

## Epidemiology of Varicella During the 2-Dose Varicella Vaccination Program — United States, 2005–2014

Adriana S. Lopez, MHS<sup>1</sup>; John Zhang, PhD<sup>1</sup>; Mona Marin, MD<sup>1</sup>

Before availability of varicella vaccine in the United States, an estimated 4 million varicella cases, 11,000–13,500 varicella-related hospitalizations, and 100–150 varicella-related deaths occurred annually. The varicella vaccination program was implemented in the United States in 1996 as a 1-dose routine childhood program. Based on data from two varicella active surveillance sites, the varicella vaccination program led to 90% decline in incidence over the next decade (1). However, because of continued varicella outbreaks, a routine 2-dose schedule (at ages 12–15 months and 4–6 years) was recommended and has been in place since 2006 (2). The declines in incidence (1,3–6) made it feasible for states to implement varicella case-based surveillance and to report varicella data to CDC through the National Notifiable Diseases Surveillance System (NNDSS). State data have become the primary source for monitoring trends in varicella incidence nationally (7). Using NNDSS data, CDC previously reported nationwide declines in varicella incidence of 72% from the end of the 1-dose to the early years of the 2-dose varicella vaccination program (2006–2010) (7). This report updates varicella incidence trends to include the most recent years in the 2-dose varicella vaccination program. Between the period 2005–2006 (before the 2-dose recommendation) and 2013–2014, overall varicella incidence declined 84.6%, with the largest declines reported in children aged 5–9 years (89.3%) and 10–14 years (84.8%). The availability of varicella-specific data varied over time. During the last 2 years examined (2013 and 2014), completeness of reporting of two critical variables monitored by CDC, vaccination status (receipt of at least 1 dose of varicella vaccine) of cases and severity of disease based on number of lesions, were 54.2% and 39.1%, respectively. State and local health departments, in collaboration with CDC, should continue working to improve reporting of cases and completeness of critical varicella-specific variables to better monitor impact of the varicella vaccination program.

Demographic, clinical, and epidemiologic data from varicella cases reported through passive surveillance from state and local health departments are electronically transmitted to CDC via NNDSS. CDC analyzed data from all states and the District of Columbia (DC) that reported varicella cases, starting with the year the state first reported varicella cases to CDC. For this report, DC is counted as a state. An earlier report had calculated varicella incidence using ad hoc inclusion criteria of adequate (incidence of  $\geq 1$  case per 100,000 population) and

consistent ( $\geq 3$  consecutive years) reporting (7); in this analysis these criteria were also examined.

Nationwide age-specific and overall varicella incidence rates from passive surveillance data were calculated for each year from 2005 to 2014 by dividing the aggregate number of confirmed and probable\* varicella cases from reporting states by the aggregate population of the same states using U.S. Census data (<https://www.census.gov/popest/data/historical/index.html>). To examine trends between the end of the 1-dose varicella vaccination program and the most recent years of the 2-dose program, incidence rates were averaged for 2005–2006 and 2013–2014 to account for year-to-year variability.

