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# Motor Vehicle Crash Deaths — United States and 28 Other High-Income Countries, 2015 and 2019

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Motor vehicle crashes are preventable, yet they continue to be a leading cause of death in the United States. An average of 36,791 crash deaths occurred each year (101 deaths each day) during 2015–2019 in the United States. To measure progress in reducing motor vehicle crash deaths, CDC calculated population-based, distance-based, and vehicle-based death rates in 2015 and 2019, as well as average rates and average percent changes from 2015 to 2019, for the United States and 28 other high-income countries for which data were available. In 2019, the population-based death rate in the United States (11.1 per 100,000 population; 36,355 deaths) was the highest among the 29 high-income countries and was 2.3 times the average rate of the 28 other high-income countries (4.8). The 2019 U.S. distance-based death rate (1.11 per 100 million vehicle miles traveled) was higher than the average rate among 20 other high-income countries (0.92), and the 2019 U.S. vehicle-based death rate (1.21 per 10,000 registered vehicles) was higher than the average rate among 27 other high-income countries (0.78). The population-based death rate in the United States increased 0.1% from 2015 to 2019, whereas the average change among 27 other high-income countries was −10.4%. Widespread implementation of proven strategies and the Safe System approach, which accounts for human error and works to protect everyone on the road, (*1*) can help reduce motor vehicle crash deaths in the United States.

CDC analyzed 2015 and 2019 data from the International Transport Forum's International Road Traffic and Accident Database (IRTAD),* which contains standardized and validated crash, population, exposure, and vehicle data regularly reported by participating countries. IRTAD data used in this report were current as of February 2022; because of data lag, 2020 and 2021 data were not complete enough to be used. All high-income† countries that provided crash death data and had populations of >1 million persons were included. Countries that met these requirements but did not have data for all study variables or had trend breaks during the study period were included in analyses for which they had comparable data. Data from other

* https://www.itf-oecd.org/irtad-road-safety-database and https://www.itf-oecd.org/irtad-publications

† https://datatopics.worldbank.org/world-development-indicators/the-world-by-income-and-region.html

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sources were included for two countries: 2019 U.S. motor vehicle crash deaths came from the Fatality Analysis Reporting System[§] (*2*); crash deaths for the Netherlands came from the Institute for Road Safety Research (SWOV).[¶] Motor vehicle crash deaths included any road user who was killed in a crash (e.g., car occupants, motorcyclists, pedestrians, and bicyclists).

The number of crash deaths is reported for each country. The following three motor vehicle crash death rates and associated percent changes were calculated: 1) population-based (per 100,000 population), 2) distance-based (per 100 million vehicle miles traveled), and 3) vehicle-based (per 10,000 registered vehicles). CDC also calculated average rates and average percent changes (comparing 2015 and 2019) with and without the United States. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.[**]

The number of crash deaths from 2015 to 2019 decreased in 21 countries and increased in seven countries (Table 1). Percent changes ranged from a 27.5% decrease in South Korea to an 11.8% increase in Denmark; the average change was –8.1%. The United States experienced a 2.5% increase (from 35,484 deaths in 2015 to 36,355 deaths in 2019).

In 2019, crash deaths per 100,000 population for all 29 countries ranged from a low of 2.0 (Norway) to a high of 11.1 (United States). The U.S. rate was 2.3 times the average rate of the other countries (4.8). The population-based death rate decreased from 2015 to 2019 in 22 countries and increased in six countries (Figure). The United States experienced a nominal 0.1% increase from 2015 to 2019, whereas the average percent change for the 27 other high-income countries was –10.4%.

Among the 21 countries with vehicle-miles–traveled data for 2019, crash deaths per 100 million vehicle miles traveled ranged from 0.38 (Norway) to 2.05 (Hungary) (Table 2). The United States had the sixth-highest distance-based crash death rate (1.11), which was higher than the average rate among 20 other high-income countries (0.92). The United States experienced a 2.9% decrease from 2015 to 2019, whereas the

[§] In the United States, two national data systems monitor motor vehicle crash deaths: the National Highway Traffic Safety Administration's Fatality Analysis Reporting System (FARS) and the National Vital Statistics System (NVSS). FARS captures detailed information on motor vehicle crash deaths from a variety of sources, including death certificates, police reports, coroner/medical examiner reports, hospitals, and emergency medical services. NVSS, coordinated and managed by CDC's National Center for Health Statistics, contains information from death certificates filed in all 50 states and the District of Columbia. These two data systems operate independently, using different methods to collect and code data; therefore, each data system provides slightly different numbers of motor vehicle crash deaths (https://www.tandfonline.com/doi/full/10.1080/15389588.2019.1576036). FARS data are regularly reported to IRTAD for the United States. At the time of the analysis, final 2019 FARS motor vehicle crash death data were available but were not yet incorporated into IRTAD; therefore, 2019 motor vehicle crash death data were taken directly from FARS.

[¶] The Netherlands determines crash deaths by comparing and combining three data sources. https://swov.nl/en/fact-sheet/road-deaths-netherlands

[**] 5 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. Motor vehicle crash deaths and deaths per 100,000 population — 29 high-income countries, 2015 and 2019***

| Country† | No. of MVC deaths | | | Population, | Population, | MVC deaths per 100,000 population** | | |
|---|---|---|---|---|---|---|---|---|
| | 2015 | 2019§,¶ | % Change,** 2015 to 2019 | 2015§ | 2019§,¶ | 2015 | 2019 | % Change, 2015 to 2019 |
| United States | 35,484 | 36,355 | 2.5 | 320,635,163 | 328,239,523 | 11.1 | 11.1 | 0.1 |
| Chile†† | NA | 1,973 | NA | 18,006,407 | 18,726,548 | NA | 10.5 | NA |
| Poland | 2,938 | 2,909 | −1.0 | 38,005,614 | 37,972,812 | 7.7 | 7.7 | −0.9 |
| New Zealand | 318 | 352 | 10.7 | 4,596,700 | 4,979,200 | 6.9 | 7.1 | 2.2 |
| Lithuania | 239 | 186 | −22.2 | 2,921,262 | 2,794,184 | 8.2 | 6.7 | −18.6 |
| South Korea | 4,621 | 3,349 | −27.5 | 51,014,947 | 51,709,098 | 9.1 | 6.5 | −28.5 |
| Greece | 793 | 688 | −13.2 | 10,858,018 | 10,724,599 | 7.3 | 6.4 | −12.2 |
| Hungary | 648 | 602 | −7.1 | 9,855,571 | 9,772,756 | 6.6 | 6.2 | −6.3 |
| Portugal | 593 | 621 | 4.7 | 10,374,822 | 10,276,617 | 5.7 | 6.0 | 5.7 |
| Czechia | 735 | 617 | −16.1 | 10,538,275 | 10,649,800 | 7.0 | 5.8 | −16.9 |
| Belgium | 762 | 644 | −15.5 | 11,237,274 | 11,455,519 | 6.8 | 5.6 | −17.1 |
| Italy | 3,428 | 3,173 | −7.4 | 60,795,612 | 60,359,546 | 5.6 | 5.3 | −6.8 |
| France | 3,461 | 3,244 | −6.3 | 64,300,821 | 64,812,052 | 5.4 | 5.0 | −7.0 |
| Slovenia | 120 | 102 | −15.0 | 2,062,874 | 2,080,908 | 5.8 | 4.9 | −15.7 |
| Austria | 479 | 416 | −13.2 | 8,584,926 | 8,858,775 | 5.6 | 4.7 | −15.8 |
| Canada | 1,887 | 1,762 | −6.6 | 35,826,748 | 37,593,384 | 5.3 | 4.7 | −11.0 |
| Australia | 1,205 | 1,187 | −1.5 | 23,815,995 | 25,365,571 | 5.1 | 4.7 | −7.5 |
| Israel | 356 | 355 | −0.3 | 8,463,400 | 9,054,100 | 4.2 | 3.9 | −6.8 |
| Netherlands | 621 | 661 | 6.4 | 16,900,726 | 17,282,163 | 3.7 | 3.8 | 4.1 |
| Finland | 270 | 211 | −21.9 | 5,471,753 | 5,517,919 | 4.9 | 3.8 | −22.5 |
| Spain | 1,689 | 1,755 | 3.9 | 46,449,565 | 46,937,060 | 3.6 | 3.7 | 2.8 |
| Germany | 3,459 | 3,046 | −11.9 | 81,197,537 | 83,019,213 | 4.3 | 3.7 | −13.9 |
| Denmark | 178 | 199 | 11.8 | 5,659,715 | 5,806,081 | 3.1 | 3.4 | 9.0 |
| Japan | 4,885 | 3,920 | −19.8 | 127,095,000 | 126,167,000 | 3.8 | 3.1 | −19.2 |
| Ireland | 162 | 140 | −13.6 | 4,677,627 | 4,904,240 | 3.5 | 2.9 | −17.6 |
| United Kingdom | 1,804 | 1,808 | 0.2 | 65,110,034 | 66,796,807 | 2.8 | 2.7 | −2.3 |
| Switzerland | 253 | 187 | −26.1 | 8,237,666 | 8,544,527 | 3.1 | 2.2 | −28.7 |
| Sweden | 259 | 221 | −14.7 | 9,747,355 | 10,230,185 | 2.7 | 2.2 | −18.7 |
| Norway | 117 | 108 | −7.7 | 5,165,802 | 5,328,212 | 2.3 | 2.0 | −10.5 |
| **Overall summary statistics** | | | | | | | | |
| Overall mean (with United States) | 2,563 | 2,441 | −8.1 | 36,814,042 | 37,446,841 | 5.4 | 5.0 | −10.0 |
| Overall median (with United States) | 692 | 644 | −7.6 | 10,858,018 | 10,724,599 | 5.3 | 4.7 | −10.8 |
| Minimum value (with United States) | 117 | 102 | −27.5 | 2,062,874 | 2,080,908 | 2.3 | 2.0 | −28.7 |
| Maximum value (with United States) | 35,484 | 36,355 | 11.8 | 320,635,163 | 328,239,523 | 11.1 | 11.1 | 9.0 |
| Overall mean (without United States) | 1,344 | 1,230 | −8.5 | 26,677,573 | 27,061,388 | 5.2 | 4.8 | −10.4 |
| Overall median (without United States) | 648 | 633 | −7.7 | 10,698,147 | 10,687,200 | 5.3 | 4.7 | −11.0 |

**Abbreviations:** MVC = motor vehicle crash; NA = not applicable.

* All data come from the International Transport Forum's International Road Traffic and Accident Database, with two exceptions. The number of MVC deaths for the United States in 2019 comes from the Fatality Analysis Reporting System's Final File, released in March 2022. The numbers of crash deaths in 2015 and 2019 for the Netherlands are reported by the Institute for Road Safety Research (SWOV) and are determined by comparing and combining three data sources. https://swov.nl/en/fact-sheet/road-deaths-netherlands

† Countries are listed in descending order by 2019 MVC deaths per 100,000 population.

§ The following numbers were considered estimates: MVC deaths for Canada in 2019 and the population for Chile and New Zealand in 2015 and 2019.

¶ The following numbers were considered provisional: MVC deaths for Portugal and Australia in 2019 and the population for Australia in 2019.

** Percent changes and MVC deaths per 100,000 population were calculated based on numbers that were not rounded. However, after being calculated, they were rounded to the nearest 10th of a decimal point.

†† Chile changed its definition for MVC deaths starting in 2019, which creates a trend break. Data for MVC deaths in Chile in 2019 cannot be compared with previous years. Therefore, 2015 MVC deaths and any calculations that would be based on 2015 MVC deaths are not reported for Chile.

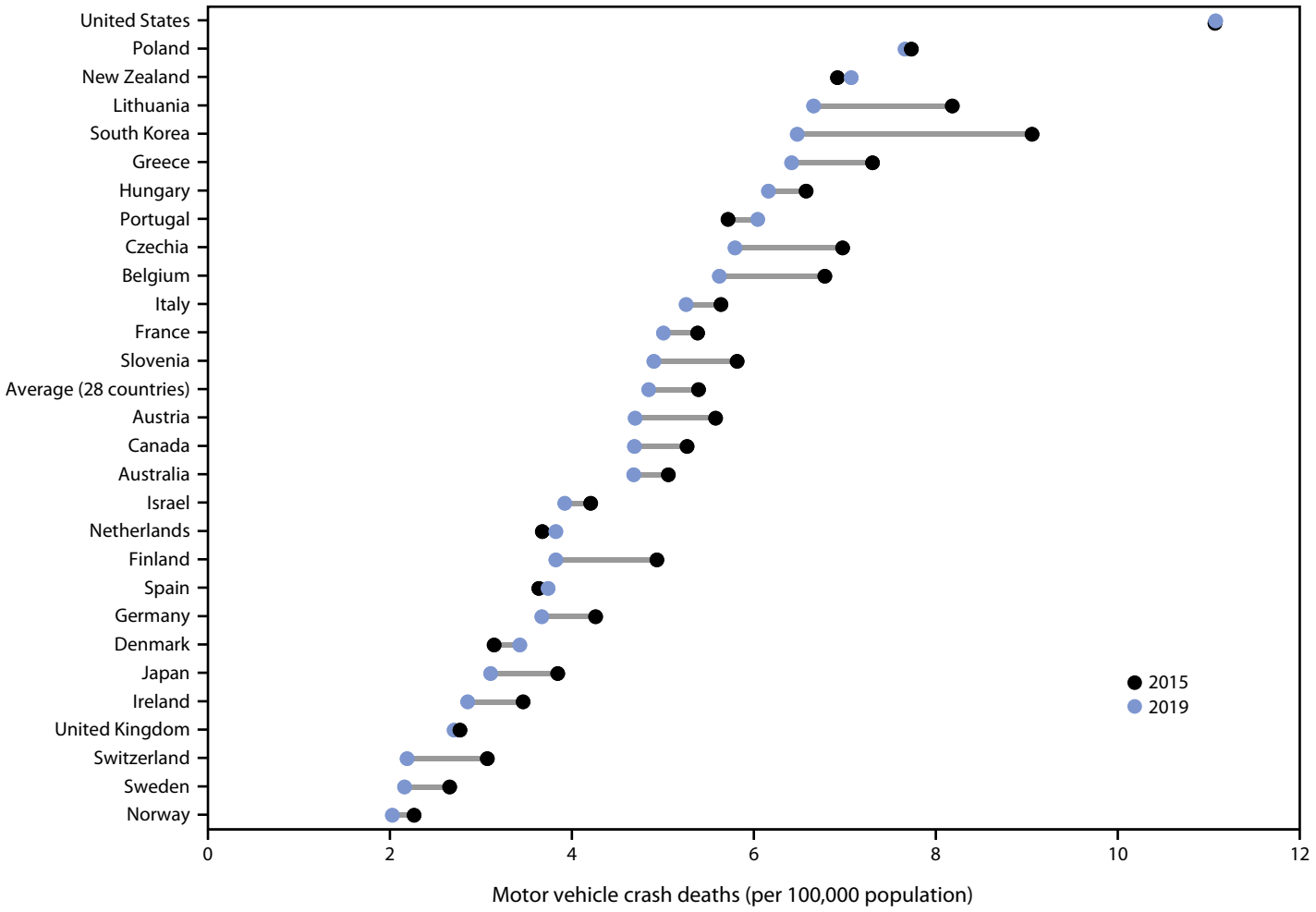
average percent change for the 16 other high-income countries was −14.2%.

Among the 28 countries with registered vehicle information for 2019, crash deaths per 10,000 registered vehicles ranged from 0.27 (Norway) to 3.52 (Chile) (Table 2). The United States had the fourth-highest vehicle-based death rate (1.21), which was 1.6 times the average rate for the 27 other countries (0.78). Denmark was the only country with a higher rate in 2019 than in 2015. The United States experienced the second-smallest decrease (−3.7%).

