ASD diagnosis also had a family member with an ASD diagnosis.

#### Preliminary Conclusions and Actions

This analysis found that among children with Zika virus exposure reported to USZPIR from Puerto Rico, the prevalence of ASD diagnosis ranged from 3.5% to 5.3%, depending on the denominator. Estimated 2018 prevalence of ASD in general population samples in the continental United States ranged from 1.3% to 4.6% among children aged 4 years (3) and from 2.3% to 4.5% among children aged 8 years (4). A systematic analysis found a prevalence of 723 autism cases per 100,000 population (<1.0%) in Latin America and the Caribbean in 2016 (5).

The findings in this report are subject to at least three limitations. First, follow-up to age 5 years is not yet complete, and ASD can be identified even later in childhood. Second, comparators of ASD prevalence in the general Puerto Rico population are not yet available. As of 2023, Puerto Rico is a participating site for the Autism and Developmental Disabilities Monitoring Network††† to conduct ASD surveillance among children aged 4 and 8 years. Finally, delays in referral of children for evaluation because of the COVID-19 pandemic might have lowered the estimated prevalence of ASD.

Additional information is needed to determine whether an association between Zika virus infection in pregnancy and ASD in children exists. Among children with prenatal Zika exposure, screening was reported for only two thirds. ASD-specific

§§ Includes maternal, placental, or infant laboratory evidence of confirmed Zika virus infection during pregnancy based on presence of Zika virus RNA by a positive nucleic acid amplification test (e.g., reverse transcription–polymerase chain reaction), possible Zika virus infection during pregnancy based on presence of serologic evidence of a Zika virus infection, or serologic evidence of an unspecified flavivirus infection.

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

\*\*\* Symptom onset date or date of earliest laboratory evidence of Zika virus infection was used to calculate trimester of exposure.

††† <https://www.cdc.gov/ncbddd/autism/addm-network-sites.html>

\* <https://www.cdc.gov/pregnancy/zika/research/registry.html>

† <https://www.salud.pr.gov/CMS/242>

§ 45 C.F.R. part 46.102(l)(2), 42 U.S.C. Sect. 241(d); 5 U.S.C. Sect. 552a.

¶ <https://www.salud.pr.gov/CMS/77>

\*\* <https://www.psychiatry.org/psychiatrists/practice/dsm>

†† <https://agesandstages.com/products-pricing/asqse-2/>; <https://mchatscreen.com/>

**TABLE. Prenatal characteristics and child outcomes among live-born infants with and without a diagnosis of autism spectrum disorder\* — U.S. Zika Pregnancy and Infant Registry, Puerto Rico, 2023**