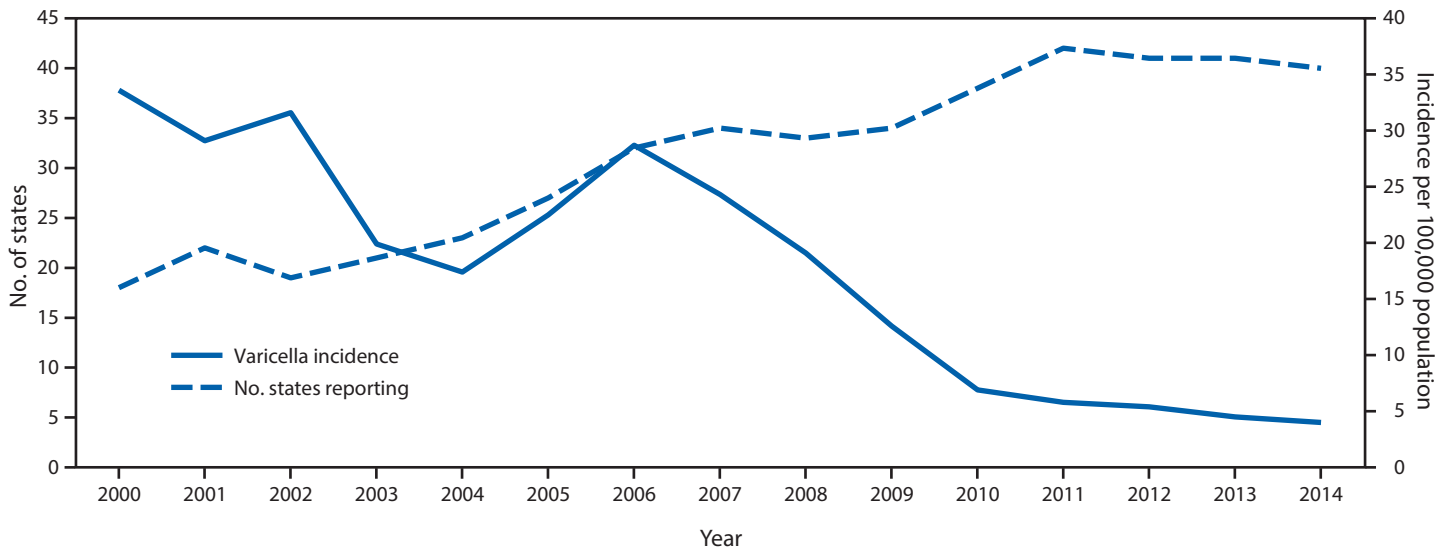
To evaluate changes in varicella incidence since the varicella vaccination program was introduced, incidence trends from 1993 to 2014, which include data from before the start of the U.S. varicella vaccination program, were analyzed for four states (Illinois, Michigan, Texas, and West Virginia) that have reported varicella cases to CDC every year since before implementation of the varicella vaccination program. Poisson regression was used to assess all trends over time.

Provisional varicella-specific case-based data from 2013 and 2014 were analyzed to assess critical variables monitored by CDC: vaccination status of cases, disease severity (based on number of lesions),<sup>†</sup> hospitalization, and association with outbreaks (defined variably by states as three or more cases or as five or more cases).

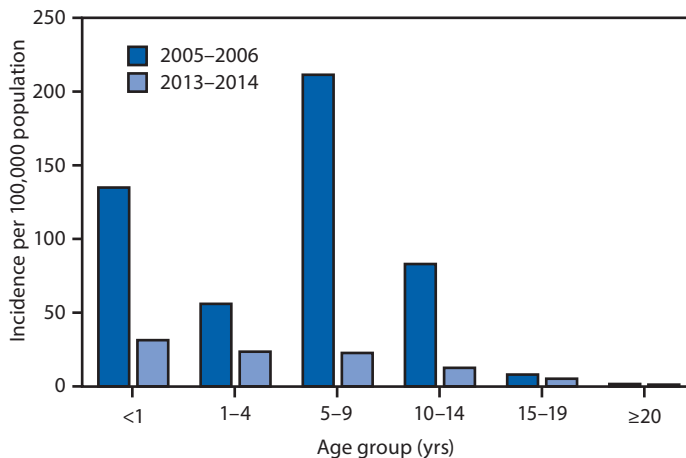
During 2005–2014, the number of states reporting varicella data to CDC through NNDSS increased 48.1%, from 27 in 2005 to 40 in 2014 (Figure 1). Among the 40 states reporting data in 2014, 38 have implemented case-based varicella surveillance. The average annual varicella incidence declined significantly (84.6%) from 25.4 per 100,000 population during 2005–2006 to 3.9 per 100,000 population during 2013–2014 ( $p < 0.001$ ) (Figure 1). Statistically significant declines in incidence were reported for all age groups during this time (Figure 2), with the largest declines among children

\* A confirmed case of varicella is an illness with acute onset of diffuse (generalized) maculopapulovesicular rash without other apparent cause that is laboratory confirmed or that meets the clinical case definition and is epidemiologically linked to a confirmed or a probable case. A probable case of varicella meets the clinical case definition, is not laboratory confirmed, and is not epidemiologically linked to another probable or confirmed case.

