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All-Cause Gastroenteritis and Rotavirus-Coded Hospitalizations Among US Children, 2000–2009

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Background. Rotavirus vaccine was recommended for US infants in 2006. We estimated baseline prevaccine burden and monitored postvaccine trends in gastroenteritis-coded and rotavirus-coded hospitalizations among US children.

Methods. We analyzed data from the State Inpatient Databases (SID) for 29–44 US states over a 10-year period (2000–2009) to calculate gastroenteritis and rotavirus-coded hospitalization rates by age group, sex, and region, among children <5 years of age. By extrapolating observed pre- and postvaccine gastroenteritis hospitalization rates to the US population <5 years and based on the 2009 cost of a diarrhea hospitalization, we estimated national reductions in diarrhea hospitalizations and associated treatment costs.

Results. The prevaccine (2000–2006) annual average gastroenteritis-coded hospitalization rate among children <5 years of age was 74 per 10 000 (annual range, 71–82 per 10 000), and declined to 51 and 50 per 10 000 in 2008 and 2009, respectively ($P < .001$). The prevaccine (2000–2006) annual average rotavirus-coded hospitalization rate among children <5 years of age was 15 per 10 000 (annual range, 13–18 per 10 000), and declined to 5 and 6 per 10 000 in 2008 and 2009, respectively ($P < .001$). The decreases in rotavirus-coded hospitalization rates in 2008 and 2009 compared with rates in prevaccine years were observed among all age groups and US regions. Nationally, during 2008 and 2009 combined, we estimated a reduction of approximately 77 000 diarrhea hospitalizations and approximately \$242 million in hospital costs.

Conclusions. Since implementation of the US rotavirus vaccination program, a marked reduction in diarrhea hospitalizations and related hospital charges has occurred among US children.

Prior to the introduction of rotavirus vaccine in the United States in 2006, rotavirus gastroenteritis annually resulted in approximately 20–60 deaths, 55 000–70 000 hospitalizations, 200 000 emergency department visits, and 400 000 outpatient visits among US children <5 years of age, with direct medical costs of \$300 million and total medical and societal costs of >\$1 billion [1]. Currently, 2 rotavirus vaccines are available in the United States—a pentavalent rotavirus vaccine

(RV5) (RotaTeq, Merck and Co) licensed in 2006 and a monovalent rotavirus vaccine (RV1) (Rotarix, GSK Biologicals) licensed in 2008.

Previous studies have shown that implementation of the rotavirus vaccine program has led to a dramatic decline in rotavirus disease burden and acute care utilization for gastroenteritis in US children [2–4]. These studies have been based on data from large discharge databases, sentinel laboratories, sentinel hospital networks with active surveillance for laboratory-confirmed rotavirus disease, or insurance claims data. They all examined data through the 2008 rotavirus season, the first year that vaccine uptake was widespread. However, there have been few comprehensive evaluations of hospitalizations and hospital charges for diarrhea through 2009 using robust and nationally representative discharge abstract data [2, 5]. Such an analysis is needed to

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confirm the trends observed through 2008 and determine whether they have continued, given the year-to-year variation in rotavirus trends before and after vaccine introduction [6].

We examined complete hospital discharge data from 29–44 US states that covered 81%–96% of the US birth cohort to examine gastroenteritis- and rotavirus-coded hospitalizations from January 2000 through December 2009. Our objectives were to examine trends in gastroenteritis- and rotavirus-coded hospitalizations at national and regional levels before and after rotavirus vaccine introduction in the United States through 2009, and to provide estimates of reduction in hospital costs following introduction of the vaccine.

METHODS

Data Source

We analyzed data from the State Inpatient Databases (SID) over a 10-year period (2000–2009) [7] to identify gastroenteritis- and rotavirus-coded hospitalization records among children <5 years of age. The SID is a component of the Healthcare Cost and Utilization Project (HCUP) produced by the Agency for Healthcare Research and Quality (AHRQ) and captures all hospitalizations that occur in community hospitals in the participating states (ie, it is not a sample of hospital discharges). The number of states participating in the intramural SID has increased over time, with 29 states representing 81% of the US birth cohort participating in 2000, and 44 states representing 96% of the US birth cohort participating by 2009 [7]. Our SID analysis was based on aggregated data, so we used the Nationwide Inpatient Sample (NIS) to estimate annual mean costs for a gastroenteritis-coded hospitalization among children <5 years of age. The NIS is a nationally representative inpatient care database that is based on data from the SID, containing data from approximately 8 million hospital stays each year, which can be up-weighted to generate national estimates [8]. The 2009 NIS contains all discharge data from 1050 hospitals located in 44 states, approximating a 20% stratified sample of US community hospitals. HCUP data from 18 states have been previously used to demonstrate postvaccine reductions in rotavirus hospitalizations [9]; our aim was to reaffirm these findings in a more nationally representative sample and determine whether reductions persisted in 2 postvaccine rotavirus seasons. Because all hospitalization data were de-identified, hospital discharge records were the unit of analysis in this study and informed consent was not required. This study was conducted through an active collaboration between the Centers for Disease Control and Prevention and the AHRQ.