Characteristic	All children reported to USZPIR N = 3,122				Children with ASQ:SE-2 or M-CHAT-R/F <sup>†</sup> at age ≥18 mos reported to USZPIR n = 1,968			
	With ASD diagnosis		Without ASD diagnosis		With ASD diagnosis		Without ASD diagnosis	
	No.	% (95% CI) <sup>§</sup>	No.	% (95% CI) <sup>§</sup>	No.	% (95% CI) <sup>§</sup>	No.	% (95% CI) <sup>§</sup>
<b>Total (row %)</b>	<b>109</b>	<b>3.5 (2.9–4.2)</b>	<b>3,013</b>	<b>96.5 (93.1–100)</b>	<b>105</b>	<b>5.3 (4.4–6.5)</b>	<b>1,863</b>	<b>94.7 (90.4–99.1)</b>
<b>Laboratory evidence of Zika virus infection</b>								
Possible Zika virus infection <sup>¶</sup>	60	55.0 (42.0–70.9)	1,668	55.4 (52.7–58.1)	57	54.3 (41.1–70.3)	944	50.7 (47.5–54.0)
Positive Zika virus NAAT result <sup>**</sup>	49	45.0 (33.3–59.4)	1,345	44.6 (42.3–47.1)	48	45.7 (33.7–60.6)	919	49.3 (46.2–52.6)
<b>Maternal symptoms<sup>††</sup></b>								
Signs and symptoms of Zika virus disease	44	40.4 (29.3–54.2)	1,275	42.3 (40.0–44.7)	44	41.9 (30.5–56.3)	863	46.3 (43.3–49.5)
No signs and symptoms of Zika virus disease	65	59.6 (46.0–76.0)	1,738	57.7 (55.0–60.5)	61	58.1 (44.4–74.6)	1,000	53.7 (50.4–57.1)
<b>Trimester with first evidence of exposure<sup>§§</sup></b>								
1st <sup>¶¶</sup>	45	41.3 (30.1–55.2)	1,102	36.6 (34.5–38.8)	44	41.9 (30.5–56.3)	685	36.8 (34.1–39.6)
2nd	42	38.5 (27.8–52.1)	1,129	37.5 (35.3–39.7)	40	38.1 (27.2–51.9)	711	38.2 (35.4–41.1)
3rd	22	20.2 (12.7–30.6)	782	26.0 (24.2–27.8)	21	20.0 (12.4–30.6)	467	25.1 (22.8–27.5)
<b>Child sex</b>								
Female	35	32.1 (22.4–44.7)	1,502	49.9 (47.4–52.4)	34	32.4 (22.4–45.3)	909	48.8 (45.7–52.1)
Male	74	67.9 (53.3–85.2)	1,511	50.1 (47.7–52.7)	71	67.6 (52.8–85.3)	954	51.2 (48.0–54.6)
<b>Zika-associated birth defects<sup>***</sup></b>								
Yes	5	4.6 (1.5–10.7)	118	3.9 (3.2–4.7)	4	3.8 (1.0–9.8)	84	4.5 (3.6–5.6)
No	104	95.4 (78.0–100.0)	2,895	96.1 (92.6–99.7)	101	96.2 (78.4–100.0)	1,779	95.5 (91.1–100.0)
<b>ASD outcomes</b>								
<b>Family member with ASD diagnosis</b>								
Yes	33	30.3 (20.8–42.5)	—	—	31	29.5 (20.0–41.9)	—	—
No	58	53.2 (40.4–68.8)	—	—	56	53.3 (40.3–69.3)	—	—
Unknown	18	16.5 (9.8–26.1)	—	—	18	17.1 (10.2–27.1)	—	—
<b>Child's age group when parent first noticed symptoms, mos</b>								
<6	6	5.5 (2.0–12.0)	—	—	6	5.7 (2.1–12.4)	—	—
6–12	27	24.8 (16.3–36.0)	—	—	26	24.8 (16.2–36.3)	—	—
13–18	31	28.4 (19.3–40.4)	—	—	29	27.6 (18.5–39.7)	—	—
19–24	19	17.4 (10.5–27.2)	—	—	18	17.1 (10.2–27.1)	—	—
25–30	5	4.6 (1.5–10.7)	—	—	5	4.8 (1.6–11.1)	—	—
31–36	10	9.2 (4.4–16.9)	—	—	10	9.5 (4.6–17.5)	—	—
37–42	3	2.8 (0.6–8.0)	—	—	3	2.9 (0.6–8.4)	—	—
43–48	3	2.8 (0.6–8.0)	—	—	3	2.9 (0.6–8.4)	—	—
49–54	2	1.8 (0.2–6.6)	—	—	2	1.9 (0.2–6.9)	—	—
Unknown	3	2.8 (0.6–8.0)	—	—	3	2.9 (0.6–8.4)	—	—
<b>Age group of ASD diagnosis, mos</b>								
Median (range)	39	(19.0–73.0)	—	—	39	(19.0–73.0)	—	—
18–25	17	15.6 (9.1–25.0)	—	—	17	16.2 (9.4–25.9)	—	—
26–33	24	22.0 (14.1–32.8)	—	—	22	21.0 (13.1–31.7)	—	—
34–41	21	19.3 (11.9–29.5)	—	—	21	20.0 (12.4–30.6)	—	—
42–49	15	13.8 (7.7–22.7)	—	—	15	14.3 (8.0–23.6)	—	—
50–57	13	11.9 (6.4–20.4)	—	—	12	11.4 (5.9–20.0)	—	—
58–65	17	15.6 (9.1–25.0)	—	—	16	15.2 (8.7–24.8)	—	—
66–73	2	1.8 (0.2–6.6)	—	—	2	1.9 (0.2–6.9)	—	—
<b>Level of support in social communication<sup>†††</sup></b>								
Level 1	22	20.2 (12.7–30.6)	—	—	22	21.0 (13.1–31.7)	—	—
Level 2	47	43.1 (31.7–57.3)	—	—	46	43.8 (32.1–58.4)	—	—
Level 3	40	36.7 (26.2–50.0)	—	—	37	35.2 (24.8–48.6)	—	—
<b>Level of support in restrictive, repetitive behaviors<sup>†††</sup></b>								
Level 1	25	22.9 (14.8–33.9)	—	—	24	22.9 (14.7–34.0)	—	—
Level 2	64	58.7 (45.2–75)	—	—	62	59.0 (45.3–75.7)	—	—
Level 3	20	18.3 (11.2–28.3)	—	—	19	18.1 (10.9–28.3)	—	—

See table footnotes on the next page.

