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Incidence of Herpes Zoster Among Children: 2003–2014

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Abstract

BACKGROUND AND OBJECTIVES: After the 1996 introduction of routine varicella vaccination in the United States, most studies evaluating pediatric herpes zoster (HZ) incidence reported lower incidence over time, with varying degrees of decline. Using the combined databases of 6 integrated health care organizations, we examined HZ incidence in children over a 12-year period in the varicella vaccine era.

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METHODS: This study included children aged 0 through 17 years from 2003 through 2014. Using electronic medical records, we identified HZ cases through International Classification of Diseases, Ninth Revision diagnosis code 053. We calculated HZ incidence rates per 100 000 person years of health plan membership for all children and among children who were vaccinated versus unvaccinated. We calculated rates for the 12-year period and examined temporal trends. Among children who were vaccinated, we compared HZ rates by month and year of age at vaccination.

RESULTS: The study included 6 372 067 children with ≥1 month of health plan membership. For the 12-year period, the crude HZ incidence rate for all subjects was 74 per 100 000 person years, and the rate among children who were vaccinated was 38 per 100 000 person years, which was 78% lower than that among children who were unvaccinated (170 per 100 000 person years; $P < .0001$). Overall HZ incidence declined by 72% ($P < .0001$) from 2003 through 2014. Annual rates in children who were vaccinated were consistently lower than in children who were unvaccinated.

CONCLUSIONS: With this population-based study, we confirm the decline in pediatric HZ incidence and the significantly lower incidence among children who are vaccinated, reinforcing the benefit of routine varicella vaccination to prevent pediatric HZ.

In 1996, the Advisory Committee on Immunization Practices (ACIP) recommended routine administration of the varicella vaccine to children in the United States aged 12 through 18 months. In 2007, the ACIP recommended the first varicella vaccine dose at ages 12 through 15 months with a second dose at ages 4 through 6 years. Similar to wild-type varicella zoster virus (VZV) infection, a vaccine-strain virus may establish a latent infection that can reactivate, causing herpes zoster (HZ).[1–6] HZ from wild-type or vaccine-strain VZV can occur in children after varicella vaccination.

In a 2013 study at Kaiser Permanente Northwest (KPNW)[7] involving children <18 years of age with laboratory-confirmed HZ, we reported that children who were vaccinated had a 79% lower incidence of HZ than children who were unvaccinated (48 vs 230 per 100 000 person years). However, among children aged 1 and 2 years, incidence was significantly higher among children who were vaccinated (100 per 100 000 vs 10 per 100 000 person years; $P = .01$). Given these results, we considered it important to examine, in a larger pediatric population, HZ incidence overall and in subgroups.

Using the databases of 6 integrated health care organizations containing the health information of almost 6.4 million children, we characterized the annual incidence of HZ among children aged 0 through 17 years from 2003 through 2014 by varicella vaccination status, age at HZ diagnosis, immunosuppressed status, sex, and other factors.

METHODS

This study included children, <18 years of age at any time from January 1, 2003, to December 31, 2014, who were members of 1 of the health care organizations participating in the Centers for Disease Control and Prevention–sponsored Vaccine Safety Datalink: the Kaiser Permanente regions of Northwest, Northern California, Southern California,

Colorado, and Washington and the Marshfield Clinic in Wisconsin.[8] All sites' institutional review boards approved the study protocol.

We identified cases of HZ using the International Classification of Diseases, Ninth Revision (ICD-9) diagnosis code 053 in outpatient, inpatient, and emergency department visits and claims from outside providers. We included those for whom there was no HZ diagnosis within the previous 6 months (and a 6-month period in 2002 for calculation of 2003 rates). We validated this ICD-9 code in earlier studies at KPNW, finding a positive predictive value of 96.8% among 0- to 17-year-olds.[9] We did not include children whose only HZ-related ICD-9 codes were 053.12 (postherpetic trigeminal neuralgia) or 053.13 (postherpetic polyneuropathy) because these may not represent incident cases. Children vaccinated ≤4 days before their first birthday were considered vaccinated 12-month-olds in accordance with ACIP guidelines.[10]

Varicella vaccination status was obtained from electronic medical records.[8] We excluded children whose only documented varicella vaccination was before vaccine licensure in 1995 ($N = 6298$) and children whose only documented varicella vaccination was before 11 months of age ($N = 4267$). If a child had a recorded varicella vaccination before 1995 or before 11 months of age followed by another varicella vaccination ($n = 13\,480$ children), we considered the latter to be the first dose.

Immunosuppressed status was defined as an immunosuppressive condition or a condition treated with immunosuppressive drugs at any time during the study period. We identified these children through an iterative process, reviewing a published list of 200 ICD-9 codes[4] and conditions associated with a comprehensive list of immunosuppressive medications[11] and adding codes from additional literature review. One author (E.L.) reviewed 300 patient charts identified by these codes, and 2 authors (E.L. and C.C.) reviewed the final list of selected codes.

Incidence rates were calculated by dividing the number of cases in each period by the number of person years in the population during that period and were expressed as cases per 100 000 person years. All *P* values were 2 sided.