<sup>†</sup> Varicella disease is classified as mild (<50 lesions), mild/moderate (50–249 lesions), moderate (250–499 lesions), or severe ( $\geq 500$  lesions or any complications such as bacterial superinfection, varicella pneumonitis, encephalitis, hospitalization, or death). <http://www.cdc.gov/vaccines/pubs/surv-manual/chpt17-varicella.html>.

**FIGURE 1. Overall varicella incidence per 100,000 population\* and number of states reporting varicella cases to CDC — United States, 2000–2014**

\* Varicella incidence declined 84.6% from 2005–2006 (the end of the 1-dose varicella vaccination program) to 2013–2014 (the most recent years of data available for the 2-dose varicella vaccination program). During the same interval, the number of states reporting varicella cases through the National Notifiable Diseases Surveillance System (NNDSS) increased from 27 to 40. NNDSS data were used to calculate national incidence starting in 2000 because before this year, data were too sparse to calculate national estimates.

**FIGURE 2. Reported varicella incidence,\* by age group† — United States, 2005–2006 compared with 2013–2014**

\* 25 states provided age data during 2005–2006, and 37 states reported data during 2013–2014.

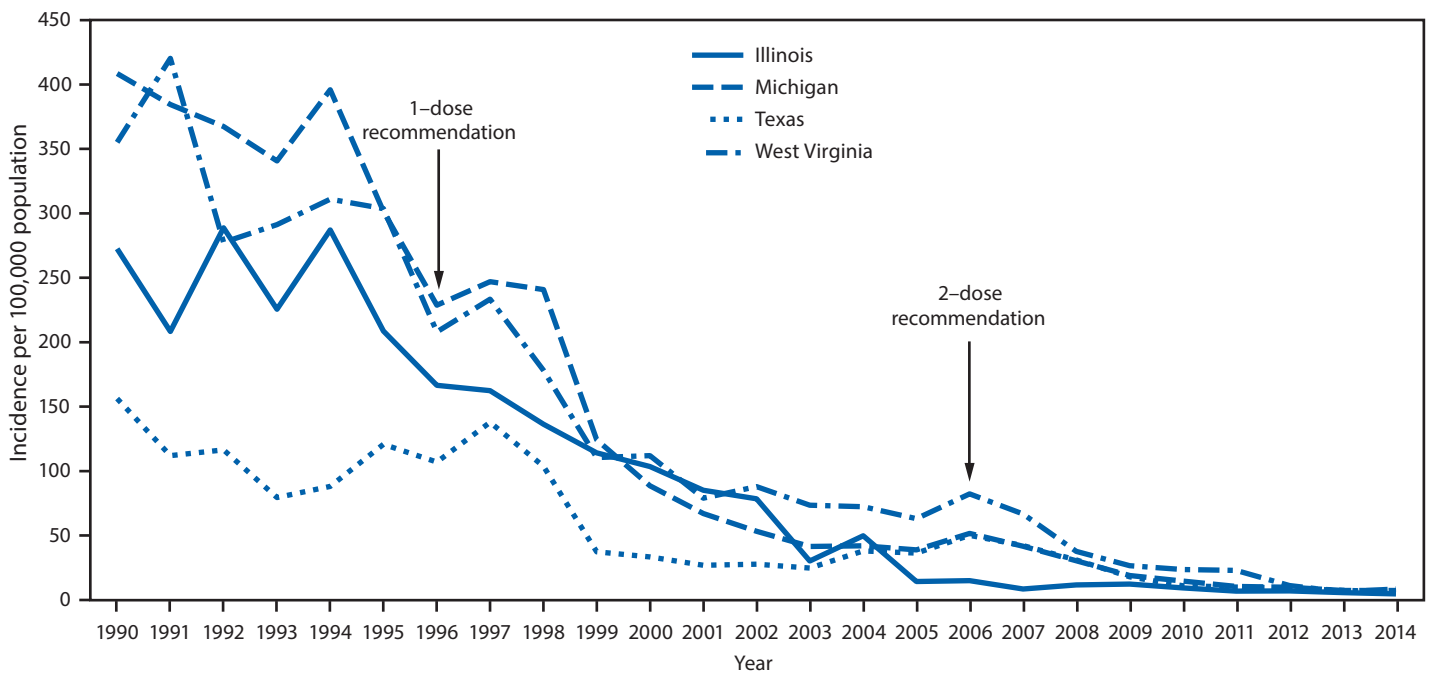
† Percentage declines for each age group are as follows: <1 year, 76.8%; 1–4 years, 58.0%; 5–9 years, 89.3%; 10–14 years, 84.8%; 15–19 years, 35.0%; ≥20 years, 25.0%. Percentage declines were statistically significant ( $p < 0.001$ ) overall and for all age groups.