**TABLE. (Continued) Prenatal characteristics and child outcomes among live-born infants with and without a diagnosis of autism spectrum disorder\* — U.S. Zika Pregnancy and Infant Registry, Puerto Rico, 2023**

**Abbreviations:** ASD = autism spectrum disorder; ASQ: SE-2 = Ages and Stages Questionnaires: Social-Emotional, Second Edition; M-CHAT-R/F = Modified Checklist for Autism in Toddlers, Revised with Follow-Up; NAAT = nucleic acid amplification test; USZPIR = U.S. Zika Pregnancy and Infant Registry.

\* ASD diagnosis by *Diagnostic and Statistical Manual for Mental Disorder, Fifth Edition* criteria. <https://www.psychiatry.org/psychiatrists/practice/dsm>

† <https://agesandstages.com/products-pricing/asqse-2/>; <https://mchatscreen.com/>

‡ CIs were calculated assuming a Poisson distribution.

¶ Includes maternal, placental, or infant laboratory evidence of possible Zika virus infection during pregnancy based on serologic evidence of a Zika virus infection, or serologic evidence of an unspecified flavivirus infection.

\*\* Includes maternal, placental, or infant laboratory evidence of confirmed Zika virus infection during pregnancy based on presence of Zika virus RNA by a positive NAAT (e.g., reverse transcription–polymerase chain reaction).

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

‡‡ Symptom onset date or date of earliest laboratory evidence of Zika virus infection was used to calculate trimester of exposure.

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

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

††† Level 1: requires support; Level 2: requires substantial support; Level 3: requires very substantial support.

screening is recommended for all children to identify concerns as early as possible and minimize delays in intervention.<sup>§§§</sup>

<sup>§§§</sup> <https://publications.aap.org/pediatrics/article/145/1/e20193447/36917/Identification-Evaluation-and-Management-of>

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### References

- Mulkey SB, Arroyave-Wessel M, Peyton C, et al. Neurodevelopmental abnormalities in children with in utero Zika virus exposure without congenital Zika syndrome. *JAMA Pediatr* 2020;174:269–76. PMID:31904798 <https://doi.org/10.1001/jamapediatrics.2019.5204>
- Shuid AN, Jayusman PA, Shuid N, Ismail J, Kamal Nor N, Mohamed IN. Association between viral infections and risk of autistic disorder: an overview. *Int J Environ Res Public Health* 2021;18:2817. PMID:33802042 <https://doi.org/10.3390/ijerph18062817>
- Shaw KA, Bilder DA, McArthur D, et al. Early identification of autism spectrum disorder among children aged 4 years—Autism and Developmental Disabilities Monitoring Network, 11 sites, United States, 2020. *MMWR Surveill Summ* 2023;72(No. SS-1):1–15. PMID:36952289 <https://doi.org/10.15585/mmwr.ss7201a1>
- Maenner MJ, Warren Z, Williams AR, et al. Prevalence and characteristics of autism spectrum disorder among children aged 8 years—Autism and Developmental Disabilities Monitoring Network, 11 sites, United States, 2020. *MMWR Surveill Summ* 2023;72(No. SS-2):1–14. PMID:36952288 <https://doi.org/10.15585/mmwr.ss7202a1>
- Olusanya BO, Davis AC, Wertlieb D, et al.; Global Research on Developmental Disabilities Collaborators. Developmental disabilities among children younger than 5 years in 195 countries and territories, 1990–2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Glob Health* 2018;6:e1100–21. PMID:30172774 [https://doi.org/10.1016/S2214-109X\(18\)30309-7](https://doi.org/10.1016/S2214-109X(18)30309-7)

## Notes from the Field

### An Outbreak of Shiga Toxin–Producing *Escherichia coli* O157:H7 Associated with a Farming Camp — Tennessee, 2022

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On June 22, 2022, the Tennessee Department of Health (TDH) was notified of a child hospitalized with Shiga toxin–producing *Escherichia coli* (STEC) O157:H7 after attending a farming camp at farm A. Three days later, TDH was notified of a second hospitalized child with hemolytic uremic syndrome, whose brother had attended the same camp, prompting an investigation. During the summer, farm A held three week-long summer camps teaching animal husbandry to children aged 6–10 years by assigning campers a baby goat (kid) to care for. STEC resides in the gastrointestinal tract of ruminants such as cattle, goats, sheep, and deer without causing illness in the animal\* (1). Outbreaks among humans associated with petting zoos are well documented (2–5).

