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Decline in Varicella-Related Ambulatory Visits and Hospitalizations in the United States Since Routine Immunization Against Varicella

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Abstract

Background—Widespread varicella vaccination has led to substantial decreases in varicella-related mortality and hospitalizations. The impact of the vaccine on ambulatory care utilization is poorly defined.

Objective—To determine trends in varicella-related ambulatory care and hospital discharges before and after vaccine licensure.

Design, Setting, and Participants—Estimates of varicella-related ambulatory and hospital discharges were calculated for the pre- (1993–1995) and post- (1996–2004) vaccine licensure periods using the National Ambulatory Medical Care Survey, National Hospital Ambulatory Medical Care Survey and National Hospital Discharge Survey.

Main Outcome Measure—Ambulatory and hospital discharge rates for varicella.

Results—The rate of varicella-related ambulatory discharges decreased by 66% from 106.6/100,000 (95 % CI: 80.5–132.6) in the pre-licensure period to 36.4/100,000 population (95% CI: 29.3–43.5) in the post-licensure period (P<0.001). The decrease was significant across all age groups <45 years, with the greatest reduction (98%) occurring among patients 0–4 years of age. The incidence of varicella-related hospital discharges decreased by 53% from 30.9/100,000 (95% CI: 24.4–37.3) to 14.5/100,000 population (95% CI: 12.1–16.8) (P<0.001). This difference was significant among patients <14 years of age. Rates of varicella-related ambulatory discharges decreased significantly for both whites and non-whites in the post-licensure period, but post-licensure ambulatory discharge rates remained higher for non-whites than for whites. Decreases in

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Conflict of Interest Statement

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Role of Medical Writer or Editor

None.

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The contributions of the authors were as follows: Study conception and design (SSS, AJR); Acquisition of data (XL); Data analysis and interpretation (all authors); First draft of manuscript (SSS, SMW, AJR); Critical manuscript revisions (all authors); Statistical expertise (all authors); Obtaining funding (SSS, AJR); Research space and resources (all authors).

varicella-related hospital discharges were statistically significant for whites and non-whites. Racial differences in the incidence of varicella-related hospital discharges also persisted following vaccine licensure.

Conclusions—Varicella-related ambulatory visits and hospitalizations have decreased significantly in the period after licensure of the varicella vaccine.

Key words for indexing

varicella; chickenpox; vaccine; varicella; epidemiology; United States

Introduction

Before availability of the live-attenuated vaccine, varicella was an exceedingly common childhood disease and an uncommon cause of hospitalization or death. The varicella vaccine was recommended for children and susceptible adults in 1995 and was widely available the following year. In the following decade, there were large decreases in mortality and hospitalization associated with varicella infection.[1–3] Active surveillance has demonstrated a declining burden of varicella disease in geographic areas with moderate to high vaccine coverage.[4] Varicella vaccine coverage rates have increased nationwide but still exhibit significant geographic variability.[5] Because varicella, in the absence of significant complications, is not a reportable disease,[6] nationally representative estimates of varicella disease are lacking.

Zhou et al.[7] used a large employer-based database to examine varicella-related hospitalizations and ambulatory visits in the United States during a 9 year period and found that both had decreased substantially (88% and 59% respectively) and calculated substantial cost savings as a result. While these data are encouraging, they may not be applicable to other populations, including uninsured people who would have been excluded from that data set. To examine trends in varicella-related ambulatory care visits and hospitalizations during the vaccine era, we used nationally representative data sets not tied to insurance status.

