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Short communication

# Vaccine-preventable, hospitalizations among American Indian/Alaska Native children using the 2012 Kid's Inpatient Database

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ABSTRACT

Our aim was to assess the odds of hospitalization for a vaccine-preventable, infectious disease (VP-ID) in American Indian/Alaska Native (AI/AN) children compared to other racial and ethnic groups using the 2012 Kid's Inpatient Database (KID) The KID is a nationally representative sample, which allows for evaluation of VP-ID in a non-federal, non-Indian Health Service setting. In a cross-sectional analysis, we evaluated the association of race/ethnicity and a composite outcome of hospitalization due to vaccine-preventable infection using multivariate logistic regression. AI/AN children were more likely (OR = 1.81, 95% CI = 1.34, 2.45) to be admitted to the hospital in 2012 for a VP-ID compared to Non-Hispanic white children after adjusting for age, sex, chronic disease status, metropolitan location, and median household income. This disparity highlights the necessity for a more comprehensive understanding of immunization and infectious disease exposure among American Indian children, especially those not covered or evaluated by Indian Health Service.



## 1. Introduction

American Indian/Alaska Native (AI/AN) children have been disproportionally affected by vaccine-preventable, infectious diseases (VP-ID) [1]. Access to the Indian Health Service (IHS) and tribal resources has reduced disparities in preventative care between AI/AN and non-Hispanic white persons [2]. In fact, immunization rates among children covered by IHS are largely the same or better than the general population of the US since 2005 [3,4]. Studies using IHS data have shown that infection rates for VP-ID like varicella, rotavirus, *Haemophilus influenzae* (Hib), Hepatitis B (Hep B), and invasive pneumococcal disease have declined among AI/AN persons since the introduction of vaccines [5–9]. Despite these improvements, AI/AN infants included in IHS reporting continued to have a higher rate of hospitalization for pertussis than the general population from 2000–2004 [10].

It is difficult to determine whether these findings extend to AI/AN children not included in IHS reporting. Only 40% of the 5.2 million AI/AN in the U.S. are serviced by IHS [11,12]. To qualify for IHS one must belong to a federally recognized tribe as well as meet certain tribal lineage requirements [2,13]. In addition, 78% of AI/ANs live outside designated AI/AN areas, where it is more difficult to access IHS or tribal health services [11,13]. Therefore, a significant proportion of people that identify as AI/AN are not captured in research evaluating VP-IDs despite sharing similar health risks and cultural practices to those serviced by IHS.

The aim of this analysis was to evaluate the rate of hospitalization for vaccine-preventable diseases in all racial/ethnic groups included in the 2012 Kids' Inpatient Database (KID) compared to white children, with a focus on AI/AN children. Given the historical disparities in VP-ID burden, we hypothesized that AI/AN children hospitalized in a non-federal, non-IHS setting were more likely to be admitted for VP-ID than white children.

## 2. Methods

### 2.1. Design and study sample

This was a cross-sectional analysis of pediatric hospitalizations for VP-ID using the 2012 KID prepared by the Agency for

*Abbreviations:* ID, Infectious Disease; VP-ID, Vaccine-preventable infectious disease; aOR, adjusted odds ratio; OR, odds ratio; CI, confidence interval.

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Healthcare Research and Quality (AHRQ) as part of the Healthcare Resource Utilization Project (HCUP). The KID is a nationally representative sample of pediatric discharges from all short-term, non-rehabilitation hospitals in 44 participating states [14]. IHS and other federal hospitals are not included in this dataset. By using this dataset we attempted to more closely capture the general population of AI children.

### 2.2. Outcomes

The primary outcome was a composite measure of VP-ID hospitalization, which we defined as any patient hospitalized with an *International Classification of Disease – ninth revision* (ICD-9) code for an infection that could reasonably be prevented with routine childhood vaccinations recommended in the 2012 CDC immunization guidelines (see Table 1) [15,16]. We examined diagnoses in all 25 diagnostic fields provided in the 2012 KID database. Individual vaccine preventable diseases with >10 cases in the AI/AN population were also analyzed as secondary outcomes.