## Discussion

In 2019, 36,355 persons in the United States were killed in motor vehicle crashes. The United States accounted for 51.4% of the deaths in this study but only 30.2% of the population. The United States had the highest population-based death rate,

**FIGURE. Motor vehicle crash deaths*,† per 100,000 population — 28 high-income countries,§,¶ 2015 and 2019****




* The numbers of motor vehicle crash deaths for Canada in 2019 and the population for New Zealand in 2015 and 2019 were considered estimates.
† The numbers of motor vehicle crash deaths for Portugal and Australia in 2019 and the population for Australia in 2019 were considered provisional.
§ Countries are listed in descending order by 2019 motor vehicle crash deaths per 100,000 population.
¶ Chile changed its definition for motor vehicle crash deaths starting in 2019, which creates a trend break. Data for motor vehicle crash deaths in Chile in 2019 cannot be compared with previous years. Therefore, data for Chile are not included.
** All data come from the International Transport Forum's International Road Traffic and Accident Database, with two exceptions. The number of motor vehicle crash deaths for the United States in 2019 (used to calculate the 2019 motor vehicle crash death rate in the United States) comes from the Fatality Analysis Reporting System's Final File, released in March 2022. The numbers of crash deaths in 2015 and 2019 (used to calculate the motor vehicle crash death rates for the Netherlands) are reported by the Institute for Road Safety Research (SWOV) and are determined by comparing and combining three data sources. https://swov.nl/en/fact-sheet/road-deaths-netherlands

the sixth-highest distance-based death rate, and the fourth-highest vehicle-based death rate among countries with data available. From 2015 to 2019, the U.S. population-based death rate increased nominally by 0.1%, whereas the average percent change of the other high-income countries was –10.4%. The United States experienced small decreases in distance-based and vehicle-based death rates, but these were well below the average decreases among other high-income countries.

If the United States were to achieve the average population-based crash death rate among all other high-income countries in this study (4.8), approximately 20,517 lives and $280.5 million in medical costs (in 2019 U.S. dollars) could be saved each year.†† However, recent data (*2*) indicate that U.S. motor vehicle crash deaths increased from 36,355 in 2019 to 38,824 in 2020 (a 6.8% increase), despite an 11.0% decrease in vehicle miles traveled. In addition, early estimates for 2021 indicate motor vehicle crash deaths further increased to 42,915. The number of motor vehicle crash deaths in 2021

†† Costs were calculated in 2019 U.S. dollars using CDC's Web-based Injury Statistics Query and Reporting System Cost of Injury Module. https://wisqars.cdc.gov/cost/

**TABLE 2. Motor vehicle crash deaths per 100 million vehicle miles traveled and per 10,000 registered vehicles — selected high-income countries,* 2015 and 2019†**

| Country§ | No. of MVC deaths, 2015 | No. of MVC deaths, 2019¶,** | Vehicle miles traveled (in billions), 2015¶,†† | Vehicle miles traveled (in billions), 2019¶,**,†† | MVC deaths§§ per 100 million vehicle miles traveled | | | No. of registered vehicles, 2015¶¶ | No. of registered vehicles, 2019¶¶ | MVC deaths§§ per 10,000 registered vehicles | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | 2015 | 2019 | % Change,†† 2015 to 2019 | | | 2015 | 2019 | % Change,†† 2015 to 2019 |
| United States | 35,484 | 36,355 | 3,089.8 | 3,261.8 | 1.15 | 1.11 | −2.9 | 281,312,446 | 299,267,114 | 1.26 | 1.21 | −3.7 |
| Chile*** | NA | 1,973 | NA | NA | NA | NA | NA | 4,647,062 | 5,599,733 | NA | 3.52 | NA |
| Poland | 2,938 | 2,909 | 138.0 | 155.1 | 2.13 | 1.88 | −11.9 | 27,409,000 | 31,989,000 | 1.07 | 0.91 | −15.2 |
| New Zealand | 318 | 352 | 26.9 | 30.4 | 1.18 | 1.16 | −2.0 | 3,514,782 | 4,403,000 | 0.90 | 0.80 | −11.6 |
| Lithuania | 239 | 186 | NA | NA | NA | NA | NA | 1,549,158 | 1,719,065 | 1.54 | 1.08 | −29.9 |
| South Korea | 4,621 | 3,349 | 185.4 | 204.8 | 2.49 | 1.64 | −34.4 | 23,853,034 | 26,990,456 | 1.94 | 1.24 | −36.0 |
| Greece | 793 | 688 | NA | NA | NA | NA | NA | 9,518,000 | 9,822,000 | 0.83 | 0.70 | −15.9 |
| Hungary | 648 | 602 | NA | 29.3 | NA | 2.05 | NA | 3,886,000 | 4,625,398 | 1.67 | 1.30 | −21.9 |
| Czechia | 735 | 617 | 31.7 | 35.7 | 2.32 | 1.73 | −25.5 | 6,499,000 | 7,643,000 | 1.13 | 0.81 | −28.6 |
| Belgium | 762 | 644 | 62.3 | NA | 1.22 | NA | NA | 7,175,062 | 7,614,082 | 1.06 | 0.85 | −20.4 |
| Italy | 3,428 | 3,173 | NA | NA | NA | NA | NA | 51,910,493 | 55,026,299 | 0.66 | 0.58 | −12.7 |
| France | 3,461 | 3,244 | 375.2 | 382.4 | 0.92 | 0.85 | −8.0 | 46,493,161 | 48,298,911 | 0.74 | 0.67 | −9.8 |
| Slovenia††† | 120 | 102 | NA | 14.0 | NA | 0.73 | NA | 1,372,751 | 1,515,329 | 0.87 | 0.67 | −23.0 |
| Austria | 479 | 416 | 47.9 | 52.8 | 1.00 | 0.79 | −21.3 | 6,466,166 | 6,895,596 | 0.74 | 0.60 | −18.6 |
| Canada | 1,887 | 1,762 | 227.3 | 248.3 | 0.83 | 0.71 | −14.5 | 23,923,806 | 25,422,635 | 0.79 | 0.69 | −12.1 |
| Australia | 1,205 | 1,187 | 154.4 | 162.8 | 0.78 | 0.73 | −6.6 | 18,007,767 | 19,505,241 | 0.67 | 0.61 | −9.1 |
| Israel | 356 | 355 | 34.1 | 39.3 | 1.05 | 0.90 | −13.5 | 3,091,636 | 3,600,693 | 1.15 | 0.99 | −14.4 |
| Netherlands | 621 | 661 | 80.5 | 85.5 | 0.77 | 0.77 | 0.2 | 10,775,799 | 11,553,132 | 0.58 | 0.57 | −0.7 |
| Finland††† | 270 | 211 | NA | 31.3 | NA | 0.67 | NA | 4,429,000 | 4,878,000 | 0.61 | 0.43 | −29.0 |
| Spain | 1,689 | 1,755 | NA | NA | NA | NA | NA | 33,412,894 | 36,343,283 | 0.51 | 0.48 | −4.5 |
| Germany††† | 3,459 | 3,046 | NA | 469.1 | NA | 0.65 | NA | 53,716,000 | 57,305,201 | 0.64 | 0.53 | −17.5 |
| Denmark | 178 | 199 | 32.4 | 34.2 | 0.55 | 0.58 | 5.9 | 3,029,000 | 3,290,000 | 0.59 | 0.60 | 2.9 |
| Japan | 4,885 | 3,920 | 454.2 | 462.7 | 1.08 | 0.85 | −21.2 | 91,315,870 | 91,457,940 | 0.53 | 0.43 | −19.9 |
| Ireland | 162 | 140 | 28.6 | 29.2 | 0.57 | 0.48 | −15.4 | 2,570,294 | 2,805,839 | 0.63 | 0.50 | −20.8 |
| United Kingdom | 1,804 | 1,808 | NA | NA | NA | NA | NA | 37,570,487 | 39,890,719 | 0.48 | 0.45 | −5.6 |
| Switzerland | 253 | 187 | 40.6 | 43.1 | 0.62 | 0.43 | −30.3 | 6,046,934 | 6,371,545 | 0.42 | 0.29 | −29.9 |
| Sweden | 259 | 221 | 50.2 | 52.0 | 0.52 | 0.42 | −17.7 | 6,021,000 | 6,363,944 | 0.43 | 0.35 | −19.3 |
| Norway | 117 | 108 | 27.5 | 28.7 | 0.43 | 0.38 | −11.6 | 3,812,144 | 4,049,449 | 0.31 | 0.27 | −13.1 |
| **Overall summary statistics** | | | | | | | | | | | | |
| Overall mean (with United States) | 2,636 | 2,506 | 282.6 | 278.7 | 1.09 | 0.93 | −13.6 | 27,618,884 | 29,437,379 | 0.84 | 0.79 | −16.3 |
| Overall median (with United States) | 735 | 653 | 56.2 | 52.0 | 0.96 | 0.77 | −13.5 | 6,837,031 | 7,628,541 | 0.74 | 0.64 | −15.9 |
| Minimum value (with United States) | 117 | 102 | 26.9 | 14.0 | 0.43 | 0.38 | −34.4 | 1,372,751 | 1,515,329 | 0.31 | 0.27 | −36.0 |
| Maximum value (with United States) | 35,484 | 36,355 | 3,089.8 | 3,261.8 | 2.49 | 2.05 | 5.9 | 281,312,446 | 299,267,114 | 1.94 | 3.52 | 2.9 |
| Overall mean (without United States) | 1,373 | 1,252 | 117.5 | 129.5 | 1.09 | 0.92 | −14.2 | 18,222,826 | 19,443,685 | 0.83 | 0.78 | −16.8 |
| Overall median (without United States) | 692 | 644 | 50.2 | 47.5 | 0.92 | 0.75 | −14.0 | 6,499,000 | 7,614,082 | 0.70 | 0.61 | −16.7 |

**Abbreviations:** MVC = motor vehicle crash; NA = not applicable.

* Portugal is not included because there were no data available for Portugal's vehicle miles traveled or for registered vehicles.

† All data come from the International Transport Forum's International Road Traffic and Accident Database, with two exceptions. The number of MVC deaths for the United States in 2019 comes from the Fatality Analysis Reporting System's Final File, released in March 2022. The numbers of crash deaths in 2015 and 2019 for the Netherlands are reported by the Institute for Road Safety Research (SWOV) and are determined by comparing and combining three data sources. https://swov.nl/en/fact-sheet/road-deaths-netherlands

§ Countries are listed in descending order by 2019 MVC deaths per 100,000 population.

¶ The following numbers were considered estimates: MVC deaths for Canada in 2019, vehicle miles traveled for Canada and Australia in 2015 and 2019, and vehicle miles traveled for Denmark, Ireland, and Switzerland in 2015.

** The following numbers were considered provisional: MVC deaths for Australia in 2019 and vehicle miles traveled for the Netherlands and Germany in 2019.

†† Vehicle miles traveled (in billions) and percent changes were calculated based on numbers that were not rounded. However, after being calculated, they were rounded to the nearest 10th of a decimal point.

§§ MVC deaths per 100 million vehicle miles traveled and per 10,000 registered vehicles were calculated based on numbers that were not rounded. However, after being calculated, they were rounded to the nearest 100th of a decimal point.

¶¶ Hungary, Belgium, Germany, and Denmark report the number of registered vehicles excluding mopeds; all other countries report the number of registered vehicles including mopeds.

*** Chile changed its definition for MVC deaths starting in 2019, which creates a trend break. Data for MVC deaths in Chile in 2019 cannot be compared with previous years. Therefore, 2015 MVC deaths and any calculations that would be based on 2015 MVC deaths are not reported for Chile.

††† Finland changed its methodology for determining vehicle kilometers traveled (which were converted to vehicle miles traveled) starting in 2016, and Germany and Slovenia changed their methodology starting in 2017. This creates a trend break. Data for vehicle miles traveled in Finland, Germany, and Slovenia in 2019 cannot be compared with previous years. Therefore, 2015 vehicle miles traveled and any calculations based on 2015 vehicle miles traveled are not reported for Finland, Germany, or Slovenia.

represents a 10.5% increase from 2020, an 18.0% increase from 2019 (even with similar levels of vehicle miles traveled), and the highest number of deaths since 2005 (*2*).

The World Health Organization (WHO) launched the first Decade of Action for Road Safety (2011–2020) and established global road safety goals,[§§] including halving crash deaths and injuries by 2020 (in line with Sustainable Development Goal Target 3.6).[¶¶] These goals were not achieved globally. Because crash deaths and injuries continue to be a major public health and development issue, WHO initiated a second Decade of Action for Road Safety. The adopted resolution[***] recommits to halving crash deaths and injuries during 2021–2030. The associated Global Action Plan[†††] emphasizes the holistic Safe System approach[§§§]: a proactive approach that prioritizes safety of all road users, accommodates for human error and human vulnerability, and incorporates road and vehicle designs that reduce crashes as well as deaths and injuries when crashes occur. The Safe System approach highlights safe road users, safe vehicles, safe speeds, safe roads, and post-crash care as its five elements.[¶¶¶] Many high-income countries, including Australia, the Netherlands, New Zealand, Spain, and Sweden, have experience implementing the Safe System approach and have observed substantial crash death reductions (*1*). Prioritizing and broadly implementing this approach could help the United States and other countries achieve global road safety goals, including Sustainable Development Goal 11.2, which calls for accessible transportation systems that are safe, affordable, and sustainable.[****]

In a previous report, CDC analyzed motor vehicle crash death data for the United States and 19 other high-income countries from 2000 to 2013 (*3*). The United States had the smallest decrease in population-based crash death rates among these countries. In that report, CDC recommended implementation of proven strategies to reduce crash deaths. Based on the results of the current study and data for 2020–2021, these recommendations are still applicable. Ample opportunities for progress and proven strategies that can save lives, prevent injuries, and avert medical costs exist.

The Road to Zero Coalition seeks to eliminate all U.S. crash deaths by 2050 through three overarching strategies: redoubling efforts to implement proven, evidence-based strategies; advancing life-saving technology in vehicles and infrastructure; and prioritizing safety by adopting the Safe System approach and creating a positive safety culture.[††††] Healthy People 2030 also aims to reduce crash deaths and transportation risk behaviors.[§§§§] The Bipartisan Infrastructure Law[¶¶¶¶] enacted in 2021 provides opportunities to complement evidence-based education and enforcement strategies with increased implementation of proven safety countermeasures designed to protect all road users and reduce transportation risk behaviors (*1*,*4*,*5*). The National Roadway Safety Strategy[*****] released in 2022 establishes a plan emphasizing the Safe System approach and outlining critical actions to address pressing motor vehicle safety issues.

Although IRTAD data precluded direct comparisons of behavioral risk factors, risk factor differences likely contributed to the United States' lack of progress in reducing crash deaths. For example, approximately 30% of U.S. motor vehicle crash deaths (>10,000 deaths a year) are attributable to alcohol-impaired driving.[†††††] Twenty-six of the 29 countries[§§§§§] in this study have blood alcohol concentration (BAC) laws set at ≤0.05 grams per deciliter (g/dL) (*6*); these laws are proven to reduce alcohol-impaired driving (*7*). In contrast, 49 U.S. states and the District of Columbia (DC) have a BAC limit of 0.08 g/dL, despite evidence indicating that impairment begins at lower BAC levels (*7*). In 2018, Utah implemented a 0.05 g/dL BAC law; a 2022 report found the law was associated with substantial reductions in motor vehicle crashes, alcohol-involved motor vehicle crashes, and motor vehicle crash deaths per mile driven (*8*).

Inconsistent restraint use and speed also remain persistent issues. In 2019, ≥47% of U.S. passenger vehicle occupants who were killed in motor vehicle crashes were unrestrained (*9*). Widespread implementation of primary enforcement seat belt laws covering all seating positions could increase seat belt use; well-publicized high-visibility enforcement of these laws can enhance the benefits (*4*). As of June 2022, only 20 U.S. states and DC have primary enforcement seat belt laws covering all seating positions[¶¶¶¶¶] despite their effectiveness. Reducing speeds would save lives of all road users, including pedestrians

[§§] https://www.who.int/groups/united-nations-road-safety-collaboration/decade-of-action-for-road-safety-2011-2020
[¶¶] https://www.un.org/sustainabledevelopment/health/
[***] https://undocs.org/en/A/RES/74/299
[†††] https://www.who.int/publications/m/item/global-plan-for-the-decade-of-action-for-road-safety-2021-2030
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[****] https://www.un.org/sustainabledevelopment/cities/
[††††] https://www.nsc.org/road-safety/get-involved/road-to-zero
[§§§§] https://health.gov/healthypeople/objectives-and-data/browse-objectives/transportation
[¶¶¶¶] The Bipartisan Infrastructure Law is also known as the Infrastructure Investment and Jobs Act. https://www.congress.gov/bill/117th-congress/house-bill/3684/text and https://www.transportation.gov/bipartisan-infrastructure-law
[*****] https://www.transportation.gov/NRSS
[†††††] https://www.iihs.org/topics/fatality-statistics/detail/alcohol
[§§§§§] The national BAC limit in the United States, the United Kingdom, and Canada is 0.08 g/dL. However, many of Canada's provinces have set lower BAC limits.
[¶¶¶¶¶] https://www.iihs.org/topics/seat-belts/seat-belt-law-table

**Summary**

What is already known about this topic?