Methods

Data sources

The National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Medical Care Survey (NHAMCS) are administered by the Ambulatory Care Statistics Branch of the National Center for Health Statistics (NCHS) of the Centers for Disease Control and Prevention. The NAMCS collects information on patient visits to non–federally funded, community, office-based physician practices throughout the United States.[8] The NHAMCS collects information on patient visits to hospital outpatient departments and hospital emergency departments as separate components.[9]

The surveys have multistage probability designs as described previously.[8, 9] The NAMCS has a 3-stage sampling design, with sampling based on geographic location, physician practices within a geographic location (stratified by physician specialty), and visits within individual physician practices. Physicians who are selected to participate in the NAMCS during a particular calendar year are not eligible to be selected again for at least another 3 years. The NHAMCS has a 4-stage sampling design, with sampling based on geographic area, hospitals within a geographic area, clinics or emergency departments within hospitals, and patient visits within clinics or emergency departments. The NHAMCS has a panel of hospitals that rotates so that a given hospital participates every 15months. Physician (NAMCS only), hospital (NHAMCS only), and patient and clinical (both surveys)

information is collected at each selected visit and is recorded on patient record forms by participating physicians, office staff, hospital staff, or Census Bureau representatives. Each visit is weighted to allow extrapolation to national estimates for all aspects of the surveys. The visit weight accounts for selection probability, adjustment for no response, and other adjustments to reflect the universe of ambulatory visits in the United States. Three diagnoses (1 primary and 2 secondary diagnoses), coded using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM), are included.

The National Hospital Discharge Survey (NHDS) is a nationally representative annual sampling of discharges from nonfederal short stay hospitals that is conducted by the NCHS. The design of the NHDS has been described in detail.[10] Briefly, a three stage survey design includes all United States hospitals with 1000 or more beds and a representative sample of others based on geographic location, size, and specialty. Each year approximately 500 hospitals participate in the survey. A random selection of discharges from each of these facilities provides a total sample of approximately 250,000 entries per year. Discharge records are weighted according to size of the hospital and region to allow calculation of national estimates. Each discharge record contains demographic information about both the patient and the hospital as well as up to 7 diagnosis codes, consistent with the *International Classification of Diseases, 9th revision, Clinical Modification* (ICD-9-CM).

Study Definitions

We examined data from the NAMCS, NHAMCS, and NHDS for the period January 1, 1993 through December 31, 2004. The pre-vaccine period was 1993–1995 while the post-vaccine period was 1996–2004. Extraction of records was based on the appearance of specific ICD-9-CM codes for varicella (052). In the primary analysis, a varicella-related ambulatory discharge (VRAD) was defined as a record in the NAMCS or the NHAMCS containing a code for varicella in any of the three discharge diagnosis fields and a varicella-related hospital discharge (VRHD) was defined as a record in the NHDS containing a code for varicella in any of the seven discharge diagnosis fields. In a secondary analysis, varicella was defined by the ICD-9-CM discharge diagnosis code 052 as the principal or primary diagnosis. For hospital discharges, appropriate ICD-9 codes for varicella-associated underlying conditions and complications were previously defined by Meyer et al.[11] Primary complications included central nervous system involvement and hematologic complications. Central nervous system complications included cerebellar ataxia, encephalitis, myelitis, encephalopathy, encephalomyelitis, meningitis, other diseases of the brain, which includes Reye's syndrome, cerebral degeneration and other central nervous system complications. Hematologic complications included purpura, thrombocytopenia, and other hematologic conditions. Secondary complications included bacterial superinfection such as bacteremia, septicemia, intracranial/intraspinal abscess, skin infections, cellulitis, necrotizing fasciitis, impetigo, infective myositis and other inflammatory diseases of tendon and fasacia, endocarditis, acute pericarditis, and bacterial pneumonia. A complete listing of ICD-9-CM codes used to identify primary and secondary varicella-related complications is available upon request.