Overall HZ Incidence Rates

For calculation of overall HZ incidence rates, children contributed person time beginning at birth, health care organization entry, or January 1, 2003 (whichever came last). Person time ended when children reached 18 years of age, died, or left their health care organization or at the end of the study period (whichever came first). We included children who left and rejoined their health care organizations but factored only the enrolled periods into the person-time calculations. A child could have multiple HZ diagnoses; the 180 days after each HZ diagnosis were excluded from person time to ensure that only new diagnoses were included in incidence calculations. Varicella vaccination status was assessed at the time of HZ diagnosis. For children who were unvaccinated, person-time calculation started on January 1, 2003; at enrollment; or at birth (whichever came last) and continued through 20 days after the first varicella vaccination, the child's 18th birthday, death, disenrollment in the health care organization, or the end of the study period (whichever came first). In calculating

incidence rates for children who were vaccinated, we started the person-time calculation 21 days after the first varicella vaccination or on January 1, 2003 (whichever came later). The 21-day window allowed time for the recipient to develop immunity to the vaccine and avoid the interval during which a localized vaccine-related rash could occur. A child could contribute unvaccinated and vaccinated person time.

Children who were immunosuppressed were included in these rates. We calculated crude incidence rates by calendar year for all ages combined, by vaccination status, and in all children regardless of vaccination status. We also calculated crude HZ incidence rates for the 12-year period by varicella vaccination status, age at HZ, sex, immunosuppressed status, site, and number of doses (1 vs ≥2). The dose-number analysis was limited to children ≥4 years of age to allow comparison of similar-aged children. Not all HZ ICD-9 codes are accurately assigned, so we created a "laboratory confirmation–adjusted rate" by multiplying crude rates by the proportion of cases that had skin lesions with VZV detected by polymerase chain reaction (PCR)in our earlier study.[7] Confidence intervals were computed assuming a Poisson distribution.[12] We evaluated linear trends in annual incidence rates using Poisson regression analysis.

HZ Incidence After Varicella Vaccination

To estimate HZ incidence rates as a function of time since the first varicella vaccination, we included only subjects who were vaccinated in 2003 or later while they were members of the health care organizations; this analysis was limited to children with 1 dose. Person-time calculation began 21 days after the first varicella vaccination and ended on the date of the second dose, first HZ diagnosis, disenrollment from the health care organization, or study end date (December 31, 2014; whichever came first). We calculated HZ incidence by age in years at vaccination (ages 1–7 years) and by age in months at vaccination (ages 11–36 months). To examine possible changes in HZ incidence over time after vaccination, we also calculated HZ incidence for each 1-year period after varicella vaccination up to 6 years. Because age at varicella vaccination may be related to a variety of immunosuppressing medical conditions, we excluded subjects who were immunosuppressed from these analyses. We evaluated linear trends using Poisson regression analysis.

RESULTS

A total of 6 372 067 children were included in the analyses: 3 186 732 (50%) were vaccinated for some or all of the study period, and 3 185 335 (50%) were not vaccinated against varicella during this period. The total population was 49% girls and 51% boys. Among children aged 1 to 17 years, the proportion with ≥1 dose of varicella vaccine ranged from 27% to 52% in 2003 and from 82% to 91% in 2014 by Vaccine Safety Datalink site.

Overall HZ Incidence Rates

The crude HZ incidence rate for all subjects was 74 per 100 000 person years (laboratory confirmation–adjusted rate: 61 per 100 000 person years; Table 1). When stratified by varicella vaccination status, the crude rate among children who were vaccinated was 38 per 100 000 person years; this was 78% lower than the rate of 170 per 100 000 person years in

children who were unvaccinated (82% lower with the laboratory confirmation–adjusted rate; $P < .0001$). HZ incidence rates were higher in girls than in boys ($P < .0001$) and 5 to 6 times higher in children who were immunosuppressed than in those who were not immunosuppressed. Crude HZ rates by study site ranged from 65 per 100 000 to 122 per 100 000 person years (Table 1).

The overall HZ incidence rate declined by 72% to its lowest rate in 2014 ($P < .0001$ for the trend over the 2003–2014 period; Fig 1). The rate among children who were vaccinated declined over time ($P < .0001$) and was consistently lower than that among those who were unvaccinated. The rate among children who were unvaccinated climbed from 2003 to 2007 ($P < .001$) and then declined sharply through the end of the study period ($P < .0001$). By site, HZ rates among those who were vaccinated were remarkably similar over time, whereas rates among those who were unvaccinated varied considerably and from year to year (data not shown). Crude HZ incidence rates by age groups of 1 to 2, 3 to 9, and 10 to 17 years are presented in Fig 2. In the group aged 1 to 2 years, the confirmation-adjusted HZ rate among children who were vaccinated was 70% higher than among those who were unvaccinated ($P < .0001$; Fig 3). In the 2 older age groups, HZ rates were significantly higher in children who were unvaccinated than in those who were vaccinated ($P < .0001$ for each group).

When stratifying by individual year of age at HZ diagnosis (Fig 4), 1-year-olds who were vaccinated had a 140% higher risk of HZ than 1-year-olds who were unvaccinated ($P < .0001$). This higher risk in those who were vaccinated disappeared by age 2 ($P = .59$). For those aged 5 to 17 years, HZ rates were much lower in children who were vaccinated than in those who were unvaccinated.

Among children ≥4 years of age who were vaccinated, the crude HZ incidence rate was 28.47 cases per 100 000 person years for those who received 1 vaccine dose and 14.11 cases per 100 000 person years for those who received 2 doses ($P < .0001$).

HZ Incidence After Varicella Vaccination

To examine whether age at vaccination was associated with a higher rate of HZ, we calculated HZ rates by year of age at vaccination up to 7 years (Fig 5). The HZ incidence rates for children aged 2 and 3 years at vaccination were approximately half the rates for 1-year-olds ($P = .06$ for comparison between 1 and 2 years of age). HZ rates for children vaccinated at >3 years of age were not statistically different from those for 1-year-olds. When HZ rates were stratified on individual month of age at varicella vaccination between 12 and 36 months, no clear pattern emerged (Fig 6). Vaccination at 11 months of age was associated with an HZ rate more than triple the other rates presented; however, the person years (1637) and HZ cases ($n = 3$) were small in this group.