#### Investigation and Outcomes

On June 28 and 29, TDH conducted an environmental assessment at farm A. In addition to an onsite interview with the farm owners and employees, the assessment included facility observations of animal pens, public petting areas, areas where children cared for the animals, food service facilities, handwashing and sanitizing facilities, play areas, and toilets. Health department staff members collected camp attendee registration and goat assignment records and conducted environmental sampling, including the collection of 41 samples from animals, animal feces, animal pens, water sources, and toilets.

TDH also sent an online survey to the parents and guardians of all 82 children who had attended camp at farm A during June 6–24 to ascertain dates of attendance, illnesses and outcomes, foods consumed, and camp activities. The outbreak-specific survey was completed by parents or guardians of 53 (65%) campers.

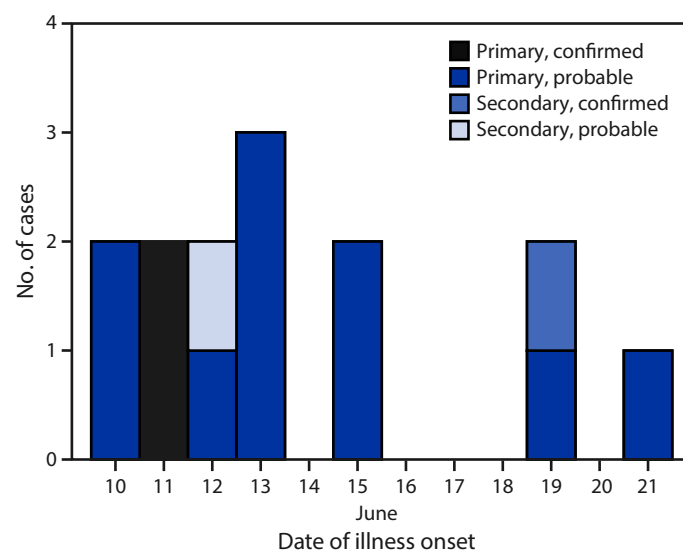
Survey responses facilitated conduct of a case-control analysis. Cases were defined in terms of 1) the person who was ill (primary versus secondary) and 2) the symptoms and laboratory results (probable versus confirmed). A primary case was defined as an illness in a person who attended any of the three camps during June 6–24; a secondary case was a compatible illness within 10 days of exposure to a primary case in

the same household or to a close contact of a summer camp attendee (irrespective of illness in the attendee). Probable cases included the onset of diarrhea within 10 days of attending the summer camp (primary cases) or within 10 days of exposure to a secondary case; confirmed outbreak cases were defined as a positive polymerase chain reaction or enzyme immunoassay Shiga toxin test result from a specimen collected after June 6.<sup>†</sup> Twelve primary cases (including two confirmed and 10 probable) and two secondary cases (one confirmed and one probable) were identified (patient age range = 2–38 years) (Figure). One patient each with a primary and secondary case was hospitalized; one death occurred in a child aged 2 years with a secondary confirmed case.

The case-control analysis included 12 ill camp attendees as case-patients and 58 healthy children identified from the

<sup>†</sup> All persons who received testing were tested by their health care provider. Providers sent two positive specimens to the Tennessee State Public Health Laboratory for sequencing, and the third was sequenced by the Florida State Public Health Laboratory because the child became ill and was hospitalized in Florida.

**FIGURE. Onset of primary,\* secondary,<sup>†</sup> probable,<sup>§</sup> and confirmed<sup>¶</sup> cases of Shiga toxin–producing *Escherichia coli* O157:H7 illness among persons associated with a farming camp (N = 14) — Tennessee, June 2022**



\* An illness in a child who attended any of the three farm A summer camps during June 6–24, 2022.

<sup>†</sup> A compatible illness in a household member or close contact of a farm A summer camp attendee.

<sup>§</sup> The onset of diarrhea within 10 days of attending the farm A summer camp (primary cases) or within 10 days of exposure to a patient with a primary case (secondary case).