Data Extraction and Analysis

Record extraction was performed using SAS^{R} v9.1. Population estimates used in the calculation of rates, including age-specific rates, were supplied by the NCHS and were consistent with census estimates. Standard errors and 95% confidence intervals (CIs) surrounding rates of varicella infection were calculated according to published NCHS guidelines[10] with SAS survey statistical procedures, including SURVEYFREQ and SURVEYLOGISTIC. According to these procedures, estimates derived from the NHDS that are based on fewer than 30 actual discharges should not be reported, because these often

have unacceptably large relative standard errors. Projected values based on 30 to 60 discharges should not be assumed to be reliable, and the same is true of any estimate with a calculated relative standard error of >30%, regardless of sample size. Potentially unreliable data points are noted when presented in this report. Because racial data are missing for approximately 20% of records in the NHDS and because the classification of race by the NCHS has changed during the study period,[12] racial categories were dichotomized as white vs. non-white race to avoid potential misclassification.

Statistical trend tests across survey years for each survey and within each age group were analyzed by logistic regression with year as the linear term. According to NCHS guidelines census-derived denominators were assumed to be free of error. Rates in the pre- and post-licensure period were compared by the univariate logistic model and involved the strata and weights used in survey design. *P*-values <0.05 were considered statistically significant.

Results

Ambulatory Discharges for Varicella

From a total of 1,044,903 records contained in either the NAMCS or the NHMACS between 1993 and 2004, 601 (0.06%) contained a discharge diagnosis code for varicella. This corresponded to an estimated 6,085,005 varicella-related ambulatory care visits during the 12-year study period. Varicella was the primary diagnosis in 81.4% of these records. We explored the potential impact of vaccine licensure in two ways. First, we compared the rates of varicella-related ambulatory discharges in the pre- and post-licensure periods. The rate of any varicella-related ambulatory discharge decreased by 65.8% from 106.6 (95 % CI: 80.5–132.6) per 100,000 population in the pre-licensure period to 36.4 (95% CI: 29.3–43.5) per 100,000 population in the post-licensure period (P<0.001) (Table 1). Second, the annual rates of varicella-related ambulatory discharges were determined. A statistically significant decreasing trend in the rate of varicella-related ambulatory visits following vaccine licensure in 1995 was noted in both the NAMCS and the NHMACS; this decrease was significant for both any (any listed diagnosis) and primary (first-listed diagnosis) varicella-related ambulatory discharges (Figure 1, Supplemental Digital Content 1). The overall rate of varicella-related discharges from the ambulatory setting (data from NAMCS and NHMACS combined) decreased from a peak of 120.3 (95% CI: 68.0–172.6) per 100,000 population in 1994 to 14.2 (95% CI: 2.3–26.2) per 100,000 population in 2004. The rate of varicella-related discharges in the NAMCS decreased sharply from 70.0 (95% CI: 29.5–110.6) per 100,000 population in 1998 to 9.0 (0–21.6) per 100,000 population in 1999; there was no significant difference in the rate of varicella-related visits in the NAMCS survey from 1999–2004. In the NHMACS, the decreasing rate of varicella-related discharges paralleled the decrease in the NAMCS except that the decrease in varicella rate in the NHMACS between 1998 (87.7 per 100,000 person years) and 1999 (76.3 per 100,000 population) was more modest.

Ambulatory Discharges for Varicella by Age

The age-specific rates of varicella-related ambulatory discharges in the post-licensure period were compared with those in the pre-licensure period. Among patients <45 years of age, the rates of varicella-related ambulatory discharges were significantly lower in the post-licensure period than in the pre-licensure period, regardless of whether varicella was listed as any or the primary diagnosis (Table 1). The annual age-specific rates of varicella-related ambulatory discharges between 1993 and 2004 are shown (Figure 2, Supplemental Digital Content 2). The overall decrease in the rate of varicella-related ambulatory discharges from 1995 to 2004 was attributable to the substantial decreases in patients <14 years of age. Among patients 0–4 years of age, the rate of varicella-related ambulatory discharges

decreased significantly from 567.1 (95% CI: 302.4–831.9) per 100,000 population in 1995 to 11.4 (95% CI: 0–24.3) per 100,000 population in 2004. Among patients 5–14 years of age, the rate of varicella decreased from 269.3 (95% CI: 60.2–478.3) per 100,000 population in 1995 to 30.7 (95% CI: 3.9–57.5) per 100,000 population in 2001. After 2001, the actual numbers of varicella-related ambulatory discharges 5–14 years of age contained in the ambulatory databases were quite small, leading to potentially unstable estimates. Therefore, the rate from 2002–2004 in this age group is more difficult to interpret.