We examined HZ incidence over time after varicella vaccination at 12 to 18 months of age to further explore risk of HZ in early childhood (Table 2). For rates calculated by using the entire study period, the risk of HZ was highest the first year after vaccination, dropping off sharply over the subsequent 5 years ($P < .0001$).

DISCUSSION

With this population-based study, we confirm that there was a decline in HZ incidence (72%) from 2003 to 2014 among children <18 years of age. HZ incidence among children who were vaccinated was significantly lower than among children who were unvaccinated. Because the population used to calculate these HZ rates included a small percentage of children who were immunosuppressed, for whom higher HZ incidence rates have been reported,[7,11,13,14] the rates among children who were immunocompetent are lower than those presented in Fig 1. We observed a significant decrease in HZ incidence among children who were unvaccinated beginning in 2010, 4 years after the introduction of a routine second varicella vaccine dose; however, the rate among children who were unvaccinated remained significantly higher than among children who were vaccinated throughout the study. The trend of decreasing HZ incidence among children who were unvaccinated is likely due to a lack of primary VZV infection resulting from herd immunity in a highly vaccinated population. We also report that among children >4 years of age, children who were unvaccinated had much higher HZ rates than children who were vaccinated.

Although HZ incidence among 1- to 2-year-olds who were vaccinated was higher than among their counterparts who were unvaccinated, the laboratory confirmation–adjusted rate from this study (34 per 100 000 person years) is only one-third of that reported for vaccinated 1- to 2-year-olds in our smaller 2005–2009 KPNW study.[7] The rate in the current study is still higher than rates reported in 2 other studies. Black et al[15] reported an HZ incidence of 15 per 100 000 person years in vaccinated 1- to 2-year-olds in 1995–1996. However, in that study, only 10 of 23 reported cases were evaluated by a physician; 2 of the 10 cases were identified as HZ and used to calculate the incidence rate. Tseng et al[16] reported a rate of 29 per 100 000 person years for the group aged 1.0 to 1.5 years and 14 per 100 000 for the group aged 1.6 to 5 years during 2002–2008; after chart review, 46% of electronically identified cases were included in the reported rates.

During the period between the first and second varicella vaccinations, we did not find statistically significant differences in HZ rates by age at vaccination for 12- to 36-month-olds. However, the HZ incidence rates for children aged 2 and 3 years at vaccination were approximately half the HZ rate for 1-year-olds.

Among the small number of children vaccinated at 11 months of age (for whom the vaccine is not recommended), the HZ incidence rate was significantly higher than in children vaccinated at ≥1 year of age. Similarly, children who contract wild-type varicella infection at ≤1 year of age also have a higher risk of HZ (relative risk: 13.5; 95% confidence interval 9.6–18.8).[17] The immature adaptive T-cell response in children <1 year of age appears less able to contain VZV as a latent infection compared with older children. Our findings for 11-month-olds who were vaccinated should be interpreted with caution because this population included only 3 cases of HZ and could have included children participating in a prelicensure study with a vaccine formulation different from Varivax.

Comparing epidemiological studies of HZ in the vaccine era is complicated by children having received 0 to 2 vaccine doses, the decreasing incidence of varicella disease, the accumulation of more children who are vaccinated, and different time intervals since vaccination. Before routine varicella vaccination, reported HZ incidence rates among 0- to 19-year-olds varied: rates were 42 per 100 000, 160 per 100 000, and 220 per 100 000 person years in the United States,[13] Iceland,[18] and France,[19] respectively. Another reported rate among US 0- to 14-year-olds before vaccine introduction was 46 per 100 000.[20] In our study, pediatric HZ incidence rates in the unvaccinated ranged from 160 per 100 000 to 213 per 100 000 person years in the early study period.

Authors of a study of HZ incidence from 1992 to 2002 among the Group Health Cooperative population reported that the HZ incidence among children and adolescents aged 0 to 19 years remained stable before and after introduction of routine childhood varicella vaccination.[21]

During 2000–2006 in Antelope Valley, California, the reported HZ rate for children <10 years of age who were vaccinated was 19.2 per 100 000 person years,[22] similar to the rates among vaccinated 3- to 9-year-olds in the 2005–2009 KPNW study[7] and in this study. Similar to our current findings (Fig 2), a follow-up study from Antelope Valley during 2000–2010 reported a continued decreasing trend of HZ incidence among children <10 years, which by 2010 had declined 84% compared with 2000.[23] Among 10- to 17-year-olds, we report a plateau in HZ incidence during 2003–2007 followed by a steady decline to 2014, whereas the Antelope Valley study reported an increase from 2003 to 2006 and a trend toward lower incidence from 2007 to 2010.[23]

Authors of studies from Canada describing the impact of routine varicella vaccination on pediatric HZ incidence report mixed results. Also, the amount of Oka strain VZV per dose differed from the Varivax (1350 plaque-forming units [PFUs]/dose; Merck) and ProQuad (9772 PFUs as part of measles-mumps-rubella-varicella vaccine; Merck) vaccines administered in the United States. A population-based study from Alberta, Canada, during 1994–2010 (Varivax [Merck], 1350 PFUs/dose; Priorix-Tetra [GlaxoSmithKline], 1995 PFUs/dose; ProQuad, 9772 PFUs/dose) revealed a significant decrease in HZ incidence among children <10 years of age after the 2002 introduction of a routine, publicly funded vaccine dose at 12 months of age. Comparing 2002–2010 with 1994–2001, authors reported an annual percent change in HZ rates for boys and girls <10 years of age of −10% ($P < .0001$ for each sex) attributed to introduction of vaccination.[24] In contrast, authors of a study from Ontario, Canada, reported HZ incidence during 1992–2010, spanning the introduction of a privately funded VZV vaccine in 1999 and a publicly funded routine 2-dose vaccination in 2005. The authors of that study reported an overall HZ incidence of 128 per 100 000 among 0- to 9-year-olds and 154 per 100 000 for 10- to 19-year-olds. There was no significant decrease in HZ rates during the study period from the prevaccine years to 5 years after the introduction of routine 2-dose vaccination.[25]