Definition of Gastroenteritis and Rotavirus-Coded Hospitalizations

Gastroenteritis hospitalizations were defined as hospital discharges that included any of the following *International*

Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes: diarrhea of determined etiology (bacterial [001–005 and 008.0–008.5, excluding 003.2]; parasitic [006–007, excluding 006.3–006.6]; and viral [008.6 and 008.8]), and diarrhea of undetermined etiology (presumed infectious [009.0–009.3] and presumed noninfectious [558.9 and 787.91]) [10]. Rotavirus-coded hospitalizations were a subset of gastroenteritis hospitalizations that included the specific *ICD-9-CM* code for rotavirus (008.61) [10]. Discharge records were queried for a gastroenteritis or rotavirus *ICD-9-CM* code through the first 15 diagnosis fields that are used by all participating US states.

Demographic and Other Characteristics

Gastroenteritis- and rotavirus-coded hospitalizations for the years 2000–2009 were examined by sex, US Census region (Midwest, Northeast, South, and West), month and year of discharge, and age group by month for children <5 years of age (0–2, 3–5, 6–11, 12–17, 18–23, 24–35, 36–47, and 48–59 months). Hospitalizations with missing information for a specific variable were excluded from analysis of that variable but were included for all other analyses.

Rate Calculations and Pre- and Postvaccine Comparisons

Hospitalization rates were calculated using the National Center for Health Statistics' Bridged Race postcensal under-5 population estimates for 2000 through 2009 [11]. The number of hospitalizations with an *ICD-9-CM* code for gastroenteritis or rotavirus was divided by the number of children <5 years of age in states participating in the SID. Eighteen states did not continuously participate in the SID for the entire time period (Supplementary Table 1). The denominators for calculating rates, both nationally and regionally, were adjusted to reflect the inclusion or exclusion of these states for a given calendar year. Hospitalization rates were calculated by month, age group, sex, and region. In addition, monthly hospitalization rates were calculated for the United States and by region.

To compare the relative difference in pre- and postvaccine years, gastroenteritis and rotavirus-coded hospitalization rates for calendar years 2000–2006 were compared with the rates in 2008 and 2009 using χ^2 tests. Data from 2007 were excluded because rotavirus vaccine uptake was low and uneven during the first year after vaccine introduction.

Hospital Stay and Costs

Median length of stay and hospital costs for gastroenteritis-coded hospitalizations were examined and compared using SID and NIS, respectively. The annual Consumer Price Index for Medical Care was used to correct for inflation, and all hospital costs are presented in 2009 US dollars [12].

National Estimates of Reduction in Gastroenteritis Hospitalizations and Charges After Rotavirus Vaccine Implementation

National estimates of gastroenteritis hospitalizations were obtained for each year by multiplying the estimated number of resident children <5 years of age by gastroenteritis hospitalization rates estimated from the SID data. The reduction in the number of gastroenteritis hospitalizations nationally in 2008 and 2009 relative to the median number in prevaccine years (2000–2006) was multiplied by the 2008 and 2009 annual mean costs, respectively, to estimate the combined cost savings due to averted gastroenteritis hospitalizations.

Results

All-Cause Gastroenteritis Hospitalization Trends Pre- and Post-Rotavirus Vaccine Implementation

There were 1 153 300 gastroenteritis-coded hospitalizations between 2000 and 2009 in the HCUP database. The prevaccine (2000–2006) annual average gastroenteritis hospitalization rate among children <5 years of age was 74 per 10 000 (annual range, 71–82 per 10 000); this rate declined 31% to 51 per 10 000 in 2008 and 33% to 50 per 10 000 in 2009 ($P < .001$

for both years) (Table 1). In both postvaccine years, rates declined similarly in males and females. Of note, in 2008 declines were similar across the groups aged 3–59 months, whereas in 2009 the declines in 3–23-month-old children were greater than those among children 24 months and older. Additionally, decreases in gastroenteritis-coded hospitalization rates compared with the rate for the prevaccine years were observed in all US regions; the decline was slightly lower in the West compared with other regions in 2008, but in 2009 all regions had a similar decline.