<sup>¶</sup> A positive stool culture test result for Shiga toxin–producing *Escherichia coli* from a specimen collected after June 6.

\* <https://www.cdc.gov/healthypets/diseases/ecoli.html>

camp attendee list as controls. Chi-square analysis was used to calculate odds ratios; 95% CIs that excluded 1 were considered statistically significant. Because the camp's food and activity schedules did not change between weeks, and no contributing factors were identified in farm A's food service establishment, neither a specific activity nor food was considered to be associated with illness. Attendance during the first week of camp, however, was significantly associated with illness (odds ratio = 13.1; 95% CI = 2.59–66.57). Camp operators reported being aware of the National Association of State Public Health Veterinarians Animal Contact Compendium<sup>§</sup> and reported incorporating handwashing stations, observing children during animal interactions, and keeping the animal areas clean and disinfected.

Investigators were able to isolate STEC by culture in six samples collected at farm A; these were further subtyped into three STEC serotypes by core genome multilocus sequence typing: H14 (one rectal swab [kid] and one stool swab [kid]), O157:H7 (one stool swab [kid] and one wood swab [inside kid barn]), and O26:H11 (two stool samples [kids]).<sup>¶</sup> Only STEC O157:H7 was associated with clinical illnesses. The two farm A STEC O157:H7 isolates were closely related by whole genome sequencing to the three outbreak-associated STEC O157:H7 patient isolates.

### Preliminary Conclusions and Actions

In response to the outbreak, farm A voluntarily closed the camp, expedited the demolition of the kid barn, euthanized two kids with positive STEC test results, and moved the kid herd off the property. During closure, farm A independently consulted with veterinarians and other petting zoos to identify additional methods for reducing disease transmission. Based on recommendations provided, the facility discontinued the animal husbandry portion of the camp, increased signage encouraging handwashing after touching animals or objects throughout the facility, and increased messaging on their website about zoonotic diseases, populations at highest risk, and ways to mitigate risk for infection. On July 18, farm A reopened their summer camp without the goat husbandry component.

TDH concluded that this outbreak was associated with STEC O157:H7-infected kids and involved secondary transmission. Hand-to-mouth contact has been observed to occur almost three times per hour among children aged 6–10 years,\*\*

<sup>§</sup> <http://nasphv.org/documentsCompendiumAnimals.html>

<sup>¶</sup> The remaining 35 samples tested negative, including one swab each from three goats, four from well water (mother goat drinking water, kid drinking water, pond, and water pipe), four from treated well water, eight from the barn environment (including one from goat feed), three from portable restrooms, 10 goat feces specimens, two lamb feces specimens, and one stool specimen from an unknown animal source.

\*\* <https://onlinelibrary.wiley.com/doi/10.1111/j.1539-6924.2007.00893.x>

supporting the potential for STEC ingestion from contaminated environmental surfaces. The hypothesis of prolonged contact between campers and kids resulting in illness is strengthened by the finding that, after conducting routine monitoring of pathogen and case report forms as well as complaint surveillance systems, STEC was not identified by patrons of the farm apart from camp attendees and their household members. Animal farms, petting zoos, and other environments where small children might have direct contact with ruminant animals should be aware of the risk for zoonotic STEC transmission and make efforts to mitigate these risks by promoting proper hand hygiene during and after animal contact.

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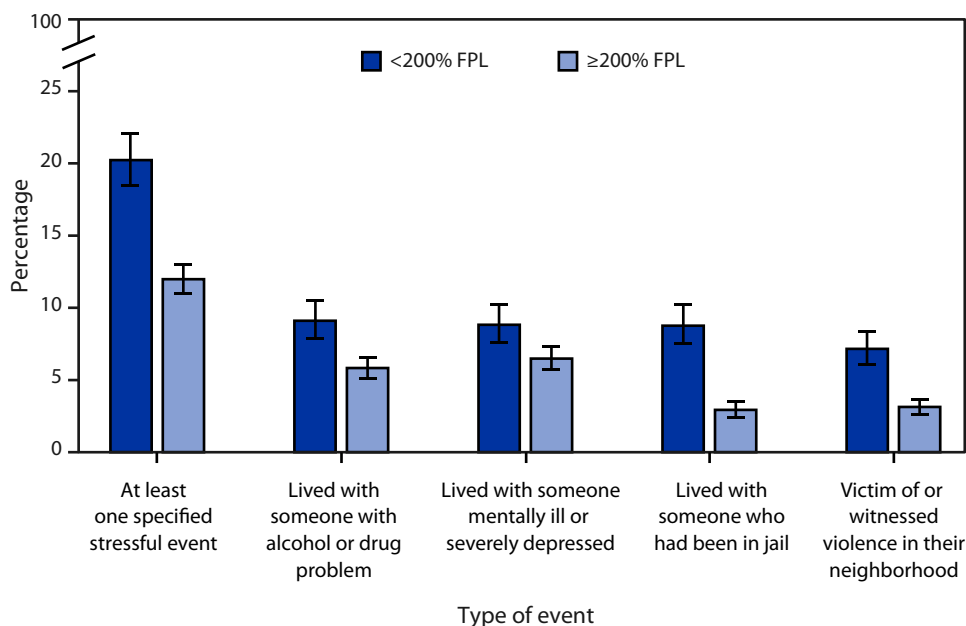
### References