A higher overall HZ incidence among girls than among boys has been reported in multiple studies before and after the introduction of routine varicella vaccination of children.[4,7,24–26]

This was also our finding. There is no known biological or behavioral basis for this excess risk in girls.[4]

To examine changes in HZ incidence postvaccine, Tseng et al[16] reported that children vaccinated at 12 to 18 months of age from 2002 to 2008 had annual HZ incidence rates that gradually increased during the subsequent 4 years (43.2 per 100 000 after 4 years) and decreased thereafter, suggesting a period of relatively higher incidence in early childhood. In contrast, in our larger study, we found a consistent decrease in HZ rates during the first 5 years after vaccination of 12- to 18-month-olds.

Our study has several strengths, including many subjects and 12 years of data from comprehensive health care plans with electronic medical records. Although our health plans were generally large and geographically diverse, there was an unequal distribution of the study population across sites. The availability of information on diagnoses associated with immunosuppression and immunodeficiencies allowed us to exclude children who were immunosuppressed from selected analyses to better reflect HZ rates in children who were not immunosuppressed.

Limitations of the study include the lack of historical data to determine pre–vaccine-era HZ rates in our population and inadequate information to calculate HZ rates by race or ethnicity. Varicella vaccination requirements varied across states in this multicenter study, which impacted the proportion of children who were vaccinated by site. We were unable to assess the unvaccinated group's underlying risk for HZ because we did not collect serological or medical record evidence of previous VZV infection. As the US varicella vaccination program matured over the study period, the likelihood of exposure to wild-type VZV decreased. Also, our study was limited to HZ in children who sought medical care. Cases did not often have PCR or culture confirmation of VZV, so some non-HZ rashes could have been included. To address the lack of VZV confirmation, we applied the laboratory confirmation adjustment based on our earlier study involving 322 subjects from 1 health plan. The retrospective nature of this study did not allow for HZ virus typing. Finally, our classification of children as immunosuppressed (yes or no) using ICD-9 codes was conservative; children who were immunosuppressed for only part of the study period were included in the immunosuppressed category. We did not exclude children who were immunosuppressed with contraindications for vaccination.

CONCLUSIONS

With this study, we reinforce the benefit of HZ prevention among children through varicella vaccination. Despite an increased HZ incidence among vaccinated 1-year-olds, the overall HZ risk in children who are vaccinated is significantly lower than among children who are unvaccinated. HZ incidence was lower in children who received 2 doses of varicella vaccine than 1 dose. Future pediatric HZ rates may be lower than those reported here during a maturing 2-dose varicella vaccination program.

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ABBREVIATIONS

ACIP	Advisory Committee on Immunization Practices
HZ	herpes zoster
ICD-9	International Classification of Diseases, Ninth Revision
KPNW	Kaiser Permanente Northwest
PCR	polymerase chain reaction
PFU	plaque-forming unit
VZV	varicella zoster virus

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WHAT'S KNOWN ON THIS SUBJECT:

Herpes zoster (HZ) is caused by wild-type or vaccine-strain varicella zoster virus. In previous studies, authors evaluated trends in pediatric HZ incidence since the varicella vaccination program began in 1996; most have shown lower incidences with varying degrees of decline.

WHAT THIS STUDY ADDS:

In this study involving 6 million children, children vaccinated against varicella had a 78% lower HZ incidence than children who were unvaccinated, and the overall HZ incidence rate declined 72%. Two-dose vaccine recipients had lower HZ incidence than 1-dose recipients.