aged 5–9 years (89.3%) and 10–14 years (84.8%). Fewer states contributed adequate (incidence  $\geq 1$  case per 100,000 population) and consistent ( $\geq 3$  consecutive years) data (26 in 2005 and 35 in 2014); however, the decline in varicella incidence, when restricted to these states, was similar (80.2%) to that in all reporting states and decreased from 27.3 cases per 100,000 population during 2005–2006 to 5.4 per 100,000 during 2013–2014 ( $p < 0.001$ ).

In the four states (Illinois, Michigan, Texas, and West Virginia) that have been reporting varicella cases annually since before implementation of the varicella vaccination program, incidence declined an average of 97.4% from 1993–1995 to 2013–2014 (range = 92.9%–97.9%) (Figure 3).

During 2013–2014, completeness of varicella-specific data from states that reported to NNDSS varied. Data on vaccination status of varicella patients was available for 12,784 (59.8%) cases; 7,000 (54.8%) of those cases occurred in persons who had received at least 1 dose of varicella vaccine. Among these reports, the number of doses received was reported for 2,266 (32.4%) patients, including 921 (39.0%) persons who had received 1 dose of varicella vaccine, 1,331 (56.4%) who had received 2 doses, and 14 (0.6%) who were reported to have received 3 doses. A total of 3,715 (17.4%) reports included information about hospitalization. Among these reports, 81 (2.2%) indicated that the patient was hospitalized. Reports from 17 (22.4%) of 76 hospitalized patients with information on vaccination status indicated receipt of varicella vaccine, and 13 vaccinated hospitalized patients had information on number of doses. Eight patients had received 1 dose, and five had received 2 doses. Among the 8,358 (39.1%) case reports with data on the number of skin lesions, 4,269 (51.1%) were considered to have had mild disease and 4,089 (48.9%) had moderate to severe disease. Mild disease occurred significantly more frequently among vaccinated patients (76.8%) than among unvaccinated patients (23.2%) ( $p < 0.001$ ). Information on outbreak association of cases was available for 13,826 (64.6%)

**FIGURE 3. Varicella incidence per 100,000 population\* in states that have reported varicella cases to CDC annually since before implementation of the varicella vaccination program — Illinois, Michigan, Texas, and West Virginia, 1990–2014**



\* Varicella incidence declined 97.4% overall from 1993–1995 to 2013–2014 (range = 92.9%–97.9%) in the four states (Illinois, Michigan, Texas, and West Virginia) that have reported varicella cases to CDC every year since before implementation of the varicella vaccination program.

reports, among which 2,279 (16.5%) cases were associated with an outbreak. Laboratory testing data were reported for 2,240 (24.6%) of 9,104 cases for which information about varicella testing was available; among these, 1,842 (82.2%) were positive by either polymerase chain reaction, direct fluorescent antibody testing, immunoglobulin M by enzyme-linked immunosorbent assay, or viral culture.