### 2.3. Clinical variables

The primary exposure of interest was race/ethnicity, which was reported in the KID using uniform coding. Race was missing in 8.24% of records, and these patients were excluded from the analysis. Covariates including age (<2, 2–6, >6 years), gender, chronic disease, location, household income, and hospital region were evaluated for association with ID hospitalization and inclusion in the adjusted model. Chronic disease was considered present if the patient had one or more conditions meeting the AHRQ definition of a chronic disease [17]. Location was dichotomized into metropolitan and nonmetropolitan per the 2013 National Center for Health Statistics' Urban-Rural Classification Scheme for Counties [18]. Median household income was separated into quartiles based on median household incomes of patients' zip codes [14].

### 2.4. Analysis

The Stata (StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP) suite of *Survey* commands was used for all analyses to account for the sampling design of the KID. Pearson Chi-square tests were used to analyze differences in patient characteristics between children hospitalized with VP-ID and all other hospitalizations.

**Table 1**
ICD-9 Codes used to create composite outcome of VP-ID hospitalization.

| Infectious disease | ICD-9 Codes |
|---|---|
| Hep B | 070.20-070.23, 070.30-070.33 |
| Rotavirus[a] | 008.61 |
| Diphtheria | 032.1-032.3, 032.81-032.85, 032.89, 032.9 |
| Tetanus | 037 |
| Pertussis[a] | 033.0-033.1, 033.8-033.9 484.3 |
| Hib[a] | 041.5, 320.0 |
| Pneumococcal[a] | 038.2, 320.1, 481 |
| Polio virus | 045.00-045.03, 045.10-045.13, 045.20-045.23, 045.90-045.93 |
| Measles | 055.0-055.2, 055.71, 055.79, 055.8, 055.9 |
| Mumps | 072.0-072.3, 072.71-072.72, 072.79, 072.8-072.9 |
| Rubella | 056.00-056.01, 056.09, 056.71, 056.79, 056.8-056.9 |
| Varicella | 052.0-052.2, 052.7-052.9 |
| Hep A | 070.0, 070.1 |
| Meningococcal | 036.0-036.3, 036.40-036.43, 036.81-036.82, 036.89, 036.9 |

[a] Infectious diseases with enough cases in AI/AN patients (>10) to conduct univariate analyses.

Univariate logistic regression was performed to assess the association between VP-ID hospitalization and race/ethnicity and clinical covariates. Collinearity was not an issue given the low to moderate correlation (max Cramer's V = 0.34) between variables. We examined each covariate for interaction with race on VP-ID hospitalizations, and significant interaction terms ($p = 0.05$) in a bivariate analysis were included in the adjusted model. All covariates associated with VP-ID ($p = 0.10$) in a univariate model were included in the multivariate model.

In sensitivity analyses, we compared the severity of illness between AI/AN and white children hospitalized with VP-ID using a Pearson Chi-square test. Severity of illness and risk of mortality measures were developed for HCUP, and they were calculated using Disease Staging, AHRQ Co morbidity Measures, and All Patient-Refined-DRGs (diagnosis related groups) [14].

## 3. Results

### 3.1. Study sample

Approximately 50% of all VP-ID hospitalizations were children <2 years old compared to only 24% of all other non-birth hospitalizations (see Table 2). Females were less likely to be hospitalized for VP-ID compared to their male counterparts ($p < 0.001$), and children hospitalized for VP-ID were less likely to have a concurrent chronic disease than those hospitalized for other reasons ($p < 0.001$). The proportion of children living in a nonmetropolitan area at the time of their hospitalization did not differ between those hospitalized for VP-ID and other hospitalizations ($p = 0.40$).