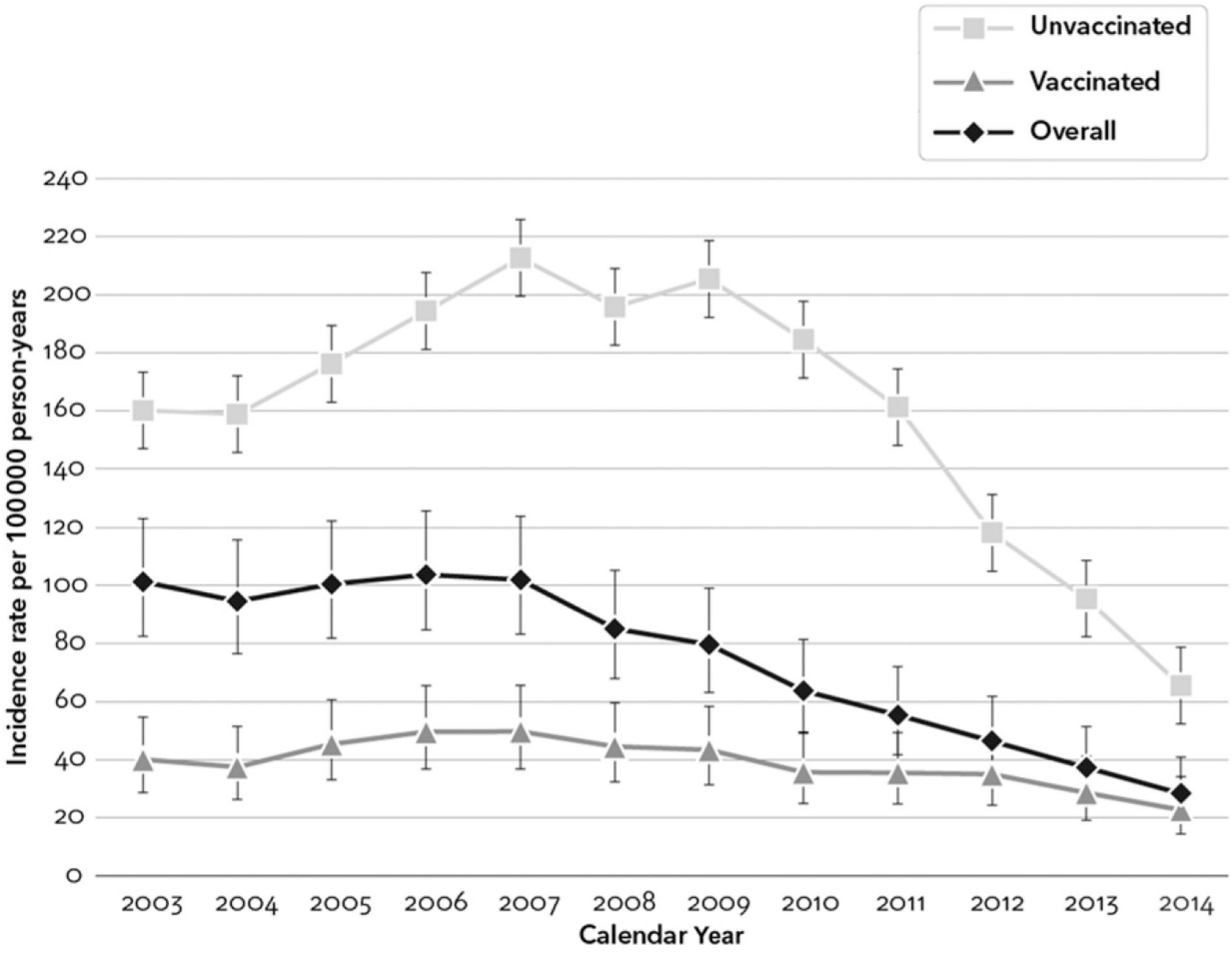

FIGURE 1.
Crude HZ incidence rates among children aged 0 to 17 years who were varicella vaccinated and unvaccinated from 6 Vaccine Safety Datalink sites (United States; 2003–2014).