Motor vehicle crashes are preventable but continue to be a leading cause of death in the United States, resulting in an average of 36,791 deaths each year (101 deaths each day) during 2015–2019.

What is added by this report?

In 2019, the population-based motor vehicle crash death rate in the United States (11.1 per 100,000 population) was the highest among 29 high-income countries. The population-based motor vehicle crash death rate decreased from 2015 to 2019 in 22 countries, but not in the United States.

What are the implications for public health practice?

Implementing proven strategies and the Safe System approach, which accounts for human error and works to protect everyone on the road, can help reduce motor vehicle crash deaths and injuries in the United States.

and bicyclists (*6*). Implementing proven speed-reducing roadway design countermeasures can reduce crashes (*5*). Speeding contributes to approximately 27% of U.S. motor vehicle crash deaths.****** Additional risk factors such as distraction, drug impairment, and fatigue also contribute to thousands of crash deaths every year.

The findings in this report are subject to at least two limitations. First, the United States surpasses all other included countries in population, vehicle miles traveled, and registered vehicles. Although various death rates were calculated to help account for these differences, other factors (e.g., population density, road infrastructure, and policies) cannot be accounted for because of data limitations. Second, although IRTAD data are standardized, small differences exist in how some countries collected and reported crash deaths and related metrics.

Compared with other high-income countries, the United States continues to lag behind in road safety. Other high-income countries have demonstrated that substantial reductions in crash deaths can be achieved. Although various U.S. cities and communities have committed to a goal of zero crash deaths and injury reductions, widespread multisectoral commitment and collaborative action toward achieving zero deaths are needed for the United States to make significant improvements. Motor vehicle crash deaths and injuries are a public health problem, but one with proven solutions. Increased and proactive implementation of proven road safety strategies, especially those addressing leading risk factors, could have an immediate effect. The United States could further reduce motor vehicle crash deaths and injuries by broadly embracing and applying the Safe System approach.

****** https://www.iihs.org/topics/fatality-statistics/detail/yearly-snapshot#speeding

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# Updated U.S. Public Health Service Guideline for Testing of Transplant Candidates Aged <12 Years for Infection with HIV, Hepatitis B Virus, and Hepatitis C Virus — United States, 2022

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The U.S. Public Health Service (PHS) has periodically published recommendations about reducing the risk for transmission of HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV) through solid organ transplantation (*1*–*4*). Updated guidance published in 2020 included the recommendation that all transplant candidates receive HIV, HBV, and HCV testing during hospital admission for transplant surgery to more accurately assess their pretransplant infection status and to better identify donor transmitted infection (*4*). In 2021, CDC was notified that this recommendation might be unnecessary for pediatric organ transplant candidates because of the low likelihood of infection after the perinatal period and out of concern that the volume of blood drawn for testing could negatively affect critically ill children.* CDC and other partners reviewed surveillance data from CDC on estimates of HIV, HBV, and HCV infection rates in the United States and data from the Organ Procurement & Transplantation Network (OPTN)† on age and weight distributions among U.S. transplant recipients. Feedback from the transplant community was also solicited to understand the impact of changes to the existing policy on organ transplantation. The 2020 PHS guideline was accordingly updated to specify that solid organ transplant candidates aged <12 years at the time of transplantation who have received postnatal infectious disease testing are exempt from the recommendation for HIV, HBV, and HCV testing during hospital admission for transplantation.

## Background

Since 1985, the U.S. PHS has made recommendations to reduce the risk for HIV transmission through solid organ transplantation (*1*–*4*). In 2013, these recommendations were expanded to include guidance on mitigating the risk for HBV and HCV transmission from solid organ donors to transplant recipients and included: 1) identifying risk factors associated with HIV, HBV, and HCV infection among organ donors, and 2) laboratory testing of donors using both serologic and nucleic acid testing for HIV, HBV, and HCV (*3*,*4*).

In 2020, the guideline was updated to reflect changes in the epidemiology of HIV, HBV, and HCV infections, advances in testing, and the availability of highly effective treatment for HIV and HBV infections and curative treatment for HCV (*4*). In addition to other updated recommendations, the 2020 PHS guideline specified that all transplant candidates should be tested for HIV, HBV, and HCV infections before transplantation, with testing to occur during hospital admission for transplant but before transplantation occurred (*4*). After implementation of the updated recommendations, CDC and the Health Resources and Services Administration (HRSA) continued to monitor the impact of guideline recommendations on organ safety and use, and received feedback from the transplant community about the requirement for repeat testing (i.e., after postnatal infectious disease testing) at the time of hospital admission for transplantation. Concerns were raised about the potential for harm that infectious disease testing might pose to some pediatric recipients because of blood volume loss from testing, including risks related to preoperative low body weight and blood volume, anemia, and exacerbation of underlying comorbid conditions (*5*). The probability of HIV, HBV, or HCV infection among some pediatric populations might be low after the perinatal period but before adolescence, thus obviating the need for additional testing (*6*,*7*). Therefore, the U.S. Department of Health and Human Services (HHS) considered changing recommendations for pediatric pretransplant testing based on age and weight.

## Methods

CDC and HRSA reviewed two relevant data sources. First, CDC HIV, HBV, and HCV surveillance data were reviewed for cases reported in the United States stratified by age group. This review was conducted to understand the risk for incident HIV, HBV, and HCV infections by age and thereby determine an age-based cutoff at which incident infections were of the lowest risk. Cases included incident HIV infections among persons aged <20 years in the United States and six territories and freely associated states during 2015–2019, and incident HBV and HCV infections among persons aged <20 years in the United States during 2019, the most recent years for which surveillance data were available (*6*). Second, data collected

* https://optn.transplant.hrsa.gov/media/4705/2021_05_24_dtac-full-cmte-mtg-summary.pdf
† https://optn.transplant.hrsa.gov/data/view-data-reports/ (Accessed June 23, 2022).

by OPTN were reviewed to ascertain the number of transplants performed in the United States during 2016–2020, by age group and by transplant recipient candidate weight. The purpose of this review was to understand the number of patients affected by the 2020 PHS policy and to ensure that an age-based cutoff for an exemption is appropriate in light of the distribution of patients' weights, because patients with low pretransplant weight are those most likely to be harmed by additional blood volume loss.

HHS then met with relevant stakeholders from the transplant community during May–December 2021, to understand the implications of policy changes on organ transplantation and organ use (*5*). In December 2021, HHS convened the Advisory Committee on Blood and Tissue Safety and Availability (ACBTSA) to present evidence and receive expert input on whether the 2020 PHS guideline recommendation pertaining to pretransplant testing of pediatric candidates should be revised (*8*). Subsequently, a draft recommendation was posted in the Federal Register to solicit public input on the proposed policy change and its anticipated impact on organ safety and use (*9*).

## Evidence

**HIV incidence among children.** Infants and children aged <13 years were at lowest risk for new HIV infections in the United States (*6*). During 2015–2019, diagnosis of 524 incident HIV infections among infants and children aged <13 years were reported in the United States and six territories and freely associated states (*6*). Overall, among children who received a diagnosis of an HIV infection, 181 (35%) were newborns aged 0–5 months, 23 (4%) were infants aged 6–11 months, 37 (7%) were children aged 12–23 months, and 283 (54%) were children aged 2–12 years (approximately 25 [5%] cases per year of age among children aged 2–12 years) (*6*). With effective efforts to eliminate perinatal transmission, prevalence and incidence of HIV infection among infants and children aged <13 years in the United States have been steadily decreasing (*6*). In contrast, persons aged 13–19 years are at substantially higher risk for acquiring a new HIV infection. Among 36,801 new HIV infections reported during 2019 in the United States and six territories and freely associated states, 1,667 (5%) were among persons aged 13–19 years (*6*).

**HBV and HCV incidence among children.** Incidence of acute HBV and HCV infection reported to CDC during 2019 among U.S. residents aged <20 years were 0 and 0.1 per 100,000 population, respectively (*7*). In addition, >90% of children aged >2 years and adolescents aged 13–17 years have been vaccinated against HBV infection[§] in the United States (*10*).

[§] https://www.cdc.gov/nchs/fastats/immunize.htm

**Pediatric transplants by age and weight.** During January 1, 2016–December 31, 2020, a total of 5,209 solid organ transplants were performed in the United States among infants and children aged <10 years (*11*). Among 5,202 (99.9%) of these recipients with weights reported, 1,528 (29%) weighed <20 pounds (9.1 kg), 2,383 (46%) weighed 20 to <40 pounds (9.1–18.1 kg), and 1,291 (25%) weighed ≥40 pounds (18.1 kg) (*11*). The 25th percentile of reported weights for this age group was 18 pounds (8.2 kg) (*11*). For transplant recipients aged 10–14 years, the 25th percentile of reported weights was 68 pounds (30.8 kg) (*11*).

ACBTSA voted in favor of changing the policy regarding the time frame for testing transplant candidates for HIV, HBV, and HCV infections pretransplant to exempt solid organ transplant recipient candidates who are aged ≤10 years at the time of transplantation. The initial policy proposal used an aged-based cutoff of <10 years because of perspectives regarding the timing of adolescence. However, members of the transplant community subsequently communicated to HHS that an age-based cutoff of ≤12 years for pretransplant infectious disease testing would more closely align with other transplant policies related to testing, organ allocation, and co-morbid disease severity classification as well as preserve patient safety (*5*).

## Updated Recommendation

Based on a review of the available data, public comment, discussions with stakeholders from the transplant community, and input from the federal advisory committee, the 2020 PHS guideline (*4*) has been amended to recommend that candidates who are aged <12 years at the time of transplantation and who have received postnatal infectious disease testing are exempt from pretransplant HIV, HBV, and HCV testing during hospital admission for transplantation.

### Discussion

This revised guideline is intended to limit the potential risk for unnecessary blood volume loss associated with infectious disease testing for specific pediatric transplant candidates during hospital admission for transplantation and continue to minimize the risk for unexpected infectious disease transmission through transplantation. Posttransplant testing recommendations remain unchanged: testing for HIV, HBV, and HCV infections should be conducted for all transplant recipients at 4–6 weeks after transplantation, including those aged <12 years regardless of postnatal infectious disease testing. In updating this recommendation, HHS considered infection risk and the effect of blood volume loss by age and by weight; the data assessed included the number of affected transplant candidates as well as the distribution of transplant candidates by weight. Data related to weight were incomplete, and patient

**Summary**

What is already known about this topic?

HIV, hepatitis B virus (HBV), and hepatitis C virus (HCV) transmission can occur through solid organ transplantation.

What is added by this report?

A 2020 U.S. Public Health Service recommendation to test transplant candidates for HIV, HBV, and HCV during the transplant hospital admission could result in potentially harmful blood loss in pediatric transplant candidates. Children aged <13 years are among those at lowest risk for new HIV infections, and incidence of acute HBV and HCV infection in U.S. residents aged <20 years is extremely low.

What are the implications for public health practice?

Children aged <12 years who have received postnatal infectious disease testing are exempt from repeat pretransplant HIV, HBV, and HCV testing during hospital admission for transplant surgery.

weight can also fluctuate because of factors including underlying health conditions. As patients move from childhood into adolescence, individual-level behaviors that increase the risk for acquiring HIV, HBV, and HCV infections become more likely, irrespective of weight (*6*,*7*). This updated recommendation is based on transplant candidate age to more effectively protect those candidates at highest risk for potential harm from blood volume loss and maintain the ability to recognize pretransplant HIV, HBV, and HCV infections among populations at highest risk. CDC, HRSA, and other federal partners will continue to monitor the impact of the 2020 PHS guideline on organ safety and use.

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# COVID-19 Vaccine Provider Availability and Vaccination Coverage Among Children Aged 5–11 Years — United States, November 1, 2021–April 25, 2022

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COVID-19 can lead to severe outcomes in children, including multisystem inflammatory syndrome, hospitalization, and death (*1*,*2*). On November 2, 2021, the Advisory Committee on Immunization Practices issued an interim recommendation for use of the BNT162b2 (Pfizer-BioNTech) vaccine in children aged 5–11 years for the prevention of COVID-19; however, vaccination coverage in this age group remains low (*3*). As of June 7, 2022, 36.0% of children aged 5–11 years in the United States had received ≥1 dose of COVID-19 vaccine (*3*). Among factors that might influence vaccination coverage is the availability of vaccine providers (*4*). To better understand how provider availability has affected COVID-19 vaccination coverage among children aged 5–11 years, CDC analyzed data on active COVID-19 vaccine providers and county-level vaccine administration data during November 1, 2021–April 25, 2022. Among 2,586 U.S. counties included in the analysis, 87.5% had at least one active COVID-19 vaccine provider serving children aged 5-11 years. Among the five assessed active provider types, most counties had at least one pharmacy (69.1%) or public health clinic (61.3%), whereas fewer counties had at least one pediatric clinic (29.7%), family medicine clinic (29.0%), or federally qualified health center (FQHC)* (22.8%). Median county-level vaccination coverage was 14.5% (IQR = 8.9%–23.6%). After adjusting for social vulnerability index (SVI)† and urbanicity, the analysis found that vaccination coverage among children aged 5–11 years was higher in counties with at least one active COVID-19 vaccine provider than in counties with no active providers (adjusted rate ratio [aRR] = 1.66). For each provider type, presence of at least one provider in the county was associated with higher coverage; the largest difference in vaccination coverage was observed between counties with and without pediatric clinics (aRR = 1.37). Ensuring broad access to COVID-19 vaccines, in addition to other strategies to address vaccination barriers, could help increase vaccination coverage among children aged 5–11 years.

This cross-sectional analysis used COVID-19 vaccine administration data reported to CDC by jurisdictions, pharmacies, and federal entities through immunization information systems, the Vaccine Administration Management System, and direct data submission.§ Among 3,142 U.S. counties, 2,586 (82.3%) were included. Two states (Texas and Idaho) and eight California counties with populations <20,000 were excluded because of restrictions on reporting of vaccine administration data to CDC, and Michigan was excluded because of incomplete data on COVID-19 vaccine administration. Counties were also excluded if provider type was missing for >25% of active providers in the county (5.1% of counties). Active providers were defined as those who reported administration of at least one Pfizer-BioNTech pediatric COVID-19 vaccine dose by April 25, 2022. COVID-19 provider enrollment data were used to classify active providers into the following provider types: pharmacies, pediatric clinics, family medicine clinics, FQHCs, and public health clinics. School-located vaccination clinics could not be included because vaccine administration in these locations was not reported separately from other provider types, such as pediatric clinics and pharmacies. For active providers and for each provider type, counties were dichotomized into those with at least one provider versus those with no providers. COVID-19 vaccination coverage was defined as the number of children aged 5–11 years who received at least one dose of pediatric COVID-19 vaccine during November 1, 2021–April 25, 2022, divided by the county population aged 5–11 years.¶

* https://www.hrsa.gov/opa/eligibility-and-registration/health-centers/fqhc/index.html

† SVI is a composite measure calculated from the following 15 indicators: 1) percentage of persons with incomes below poverty threshold, 2) percentage of civilian population (aged ≥16 years) unemployed, 3) per capita income, 4) percentage of persons aged ≥25 years with no high school diploma, 5) percentage of persons aged ≥65 years, 6) percentage of persons aged ≤17 years, 7) percentage of civilian noninstitutionalized population with a disability, 8) percentage of single-parent households with children aged <18 years, 9) percentage of persons who are racial or ethnic minorities (i.e., all persons except those who are non-Hispanic White), 10) percentage of persons aged ≥5 years who speak English "less than well," 11) percentage of housing in structures with ≥10 units (multiunit housing), 12) percentage of housing structures that are mobile homes, 13) percentage of households with more persons than rooms (crowding), 14) percentage of households with no vehicle available, and 15) percentage of persons in group quarters. The 15 indicators are categorized into four themes: 1) socioeconomic status (indicators 1–4), 2) household composition and disability (indicators 5–8), 3) racial and ethnic minority status and language (indicators 9 and 10), and 4) housing type and transportation (indicators 11–15). These indicators are combined into a final score that is ranked from 0 (lowest vulnerability) to 1 (highest vulnerability). https://www.atsdr.cdc.gov/placeandhealth/svi/index.html

§ https://www.cdc.gov/coronavirus/2019-ncov/vaccines/distributing/about-vaccine-data.html

¶ County population totals used to calculate vaccination coverage among children aged 5–11 years were obtained from the National Center for Health Statistics (NCHS) vintage 2019 bridged-race postcensal population estimates (https://www.cdc.gov/nchs/nvss/bridged_race.htm). The population of children aged 5–11 years in counties included in the analysis ranged from 33 to 839,738.

