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# Sustained Decline in Acute Gastroenteritis-Associated Hospitalizations and Outpatient Visits among American Indian/ Alaska Native Children after Rotavirus Vaccine Introduction, 2001–2014

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## Abstract

We examined uptake of rotavirus vaccine and compared trends in acute gastroenteritis (AGE)associated hospitalizations and outpatient visits among AI/AN children <5 years of age in the preand post-rotavirus vaccine era. Rates of AGE-associated hospitalization and outpatient visits among AI/AN children remain below prevaccine levels.

#### Keywords

rotavirus; American Indian; Alaska Native; children; infants

# Introduction

Before the introduction of the pentavalent and monovalent rotavirus vaccines (RotaTeq®, Merck and Co., New York, New York, and Rotarix®, GSK Biologicals, Brentford, United Kingdom, respectively) in the United States in 2006 and 2008, respectively, rotavirus was a leading cause of AGE-associated hospitalizations and outpatient visits among children <5 years of age.[1, 2] Introduction of these vaccines into the routine childhood immunization schedule has resulted in declines in healthcare utilization for rotavirus-associated AGE among US children.[3–5]

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Infectious acute gastroenteritis, including AGE caused by rotavirus, has been a particular public health problem among American Indian/Alaska Native (AI/AN) populations.[6, 7] AGE-associated hospitalization rates among AI/AN children were almost twice the rate among children in the general United States (US) population in the early 1980s,[6] but by the mid-1990s AGE-associated hospitalization rates were similar among AI/AN children and US children <5 years of age. However, AGE-associated hospitalization rates among AI/AN children through the mid-2000s.[8] Additionally, AGE-associated outpatient visit rates among AI/AN children <5 years of age were greater than that among US children.[8]

The Indian Health Service (IHS), the federal agency responsible for providing health services to AI/AN people, began using rotavirus vaccine in all IHS areas in 2006. AGE-associated hospitalization and outpatient visit rates among AI/AN children declined after implementation of rotavirus vaccines,[9] but this early examination of vaccine impact on AGE-associated hospitalization and outpatient visit rates was limited to the first three years after vaccine implementation. To further examine vaccine impact, we examined AGE-associated hospitalization and outpatient visit rates in the prevaccine era compared with the first six years after rotavirus vaccine implementation among AI/AN children <5 years of age.

## Materials and Methods

The IHS provides health care to AI/ANs through a network of IHS, tribal, and Urban Indian health care facilities. Rotavirus vaccination coverage estimates were obtained from the IHS Division of Epidemiology and Disease Prevention, which reports vaccination information from IHS electronic health records on a quarterly basis.[10] Average rotavirus vaccination coverage for the first and second dose of vaccine among infants aged 3–4 months (dose 1) and 5–6 months (dose 2) of age were calculated from calendar years 2008 to 2014. Third dose coverage was not assessed due to site-to-site differences in the use of RotaTeq® and Rotarix®.

AGE-associated hospitalization and outpatient visit data for AI/AN children <5 years of age from calendar years 2001 to 2014 were obtained from the IHS National Patient Information Reporting System. These data consist of records of hospital discharges and outpatient visits to IHS-operated, tribally operated, and community hospitals and clinics as well as health services that are contracted with the IHS or specific tribes. As in the previous examination of these data, the West region was excluded from the hospitalization analysis due to the lack of IHS- or tribally-funded hospitals as well as limitations in contract health service data.[9] Data were categorized by age group (<1 year and 1–4 years of age), and time period with respect to rotavirus vaccine availability (2001–2006 classified as prevaccine period; 2007 classified as a transitional year; [3, 4, 9] and 2008–2014 classified as postvaccine period). AGE-associated outpatient visits for calendar years 2001–2014 among AI/AN children <5 years of age were obtained from all regions, including the West region. Hospital discharge and outpatient visit records were classified as AGE-associated when one of up to 15 discharge diagnosis codes matched an *International Classification of Diseases, Ninth* 

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*Revision, Clinical Modification* (ICD-9-CM) code list for acute gastroenteritis.[9] Newborn birth hospitalizations were excluded in this study.

Annual and average annual hospitalization or outpatient AGE-associated visit rates were expressed as the number of hospitalizations or visits per 10,000 AI/AN children <5 years of age in the corresponding population. Population denominators for rate calculation estimates were identified by using the IHS/tribal user population counts for each age category for calendar years 2001–2014; the IHS user population includes all registered AI/AN persons who had received IHS-funded health care services at least once in the preceding three years. Poisson regression was used to compare rates and test for trends. Statistical significance was determined at p-values < 0.05. All analyses were completed using SAS/STAT<sup>®</sup> software.

#### Results

Average annual rotavirus vaccine coverage for dose 1 among AI/AN infants 3 to 4 months of age and for dose 2 among infants 5 to 6 months of age increased significantly (p<0.05) over the study period (Figure 1).