Rotavirus-Coded Hospitalization Trends Pre- and Post-Rotavirus Vaccine Implementation

There were 212 077 rotavirus-coded hospitalizations between 2000 and 2009 in the HCUP database, which is approximately 20% of all coded gastroenteritis discharges. The prevaccine (2000–2006) average annual rotavirus-coded hospitalization rate among children <5 years of age was 15 per 10 000 (annual range, 13–18 per 10 000); this rate declined 71% to 4 per 10 000 in 2008 and 62% to 6 per 10 000 in 2009 ($P < .001$ for both years) (Table 2). The declines were similar among males and females in both years. In prevaccine years (2001–2006), the annual average rotavirus-coded hospitalization rate was

Table 1. Gastroenteritis-Coded Hospitalization Rates in the Prevaccine Years (2000–2006) and Rates and Rate Reduction in Postvaccine Years (2008 and 2009)^a

	2000–2006	2008		2009	
	Rate, Average Annual (Minimum–Maximum) Hospitalizations per 10 000 Children ^b	Rate, Hospitalizations per 10 000 Children ^b	Rate Reduction (%)	Rate, Hospitalizations per 10 000 Children ^b	Rate Reduction (%)
Total	74 (71–82)	51	31	50	33
Sex					
Male	79 (76–88)	54	31	53	33
Female	69 (67–76)	47	32	46	33
Age					
0–2 months	163 (149–188)	130	20	124	24
3–5 months	125 (113–144)	89	29	81	35
6–11 months	142 (129–156)	91	36	81	43
12–17 months	122 (113–133)	78	36	69	43
18–23 months	89 (80–98)	58	34	56	37
24–35 months	53 (49–58)	37	30	40	25
36–47 months	32 (29–37)	22	31	27	15
48–59 months	23 (21–26)	16	30	18	22
Region					
Midwest	71 (66–77)	46	35	50	30
Northeast	79 (72–88)	55	30	53	33
South	86 (80–96)	58	33	56	35
West	57 (53–63)	42	27	38	33

^a Primary data obtained from Healthcare Cost and Utilization Project State Inpatient Databases Documentation, March 2011. Agency for Healthcare Research and Quality.

^b Rates represent gastroenteritis hospitalizations per 10 000 children <5 years of age.

Table 2. Rotavirus-Coded Hospitalization Rates in the Prevaccine Years (2000–2006) and Rates and Rate Reduction in Postvaccine Years (2008 and 2009)^a

	2000–2006	2008		2009	
	Rate, Average Annual (Minimum–Maximum) Hospitalizations per 10 000 Children ^b	Rate, Hospitalizations per 10 000 Children ^b	Rate Reduction (%)	Rate, Hospitalizations per 10 000 Children ^b	Rate Reduction (%)
Total	15 (13–18)	4	71	6	62
Sex					
Male	17 (14–20)	5	71	6	62
Female	14 (11–17)	4	71	5	63
Age					
0–2 months	19 (16–23)	7	61	8	57
3–5 months	24 (21–27)	5	78	5	81
6–11 months	36 (34–39)	7	82	6	83
12–17 months	32 (25–40)	8	76	8	76
18–23 months	22 (16–29)	8	64	8	62
24–35 months	11 (8–14)	5	55	7	35
36–47 months	5 (3–6)	2	64	4	7
48–59 months	2 (2–3)	1	72	2	22
Region					
Midwest	18 (13–22)	4	75	8	56
Northeast	12 (8–15)	3	74	5	61
South	15 (12–21)	5	65	7	54
West	10 (8–11)	4	58	3	70

^a Primary data obtained from Healthcare Cost and Utilization Project State Inpatient Databases Documentation, March 2011. Agency for Healthcare Research and Quality.