Associations between provider availability and vaccination coverage among children aged 5–11 years were measured using generalized estimating equation models with negative binomial regression to account for clustering of counties within states.** Because the active provider definition might have undercounted providers that did not report identifying information with their vaccine administrations, a sensitivity analysis was also conducted in which active providers were defined as those reporting either administration or inventory of ≥1 Pfizer-BioNTech pediatric COVID-19 vaccine dose. Rate ratios were calculated with 95% CIs to compare vaccination coverage among counties with and without active COVID-19 vaccine providers overall and by each provider type, with multivariable models controlling for SVI and urbanicity.†† P-values <0.05 were considered statistically significant. Analyses were performed in SAS (version 9.4; SAS Institute). This study was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.§§

Active providers of COVID-19 vaccine to children aged 5–11 years were primarily concentrated in parts of the Northeast, Midwest, and several counties in the West (Figure); this distribution approximately corresponded with COVID-19 vaccination coverage among children aged 5–11 years. Most counties had at least one active provider (87.5%), with the most common being a pharmacy (69.1%) or public health clinic (61.3%); fewer counties had at least one pediatric clinic (29.7%), family medicine clinic (29.0%), or FQHC (22.8%) (Table 1). More than one half (1,322; 51.1%) of counties had no pediatric clinic, family medicine clinic, or FQHC. Among all counties, median vaccination coverage among children aged 5–11 years was 14.5% (IQR = 8.9%–23.6%).

In univariate models, the presence of at least one active provider in a county was associated with higher vaccination coverage when compared with having no active provider in a county, irrespective of provider type (Table 2). These associations remained significant after adjusting for SVI and urbanicity. In the adjusted models, the largest associations with vaccination coverage were found for active providers (aRR = 1.66) and pediatric clinics (aRR = 1.37). Public health clinics were associated with the smallest difference in vaccination coverage (aRR = 1.16). The sensitivity analysis in which active providers were defined as those reporting either administration or inventory of at least one Pfizer-BioNTech pediatric COVID-19 vaccine dose yielded similar results.

** Robust SEs were used.

†† County-level SVI data were obtained from CDC/Agency for Toxic Substances and Disease Registry 2018 SVI database. County-level urbanicity data were obtained from the 2013 NCHS Urban-Rural Classification Scheme. https://www.cdc.gov/nchs/data_access/urban_rural.htm

§§ 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.

## Discussion

The availability of any active pediatric COVID-19 vaccine provider in a county was associated with higher county-level vaccination coverage among children aged 5–11 years during November 1, 2021–April 25, 2022. This association remained significant within individual provider types, including pediatric clinics, family medicine clinics, FQHCs, pharmacies, and public health clinics, underscoring the importance of COVID-19 vaccine provider availability to increasing vaccination coverage among children in this age group.

Although most counties had at least one active COVID-19 vaccine provider serving children aged 5–11 years, approximately one half of counties did not have an active pediatric clinic, family medicine clinic, or FQHC. This gap in access to COVID-19 vaccines through providers that serve as a medical home for routine pediatric care has important implications for COVID-19 vaccination coverage. Survey data have indicated that pediatricians are among the most trusted sources of reliable information about COVID-19 vaccines (*5*). Furthermore, among provider types included in this report, the availability of pediatric clinics was associated with the largest difference in vaccination coverage. Lack of access to a pediatrician or other regular health care provider that administers COVID-19 vaccines could be a barrier to vaccination for children aged 5–11 years.

In counties without a pediatric clinic, family medicine clinic, or FQHC, access to COVID-19 vaccines was primarily available through pharmacies and public health clinics. Leveraging these alternative vaccine access points is critical to reaching parents and children who remain unvaccinated. Pharmacies have played an important role in expanding access to COVID-19 vaccines through their availability and extended hours of operation. A previous study found that 46.4% of COVID-19 pediatric vaccine doses were administered in pharmacies (*6*), indicating that pharmacy vaccine providers are acceptable to many parents. Strategies to improve vaccination coverage among children aged 5–11 years could include encouraging interactions between pharmacy staff members and parents around COVID-19 vaccination.

Whereas ensuring access to COVID-19 vaccine providers might increase vaccination coverage, several other barriers to COVID-19 vaccination exist in pediatric populations. Concerns about vaccine safety and effectiveness continue to deter many parents from seeking COVID-19 vaccination for their children (*7*). Parents might also perceive the risk for serious COVID-19–associated illness to be low in children, leading them to defer vaccination (*7*). Beyond maintaining access to COVID-19 vaccine providers, interventions to overcome vaccine hesitancy are needed to improve vaccination coverage

**FIGURE. Number of active COVID-19 vaccine providers per 10,000 children aged 5–11 years and COVID-19 vaccination coverage among children aged 5–11 years, by county — United States, November 1, 2021–April 25, 2022**

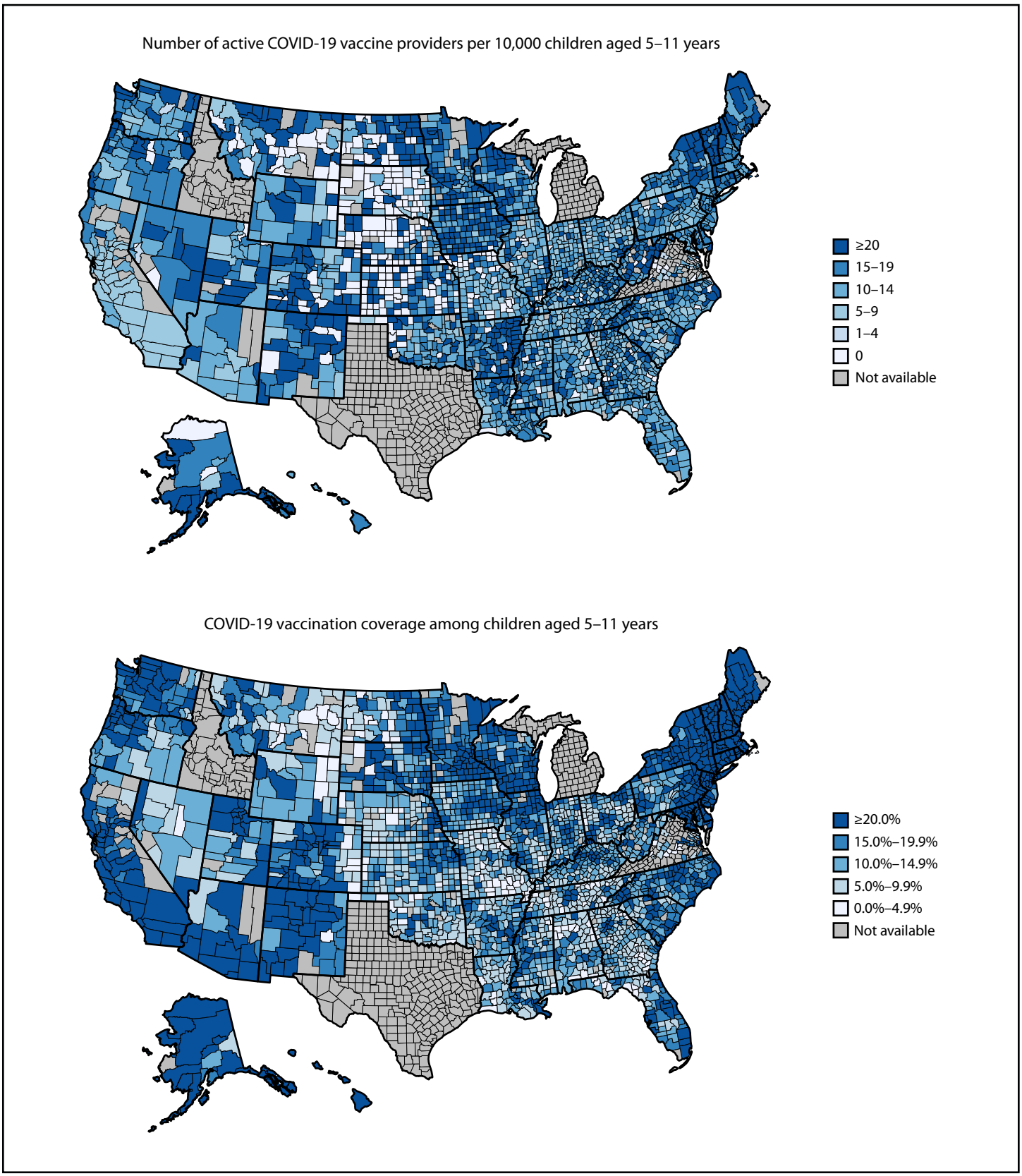

**TABLE 1. Number of pediatric COVID-19 vaccine providers per county and county-level vaccination coverage among children aged 5–11 years, by availability of provider type — United States, November 1, 2021–April 25, 2022**

| Characteristic | No. of counties (%) | Median (IQR) | | |
|---|---|---|---|---|
| | | No. of providers per county* | No. of providers per 10,000 children aged 5–11 years per county* | County-level vaccination coverage |
| **Total** | **2,586 (100.0)** | **4 (1–9)** | **14 (9–19)** | **14.5 (8.9–23.6)** |
| **Any active provider** | | | | |
| 0 | 323 (12.5) | 0 | 0 | 8.4 (5.3–13.1) |
| ≥1 | 2,263 (87.5) | 4 (2–11) | 15 (11–20) | 15.4 (9.7–25.2) |
| **Provider type** | | | | |
| **Pharmacy** | | | | |
| 0 | 800 (30.9) | 0 | 0 | 10.3 (6.6–16.2) |
| ≥1 | 1,786 (69.1) | 3 (1–8) | 8 (5–11) | 16.6 (10.5–27.3) |
| **Pediatric clinic** | | | | |
| 0 | 1,817 (70.3) | 0 | 0 | 11.9 (7.5–18.1) |
| ≥1 | 769 (29.7) | 2 (1–5) | 2 (1–4) | 23.8 (15.0–37.3) |
| **Family medicine clinic** | | | | |
| 0 | 1,836 (71.0) | 0 | 0 | 11.8 (7.5–18.2) |
| ≥1 | 750 (29.0) | 1 (1–3) | 2 (1–5) | 24.0 (15.0–37.1) |
| **Federally qualified health center** | | | | |
| 0 | 1,996 (77.2) | 0 | 0 | 12.7 (8.0–19.4) |
| ≥1 | 590 (22.8) | 1 (1–3) | 2 (1–4) | 24.3 (14.7–38.3) |
| **Public health clinic** | | | | |
| 0 | 1,002 (38.7) | 0 | 0 | 12.9 (7.6–20.9) |
| ≥1 | 1,584 (61.3) | 1 (1–1) | 3 (1–8) | 15.2 (9.7–25.5) |
| **Social vulnerability index** | | | | |
| Quartile 1 (lowest vulnerability) | 697 (27.0) | 2 (1–8) | 13 (5–20) | 17.1 (9.7–29.5) |
| Quartile 2 | 656 (25.4) | 4 (2–11) | 14 (9–19) | 15.1 (9.9–25.6) |
| Quartile 3 | 612 (23.7) | 4 (2–12) | 13 (10–18) | 12.8 (7.9–21.7) |
| Quartile 4 (highest vulnerability) | 621 (24.0) | 4 (2–7) | 14 (10–19) | 12.9 (8.0–18.8) |
| **Urbanicity** | | | | |
| Large central metropolitan | 55 (2.1) | 116 (81–184) | 14 (10–16) | 39.5 (31.7–53.4) |
| Large fringe metropolitan | 301 (11.6) | 11 (4–35) | 12 (9–15) | 23.1 (13.8–35.7) |
| Medium metropolitan | 320 (12.4) | 12 (4–33) | 13 (10–17) | 20.4 (13.6–29.3) |
| Small metropolitan | 297 (11.5) | 8 (2–16) | 13 (9–16) | 16.6 (10.6–25.5) |
| Micropolitan | 535 (20.7) | 5 (3–7) | 14 (10–19) | 13.9 (9.4–20.0) |
| Noncore | 1,078 (41.7) | 1 (1–3) | 15 (6–25) | 10.8 (6.8–16.4) |

* For social vulnerability and urbanicity, medians and IQRs were calculated using the total number of COVID-19 vaccine providers per county.

among children aged 5–11 years. Educating parents about the impact of COVID-19 illness in children (*1*,*2*) and the safety and effectiveness of pediatric COVID-19 vaccines (*8*,*9*) is vital.

The findings in this report are subject to at least five limitations. First, 17.7% of U.S. counties were excluded from this analysis because of insufficient data; therefore, findings might not be generalizable to all U.S. counties. Second, providers that did not report identifying information with their vaccine administrations might not have been counted as active providers; however, a sensitivity analysis in which active providers were defined as those with either administration or inventory of ≥1 Pfizer-BioNTech pediatric COVID-19 vaccine dose yielded similar results. Third, providers identified in this analysis refer to provider locations as opposed to individual providers; the capacity of each provider location to administer COVID-19 vaccines might differ. Fourth, because provider-type data were self-reported by providers enrolling in

**Summary**

What is already known about this topic?

Although COVID-19 vaccination has been recommended for children aged 5–11 years since November 2021, coverage among this age group remains low.

What is added by this report?

By April 25, 2022, most U.S. counties had a pharmacy or public health clinic offering COVID-19 vaccines to children aged 5–11 years; fewer counties had a pediatric clinic, family medicine clinic, or federally qualified health center. The availability of each provider type was associated with higher county-level vaccination coverage among children aged 5–11 years.

What are the implications for public health practice?

Ensuring broad access to COVID-19 vaccines, in addition to other strategies to address vaccination barriers, could help increase vaccination coverage among children aged 5–11 years.

**TABLE 2. Univariate and multivariable models* describing the association between county-level pediatric COVID-19 provider availability (≥1 versus 0) and county-level vaccination coverage among children aged 5–11 years, by provider type† — United States, November 1, 2021–April 25, 2022**

| | RR (95% CI) | |
|---|---|---|
| Provider type (≥1 versus 0) | Univariate model | Multivariable model§ |
| Active provider | 1.82 (1.67–1.99) | 1.66 (1.49–1.84) |
| Pharmacy | 1.47 (1.38–1.57) | 1.25 (1.17–1.33) |
| Pediatric clinic | 1.69 (1.59–1.79) | 1.37 (1.31–1.44) |
| Family medicine clinic | 1.48 (1.38–1.59) | 1.25 (1.17–1.34) |
| Federally qualified health center | 1.46 (1.36–1.56) | 1.22 (1.15–1.29) |
| Public health clinic | 1.24 (1.14–1.36) | 1.16 (1.07–1.26) |

**Abbreviation:** RR = rate ratio.
* Analysis performed using generalized estimating equation models with negative binomial regression to account for clustering of counties within states.
† RRs compare the vaccination rate in counties with at least one provider overall and of a given type to counties with 0 providers overall and of the same type.
§ Models controlled for social vulnerability index quartile and urbanicity.

the COVID-19 vaccination program, some providers might have been misclassified. Finally, the impact of school-located vaccination clinics could not be evaluated, because vaccine administration in these locations was not reported separately from other provider types.

Ensuring widespread access to COVID-19 vaccines in addition to other strategies to address barriers to vaccination could increase vaccination coverage among children aged 5–11 years. Coverage might be improved by engaging health care providers and pharmacists, as well as school officials, community leaders, and faith leaders, to increase vaccine confidence. In areas with few pediatric medical practices, promoting vaccination through alternative sources, including pharmacies, public health clinics, and school-based vaccination clinics, is essential.

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# Interim Analysis of Acute Hepatitis of Unknown Etiology in Children Aged <10 Years — United States, October 2021–June 2022

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On April 21, 2022, CDC issued a health advisory† encouraging U.S. clinicians to report all patients aged <10 years with hepatitis of unknown etiology to public health authorities, after identification of similar cases in both the United States (*1*) and Europe.§ A high proportion of initially reported patients had adenovirus detected in whole blood specimens, thus the health advisory encouraged clinicians to consider requesting adenovirus testing, preferentially on whole blood specimens. For patients meeting the criteria in the health advisory (patients under investigation [PUIs]), jurisdictional public health authorities abstracted medical charts and interviewed patient caregivers. As of June 15, 2022, a total of 296 PUIs with hepatitis onset on or after October 1, 2021, were reported from 42 U.S. jurisdictions. The median age of PUIs was 2 years, 2 months. Most PUIs were hospitalized (89.9%); 18 (6.1%) required a liver transplant, and 11 (3.7%) died. Adenovirus was detected in a respiratory, blood, or stool specimen of 100 (44.6%) of 224 patients.¶ Current or past infection with SARS-CoV-2 (the virus that causes COVID-19) was reported in 10 of 98 (10.2%) and 32 of 123 (26.0%) patients, respectively. No common exposures (e.g., travel, food, or toxicants) were identified. This nationwide investigation is ongoing. Further clinical data are needed to understand the cause of hepatitis in these patients and to assess the potential association with adenovirus.