During 2001 through 2014, a total of 7,257 AGE-associated hospitalizations among AI/AN children <5 years of age were reported to IHS. The prevaccine (2001–2006) average annual AGE-associated hospitalization rate among AI/AN children <5 years of age was 61 per 10,000 (annual range: 52–78 per 10,000). The rate declined progressively to reach a low of 24 per 10,000 in 2014, a decrease of 61% (p<0.0001) (Figure 1A). The prevaccine average annual AGE-associated hospitalization rate among AI/AN children <1 year of age was 232 per 10,000 and declined to 80 per 10,000 in 2014, a 66% decrease (p<0.0001).

During 2001 through 2014, a total of 342,188 AGE-associated outpatient visits among AI/AN children <5 years of age were reported to IHS. The prevaccine average annual AGE-associated outpatient visit rate among AI/AN children <5 years of age was 2,188 per 10,000 (annual range: 2095–2401 per 10,000) and declined to 1,438 per 10,000 in 2014, a decrease of 34% (p<0.0001) (Figure 1B). The prevaccine average annual AGE-associated outpatient visit rate among AI/AN children <1 year of age was 5,865 per 10,000 and declined to 2,982 per 10,000 in 2014, a 49% decrease (p<0.0001).

#### Discussion

We previously highlighted the decrease in AGE-associated hospitalization and outpatient visit rates among AI/AN children for the first 3 years following the introduction of rotavirus vaccine,[9] and now demonstrate that these decreases have been sustained from 2010–2014.

The sustained declines in AGE-associated hospitalization and outpatient visit rates are likely attributable to rotavirus vaccination. The declines in AGE-associated hospitalization were found to be more pronounced almost every subsequent year following vaccine introduction, as increasing numbers of children were being vaccinated. Additionally, while we observed dramatic reductions in AGE-associated hospitalization rates since the introduction of rotavirus vaccine, the reduction in AGE-associated outpatient visit rates were more modest. This observation provides additional evidence that the introduction of rotavirus vaccine has

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contributed to the substantial decrease in more severe AGE-associated illness. Rotavirus gastroenteritis among children is commonly more severe than that from other causes [1], therefore a greater proportion of AGE-associated hospitalizations would be prevented through vaccination than the proportion of less severe episodes of gastroenteritis leading to outpatient visits.

We estimated that annual AGE-associated hospitalization rates among AI/AN children <5 years of age declined up to 64% annually compared to 2001–2006. Our estimated hospitalization rates are consistent with another study that reported acute gastroenteritis hospitalization rates among US children <5 years of age, which ranged between 39 per 10,000 in 2008 to 27 per 10,000 in 2010,[5] but were somewhat lower than those reported by another study that examined hospitalization rates among U.S. children <5 years of age in 24 states.[4] Additionally, our estimated hospitalization rate reductions are similar or greater to the rate reductions (ranging from 25%–55% annually) reported by these studies.

We estimated that annual AGE-associated outpatient visit rates among AI/AN children <5 years of age declined up to 39% annually compared to 2001–2006. Our estimated AI/AN outpatient visit rates are notably higher than those reported among U.S. children <5 years of age from 2008 to 2010; in 2014, the estimated AGE-associated outpatient visit rate among AI/AN children was 1,438 per 10,000, while the outpatient visit rate among U.S. children <5 years of age was 1,360 per 10,000 in 2008.[5] However, AGE-associated outpatient visit rates decreased more dramatically among AI/AN children when compared to U.S. children from 2008–2010.

Our study has some limitations. First, ICD9-coded AGE-associated diagnoses may be incomplete or inaccurate. While our results strongly suggest that use of rotavirus vaccine led to decreases in AGE-associated hospitalization and outpatient visit rates, we could not directly detect any decreases in rotavirus-coded AGE due to the small number of rotavirus-coded outpatient visits and hospitalizations, and did not directly analyze laboratory-confirmed rotavirus infections. Additionally, annual trends in other pathogens associated with less severe gastroenteritis (e.g., norovirus) would likely affect our findings, particularly AGE-associated outpatient visit rates. Furthermore, our ecologic analysis of hospitalization and outpatient visit rates is susceptible to variability across IHS regions including host factors such as comorbidities; disease factors such as rotavirus strain differences and AGE outbreaks; variations in use of vaccines that require two vs. three doses; and social factors such as access to health care and variability in physician treatment practices. Finally, AI/AN patients within the IHS healthcare system may receive care outside the IHS system, and such care episodes would not be included in this study.

#### Conclusions

Sustained decreases in AGE-associated hospitalization and outpatient rates in the years after the introduction of rotavirus vaccine among AI/AN children in the IHS underscores the health benefits of vaccination. Continued efforts to increase rotavirus vaccination coverage among AI/AN children are expected to further reduce AGE-associated hospitalizations and outpatient visits.

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#### Summary

Decreasing trends in acute gastroenteritis-associated hospitalization and outpatient visit rates have been sustained during the seven years following rotavirus vaccine introduction within the Indian Health Service. These decreases underscore the importance of vaccination uptake among American Indian and Alaska Native children.

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Note: Prevaccine years (black), transition year (white), and postvaccine years (gray) are shown