Ambulatory Discharges for Varicella by Race

The overall rates of varicella-related ambulatory discharges decreased significantly in the post-licensure period compared with the pre-licensure period for both whites and non-whites (Table 1). The rates of varicella-related ambulatory discharges in the post-licensure period remained higher for non-whites than for whites; the rates were 29.7% and 45.1% higher for primary and any-listed diagnosis of varicella, respectively. However, the magnitude of the racial disparity for any-listed diagnosis of varicella-related ambulatory discharges was similar in the pre- and post-licensure periods.

Hospital Discharges for Varicella

From a total of 3,626,198 records in the NHDS from 1993 through 2004, 716 (0.02%) contained a discharge diagnosis code for varicella. This corresponded to an estimated 79,309 VRHD during the study period. Varicella was the primary diagnosis in 49.9% of these records. The potential impact of varicella vaccine licensure on VRHD was explored comparing both the overall rate in the pre- and post-licensure periods (Table 1) and the annual trends following vaccine licensure (Figure 1, Supplemental Digital Content 1). The rate of any VRHD decreased by 53.1% from 30.9 (95% CI: 24.4–37.3) per 100,000 population in the pre-licensure period to 14.5 (95% CI: 12.1–16.8) per 100,000 population in the post-licensure period ($P<0.001$). The rate of VRHD decreased from 29.7 (95% CI: 18.1–41.3) per 100,000 population in 1995 to 10.5 (95% CI: 4.6–16.5) per 100,000 population in 2001 to 6.0 (2.6–9.4) per 100,000 population in 2004 (Figure 1, Supplemental Digital Content 1).

Hospital Discharges for Varicella by Age

In the NHDS, the rate of VRHD was significantly lower in the post-licensure period compared with the pre-licensure period among patients <14 years of age (Table 1). For those 15–44 years, the rate was significantly lower only when varicella was listed as the primary diagnosis; the difference in VRHD in the pre- and post-licensure periods when varicella was listed as any diagnosis was not significant. Among patients, >45 years of age, there was no significant difference in VRHD in the post-licensure period compared with the pre-licensure period. The annual age-specific rates of VRHD are shown in Figure 3 (Supplemental Digital Content 3). Similar to the decreasing rates in patients discharged from the ambulatory setting, the most prominent decreases occurred in children <14 years of age. The rates in 1995 were 98.7 (32.7–164.7) and 323.7 (134.0–513.5) per 100,000 population for patients <4 and 5–14 years, respectively. After 2001, there were so few actual VRHD among children 0–14 years of age contained in the NHDS that stable estimates could not be calculated; this precluded meaningful statistical comparison of changes in age-specific rates of VRHD from 2002–2004.

Hospital Discharges for Varicella by Race

In the NHDS, the decreases in VRHD were also statistically significant for both whites and non-whites. The racial difference in the rate of VRHD persisted following vaccine licensure when varicella was listed as the primary diagnosis; the rate was 47.8% higher for non-whites

in the pre-licensure period and 43.3% higher in the post-licensure period. In contrast, when any-listed varicella diagnosis was considered, the racial disparity decreased for VRHD; the rates were 63.1% higher for non-whites compared with whites in the pre-licensure period and 31.7% higher in the post-licensure period.

Varicella-Related Complications

Primary varicella-related complications occurred less commonly overall in the post-licensure period; the age-specific decreases were significant only for patients 5–14 years of age, the group with the highest overall complication rate (Table 2). Primary varicella-related complications among whites decreased by 62% between the pre- to the post-licensure periods. The difference was not significant among non-whites though the relatively small number of reported cases in the pre-licensure period among non-whites makes comparison with the post-licensure estimate unreliable. Rates of secondary complications attributable to varicella decreased by 47% between the pre- and post-licensure periods.