### Discussion

Previous reports have documented significant declines in varicella incidence in the United States since the varicella vaccination program was implemented in 1996 through the early years of the 2-dose program (1,3–8). During 1995–2010, data to assess impact of the varicella vaccination program were obtained from a varicella active surveillance project, which was discontinued in 2010 (3). Since 2000, more states are reporting to NNDSS; these data can now be used to assess impact of the program (7). NNDSS data documented an 85% decline in varicella incidence from the 2-year period 2005–2006 (the end of the 1-dose varicella vaccination program) through 2013–2014, and a 97% decline since the varicella vaccination program was implemented. Since recommendation of the second varicella vaccine dose, the largest declines in incidence have occurred in the age groups more likely to have received the second dose (children and adolescents aged 5–14 years).

During 2013–2014, 55% of all reported varicella cases occurred in persons who had received varicella vaccine; this finding is not unexpected in a highly vaccinated population, in which overall incidence declines, but among cases that still occur, a high percentage will be among vaccinated persons.

As varicella incidence continues to decline, more states are able to conduct case-based surveillance. Almost 80% of states are reporting case-based varicella data to CDC for use in national surveillance. However, the completeness of reported data varies, and data from critical variables are missing for approximately 40% of cases. Continued efforts by states to improve reporting and completeness of reported data will be valuable for accurately describing trends and epidemiology of varicella disease.

Although incidence rates were slightly higher when only states with adequate and consistent reporting (7) were included in trend analyses, the percentage declines between 2005–2006 and 2013–2014 were similar. Therefore, removing the adequacy and consistency of reporting criteria for calculating incidence allows for the inclusion of more states to provide a better representation of varicella incidence nationwide.

Varicella surveillance data can also provide information about characteristics of cases that result in severe outcomes such as hospitalization and death. Analyses of administrative (hospital discharge, medical claims, and vital statistics) data

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

The introduction of a routine childhood dose of varicella vaccine in the United States in 1996 led to an approximate 90% decline in varicella incidence. However, because of continued outbreaks, a second routine childhood dose of varicella vaccine was introduced in 2006. Declines in incidence have continued during the early years since implementation of the 2-dose vaccination recommendation and have made it feasible for more states to conduct varicella case-based surveillance, such that state data reported to CDC through the National Notifiable Diseases Surveillance System (NNDSS) are now used to monitor trends in varicella incidence.

**What is added by this report?**

Among all states that reported varicella data to NNDSS, there was an 85% decline in varicella incidence from 2005–2006 (the end of the 1-dose varicella vaccination program) to 2013–2014. The largest declines occurred among children and adolescents aged 5–14 years (those age groups likely to receive a second dose). Although the number of states reporting varicella data to CDC has increased over time, >40% of reported cases are missing data for varicella-specific variables important for monitoring the varicella vaccination program.

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

Further reduction in the number of varicella cases will provide states with increased opportunities for enhancing varicella surveillance and improving completeness of reporting to monitor impact of the vaccination program. These efforts will improve the accuracy of national data, provide important information for further assessment of varicella vaccination, and inform vaccination policy.

have demonstrated significant declines in hospitalizations (86%–93%) and deaths (87%) among all age groups since implementation of the varicella vaccination program (9,10). However, it is important to understand why severe outcomes still occur and whether these outcomes are occurring among vaccinated persons. Improvements in completeness of NNDSS data will permit evaluation of severe outcomes by vaccination status.