^b Rates represent rotavirus-coded hospitalizations per 10 000 children <5 years of age.

highest among children 6–11 months at 36 per 10 000 (annual range, 34–39 per 100 000); rates in this age group declined 82% to 7 and 83% to 6 per 10 000 in 2008 and 2009, respectively ($P < .001$). Of note, among children 24–59 months of age, in 2009 there were smaller declines in rotavirus-coded hospitalization rates of 7%–35% compared to much larger declines of 55%–72% in 2008. In the prevaccine (2001–2006) years, among children <5 years of age hospitalized with rotavirus-coded diarrhea, 24% (annual range, 21%–26%) were 24–59 months of age. This proportion increased to 33% in 2008 and 48% in 2009, respectively ($P < .001$). Additionally, decreases in rotavirus-coded hospitalization rates were observed in all US regions; the decline was slightly lower in the West compared with other regions in 2008 but in 2009 the West had the greatest decline.

Seasonal Patterns of Gastroenteritis and Rotavirus-Coded Hospitalizations Pre- and Post-Rotavirus Vaccine Implementation

In prevaccine years, the median monthly gastroenteritis-coded hospitalization rate was highest in March at 152 per 10 000 (annual range, 118–172 per 10 000). After vaccine introduction,

gastroenteritis-coded hospitalization rates peaked at 69 per 10 000 in April 2008 and 89 per 10 000 in March 2009 (Figure 1A). In prevaccine years, the median monthly rotavirus-coded hospitalization rate was highest in March at 54 per 10 000 (annual range, 33–63 per 10 000) (Figure 1B). After vaccine introduction, rotavirus-coded hospitalization rates peaked at 14 per 10 000 in April 2008 and 20 per 10 000 in March 2009. During each of the 4 months from January through April with highest prevaccine rotavirus-coded hospitalization rates, the rates in both 2008 and 2009 were substantially lower. However, because of a delay in the onset of the 2008 rotavirus season, rotavirus-coded hospitalization rates during May and June of 2008 exceeded prevaccine rates, although rates in these 2 months were substantially lower than during the peak months from January through April.

Gastroenteritis Hospitalization Costs and Length of Stay

The median hospital cost for a gastroenteritis hospitalization in adjusted 2009 dollars increased during the study period from \$1469 in 2000 to \$3210 in 2009. The median length of stay for a gastroenteritis-coded hospitalization was relatively stable during the study period, ranging from 2.2 to 2.6 days.