Discussion

We report a significant decrease in rates of varicella-related ambulatory and hospital discharges since introduction of the varicella immunization program in the United States. Childhood varicella vaccination rates increased from 12.2% in 1996 to 87.5% in 2004.[13,14] Our study identified a 66% decrease in varicella-related ambulatory discharges and a 53% decrease in VRHD between the pre- and post-licensure periods. In the ambulatory setting, the decreases were most pronounced among patients <4 years of age, where the rate of varicella-related ambulatory discharges decreased by 98%. The post-licensure decrease in VRHD noted from 1995–2001 by previous authors[1, 4, 7, 15–20] continued between 2001 and 2004. These decreases parallel national increases in varicella vaccination coverage.[5] In addition, primary varicella-related complications occurred less commonly overall in the post-licensure period with significant age-specific decreases among patients 5–14 years of age, the group with the highest overall complication rate. These results further emphasize the benefits of the national childhood varicella vaccination program in reducing rates of primary varicella infection.

Our study is the first to examine national trends in varicella-related ambulatory discharges in insured and uninsured patients. A major goal of the varicella vaccination program in the United States was to reduce the rates of morbidity and death associated with varicella infections. While previous studies have utilized hospitalization and mortality data to assess vaccine effectiveness, most cases of varicella are managed in the ambulatory setting. Ambulatory practices may also be the sentinel setting for tracking the post-vaccine epidemiology of varicella. Following licensure of the vaccine, we found that decreases in varicella-related ambulatory discharges occurred earlier and were more dramatic than decreases in VRHD. While examining epidemiologic trends in varicella in the outpatient setting is essential to describing the impact of the vaccine, few studies have addressed the burden of varicella infection in the ambulatory setting.[7, 17, 21] Ambulatory visits also contribute significantly to the economic burden of varicella infection. Zhou et al[7] demonstrated that ambulatory visits comprised 52.1% of varicella-related healthcare expenditures in the pre-licensure period, and 78% in the post-licensure period. These data suggest that as VRHD declines, tracking varicella in the ambulatory setting is the most accurate method of examining vaccine cost-effectiveness and efficacy. Tracking rates of varicella in the ambulatory setting is particularly important because outbreaks of varicella continue to occur, even in highly vaccinated populations.[22, 23] Breakthrough varicella in vaccinated persons is often mild, making it unlikely that affected persons will require hospitalization.[23]

Widespread use of the heptavalent pneumococcal conjugate vaccine was associated with elimination of racial differences in the incidence of invasive pneumococcal disease.[24] In contrast, despite significant decreases in varicella-related ambulatory discharges in both whites and non-whites in the post-licensure period, racial differences in varicella rates persisted in the post-vaccine period, with rates of ambulatory discharges remaining higher for non-whites than whites. VRHD also remained higher for non-whites in the post-licensure period when varicella was listed as the primary diagnosis. Staat et al[17] found that varicella-related emergency department visit rates were higher for black children than white children in the post-vaccine period. While racial disparities in vaccine coverage existed in the early post-licensure period, there have been no significant differences in national coverage rates between whites and blacks after 1998.[5] Lack of access to primary care or delayed diagnosis among non-whites may also lead to these racial differences. However our data, which are based in the outpatient setting, suggest that non-white patients frequently utilize primary care for diagnoses of varicella. The persistent difference in rates of disease may be due to baseline racial differences in varicella susceptibility, which have been previously reported,[25] or to differences in the threshold for seeking medical attention for this condition.