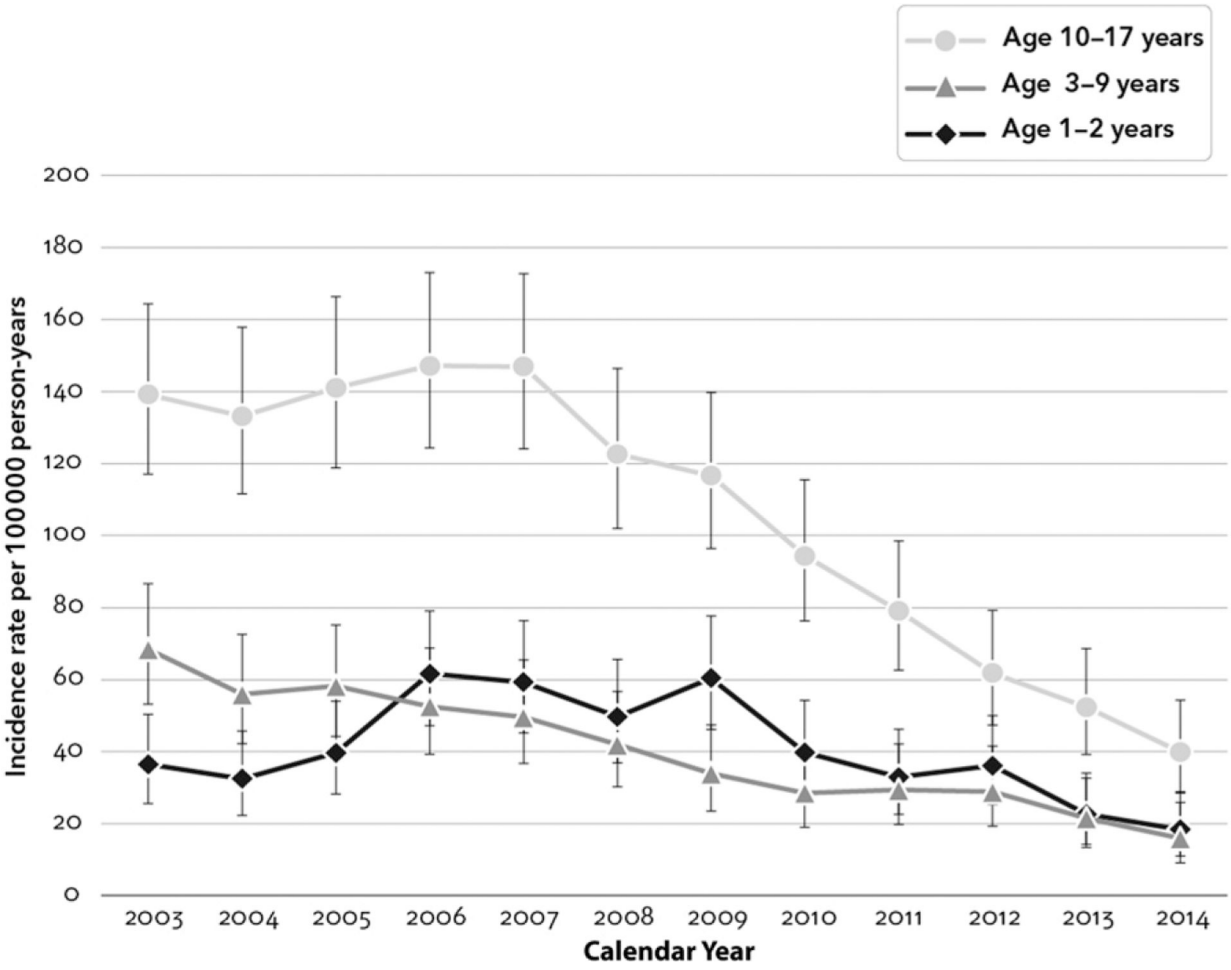

FIGURE 2.

Crude HZ incidence rates by age group (each group includes subjects who were varicella vaccinated and unvaccinated) from 6 Vaccine Safety Datalink sites (United States; 2003–2014). The decreasing trend in incidence from 2008 to 2014 is significant for all 3 age groups ($P < .0001$).

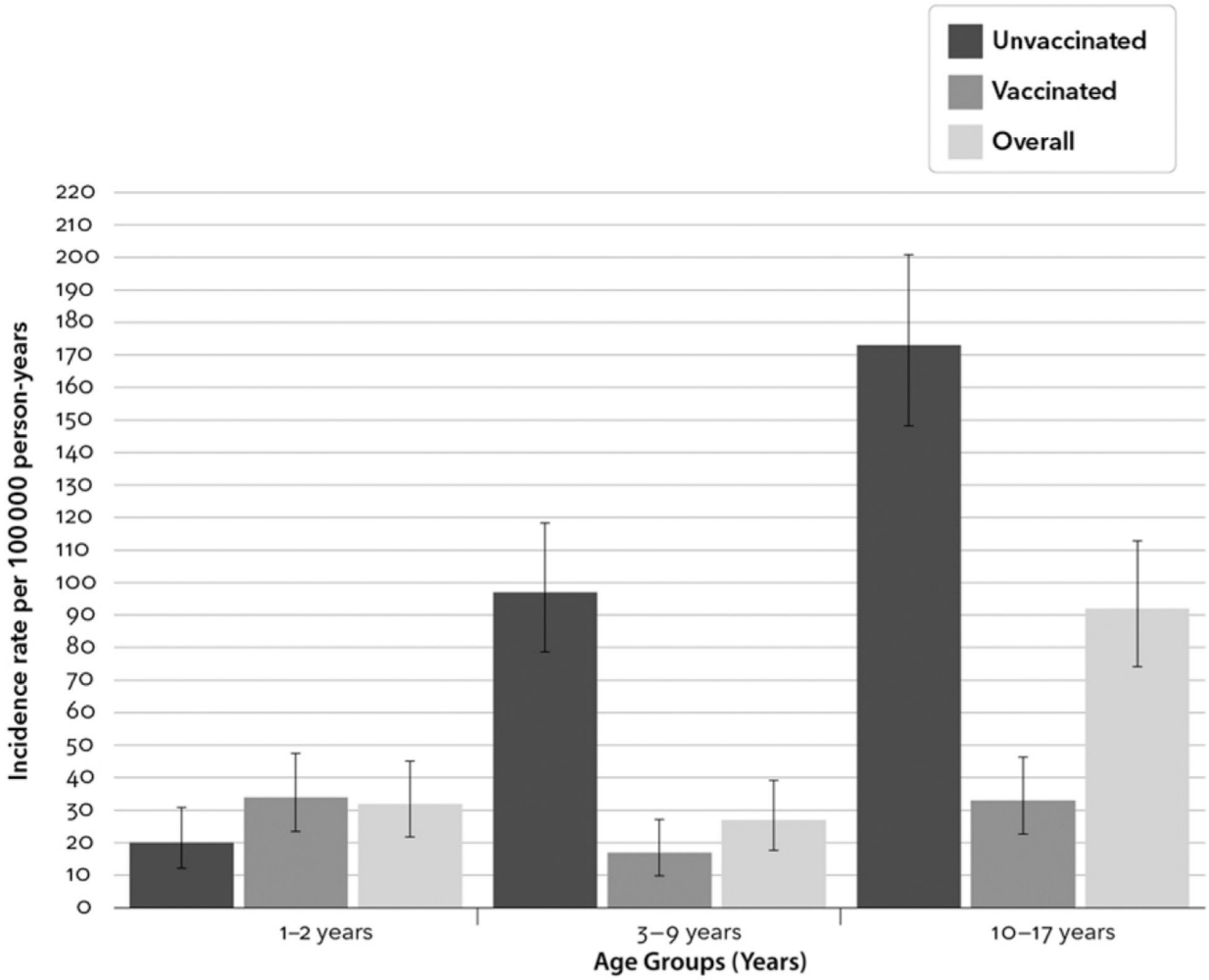

FIGURE 3.
Laboratory confirmation–adjusted HZ incidence rates by age group and varicella vaccination status from 6 Vaccine Safety Datalink sites (United States; 2003–2014).