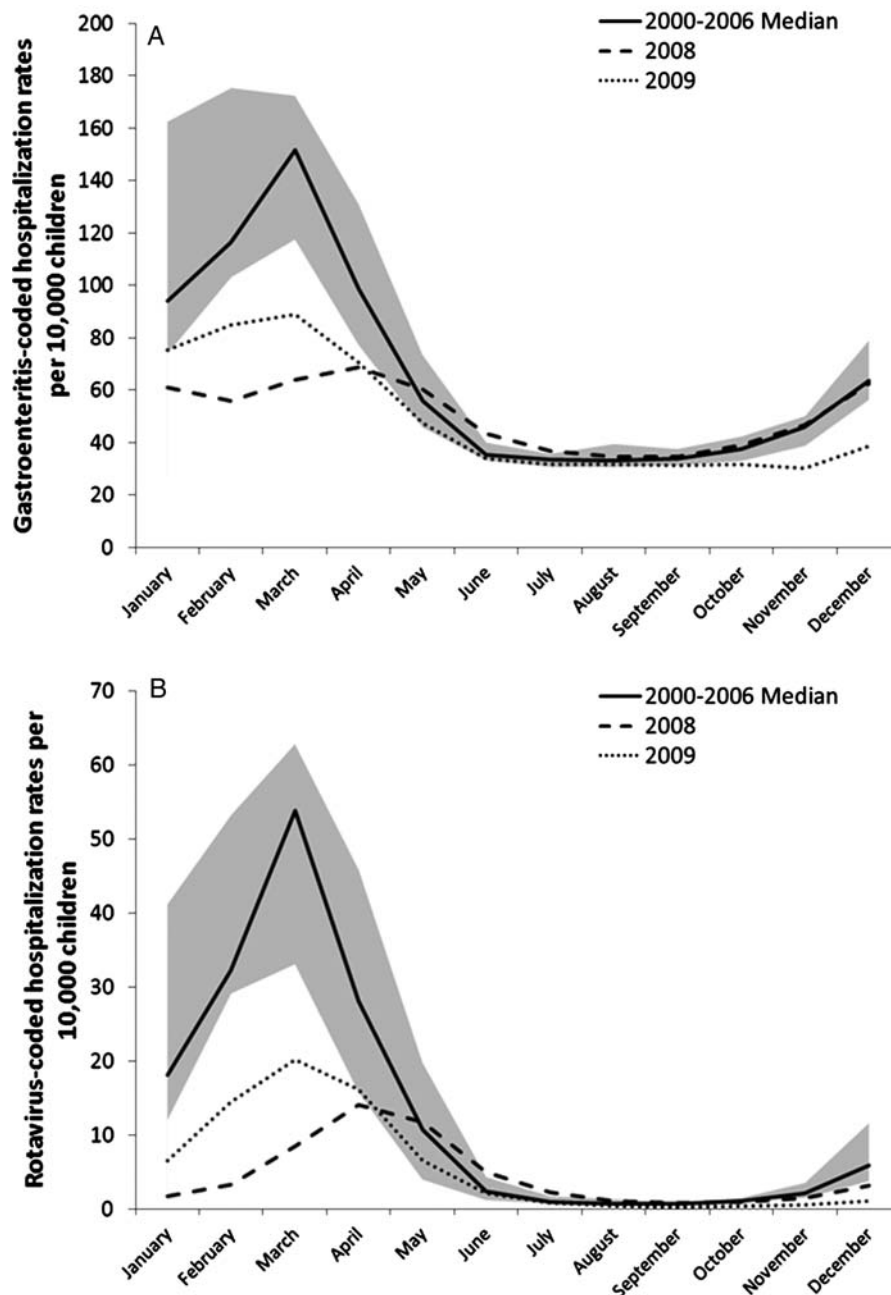


Figure 1. A, Gastroenteritis hospitalization rates in prevaccine years and postvaccine years (2008 and 2009) by month of year. B, Rotavirus hospitalization rates in prevaccine years and postvaccine years (2008 and 2009) by month of year. Black line, 2000–2006 median; gray line, maximum–minimum range. All rates are for children <5 years of age.

National Estimates of Reduction in Gastroenteritis Hospitalizations and Charges After Rotavirus Vaccine Implementation

Extrapolating the observed gastroenteritis hospitalization rates in our study to the US population <5 years of age yields a median of 145 051 gastroenteritis hospitalizations annually in prevaccine years; this declined to 107 354 and 105 952

gastroenteritis hospitalizations in 2008 and 2009, respectively. Combining the average charge per gastroenteritis hospitalization in 2008 (\$3080) and 2009 (\$3210) and the reduction in gastroenteritis hospitalizations in 2008 (37 697) and 2009 (39 099) yields an overall reduction of \$116 087 912 and \$125 488 241 in hospital charges in the United States in 2008 and 2009, respectively.

DISCUSSION

Since implementation of the US rotavirus vaccination program in 2006, a marked reduction in both gastroenteritis- and rotavirus-coded hospitalizations and related direct medical costs has occurred among US children <5 years of age. During the 2008 and 2009 postvaccine years, we observed annual reductions in all-cause gastroenteritis hospitalizations of 31%–33% and reductions in rotavirus-coded hospitalizations of 62%–71% compared with prevaccine years from 2000 to 2006. Reductions in gastroenteritis- and rotavirus-coded hospitalizations occurred across all US census regions and among most racial groups. The most notable decreases occurred during the winter rotavirus season and among children 6–11 months of age, a group with the highest rates of rotavirus disease in prevaccine years and with greatest levels of vaccine coverage in both years. These findings strongly suggest that the reductions in gastroenteritis- and rotavirus-coded hospitalizations were due to rotavirus vaccine, as opposed to unmeasured contemporaneous factors or changes in hospital coding practices. In the 2 postvaccine years 2008 and 2009 combined, we estimated a reduction of approximately 77 000 hospitalizations for gastroenteritis, yielding a national reduction in hospital charges of >\$240 million.

While declines in gastroenteritis and rotavirus-coded hospitalizations were seen in both postvaccine years 2008 and 2009, some differences were observed between the 2 years. In particular, large declines were seen across all age groups in 2008, including among children 24 months and older who were not age-eligible for rotavirus vaccination, whereas in 2009 the declines in these older nonvaccine-eligible age groups were much less prominent. The slight rebound in rotavirus hospitalization rates during 2009, particularly among children aged 24–59 months, has been seen in an analysis of hospital discharge data from a network of US pediatric hospitals as well as in prospective, population-based surveillance of laboratory-confirmed rotavirus hospitalizations and emergency room visits in 3 US counties [2, 5]. One possible explanation may be that a markedly diminished 2008 season, as a result of indirect protection of unvaccinated infants due to reduced rotavirus transmission in the community (ie, herd immunity), resulted in a larger susceptible cohort of unvaccinated older children in 2009 that were not exposed to natural rotavirus infection in the previous 2008 season. The increased pool of susceptible individuals and herd immunity likely combine to generate a biennial pattern which is superimposed on a general decreased rotavirus disease trend after vaccine introduction. This pattern of biennial epidemics was predicted by a mathematical model of rotavirus dynamics [13] and is corroborated by laboratory-based rotavirus surveillance showing a similar pattern in 2010 and 2011 [14]. Also, important regional differences were