Clinicians and health departments began retrospectively and prospectively identifying PUIs on April 21, 2022. A PUI was defined as a person aged <10 years with elevated (>500 U/L) aspartate aminotransferase (AST) or alanine aminotransferase (ALT), an unknown etiology for the hepatitis, and onset on or after October 1, 2021. Comprehensive investigations of PUIs included rapid reporting of preliminary information, medical chart abstractions, caregiver interviews, laboratory testing, and tissue specimen examination. Upon identification of a PUI, jurisdictional health departments sent preliminary information (basic demographic information, date of hepatitis diagnosis, adenovirus testing results, and patient outcome) to CDC. Medical chart abstraction used standardized forms to collect information on demographic characteristics, signs and symptoms of illness, underlying health conditions, laboratory results (pathogen testing, biomarkers, and toxicology), radiologic findings, tissue pathology findings, vaccination history, and diagnoses and treatment received. Patient caregiver interviews collected information on demographic characteristics, household structure, symptoms, health care use, medical and medication history, and potential exposures (e.g., close contacts, diet, and toxicants). Adenovirus nucleic acid amplification testing (e.g., polymerase chain reaction [PCR]) of blood, respiratory, or stool specimens or rectal swabs was requested at the discretion of the treating clinician and conducted at a diagnostic or reference laboratory.** Available specimens that yielded positive results for adenovirus were further characterized using Sanger sequencing of the six hypervariable regions of the hexon gene to determine adenovirus type (*2*). Formalin-fixed, paraffin-embedded (FFPE) liver biopsy, explant, or autopsy tissue specimens underwent routine evaluation at the clinical institutions, and residual FFPE tissue specimens were submitted to CDC for additional pathologic evaluation and diagnostic testing (*3*,*4*). This investigation was reviewed by CDC and conducted consistent with applicable federal law and CDC policy.†† Data were managed using REDCap electronic data tools hosted at CDC,§§ and SAS (version 9.4; SAS Institute) was used to conduct all analyses.

As of June 15, 2022, a total of 296 PUIs were reported from 42 U.S. jurisdictions. There was no apparent temporal clustering of hepatitis diagnoses among these children, although a peak in diagnoses coincided with the release of the health advisory (Figure 1). The median age at time of illness was 2 years, 2 months (range = 1 month–9 years, 8 months), and the largest percentage of PUIs (37.8%, 112) were Hispanic or Latino children, followed by White, non-Hispanic children (32.4%, 96) (Table). Among all reported PUIs, 266 (89.9%) required hospitalization, 18 (6.1%) required a liver transplant, and 11 (3.7%) died. Preliminary reports indicated that among

* These authors contributed equally to this report.
† https://emergency.cdc.gov/han/2022/han00462.asp
§ https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON368
¶ Adenovirus-positive results on respiratory, blood, or stool specimen types but excluded PUIs with pending or unknown test results (test results might not have been available at the time of data collection).
** https://www.cdc.gov/ncird/investigation/hepatitis-unknown-cause/laboratories-testing-typing.html
†† 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.
§§ https://projectredcap.org/

224 PUIs receiving adenovirus testing, 100 (44.6%) had a positive result in any specimen type, including 31 of 71 (43.7%) who underwent testing of whole blood (Figure 1).

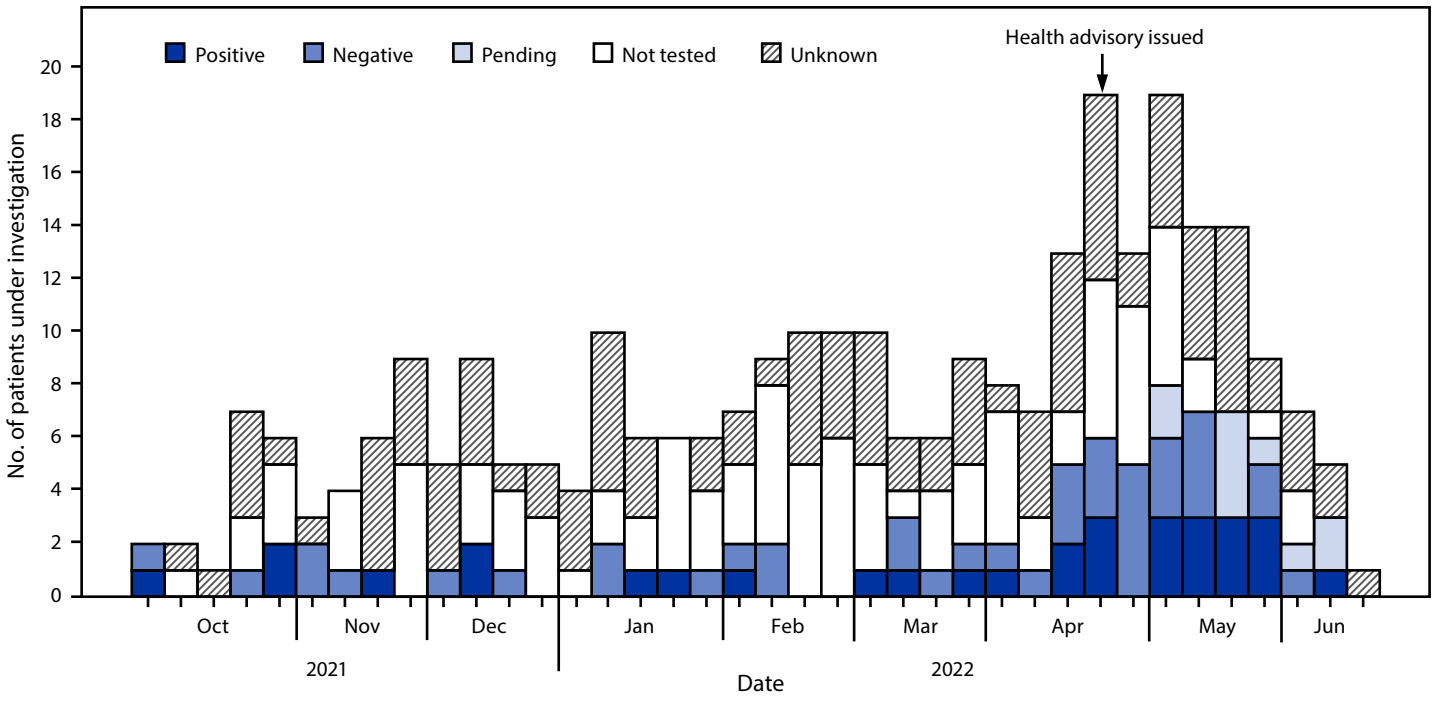
Data from 123 PUIs with medical chart abstraction and interviews were available for detailed analyses; completion of data collection is pending for the remaining 173 PUIs. Compared with all reported PUIs, those with completed medical chart abstraction and interview data were similar demographically, by date of hepatitis diagnosis and by percentage of positive adenovirus test results. Systemic and gastrointestinal signs and symptoms (86.2% and 87.8%, respectively) were common and included vomiting (61.8%), fatigue (55.3%), and jaundice (57.7%) (Table). The median interval between symptom onset and clinical evaluation was 4 days (IQR = 2–9 days). The median peak AST and ALT levels were 2,254.5 U/L (IQR = 802.5–4,266.5) and 1,744.5 U/L (IQR = 710.5–3,358.5), respectively. Thirty-seven (30.1%) patients received a diagnosis of acute liver failure[¶¶] and 15 (12.2%) had hepatic encephalopathy. The clinical assessments of four PUIs were consistent with potential autoimmune hepatitis based on liver biopsy results or other laboratory testing.

Medical records of the 123 PUIs with available chart abstractions and interviews indicated testing for and identification of a range of pathogens; adenovirus was detected most frequently (Figure 2). Among PUIs with adenovirus test results from any specimen type, 49.5% (48 of 97) received a positive test result (Table). Adenovirus was detected in 37.8% (14 of 37) of whole blood specimens, 34.4% (11 of 32) of plasma specimens, 30.0% (12 of 40) of stool specimens, and 30.1% (22 of 73) of respiratory specimens. Typing was attempted for 13 specimens, six of which were species F (type 41), one was species C (type C1); six could not be typed.[***] Overall, 98 (79.7%) PUIs with available chart data received testing for current SARS-CoV-2 infection, 10 (10.2%) which received a positive test result. History of SARS-CoV-2 infection, based on documentation in the medical chart, antibody testing, or parental report, was reported for 32 (26.0%) patients. The median interval from prior SARS-CoV-2 infection to hepatitis diagnosis

[¶¶] Acute liver failure (ALF) was based on the number of patients reported to have ALF in their medical chart. Twenty-four (64.9%) of the 37 patients were confirmed to meet the clinical definition for ALF based on laboratory markers and hepatic encephalopathy diagnosis (AST >500 U/L or ALT >500 U/L and either international normalized ratio (INR) >1.5 with hepatic encephalopathy or INR >2 without hepatic encephalopathy.

[***] Adenovirus type C1 was identified in a nasopharyngeal swab. Specimens reported as "could not be typed" were those in which sequencing was attempted, and insufficient sequencing information was obtained to identify the adenovirus type.

**FIGURE 1. Patients under investigation for pediatric hepatitis of unknown etiology* reported to CDC (N = 296), by week of hepatitis presentation and stratified by results of preliminary adenovirus testing using whole blood — United States, October 2021–June 2022**




* https://emergency.cdc.gov/han/2022/han00462.asp

**TABLE. Demographic and clinical characteristics and potential exposures of patients under investigation for hepatitis of unknown etiology (N = 296) — United States, October 2021–June 2022**

| Characteristic | No. (%) |
|---|---|
| **All PUIs (N = 296, 100%)** | |
| **Age, yrs, median (range)** | **2.2 (0–9.7)** |
| **Sex** | |
| Male | 172 (58.1) |
| Female | 121 (40.9) |
| Unknown | 3 (1.0) |
| **Race and ethnicity** | |
| Hispanic or Latino | 112 (37.8) |
| White, non-Hispanic | 96 (32.4) |
| Black, non-Hispanic | 29 (9.8) |
| Asian, non-Hispanic | 11 (3.7) |
| Multiple race, non-Hispanic | 9 (3.0) |
| American Indian or Alaska Native, non-Hispanic | 5 (1.7) |
| Native Hawaiian or other Pacific Islander, non-Hispanic | 3 (1.0) |
| Unknown or missing | 31 (10.5) |
| **Outcome** | |
| Hospitalized* | 266 (89.9) |
| Received liver transplant† | 18 (6.1) |
| Died§ | 11 (3.7) |
| **PUIs with completed medical chart abstractions and interviews (n = 123, 42%)** | |
| **Measure of severity of acute hepatitis¶** | |
| Acute hepatitis with acute liver failure | 37 (30.1) |
| Acute hepatitis without acute liver failure | 86 (69.9) |
| **Signs and symptoms during illness** | |
| Any respiratory | 49 (39.8) |
| Cough | 34 (27.6) |
| Rhinorrhea | 22 (17.9) |
| Congestion | 20 (16.3) |
| Any gastrointestinal | 108 (87.8) |
| Vomiting | 76 (61.8) |
| Diarrhea | 61 (49.6) |
| Abdominal pain | 48 (39.0) |
| Any systemic | 106 (86.2) |
| Fatigue | 68 (55.3) |
| Decreased appetite | 65 (52.9) |
| Fever | 51 (41.5) |
| Hepatitis signs and symptoms | 84 (68.3) |
| Jaundice | 71 (57.7) |
| Dark-colored urine | 44 (35.8) |
| Hepatic encephalopathy | 15 (12.2) |
| **Underlying medical conditions** | |
| Any** | 44 (35.8) |
| None | 74 (60.2) |
| Unknown | 5 (4.1) |
| History of previous liver transplant | 1 (0.8) |
| **Other testing or etiologies** | |
| Potential autoimmune hepatitis | 4 (3.3) |
| Potential acetaminophen toxicity | 1 (0.8) |
| **Adenovirus positivity, no. positive/total no. tested (%)** | |
| Any specimen type | 48/97 (49.5) |
| Whole blood | 14/37 (37.8) |
| Plasma | 11/32 (34.4) |
| Respiratory | 22/73 (30.1) |
| Stool | 12/40 (30.0) |
| Serum | 0/3 (—) |
| **SARS-CoV-2** | |
| Current SARS-CoV-2 infection,†† no. positive/total no. tested (%) | 10/98 (10.2) |
| History of SARS-CoV-2 infection | 32 (26.0) |
| Received ≥1 dose of a COVID-19 vaccine | 5 (4.1) |
| **Household structure and exposures inside and outside the home** | |
| No. of children aged <10 yrs in household,§§ median (range) | 1 (0–4) |
| Parental report of daily acetaminophen use during 2 mos preceding illness (any duration) | 11 (8.9) |
| Attended a child care facility or school during month preceding illness | 51 (42.5) |
| Patient never attended a child care facility or school | 69 (56.1) |
| Any domestic or international travel during 2 mos preceding illness | 24 (20.2) |
| Any international travel during 2 mos preceding illness¶¶ | 2 (1.6) |
| Any pets in the household*** | 53 (43.1) |

**Abbreviations:** ALF = acute liver failure; PUI = patient under investigation.

* Denominator includes four PUIs with unknown hospitalization data.

† Denominator includes 16 PUIs with unknown liver transplant data. Medical chart abstraction is pending for six (33.3%) of the 18 PUIs who received a liver transplant.

§ Denominator includes 25 PUIs with unknown death data. Medical chart abstraction is pending for four (36.4%) of the 11 deaths.

¶ ALF was based on the number of patients reported to have ALF in their medical chart. Twenty-four (64.9%) of the 37 cases were confirmed as meeting the clinical definition of ALF based on laboratory markers and hepatic encephalopathy diagnosis (aspartate aminotransferase >500 or alanine aminotransferase >500 and either [international normalized ratio >1.5 and hepatic encephalopathy] or [international normalized ratio >2 without hepatic encephalopathy]). Denominator includes 12 PUIs with unknown status for ALF.

** The specific underlying conditions reported included asthma (five, 4.1%), congenital heart disease (five, 4.1%), diabetes mellitus (one, 0.8%), seizure (one, 0.8%), history of liver transplant (one, 0.8%) premature birth (12, 9.8%), developmental disorder (eight, 6.5%), atopic or allergic conditions excluding asthma (eight, 6.5%), other chromosomal or congenital disorder (five, 4.1%), abnormal gastrointestinal tract or nutritional disorders (six, 4.9%), other disorders (11, 8.9%) (tracheomalacia, spinal arteriovenous malformation, obesity, history of elevated hepatic enzymes of unclear etiology, neonatal abstinence syndrome, anemia, pseudohypoaldosteronism, or heart murmur).

†† For SARS-CoV-2 infection, nine patients received positive reverse transcription–polymerase chain reaction test results and one received a positive antigen test result.

§§ Excluding the patient under investigation.

¶¶ Country visited was Mexico.