The findings in this report are subject to at least three limitations. First, because data are passively reported and case ascertainment is likely incomplete, varicella cases might be missed, resulting in an underestimate of incidence. Conversely, because varicella disease in vaccinated persons is mild and atypical (fewer lesions and predominantly maculopapular rash) and increasingly challenging to diagnose clinically, nonvaricella cases might be misclassified, resulting in possible overestimates of incidence. Second, laboratory testing is still not routinely done for varicella diagnosis; only 25% of reported cases had available information about testing, although some states might not receive laboratory data if results are negative. Finally, approximately 40% of data for important varicella-specific

variables were missing; therefore, the reported findings describing patient characteristics should be interpreted with caution.

With the reduction in the number of varicella cases, states have increased opportunities for improving varicella surveillance to better monitor impact of the vaccination program. Starting in 2015, 48 jurisdictions have been funded through CDC's Epidemiology and Laboratory Capacity program to add a vaccine preventable disease surveillance coordinator to help enhance varicella surveillance. Jurisdictions with varicella case-based surveillance are working to improve reporting of cases and completeness of reporting. In addition, CDC will receive data on varicella outbreaks from all funded jurisdictions, to allow better assessment of impact of the second dose on varicella outbreaks. These efforts will improve the accuracy of national data, provide important information for further assessment of varicella vaccination, and inform vaccination policy.

<sup>1</sup>Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, CDC.

Corresponding author: Adriana S. Lopez, MHS, alopez@cdc.gov, 404-639-8369.

**References**

1. Guris D, Jumaan AO, Mascola L, et al. Changing varicella epidemiology in active surveillance sites—United States, 1995–2005. *J Infect Dis* 2008;197(Suppl 2):S71–5. <http://dx.doi.org/10.1086/522156>
2. Marin M, Güris D, Chaves SS, Schmid S, Seward JF; Advisory Committee on Immunization Practices. Prevention of varicella: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2007;56(No. RR-4).
3. Bialek SR, Perella D, Zhang J, et al. Impact of a routine two-dose varicella vaccination program on varicella epidemiology. *Pediatrics* 2013;132:e1134–40. <http://dx.doi.org/10.1542/peds.2013-0863>
4. Daly ER, Anderson L, Dreisig J, Dionne-Odom J. Decrease in varicella incidence after implementation of the 2-dose recommendation for varicella vaccine in New Hampshire. *Pediatr Infect Dis J* 2013;32:981–3. <http://dx.doi.org/10.1097/INF.0b013e318293308e>
5. Sosa LE, Hadler JL. Epidemiology of varicella in Connecticut, 2001–2005. *J Infect Dis* 2008;197(Suppl 2):S90–3. <http://dx.doi.org/10.1086/522128>
6. Mullins J, Kudish K, Sosa L, Hadler J. Continuing decline in varicella incidence after the 2-Dose Vaccination Recommendation—Connecticut, 2009–2014. *Open Forum Infect Dis* 2015;2:ofv150. <http://dx.doi.org/10.1093/ofid/ofv150>
7. CDC. Evolution of varicella surveillance—selected states, 2000–2010. *MMWR Morb Mortal Wkly Rep* 2012;61:609–12.
8. Leung J, Lopez AS, Blostein J, et al. Impact of the US two-dose varicella vaccination program on the epidemiology of varicella outbreaks: data from nine states, 2005–2012. *Pediatr Infect Dis J* 2015;34:1105–9. <http://dx.doi.org/10.1097/INF.0000000000000821>
9. Leung J, Harpaz R. Impact of the maturing varicella vaccination program on varicella and related outcomes in the United States: 1994–2012. *J Pediatric Infect Dis Soc* 2015;pii044 Epub August 12, 2016. <http://dx.doi.org/10.1093/jpids/piv044>
10. Leung J, Bialek SR, Marin M. Trends in varicella mortality in the United States: Data from vital statistics and the national surveillance system. *Hum Vaccin Immunother* 2015;11:662–8. <http://dx.doi.org/10.1080/21645515.2015.1008880>