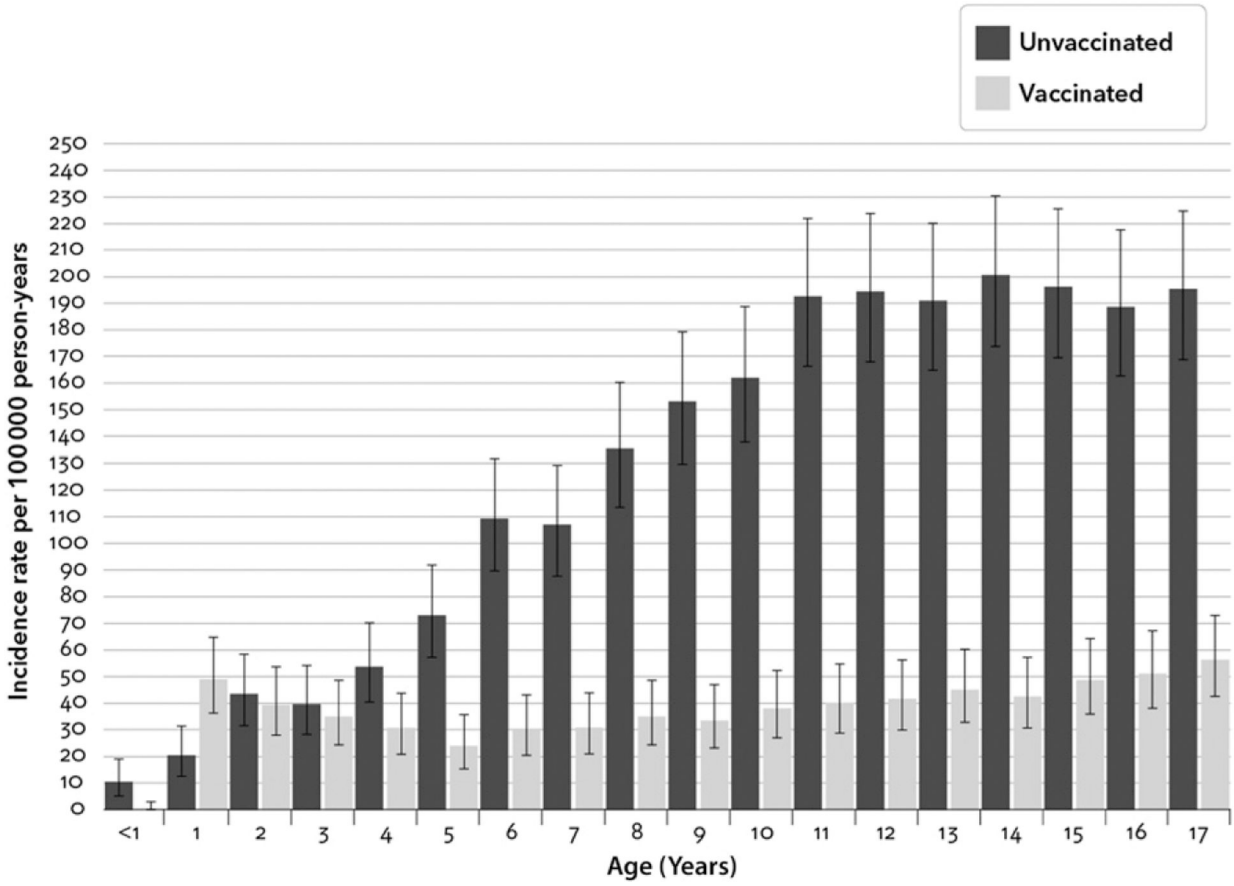

FIGURE 4.

Crude HZ incidence rates by age (years) and varicella vaccination status from 6 Vaccine Safety Datalink sites (United States; 2003–2014).

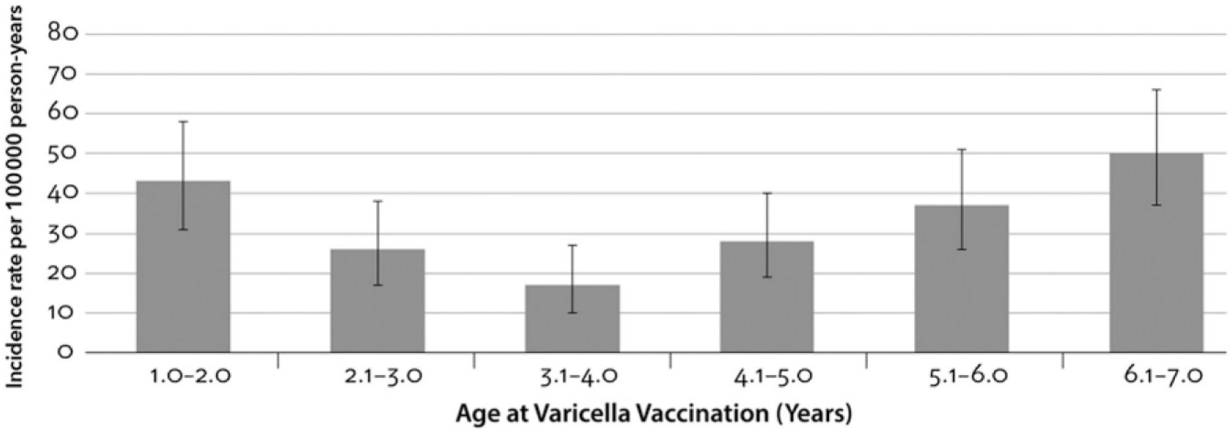

FIGURE 5.

Crude HZ incidence rates by age (years) at first varicella vaccination and before second vaccine dose from 6 Vaccine Safety Datalink sites (United States; 2003–2014). Excludes children vaccinated before 2003 and those classified as immunosuppressed during the study period.