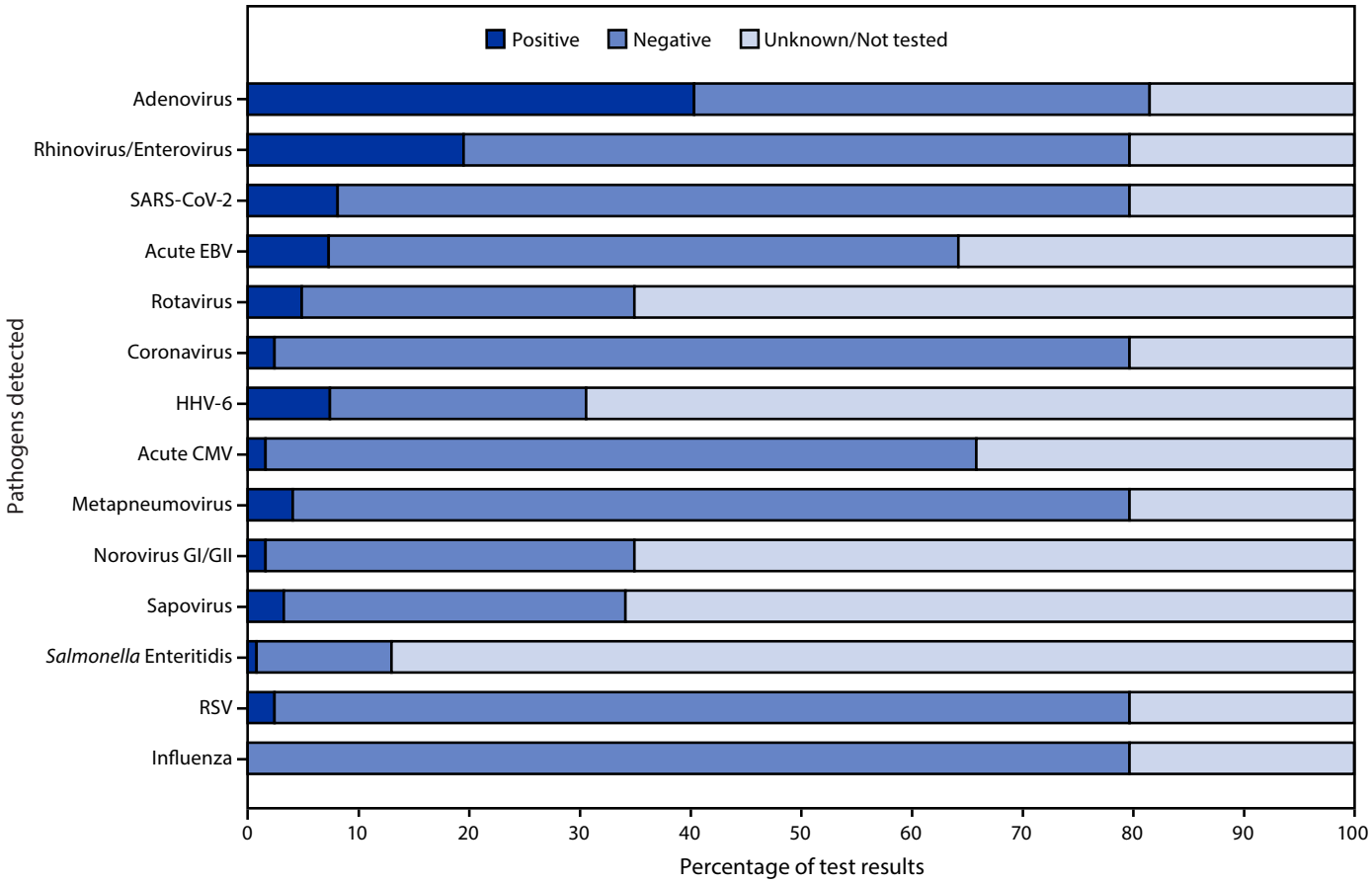
*** Thirty-nine (73.6%) reported a dog.

was 133 days (IQR = 77–283; nine with unknown date of prior infection). Five (4.1%) patients had received at least 1 dose of a COVID-19 vaccine. Other commonly detected pathogens included rhinovirus/enterovirus (24.5%, 24 of 98 tested), acute Epstein-Barr virus††† (11.4%, nine of 79), and rotavirus (14.0%, six of 43). Adenovirus and SARS-CoV-2 were co-detected in 3.5% (three of 86) of patients receiving testing.

Among 36 PUIs for whom information on pathologic evaluation of liver biopsy, explant, or autopsy tissues was available, 25 (65.8%) had evidence of active or acute hepatitis, and none had viral inclusions. As previously reported, liver biopsies from six patients with adenovirus infection had no

††† Acute Epstein-Barr virus (EBV) infection was defined as a positive EBV viral capsid antigen immunoglobulin (Ig) M or early antigen IgG test result, or diagnosis of primary EBV infection in the medical chart.

**FIGURE 2. Pathogens*,†,§,¶ detected during illness among a subset of patients under investigation for pediatric hepatitis of unknown etiology with completed medical chart abstraction and parental interviews (N = 123) — United States, October 2021–June 2022**




**Abbreviations:** CMV = cytomegalovirus; EA = early antigen; EBV = Epstein-Barr virus; HHV = human herpesvirus; IgG = immunoglobulin G; IgM = immunoglobulin M; PCR = polymerase chain reaction; RSV = respiratory syncytial virus; RT-PCR = reverse transcription–polymerase chain reaction; VCA = viral capsid antigen.
* Adenovirus test results: positive = adenovirus detected in any specimen type; negative = all tested specimens negative.
† Current SARS-CoV-2 detection: positive SARS-CoV-2 RT-PCR or antigen test result during current illness.
§ Acute EBV: positive EBV VCA IgM or EA IgG test result, or diagnosis of primary EBV in the medical chart.
¶ Acute CMV: based on clinical diagnosis, verified by PCR/IgM test result.

immunohistochemical evidence of adenovirus and no viral particles identified by electron microscopy (*1*).

Approximately one third of patients were the only child in the household aged <10 years. Fewer than one half (42.5%) of children attended a child care facility or school in the month before becoming ill, and 56.1% had never attended a child care facility or school. At present, no exposures (e.g., travel, food, or toxicants) were common among the PUIs, and no epidemiologic links were identified among PUIs in preliminary analyses.

## Discussion

As of June 15, 2022, a total of 296 PUIs with pediatric hepatitis of unknown etiology have been reported to CDC. Illness severity at the time of initial clinical evaluation ranged from elevated liver enzymes without acute liver failure to acute liver failure requiring liver transplantation, and there were 11 deaths. Most cases occurred in children aged <5 years. Adenovirus was the most commonly detected pathogen (45% of PUIs), and among a limited subset of 13 patients with typing data available, adenovirus type 41 was the predominant type.

This ongoing U.S. investigation coincides with and complements investigations of similar cases globally. As of May 26, 2022, the World Health Organization had reported 434 probable cases[§§§] of acute pediatric hepatitis of unknown etiology in 32 other countries, primarily in Europe.[¶¶¶] Notable similarities among cases identified across these investigations

[§§§] World Health Organization probable case definition: acute hepatitis (non hep A–E) with serum transaminase >500 IU/L (AST or ALT) in a person aged ≤16 years, since October 1, 2021.
[¶¶¶] https://www.who.int/emergencies/disease-outbreak-news/item/DON-389

are emerging, including young age (77.9% of European cases were in children aged ≤5 years), frequent adenovirus detection (53.9% of European cases), and identification of adenovirus type 41.[****]

It is not unusual for the cause of hepatitis in children to remain unknown; some estimates suggest that no etiology is identified in nearly one third of children with acute liver failure (*5*). The patients included in this investigation likely represent a heterogenous group of hepatitis etiologies. The findings from liver tissue examinations were nonspecific and can be observed in hepatitis due to infectious or noninfectious causes; however, the findings were not consistent with typical adenoviral hepatitis observed among immunocompromised children (*6*). Adenovirus is not a known cause of hepatitis in otherwise healthy children (*7*); however, the recent identification of adenovirus in specimens from several PUIs raises the question of whether a new pattern of disease is emerging in this population or if adenovirus might be an underrecognized cause or cofactor in previously indeterminate cases of pediatric hepatitis.

Current U.S. data do not suggest an increase in pediatric hepatitis of unknown etiology or percent positivity for adenovirus types 40/41 over baseline levels (*8*). Additional hypotheses are under investigation, including the potential role of previous SARS-CoV-2 infection and adeno-associated virus-2, a nonpathogenic parvovirus that has been detected in a high proportion of cases in the United Kingdom (*9*). Potential changes in patterns of exposure to adenovirus and immune naivety are also being considered. COVID-19 vaccination is unlikely to be related to these cases, given the low percentage of PUIs who were vaccinated and that nearly three quarters of PUIs were ineligible for COVID-19 vaccination based on age <5 years.

The findings in this report are subject to at least four limitations. First, this was a descriptive analysis, precluding definitive conclusions regarding potential associations between adenovirus or other risk factors and hepatitis. Second, this report describes preliminary data; CDC continues to receive data for current and new (including retrospectively identified) PUIs. Third, the retrospective identification of PUIs might limit the accuracy of both ascertainment and information obtained during interviews. Children with the most severe outcomes might have been more likely to be recalled by clinicians and reported retrospectively. Among the children who died, limitations in information that was immediately available made it difficult to further characterize the deaths. Finally, the hypothesized association between adenovirus and hepatitis might have led to increased adenovirus testing and reporting of children having positive test results.

CDC continues to partner with U.S. jurisdictions to investigate cases of pediatric acute hepatitis of unknown etiology. Clinicians are encouraged to continue to report patients meeting the criteria in the health advisory to jurisdictional public health authorities and to consider adenovirus testing of blood, respiratory, stool, and residual fixed liver tissue specimens, as well as SARS-CoV-2 antibody testing. Hepatitis of unknown etiology remains rare among young children. Nonetheless, parents and caregivers should contact their child's health care provider if their child shows any signs or symptoms of hepatitis.[††††] Additional data from this ongoing investigation are needed to better understand the cause and pathophysiologic mechanism of hepatitis in these patients.

[****] https://cdn.ecdc.europa.eu/novhep-surveillance/

[††††] Signs and symptoms of liver inflammation include fever, fatigue, loss of appetite, nausea, vomiting, abdominal pain, dark urine, light-colored stools, joint pain, and jaundice.

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**Summary**

What is already known about this topic?

During October 2021–February 2022, a cluster of children with hepatitis of unknown etiology and adenovirus infection was identified in the United States. On April 21, after reports of similar cases in other countries, CDC advised clinicians to report patients aged <10 years with hepatitis of unknown etiology to public health authorities.

What is added by this report?

During October 1, 2021–June 15, 2022, a total of 296 U.S. pediatric patients received a diagnosis of hepatitis of unknown etiology, with adenovirus detected among 45%. Preliminary analyses have not identified common exposures (e.g., travel or toxicants).

What are the implications for public health practice?

The investigation is ongoing; further clinical data are needed to understand the cause of these cases and to assess the potential association with adenovirus.

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# Interim Recommendations of the Advisory Committee on Immunization Practices for Use of Moderna and Pfizer-BioNTech COVID-19 Vaccines in Children Aged 6 Months–5 Years — United States, June 2022

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On June 17, 2022, the Food and Drug Administration (FDA) issued Emergency Use Authorization (EUA) amendments for the mRNA-1273 (Moderna) COVID-19 vaccine for use in children aged 6 months–5 years, administered as 2 doses (25 μg [0.25 mL] each), 4 weeks apart, and BNT162b2 (Pfizer-BioNTech) COVID-19 vaccine for use in children aged 6 months–4 years, administered as 3 doses (3 μg [0.2 mL] each), at intervals of 3 weeks between doses 1 and 2 and ≥8 weeks between doses 2 and 3. On June 18, 2022, the Advisory Committee on Immunization Practices (ACIP) issued separate interim recommendations for use of the Moderna COVID-19 vaccine in children aged 6 months–5 years and the Pfizer-BioNTech COVID-19 vaccine in children aged 6 months–4 years for the prevention of COVID-19.* Both the Moderna and Pfizer-BioNTech COVID-19 vaccines met the criteria for immunobridging, which is the comparison of neutralizing antibody levels postvaccination in young children with those in young adults in whom efficacy had been demonstrated. Descriptive efficacy analyses were also conducted for both Moderna and Pfizer-BioNTech COVID-19 vaccines during the period when the Omicron variant of SARS-CoV-2 (the virus that causes COVID-19) predominated. No specific safety concerns were identified among recipients of either vaccine. ACIP recommendations for the use of the Moderna COVID-19 vaccine and the Pfizer-BioNTech COVID-19 vaccine in children aged 6 months–5 years and 6 months–4 years, respectively, are interim and will be updated as additional information becomes available. Vaccination is important for protecting children aged 6 months–5 years against COVID-19.

The Moderna and Pfizer-BioNTech COVID-19 vaccines are lipid nanoparticle–formulated, nucleoside-modified mRNA vaccines encoding the prefusion spike glycoprotein of SARS-CoV-2. On January 31, 2022, FDA approved a Biologics License Application (BLA) for use of the Moderna COVID-19 vaccine (Spikevax, ModernaTX, Inc.) in persons aged ≥18 years, and the Moderna COVID-19 vaccine is also recommended under EUA for children and adolescents aged 6–17 years (*1*). On August 23, 2021, FDA approved a BLA for use of the Pfizer-BioNTech COVID-19 vaccine (Comirnaty, Pfizer, Inc.) in persons aged ≥16 years, and the Pfizer-BioNTech COVID-19 vaccine is also recommended under EUA for children and adolescents aged 5–15 years (*2*). Recommendations regarding products, dosing intervals, and booster doses and for persons who are moderately to severely immunocompromised, which differ from recommendations for persons without immunocompromising conditions, are available at https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html. As of June 17, 2022, among persons aged ≥18 years, 223 million doses of the Moderna COVID-19 vaccine have been administered in the United States, and among persons aged ≥5 years, 349 million doses of the Pfizer-BioNTech COVID-19 vaccine have been administered (*3*).

Since June 2020, ACIP has convened 28 public meetings to review data relevant to the epidemiology of COVID-19 and considerations for the use of COVID-19 vaccines, including the Moderna and Pfizer-BioNTech COVID-19 vaccines.† The ACIP COVID-19 Vaccines Work Group (Work Group), comprising experts in pediatrics, infectious diseases, vaccinology, vaccine safety, public health, and ethics, has held weekly meetings to review COVID-19 surveillance data; evidence for vaccine efficacy, postauthorization effectiveness, and safety; and implementation considerations for COVID-19 vaccines. To guide its deliberations regarding recommendations for use of these vaccines, ACIP used the Evidence to Recommendation (EtR) Framework§ and incorporated a Grading of Recommendations, Assessment, Development and Evaluation (GRADE) approach.¶ Within the EtR Framework, ACIP considered the importance of COVID-19 as a public health problem, as well as parents' values and preferences, acceptability, feasibility, resource use, and equity regarding use of mRNA COVID-19 vaccines among children aged 6 months–5 years. Consistent with the age groups for each

* On June 18, 2022, ACIP voted 12 to 0 (three members absent) in favor of the interim recommendation for the use of the Moderna COVID-19 vaccine for children aged 6 months–5 years. ACIP voted 12 to 0 (three members absent) in favor of the interim recommendation for the use of the Pfizer-BioNTech COVID-19 vaccine for children aged 6 months–4 years.

† https://www.cdc.gov/vaccines/acip/meetings/index.html

§ https://www.cdc.gov/vaccines/acip/recs/grade/downloads/acip-evidence-recs-framework.pdf

¶ https://www.cdc.gov/vaccines/acip/recs/grade/about-grade.html

vaccine included under EUA, ACIP also considered, within the EtR Framework, the benefits and harms of using each vaccine (i.e., the Moderna COVID-19 vaccine among children aged 6 months–5 years and the Pfizer-BioNTech COVID-19 vaccine among children aged 6 months–4 years), independently compared with no vaccine. After conducting systematic reviews of published and unpublished evidence for benefits and harms, the Work Group used the GRADE approach to independently assess the certainty of evidence for outcomes related to the Moderna and Pfizer-BioNTech COVID-19 vaccines, rated on a scale of type 1 (high certainty) to type 4 (very low certainty).** Work Group conclusions regarding evidence for the use of Moderna COVID-19 vaccine among children aged 6 months–5 years and Pfizer-BioNTech COVID-19 vaccine among children aged 6 months–4 years were presented to ACIP at a public meeting during June 17–18, 2022.