The use of national health statistics is both a strength and limitation of this study. While active surveillance may be the most precise method for tracking varicella epidemiology, it is both costly and impractical for demonstrating the true nationwide impact of the vaccination program. Use of databases such as the NAMCS, NHAMCS, and NHDS is an accurate and low-cost method of monitoring national trends in disease. The results of our study closely parallel those of the Varicella Active Surveillance Project (VASP), a varicella active surveillance project implemented in Antelope Valley, California, and Philadelphia, Pennsylvania, which describe an approximately 90% decrease in the rate of primary varicella from 1995–2005.[15] Both VASP and our study identified large decreases in cases of varicella, with the sharpest decline occurring from 1998–1999 and the greatest reduction in the rate among children under 4 years of age.[4]

One limitation of using national health statistics is the reliability of estimates based on smaller number of discharges. As noted previously, we were unable to compare post-licensure hospitalization rates after 2001 due to the relatively small number of VRHDs among children 0–14 years of age. Similarly, although there may have been a trend toward an increase in ambulatory discharges among children 5–14 years of age after 2002, the small number of cases precludes meaningful interpretation of this data. However, this increase may represent a true increase in varicella cases in older children. This may represent normal year-to-year variation of disease, or reflect the increased rates in breakthrough disease that prompted the Advisory Committee on Immunization Practices to recommend a booster varicella vaccine at 4–6 years of age in 2006.[26]

Additionally, we presumed that decreases in varicella cases and varicella-related complications were a consequence of vaccination. Although our findings are likely to be causal, we cannot make such inferences about causality with administrative data. The decline in varicella could also be due to underdiagnosis by physicians because in immunized populations the rash may be modified or atypical, and thus more difficult recognize. It is also possible that patients are less likely to present for care, especially in cases where vaccination has attenuated the severity of the disease. Finally, it is possible that varicella rates incrementally increased between 2001 and 2004 as a consequence of waning immunity in vaccinated children or increased numbers of vulnerable immunocompromised patients. However, because relatively few patients in the databases had varicella in this time period, our study was not powered to detect small increases in varicella rates.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Rates of varicella infection comparing the pre- and post-licensure periods for the varicella vaccine. The pre-licensure period is 1993–1995 and the post-licensure period is 1996–2004. Ambulatory visits represent population estimates combined from the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey. Hospitalizations represent population estimates from the National Hospital Discharge Survey. Rates are presented per 100,000 population.

			Pre-licensure Period (1993–1995)		Post-licensure Period (1996–2004)		
Survey Types	**Diagnosis**		**# Cases**	**Rate**	**# Cases**	**Rate**	**P-value**
Ambulatory	Primary	**Overall**	218	88.9 (64.8, 112.9)	271	29.9 (23.1, 36.8)	<0.001
		Age group					
		<=4	91	357.9 (235.7, 480.0)	100	121.8 (76.3,	<0.001
		5–14	66	397.0 (194.0, 599.9)	94	139.5 (85.8,	<0.001
		15–44	57	42.6 (21.3, 64.0)	64	11.8 (6.0, 17.7)	<0.001
		>=45	4	1.4 (0.0, 3.0)	13	5.3 (0.1, 10.5)	0.057
		Race					
		Non-white	68	119.0 (65.3, 172.7)	85	37.1 (19.6, 54.5)	<0.001
		White	150	83.8 (57.2, 110.3)	186	28.6 (21.2, 35.9)	<0.001
	Any Diagnosis	**Overall**	263	106.6 (80.5, 132.6)	338	36.4 (29.3, 43.5)	<0.001
		Age group					
		<=4	117	475.4 (337.4, 613.4)	130	158.4 (107.5,	<0.001
		5–14	74	425.7 (219.6, 631.8)	110	158.8 (102.6,	<0.001
		15–44	66	50.5 (27.4, 73.5)	84	15.8 (9.0, 22.7)	<0.001
		>=45	6	1.5 (0.0, 3.1)	14	5.4 (0.1, 10.6)	0.061
		Race					
		Non-white	79	142.9 (86.1, 199.6)	102	49.2 (29.1, 69.4)	<0.001
		White	184	100.5 (71.9, 129.0)	236	33.9 (26.4, 41.5)	<0.001
Hospitalization	Primary	**Overall**	125	15.9 (11.3, 20.5)	232	7.0 (5.4, 8.5)	<0.001
		Age group					
		<=4	46	42.9 (19.6, 66.3)	70	15.3 (8.0, 22.6)	0.003
		5–14	49	153.3 (84.4, 222.2)	90	65.7 (44.9, 86.5)	0.002
		15–44	25	14.2 (6.9, 21.4)	50	5.9 (3.3, 8.5)	0.009
		>=45	5	1.0 (0.0, 2.1)	22	1.8 (0.7, 2.9)	0.359
		Race					