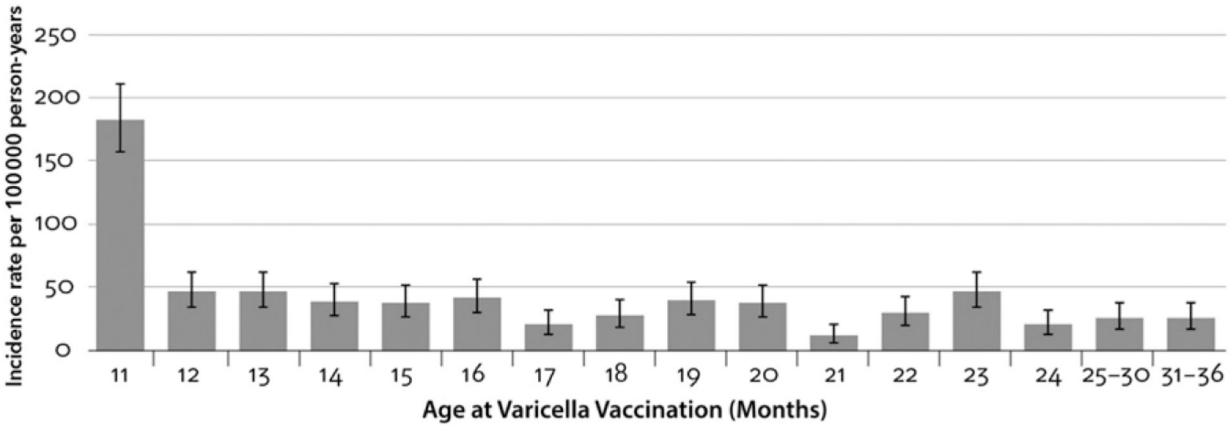

FIGURE 6.

Crude HZ incidence rates by age (months) at first varicella vaccination and before second vaccine dose from 6 Vaccine Safety Datalink sites (United States; 2003–2014). Excludes children vaccinated before 2003 and those classified as immunosuppressed during the study period.

TABLE 1

Crude and Laboratory Confirmation–Adjusted HZ Incidence Rates by Selected Demographic and Clinical Characteristics, 2003–2014

Characteristics	No. Children in the Study Population	Person y	HZ Cases	Incidence Rates (Crude) per 100 000 Person y	Proportion KPNW Study Participants Positive for VZV by PCR per No. Adequate Specimens (*N* = 309), *n* (%)[a]	Incidence Rates (Adjusted) per 100 000 Person y (95% CI)
Sex[b]						
Male	3 232 096	9 864 319	6894	70	120 of 155 (77.4)	54 (41–70)
Female	3 139 609	9 449 629	7489	79	134 of 154 (87.0)	69 (54–87)
Immunocompromised						
Yes	31 655	65 669	271	413	4 of 5 (80.0)	330 (295–368)
No	6 340 412	19 248 702	14 122	73	250 of 305 (82.2)	60 (46–77)
Vaccination status						
Unvaccinated	3 185 335	5 311 456	9044	170	174 of 194 (89.7)	153 (128–179)
Vaccinated	3 186 732	14 002 915	5339	38	80 of 115 (69.6)	27 (17–39)
Site						
A	468 373	1 061 893	1296	122	254 of 309 (82.2)	100 (81–122)
B	395 715	944 341	991	105	254 of 309 (82.2)	86 (69–106)
C	136 481	487 965	492	101	254 of 309 (82.2)	83 (66–102)
D	2 241 579	7 463 212	4866	65	254 of 309 (82.2)	54 (41–70)
E	378 400	968 230	1010	104	254 of 309 (82.2)	86 (69–106)
F	2 751 519	8 388 730	5728	68	254 of 309 (82.2)	56 (42–73)
Age group, y						
1–2	N/A	1 872 775	763	41	25 of 32 (78.1)	32 (22–45)
3–9	N/A	7 373 895	2943	40	38 of 56 (67.9)	27 (18–39)
10–17	N/A	10 067 701	10 677	106	191 of 221 (86.4)	92 (74–113)
All subjects	6 372 067	19 314 371	14 383	74	254 of 309 (82.2)	61 (47–78)

CI, confidence interval; N/A, not applicable.

[a]These laboratory confirmation proportions were calculated for each category from the Weinmann et al[7] study at KPNW. The overall proportion, calculated by combining the previous study's vaccinated and unvaccinated groups, was applied to each of the site-specific groups.

[b]Reported numbers of boys and girls omit 362 children without documented sex.

TABLE 2

Crude HZ Incidence Rates per 100 000 Person Years for Each Year After the First Dose of Varicella Vaccine at 12–18 Months of Age and Before Administration of a Second Dose

Vaccination y[a]	Time Since Vaccination, y					
	<1	1–<2	2–<3	3–<4	4–<5	5–<6
2003	37	17	13	9	7	4
2004	44	29	18	10	3	0
2005	57	36	17	11	7	13
2006	73	28	14	7	8	14
2007	66	25	6	9	9	18
2008	79	24	9	6	5	0
2009	56	21	10	8	0	0
2010	32	14	10	1	0	—
2011	46	15	8	2	—	—
2012	44	10	2	—	—	—
2013	28	9	—	—	—	—
2014	24	—	—	—	—	—
All y[b]	50	21	11	7	5	6

Excludes children vaccinated before 2003, children vaccinated at 11 months of age, and those classified as immunosuppressed during the study period. —, not applicable.

[a]Each row of the table reveals annual HZ incidence rates over the subsequent 6-year period for the cohort of children vaccinated in that calendar year; follow-up for calendar years 2010–2014 is truncated at December 31, 2014, study end date.

[b]Annual HZ incidence rates over the 6-year period after varicella vaccination for all study years combined (2003–2014; $P < .0001$).