## Summary of Evidence for Use of the Moderna COVID-19 Vaccine in Children Aged 6 Months–5 Years

The body of evidence regarding immunogenicity, efficacy, and safety of the Moderna COVID-19 vaccine among children aged 6 months–5 years was guided by one randomized, double-blind, placebo-controlled phase II/III clinical trial in which 6,388 participants aged 6 months–5 years were enrolled and randomized 3:1 to receive either 2 doses of vaccine (25 μg) or saline placebo, separated by an interval of 28 days (*4*). Interim findings from this clinical trial were based on data from participants with a median blinded follow-up after dose 2 of 68 days for children aged 6–23 months and 71 days for children aged 2–5 years. Vaccine efficacy against symptomatic, laboratory-confirmed COVID-19 was supported by two types of evidence: 1) direct efficacy of 2 doses against symptomatic COVID-19, and 2) immunobridging (i.e., comparing neutralizing antibody levels in one population [e.g., young children] with antibody levels in another population [e.g., young adults] with demonstrated efficacy). Vaccine efficacy ≥14 days after dose 2 was 37.8% (95% CI = 20.9%–51.1%) in preventing symptomatic, laboratory-confirmed COVID-19†† in children aged 6 months–5 years with or without evidence of previous SARS-CoV-2 infection.§§ This estimate was based on symptomatic illness in 181 vaccine recipients and 97 placebo recipients, none of whom were hospitalized. Vaccine efficacy against symptomatic COVID-19 was also inferred based on immunobridging criteria. The measure of immune response to 2 doses (25 μg each) of the Moderna COVID-19 vaccine in children aged 6–23 months and 2–5 years without evidence of previous SARS-CoV-2 infection was at least as high as the response observed in young adults aged 18–25 years after 2 doses (100 μg each) of the Moderna COVID-19 vaccine, with a geometric mean ratio (GMR) for 50% neutralizing antibody titer of 1.28 (95% CI = 1.12–1.47) for children aged 6–23 months and 1.01 (95% CI = 0.88–1.17) for children aged 2–5 years, satisfying the noninferiority criteria¶¶ for both age groups. In addition, vaccine efficacy against asymptomatic, laboratory-confirmed SARS-CoV-2 infection*** was 16.0% (95% CI = –18.5%–40.5%) among children aged 6 months–5 years with or without evidence of previous SARS-CoV-2 infection, based on asymptomatic infection in 111 vaccine recipients and 44 placebo recipients.

Among vaccine recipients aged 6 months–5 years, reactogenicity, defined as solicited local and systemic adverse reactions during the 7 days after vaccination, were reported frequently. After dose 2, 66.1% of caregivers reported any local reaction among the child vaccine recipients after vaccination, and 65.9% reported any systemic reaction; most reactions were mild to moderate with symptom onset 1–2 days after vaccination and resolving after 2–3 days. Reactogenicity was usually less frequent in children aged 6 months–5 years than in those aged 6–11 years. Among children aged 6 months–5 years, severe local and systemic adverse reactions (grade 3 or higher, defined as interfering with daily activity) occurred in 7.7% of vaccine recipients, more commonly after dose 2, and in 4.1% of placebo recipients. The most common grade 3 or higher local symptom reported by vaccine recipients after dose 2 was pain at the injection site (0.4%). The most commonly reported reactions of grade 3 or higher after dose 2 were fever (2.6%) and irritability or crying (1.2%) among vaccine recipients aged 6–36 months and fever (3.1%) and fatigue (2.3%) among those aged 37 months–5 years. Serious adverse events††† were

** https://www.cdc.gov/vaccines/acip/recs/grade

†† In the Moderna COVID-19 vaccine clinical trial, symptomatic, laboratory-confirmed COVID-19 was defined based on the CDC case definition, which required at least one clinical symptom (fever ≥100.4°F [≥38°C], chills, fatigue, headache, myalgia, nasal congestion or rhinorrhea, new loss of taste or smell, sore throat, abdominal pain, diarrhea, nausea or vomiting, poor appetite or poor feeding, cough, or shortness of breath or difficulty breathing), and a positive COVID-19 test result using reverse transcription–PCR (RT-PCR).

§§ In the Moderna COVID-19 vaccine clinical trial, approximately 10% of children aged 6 months–5 years were seropositive, indicating previous SARS-CoV-2 infection, at baseline.

¶¶ Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR is >0.67 and the point estimate of GMR is ≥0.8.

*** In the Moderna COVID-19 vaccine clinical trial, asymptomatic SARS-CoV-2 infection was identified by absence of symptoms and at least one of the following conditions: 1) binding antibody level against SARS-CoV-2 nucleocapsid protein negative at baseline (or day 1) that became positive post-baseline (testing performed only on the immunogenicity subset [494]), or 2) a positive COVID-19 test result using RT-PCR post-baseline at a scheduled (29 days after dose 2) or unscheduled visit.

††† Serious adverse event is defined as any untoward medical occurrence that results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability or incapacity, or is a congenital anomaly or birth defect. Serious adverse events occurring after dose 1 or dose 2 were reported.

uncommon and occurred with similar frequency among vaccine (0.5%) and placebo (0.2%) recipients, with no statistically significant difference in frequency. Two serious adverse events in one participant were determined to be potentially related to vaccination.[§§§] No specific safety concerns were identified among vaccine recipients aged 6 months–5 years. A detailed summary of safety data, including information on reactogenicity, is available at https://www.cdc.gov/vaccines/covid-19/info-by-product/moderna/reactogenicity.html.

From the GRADE evidence assessment, the level of certainty for the benefits of Moderna COVID-19 vaccination among children aged 6 months–5 years was type 1 (high certainty) for the prevention of symptomatic laboratory-confirmed COVID-19 assessed using direct efficacy and type 2 (moderate certainty) assessed using immunobridging, because of serious concerns for indirectness, because immunogenicity is a surrogate measure of efficacy. The level of certainty for prevention of asymptomatic SARS-CoV-2 infection was type 3 (low certainty) because of serious concerns of indirectness, because serial SARS-CoV-2 polymerase chain reaction (PCR) testing was not performed, and serology was only performed for a subset of participants[¶¶¶]; serious concerns of imprecision were also noted because of the width of the 95% CI. Regarding potential harms after vaccination, evidence was type 4 (very low certainty) for serious adverse events because of short follow-up time (median = 68 and 71 days after dose 2 for children aged 6–23 months and 2–5 years, respectively), study size, and the width of the 95% CI. Evidence was type 1 (high certainty) for reactogenicity. No data were available to assess the other GRADE benefits, including prevention of COVID-19–associated hospitalization or multisystem inflammatory syndrome in children (MIS-C).

## Summary of Evidence for Use of the Pfizer-BioNTech COVID-19 Vaccine in Children Aged 6 Months–4 Years

The body of evidence regarding immunogenicity, efficacy, and safety of the Pfizer-BioNTech COVID-19 vaccine among children aged 6 months–4 years was composed of data from one randomized, double-blind, placebo-controlled phase II/III clinical trial in which 4,526 participants aged 6 months–4 years were enrolled and randomized 2:1 to receive either vaccine or saline placebo (*5*). The protocol initially specified 2 doses of vaccine (3 $\mu$g) or saline placebo separated by an interval of 3 weeks. Per protocol, participants were unblinded 6 months after dose 2 or at age 5 years (whichever occurred first). Based on an interim analysis where the predefined criteria for immunobridging and efficacy of the trial were not met after 2 doses, a protocol amendment was implemented on February 1, 2022, to include a third dose of either vaccine (3 $\mu$g) or saline placebo, administered ≥56 days after dose 2. Dose 3 was offered to blinded and unblinded participants in the vaccine arm, and blinded participants in the placebo arm were offered a third dose of placebo. Among trial participants, 1,456 (32.2%) received a blinded third dose and were included in a 3-dose efficacy analysis (992 in the vaccine arm and 464 in the placebo arm). The median interval between doses 2 and 3 was 16 weeks among children aged 6–23 months and 11 weeks among children aged 2–4 years. Safety analyses included blinded participants and assessed outcomes starting at dose 1. Interim findings from this clinical trial were based on data from participants with a median blinded follow-up of 35 days after dose 3 for children aged 6–23 months and 40 days for children aged 2–4 years.

Vaccine efficacy was supported by two types of evidence: 1) direct efficacy of 3 doses against symptomatic laboratory-confirmed COVID-19[****] and 2) immunobridging data. Vaccine efficacy ≥7 days after dose 3 was 80.0% (95% CI = 22.8%–94.8%)[††††] in preventing symptomatic, laboratory-confirmed COVID-19 in children aged 6 months–4 years with and without evidence of previous SARS-CoV-2 infection,[§§§§] based on infection in three vaccine recipients and seven placebo recipients, none of whom were hospitalized. In the immunobridging analysis, the measure of immune response to 3 doses (3 $\mu$g each) of the Pfizer-BioNTech COVID-19 vaccine in children aged 6 months–4 years without evidence of previous SARS-CoV-2 infection was at least as high as the response observed in persons aged 16–25 years who had received 2 doses (30 $\mu$g each) of the Pfizer-BioNTech COVID-19 vaccine, with a GMR for 50% neutralizing

[§§§] One recipient in the Moderna COVID-19 vaccine clinical trial experienced two serious adverse events (i.e., fever and febrile seizure) that the investigator and FDA determined to be potentially related to the vaccine.

[¶¶¶] The definition of asymptomatic SARS-CoV-2 infection specified for GRADE: SARS-CoV-2 infection with no reported symptoms identified through 1) serial RT-PCR testing, or 2) testing of binding antibody level against SARS-CoV-2 nucleocapsid protein, on the entire cohort or a representative sample.

[****] In the Pfizer-BioNTech COVID-19 vaccine clinical trial, symptomatic laboratory-confirmed COVID-19 was defined based on the CDC case definition, which required at least one clinical symptom (fever, new or increased cough, new or increased shortness of breath, chills, new or increased muscle pain, new loss of taste or smell, sore throat, diarrhea, vomiting, and inability to eat or poor feeding), and a positive SARS-CoV-2 nucleic acid amplification test result within 4 days of the symptomatic period.

[††††] For GRADE, relative risks (RR) were calculated from numerators and denominators available in the body of evidence. Vaccine efficacy estimates were defined as 100% x (1–RR). Manufacturer vaccine efficacy estimates were calculated using incident rate ratios. Based on the Pfizer-BioNTech COVID-19 vaccine clinical trial analysis, the vaccine efficacy against symptomatic SARS-CoV-2 infection was 80.3% (95% CI = 13.9%–96.7%).

[§§§§] In the Pfizer-BioNTech COVID-19 vaccine clinical trial, approximately 30% of children aged 6 months–4 years were seropositive, indicating a previous SARS-CoV-2 infection, before dose 3.

antibody titer of 1.19 (95% CI = 1.00–1.43) for children aged 6–23 months and 1.30 (95% CI = 1.13–1.50) for children aged 2–4 years, satisfying the noninferiority criteria[¶¶¶¶] for both age groups.

Among vaccine recipients aged 6 months–4 years, reactogenicity, defined as solicited local injection site or systemic signs or symptoms during the 7 days after vaccination, were common (47.8% reported any local reaction, and 63.8% reported any systemic reaction); most reactions were mild to moderate. Local and systemic reactogenicity symptoms were usually less frequent in children aged 6 months–4 years (63.8%) than in children aged 5–11 years (86.2%) (*6*). Severe local and systemic adverse reactions (grade 3 or higher, defined as interfering with daily activity) occurred in 4.3% and 3.6% of vaccine recipients and placebo recipients, respectively. The most commonly reported reactions of grade 3 or higher among vaccine recipients aged 6–23 months were fever (4.0%) and irritability (1.3%), and among recipients aged 2–4 years, were fatigue (0.8%) and fever (2.2%). Overall, reactions of grade 3 or higher were also more commonly reported after the second dose than after the first or third dose. Serious adverse events[*****] were uncommon and occurred with similar frequency among recipients of vaccine (1.0%) and placebo (1.5%), with no statistically significant difference in frequency. Two serious adverse events in one participant in the vaccinated group were determined to be potentially related to vaccination.[†††††] No specific safety concerns were identified among vaccine recipients aged 6 months–4 years. A detailed summary of safety data, including information on reactogenicity, is available at https://www.cdc.gov/vaccines/covid-19/info-by-product/pfizer/reactogenicity.html.

From the GRADE evidence assessment, the level of certainty for the benefits of Pfizer-BioNTech COVID-19 vaccination among children aged 6 months–4 years was type 4 (very low certainty) for the prevention of symptomatic laboratory-confirmed COVID-19 assessed using direct efficacy because of serious concern about the short duration of follow-up (median = 35 and 40 days for children aged 6–23 months and 2–4 years, respectively) and very serious concerns about imprecision because of case accrual and study size. For the prevention of symptomatic, laboratory-confirmed COVID-19 assessed using immunobridging, the evidence was type 2 (moderate certainty) because of serious concerns for indirectness, because immunogenicity is a surrogate measure of efficacy. Regarding potential harms after vaccination, the evidence was type 4 (very low certainty) for serious adverse events because of very serious concerns for indirectness because of the short duration of follow-up of 1 month after dose 3 and because only 31% of trial participants received dose 3, limiting the ability to detect serious adverse events that might occur at a higher rate after dose 3, and serious concern of imprecision because of the study size. For reactogenicity, the evidence was type 2 (moderate certainty) because of serious concern for indirectness, as only 31% of trial participants received dose 3, limiting the ability to detect severe reactogenicity that might occur specifically after dose 3. No data were available to assess the other GRADE benefits, specifically prevention of COVID-19–associated hospitalization, MIS-C, or asymptomatic SARS-CoV-2 infection.

[¶¶¶¶] Noninferiority is declared if the lower bound of the 2-sided 95% CI for the GMR >0.67 and the point estimate of GMR is ≥0.8.

[*****] Serious adverse event is defined as any untoward medical occurrence that results in death, is life threatening, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent disability or incapacity, or is a congenital anomaly or birth defect. Serious adverse events occurring after dose 1, dose 2, or dose 3 were reported.

[†††††] One recipient in the Pfizer-BioNTech COVID-19 vaccine clinical trial had two serious adverse events (i.e., fever and pain in extremity requiring hospitalization) that the investigator and FDA determined to be potentially related to the vaccine. FDA noted that the events were also consistent with viral myositis.

## Recommendations for the Use of the Moderna COVID-19 Vaccine in Children Aged 6 Months–5 Years and the Pfizer-BioNTech COVID-19 Vaccine in Children Aged 6 Months–4 Years

Data reviewed with the EtR Framework supported the use of COVID-19 vaccine in children aged 6 months–5 years. COVID-19 is a major public health problem among young children. As of June 12, 2022, approximately 2 million COVID-19 cases, 20,000 hospitalizations, and 200 deaths from COVID-19 have been reported among U.S. children aged 6 months–4 years (*7*,*8*). The SARS-CoV-2 Omicron variant emerged in the United States in December 2021 and led to the highest COVID-19 incidence, rates of COVID-19–associated emergency department visits and COVID-19–associated hospitalization among children aged 6 months–4 years yet seen during the pandemic (*9*). Approximately one half (51%–54%) of children aged 6 months–4 years with a COVID-19–associated hospitalization had no underlying health conditions, highlighting the risk for severe COVID-19 even among young children without underlying health conditions (*9*). During the period of Omicron predominance, illness among children aged 6 months–4 years with COVID-19–associated hospitalizations was as severe or more severe than that among children and adolescents aged 5–17 years, who were eligible for COVID-19 vaccination during that period (*9*). Furthermore, COVID-19 hospitalization rates among children aged 6 months–4 years during October 2021–April 2022 were as high or higher than were influenza-associated hospitalization rates during the 2017–18, 2018–19, and 2019–20 influenza seasons (*10*).

SARS-CoV-2 can also lead to complications after acute infection. MIS-C is a severe illness in persons aged <21 years that occurs 2–6 weeks after SARS-CoV-2 infection and is characterized by fever, multisystem organ involvement, and laboratory evidence of inflammation (*11*). As of May 31, 2022, CDC has received 8,525 reports of cases of MIS-C in the United States, including 69 deaths (*12*); children aged 6 months–4 years account for 1,990 (23%) of these cases and 9 (13%) of the deaths among MIS-C cases (*9*). Post–COVID-19 conditions, which include a range of new, returning, or ongoing, health problems occurring ≥4 weeks after acute SARS-CoV-2 infection, also occur in children, including those aged <5 years (*13*–*15*). However, evidence regarding the prevalence and spectrum of these conditions in children, especially young children, is limited by the inability of younger children to verbalize symptoms, few studies that include children, lack of appropriate control groups, and because symptoms similar to those seen in post–COVID-19 conditions are frequently reported among children without known SARS-CoV-2 infection (*13*,*14*,*16*).

The pandemic has also had additional indirect effects on children and families, including missed routine childhood immunizations and health care visits; worsening of children's social, emotional, and mental well-being; and disruptions in early child care and education programs (*17*–*19*). In a survey conducted during July 15–August 2, 2021, 39% of parents reported that an adult in their household either left a job or changed work schedules to care for children during the past year; parents of a child aged <5 years, Black and African American parents, Hispanic or Latino parents, and parents with an annual household income of <$40,000 were most likely to report household job disruptions (*20*). COVID-19 vaccination in this age group may provide parents with increased confidence to return to prepandemic activities, improving social interactions in young children.