observed in the postvaccine era. The rotavirus-coded hospitalization rate in the West lagged behind other regions in 2008 but was highest among all regions in 2009, a geographic pattern consistent with previously published data on rotavirus laboratory detections [15].

Prior evaluations of rotavirus vaccine impact in the United States have been performed. A study evaluating the HCUP database also demonstrated postvaccine reductions in rotavirus hospitalizations, but only included 1 complete postvaccine season and a limited number of US states [9]. Our study addresses both of these limitations, making this vaccine impact analysis more reliable and generalizable to the entire US population. Another analysis of private- and public-sector insurance claims in the MarketScan databases estimated national reductions of 64 855 gastroenteritis hospitalizations and \$278 million in cost savings over the combined 2008 and 2009 rotavirus seasons [4], estimates that were strikingly similar to those presented here. Finally, a study using a database of 62 US pediatric hospitals found reductions in gastroenteritis hospitalizations of 50% and 29% in the 2008 and 2009 rotavirus seasons, respectively, relative to prevaccine years [5]. Again, these figures are similar to our estimates based on more robust and nationally representative data of reductions in gastroenteritis hospitalizations in 2008 (31%) and 2009 (33%). Collectively, these findings from multiple hospital-based and payer databases conclusively demonstrate a reduction in gastroenteritis hospitalizations and associated costs in 2 postvaccine rotavirus seasons.

The hospitalization data from the SID have limitations. First, the rotavirus code has been shown to be specific for identifying rotavirus laboratory-confirmed hospitalizations; however, rotavirus-coded events underestimate the true burden of rotavirus hospitalizations, because laboratory testing and coding for rotavirus are not routinely performed for all patients with gastroenteritis [16, 17]. This is particularly true for rotavirus mortality trends, which have been documented in the prevaccine era but not in the postvaccine years [18]. Additionally, aggregate de-identified patient data preclude analyses by vaccination status. Because no patient-level data are available, a given patient might have multiple gastroenteritis- and/or rotavirus-coded hospitalizations reported. Secular variation may account for part of the decrease in gastroenteritis- and rotavirus-coded hospitalization rates; however, it is unlikely to account for the large declines we consistently observed in 2 postvaccine years. Finally, the national reduction in hospital charges must be compared against the cost of the rotavirus vaccination program. An evaluation performed in 2007 revealed that although the rotavirus vaccine is unlikely to be cost-saving in the United States, it may still be considered a cost-effective intervention [19].

In summary, we demonstrate a marked reduction in both gastroenteritis- and rotavirus-coded hospitalizations and related direct medical costs among US children through 2

rotavirus seasons after vaccine implementation. Disease reductions were greatest among 0–23-month-old infants, compared to older, largely unvaccinated birth cohorts, particularly in 2009. This suggests that gastroenteritis- and rotavirus-coded hospitalization rates among children <5 years will continue to decrease in future years, as successive birth cohorts are vaccinated. Ongoing surveillance will enable monitoring of the long-term impact of vaccination on rotavirus hospitalizations and associated costs.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online (<http://cid.oxfordjournals.org>). Supplementary materials consist of data provided by the author that are published to benefit the reader. The posted materials are not copyedited. The contents of all supplementary data are the sole responsibility of the authors. Questions or messages regarding errors should be addressed to the author.

Notes

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Disclaimer. The findings and conclusions in this report are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention or the Agency for Healthcare Research and Quality.

Potential conflicts of interest. All authors: No reported conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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West	UT	UT	UT	UT	UT	UT	UT	UT	UT	UT
West	WA	WA	WA	WA	WA	WA	WA	WA	WA	WA
West	[REDACTED]		NV	NV	NV	NV	NV	NV	NV	NV
West	[REDACTED]							WY	WY	WY
West	[REDACTED]									NM
West	[REDACTED]									MT