- Schlager S, Lepuschitz S, Ruppitsch W, et al. Petting zoos as sources of Shiga toxin-producing *Escherichia coli* (STEC) infections. *Int J Med Microbiol* 2018;308:927–32. PMID:30257809 <https://doi.org/10.1016/j.ijmm.2018.06.008>
- CDC. Outbreak of Shiga toxin-producing *Escherichia coli* O157 infection associated with a day camp petting zoo—Pinellas County, Florida, May–June 2007. *MMWR Morb Mortal Wkly Rep* 2009;58:426–8. PMID:19407735
- Laughlin M, Gambino-Shirley K, Gacek P, et al. Notes from the field: outbreak of *Escherichia coli* O157 infections associated with goat dairy farm visits—Connecticut, 2016. *MMWR Morb Mortal Wkly Rep* 2016;65:1453–4. PMID:28033314 <https://doi.org/10.15585/mmwr.mm655051a6>
- CDC. Outbreaks of *Escherichia coli* O157:H7 associated with petting zoos—North Carolina, Florida, and Arizona, 2004 and 2005. *MMWR Morb Mortal Wkly Rep* 2005;54:1277–80. PMID:16371942
- Daly RF, House J, Stanek D, Stobierski MG; National Association of State Public Health Veterinarians Animal Contact Compendium Committee. Compendium of measures to prevent disease associated with animals in public settings, 2017. *J Am Vet Med Assoc* 2017;251:1268–92. PMID:29154705 <https://doi.org/10.2460/javma.251.11.1268>

## QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

## Percentage\* of Children and Adolescents Aged ≤17 Years Who Have Experienced a Specified Stressful Life Event,<sup>†</sup> by Type of Event and Family Income<sup>§</sup> — National Health Interview Survey,<sup>¶</sup> United States, 2021



**Abbreviation:** FPL = federal poverty level.

\* With 95% CIs indicated by error bars.

<sup>†</sup> Percentages for the specified stressful life events are based on the following questions: 1) "Has child ever been the victim of violence or witnessed violence in their neighborhood?"; 2) "Has child ever been separated from a parent or guardian because the parent or guardian went to jail, prison, or a detention center?"; 3) "Did child ever live with anyone who was mentally ill or severely depressed?"; 4) "Did child ever live with anyone who had a problem with alcohol or drugs?" Having any stressful event was based on having answered "yes" to any of these four questions. The four stressful life event questions come from a larger battery of questions on adverse childhood experiences.

<sup>§</sup> As a percentage of FPL, which is based on family income and family size, using the U.S. Census Bureau's poverty thresholds. Family income was imputed when missing.

<sup>¶</sup> Estimates are based on household interviews of a sample of the civilian, noninstitutionalized U.S. population.

In 2021, 20.2% of children and adolescents in families with incomes <200% of FPL and 12.0% of those in families with incomes ≥200% of FPL had experienced at least one specified stressful life event. Children and adolescents in families with incomes <200% of FPL were more likely than those in families with incomes ≥200% of FPL to have had the following experiences: lived with someone with alcohol or drug problems (9.1% versus 5.8%); lived with someone who was mentally ill or severely depressed (8.8% versus 6.5%); lived with someone who had been in jail (8.8% versus 2.9%); or been the victim of or witnessed violence in their neighborhood (7.2% versus 3.1%).

**Source:** National Center for Health Statistics, National Health Interview Survey, 2021. <https://www.cdc.gov/nchs/nhis/index.htm>

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For more information on this topic, CDC recommends the following link: <https://www.cdc.gov/violenceprevention/aces/index.html>

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