Survey Types	Diagnosis		Pre-licensure Period (1993–1995) # Cases	Pre-licensure Period (1993–1995) Rate	Post-licensure Period (1996–2004) # Cases	Post-licensure Period (1996–2004) Rate	P-value
		Non-white	56	20.1 (11.5, 28.6)	124	8.6 (6.3, 10.8)	<0.001
		White	69	13.6 (8.3, 19.0)	108	6.0 (3.9, 8.1)	0.002
	Any Diagnosis	**Overall**	253	30.9 (24.4, 37.3)	463	14.5 (12.1, 16.8)	<0.001
		Age group					
		<=4	86	78.4 (46.8,110.1)	127	32.1 (20.7, 43.5)	<0.001
		5–14	90	311.5 (207.6,415.4)	154	103.9 (78.4,	<0.001
		15–44	55	21.7 (12.9, 30.4)	125	15.1 (10.7, 19.5)	0.155
		>=45	22	5.9 (2.3, 9.5)	57	4.1 (2.5, 5.8)	0.349
		Race					
		Non-white	125	41.1 (28.6, 53.6)	238	17.0 (13.6, 20.5)	<0.001
		White	128	25.2 (17.9, 32.4)	225	12.9 (9.7, 16.1)	<0.001

Table 2

Rate of primary and secondary complications of varicella comparing the pre- and post-varicella vaccine licensure periods. The pre-Licensure period is 1993–1995 and the post licensure period is 1996–2004. Rates are presented per 100,000 population.

		Pre-licensure Period (1993–1995)		Post-licensure Period (1996–2004)		
Variable		**# Cases**	**Rate**	**# Cases**	**Rate**	**P-value**
Primary complication	**Overall**	49	6.9 (3.6, 10.3)	98	2.9 (1.7, 4.1)	0.006
	Age group					
	<=4	20	16.3 (0.0, 33.4)	31	9.7 (2.0, 17.4)	0.429
	5–14	19	89.4 (29.0,149.8)	28	16.4 (8.1, 24.7)	<0.001
	15–44	3	2.0 (0.0, 4.6)	21	1.9 (0.7, 3.1)	0.924
	>=45	7	2.2 (0.2, 4.2)	18	0.9 (0.3, 1.6)	0.134
	Race					
	Non-white	17	5.4 (0.9, 9.9)	50	2.8 (1.7, 3.8)	0.142
	White	32	7.8 (3.2, 12.4)	48	3.0 (1.2, 4.8)	0.021
Secondary complication	**Overall**	30	3.2 (1.6, 4.9)	49	1.7 (0.6, 2.7)	0.101
	Age group					
	<=4	15	7.4 (2.0, 12.8)	17	6.8 (0.0, 14.2)	0.907
	5–14	10	37.6 (6.5, 68.8)	16	10.8 (3.3, 18.3)	0.016
	15–44	1	1.1 (0.0, 3.3)	5	0.2 (0.0, 0.5)	0.131
	>=45	4	1.2 (0.0, 2.7)	11	0.5 (0.1, 0.9)	0.248
	Race					
	Non-white	10	2.7 (0.1, 5.3)	25	1.7 (0.7, 2.6)	0.376
	White	20	3.5 (1.4, 5.6)	24	1.7 (0.1, 3.3)	0.184