Implementation of these recommendations will require educating vaccine providers about the correct age-appropriate product (Table 1) and vaccination schedule (Table 2) for each vaccine, to avoid vaccine administration errors. ACIP determined that use of the Moderna and Pfizer-BioNTech COVID-19 vaccines among children is a reasonable and efficient allocation of resources. To expand COVID-19 vaccine access, additional considerations should be given to demographic groups that have experienced disproportionate COVID-19 morbidity and mortality, as well as those with barriers to routine health care (e.g., members of certain racial and ethnic groups and those living in a rural area, experiencing homelessness, or lacking health insurance). Children from racial and ethnic minority groups have experienced a disproportionately high incidence of COVID-19, associated hospitalization, and MIS-C (*7*,*12*,*21*). Pediatricians and health care providers remain the most trusted source among parents for information about COVID-19 vaccines for children (*22*). Based on the National Immunization Survey-Child COVID Module interviews conducted in May 2022, 33.5% of parents said they would definitely vaccinate their child aged 6 months–4 years for COVID-19, once eligible, and 19.6% said they would probably vaccinate their child aged 6 months–4 years (*7*). Thus, pediatricians and other primary care providers who care for children will be critical to increasing COVID-19 vaccine confidence among parents and coverage with COVID-19 vaccine among young children.

ACIP reviewed the balance of known and potential benefits and risks regarding the use of the Moderna COVID-19 vaccine in children aged 6 months–5 years and Pfizer-BioNTech COVID-19 vaccine in children aged 6 months–4 years, each compared with no vaccine. Both vaccines demonstrated ability to prevent COVID-19 and met noninferiority criteria based on immunobridging data. Although both the Moderna and Pfizer-BioNTech COVID-19 vaccine trials were conducted when Omicron was the predominant circulating SARS-CoV-2 variant, case accrual after the final dose occurred in different months, resulting in differences in COVID-19 incidence across the trials. Thus, efficacy estimates cannot be directly compared between these two vaccines. Moreover, vaccine efficacy from these trials should be interpreted in the context of what is known about vaccine effectiveness against Omicron infection. Postauthorization observational studies in persons aged ≥5 years have demonstrated that the vaccine effectiveness against Omicron infection is lower than that observed against earlier SARS-CoV-2 variants (*23*,*24*). However, postauthorization observational data also indicate that mRNA vaccine effectiveness is higher, even during Omicron predominance, against hospitalization (68% a median of 37 days after the second dose in children aged 5–11 years) than against infection (40% during the 2 months after the second dose in children aged 5–11 years) (*25*). Importantly, during Omicron predominance, mRNA vaccine effectiveness against MIS-C remained high (78%) among children aged 5–11 years (*25*). The clinical trials were not powered to detect efficacy against severe disease in young children, but similar patterns are expected in this age group to what has been observed in persons aged ≥5 years.

ACIP also considered evidence from known and potential harms from COVID-19 vaccines. Myocarditis and pericarditis are rare adverse events that have been reported after receipt of mRNA COVID-19 vaccines (*26*,*27*). Among vaccine recipients aged ≥5 years, the observed risk for myocarditis is highest among males aged 12–39 years (*26*,*28*,*29*). Cases of myocarditis among children aged 5–11 years after Pfizer-BioNTech COVID-19 vaccination have been rarely reported, primarily in boys and after dose 2 (*28*,*29*). To date, monitoring in CDC's

**TABLE 1. COVID-19 vaccines approved or authorized by the Food and Drug Administration for children aged 6 months–17 years — United States, June 2022**

| Vaccine manufacturer | Age group at vaccination | Vial cap color | Label border color | Concentration of mRNA per primary dose | Injection volume per primary dose | Diluent volume | Primary doses per vial |
|---|---|---|---|---|---|---|---|
| **Moderna** | 6 mos–5 yrs | Dark blue | Magenta | 25 μg | 0.25 mL | None | 10 |
| | 6–11 yrs | Dark blue | Purple* | 50 μg | 0.5 mL | None | 5 |
| | 6–11 yrs | Dark blue | Teal* | 50 μg | 0.5 mL | None | 5 |
| | 12–17 yrs | Red | Light blue | 100 μg | 0.5 mL | None | 10–11 |
| **Pfizer-BioNTech** | 6 mos–4 yrs | Maroon | Maroon | 3 μg | 0.2 mL | 2.2 mL | 10† |
| | 5–11 yrs | Orange | Orange | 10 μg | 0.2 mL | 1.3 mL | 10† |
| | 12–17 yrs | Gray | Gray | 30 μg | 0.3 mL | None | 6 |

**Abbreviation:** FDA = Food and Drug Administration.

* Moderna COVID-19 vaccine supplied in a vial with a dark blue cap and a label with a teal border stating "Age 6y through 11y" is currently not available. Moderna COVID-19 vaccine supplied in a vial with a dark blue cap and a label with a purple border stating "BOOSTER DOSES ONLY" is FDA-authorized for use in children aged 6–11 years to provide primary series doses.

† After dilution with 0.9% sodium chloride (normal saline, preservative-free).

Vaccine Safety Datalink have not detected an increased risk for myocarditis and pericarditis in children aged 5–11 years (*29*). No cases of myocarditis occurred among 7,804 children aged 6 months–5 years in the Moderna and Pfizer-BioNTech COVID-19 vaccine clinical trials who received an mRNA vaccine and had ≥7 days of follow-up, although the trials were not adequately powered to detect rare adverse events. Postauthorization safety monitoring, including monitoring for myocarditis and pericarditis after mRNA COVID-19 vaccination, is conducted through multiple national safety surveillance systems.

ACIP determined that the benefits of COVID-19 vaccination outweigh the known and potential risks, even in the setting of high seroprevalence among young children; by April 2022, in a national sample of children aged 6 months–4 years, 71% had infection-induced SARS-CoV-2 antibodies (*9*). Past infection with SARS-CoV-2 provides some protection against reinfection, but the immune response to infection can vary, especially by disease severity, and might not provide broad protection against all SARS-CoV-2 variants (*30*). The Omicron-wave surges of pediatric COVID-19 hospitalizations occurred even in the setting of high seroprevalence, suggesting this alone is not sufficient to provide broad population-level protection. Vaccination in previously infected persons enhances protection against reinfection (*30*–*32*) and COVID-19–associated hospitalization, including infections and hospitalizations due to the Omicron variant (*32*,*33*). No concerns have been identified in postauthorization safety surveillance associated with vaccination of seropositive persons aged ≥5 years. After assessing the balance of benefits and risks for COVID-19 vaccination, ACIP made an interim recommendation for vaccination with the Moderna COVID-19 vaccine for children aged 6 months–5 years as a 2-dose primary series as authorized under the EUA and an interim recommendation for vaccination with the Pfizer-BioNTech COVID-19 vaccine for children aged 6 months–4 years as a 3-dose primary series as authorized under the EUA. ACIP does not state a product preference between the two recommended vaccines for children aged 6 months–5 years; children may receive any ACIP-recommended COVID-19 vaccine and are encouraged to receive the earliest vaccine available to them. Once a primary series is started, the same mRNA vaccine product should be used for all doses in the series.

The GRADE evidence profiles, which provide details on the identification and assessment of relevant evidence, are available for the Moderna COVID-19 vaccine at https://www.cdc.gov/vaccines/acip/recs/grade/covid-19-moderna-vaccine-6-months-5-years.html and for the Pfizer-BioNTech COVID-19 vaccine at https://www.cdc.gov/vaccines/acip/recs/grade/covid-19-pfizer-biontech-vaccine-6-months-4-years.html. The EtR supporting evidence for both the Moderna COVID-19 vaccine and the Pfizer-BioNTech COVID-19 vaccine is available at https://www.cdc.gov/vaccines/acip/recs/grade/covid-19-moderna-pfizer-children-vaccine-etr.html. Additional clinical considerations, including recommendations for children who are moderately or severely immunocompromised, are available at https://www.cdc.gov/vaccines/covid-19/clinical-considerations/covid-19-vaccines-us.html.

These interim recommendations and clinical considerations are based on use of the Moderna COVID-19 vaccine under an EUA and on the Pfizer-BioNTech COVID-19 vaccine under an EUA and might change as more evidence becomes available. COVID-19 vaccines must be administered according to applicable state and territorial vaccination laws. Before vaccination, the EUA Fact Sheet (available at https://www.fda.gov/media/159309/download for the Moderna COVID-19 vaccine and https://www.fda.gov/media/159313/download for the Pfizer-BioNTech COVID-19 vaccine) should be provided to parents or guardians. ACIP will continue to review additional data as they become available; updates to recommendations or clinical considerations will be posted on the ACIP website (https://www.cdc.gov/vaccines/hcp/acip-recs/vacc-specific/covid-19.html).

**TABLE 2. Interim COVID-19 immunization schedule for children aged 6 months–17 years — United States, June 2022**

| Vaccine manufacturer* | Age group at vaccination | Immunocompromise status: Not moderately or severely immunocompromised† — Primary series§ | Not moderately or severely immunocompromised† — Booster dose | Moderately or severely immunocompromised† — Primary series | Moderately or severely immunocompromised† — Booster doses |
|---|---|---|---|---|---|
| **Moderna** | 6 mos–5 yrs | 2 doses<br>4–8 weeks between doses 1 and 2 | Not authorized | 3 doses<br>4 weeks between doses 1 and 2; ≥4 weeks between doses 2 and 3 | Not authorized |
| | 6–11 yrs | 2 doses<br>4–8 weeks between doses 1 and 2 | Not authorized | 3 doses<br>4 weeks between doses 1 and 2; ≥4 weeks between doses 2 and 3 | Not authorized |
| | 12–17 yrs | 2 doses<br>4–8 weeks between doses 1 and 2 | Not authorized | 3 doses<br>4 weeks between doses 1 and 2; ≥4 weeks between doses 2 and 3 | Not authorized |
| **Pfizer-BioNTech** | 6 mos–4 yrs | 3 doses<br>3–8 weeks between doses 1 and 2; ≥8 weeks between doses 2 and 3 | Not authorized | 3 doses<br>3 weeks between doses 1 and 2; ≥8 weeks between doses 2 and 3 | Not authorized |
| | 5–11 yrs | 2 doses<br>3–8 weeks between doses 1 and 2 | ≥5 mos after primary series | 3 doses<br>3 weeks between doses 1 and 2; ≥4 weeks between doses 2 and 3 | ≥3 mos after primary series |
| | 12–17 yrs | 2 doses<br>3–8 weeks between doses 1 and 2 | ≥5 mos after primary series | 3 doses<br>3 weeks between doses 1 and 2; ≥4 weeks between doses 2 and 3 | 2 booster doses<br>First: ≥3 mos after primary series<br>Second: ≥4 mos after first booster |

**Abbreviation:** FDA = Food and Drug Administration.

* More information on product and dosage is available at https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html.

† https://www.cdc.gov/vaccines/covid-19/clinical-considerations/interim-considerations-us.html#immunocompromised

§ mRNA COVID-19 vaccines are FDA-approved or FDA-authorized for a 3-week (Pfizer-BioNTech vaccine) or 4-week (Moderna vaccine) interval between the first and second dose. CDC recommends that an 8-week interval might be optimal for some persons aged 6 months–64 years, especially for males aged 12–39 years because it might reduce the small risk of myocarditis or pericarditis associated with mRNA COVID-19 vaccines. A shorter interval (3 weeks for Pfizer-BioNTech and 4 weeks for Moderna) between the first and second doses remains the recommended interval for persons who are moderately or severely immunocompromised, adults aged ≥65 years, and those in situations in which there is increased concern about COVID-19 community levels or a person's higher risk for severe disease.

## Reporting of Vaccine Adverse Events

FDA requires that vaccination providers report vaccination administration errors, serious adverse events, multisystem inflammatory syndrome cases, and COVID-19 cases that result in hospitalization or death after administration of COVID-19 vaccine under an EUA. Adverse events that occur after receipt of any COVID-19 vaccine should be reported to the Vaccine Adverse Events Reporting System (VAERS). Information on how to submit a report to VAERS is available at https://vaers.hhs.gov/index.html or 1-800-822-7967. Any person who administers or receives a COVID-19 vaccine (or their parent or guardian) is encouraged to report any clinically significant adverse event, whether it is clear that a vaccine caused the adverse event. In addition, CDC has developed a voluntary smartphone-based online tool (v-safe) that uses text messaging and online surveys to provide near real-time health check-ins after receipt of a COVID-19 vaccine. Parents or guardians can register their children in v-safe and complete

**Summary**

What is already known about this topic?

On June 17, 2022, the Food and Drug Administration granted Emergency Use Authorization for the Moderna and Pfizer-BioNTech COVID-19 vaccines for children aged 6 months–5 years and 6 months–4 years, respectively.

What is added by this report?

On June 18, 2022, the Advisory Committee on Immunization Practices (ACIP) issued interim recommendations for the use of the Moderna COVID-19 vaccine for children aged 6 months–5 years and for the Pfizer-BioNTech COVID-19 vaccine for children aged 6 months–4 years in the United States for prevention of COVID-19. ACIP determined that the benefits of vaccination outweigh risks for this population.

What are the implications for public health practice?

Vaccination is important for protecting children aged 6 months–5 years against COVID-19.

the health surveys on their behalf. CDC's v-safe call center follows up on reports to v-safe that include possible medically significant health events to collect additional information for completion of a VAERS report. Information about v-safe is available at https://www.cdc.gov/vsafe.

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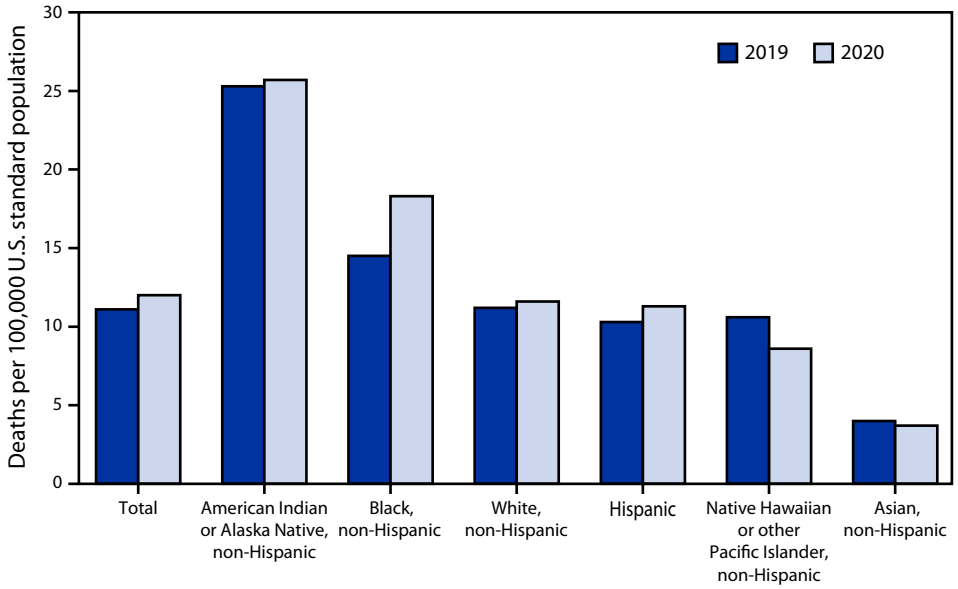
# QuickStats

FROM THE NATIONAL CENTER FOR HEALTH STATISTICS

## Age-Adjusted Death Rates* for Motor Vehicle Traffic Injury,† by Race and Hispanic Origin — United States, 2019 and 2020




* Age-adjusted death rates are deaths per 100,000 adjusted to 2000 U.S. standard population.
† Motor vehicle traffic injuries are identified as underlying cause of death using *International Classification of Diseases, Tenth Revision* codes V02–V04[.1,.9], V09.2, V12–V14[.3–.9], V19[.4–.6], V20–V28[.3–.9], V29–V79[.4–.9], V80[.3–.5], V81.1, V82.1, V83–V86[.0–.3], V87[.0–.8], and V89.2.

Age-adjusted death rates for motor vehicle traffic injury increased from 11.1 per 100,000 population in 2019 to 12.0 in 2020. The rates increased from 10.3 to 11.3 for Hispanic persons, from 14.5 to 18.3 for non-Hispanic Black persons, and from 11.2 to 11.6 for non-Hispanic White persons. The changes in rates among other groups were not statistically significant. During 2019 and 2020, the rates were highest for non-Hispanic American Indian or Alaska Native persons (25.3 and 25.7) and lowest for non-Hispanic Asian persons (4.0 and 3.7), respectively.

**Source:** National Vital Statistics System, Underlying Cause of Death by Single-Race Categories, 2018–2020. https://wonder.cdc.gov/ucd-icd10-expanded.html

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

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