**Table 2**
Patient characteristics of all non-birth hospitalizations of children in 2012.

| | VP_ID diagnosis[a] N = 12,732 | Other diagnoses N = 2,928,730 | $\chi^2$ p-value |
|---|---|---|---|
| **Characteristics** | Weighted %[b] (95% CI) | Weighted %[b] (95% CI) | |
| Racial/Ethnic Groups | | | <0.0001 |
| American Indian/ Alaska Native | 1.7 (1.2, 2.4) | 1.0 (0.8, 1.3) | |
| Non-Hispanic white | 48.3 (45.3, 51.3) | 49.8 (47.9, 51.6) | |
| African American | 15.3 (13.9, 16.9) | 18.9 (17.8, 20.1) | |
| Hispanic | 26.3 (23.2, 29.6) | 22.4 (20.6, 24.3) | |
| Asian | 3.2 (2.5, 3.9) | 2.5 (2.2, 2.9) | |
| Other | 5.3 (4.6, 6.2) | 5.4 (4.8, 6.0) | |
| Age | | | <0.0001 |
| <2 years | 49.5 (47.9, 51.1) | 23.8 (23.2, 24.5) | |
| 2–6 years | 24.5 (23.4, 25.6) | 15.2 (14.7, 15.7) | |
| >6 years | 26.0 (24.8, 27.3) | 61.0 (59.9, 62.0) | |
| Sex | | | <0.0001 |
| Female | 46.8 (45.7, 47.9) | 56.3 (55.6, 56.9) | |
| Chronic Disease Present | 53.8 (52.0, 55.6) | 59.4 (58.4, 60.4) | <0.0001 |
| Location | | | 0.40 |
| Nonmetropolitan | 17.3 (15.8, 19.0) | 16.9 (15.9, 17.9) | |
| Median Household Income | | | <0.0001 |
| ≥63,000 | 15.9 (14.3, 17.7) | 18.4 (17.1, 19.7) | |
| 48,000–62,999 | 21.9 (20.4, 23.5) | 22.4 (21.6, 23.2) | |
| 39,000–47,999 | 25.2 (23.7, 26.6) | 25.1 (24.3, 25.9) | |
| ≤38,999 | 37.0 (34.5, 39.6) | 34.2 (32.7, 35.6) | |
| Region | | | 0.10 |
| Northeast | 16.4 (13.1, 20.3) | 17.5 (14.8, 20.5) | |
| Midwest | 21.3 (17.3, 26.0) | 22.3 (19.4, 25.6) | |
| South | 41.6 (36.3, 47.0) | 38.8 (35.4, 42.4) | |
| West | 20.7 (16.8, 25.3) | 21.4 (18.5, 24.7) | |

[a] VP-ID diagnosis if patient was discharged with any diagnosis described in Table 1.
[b] Weighted using scaled weights provided by HCUP to produce national level estimates.

### 3.2. Race/ethnicity and VP-ID

AI/AN children constituted 1.7% of the estimated 8999 VP-ID hospitalizations and 1.0% of the estimated 2,079,210 other childhood hospitalizations in 2012. Results of the univariate and multivariate regression analyses are described in Table 3. Hospital region was not included in the model due to insufficient numbers by race ($n \leq 10$). Metropolitan status was not associated with VP-ID hospitalization, so it was excluded from the multivariate analysis. AI/AN, Hispanic, and Asian race/ethnicity were all associated with greater odds of hospitalization for VP-ID compared to whites. There was significant interaction between race and age in a bivariate analysis, so it was included in the adjusted model. After adjusting for the interaction between age and race as well as potential confounders, only AI/AN and Hispanic race/ethnicity was associated with greater odds of VP-ID hospitalization. The association of AI/AN race and VP-ID hospitalization was significant in the unadjusted (OR = 1.66, 95% CI = 1.28, 2.15) and adjusted (aOR = 1.81, CI = 1.34, 2.45) models, indicating AI/AN children had greater odds of being admitted to the hospital in 2012 for a VP-ID compared to whites. The results were similar using only the primary diagnosis in the unadjusted (OR = 1.51, CI = 1.08, 2.11) and adjusted (aOR = 1.72, CI = 1.16, 2.54) models.

**Table 3**
Adjusted and unadjusted OR for vaccine-preventable infectious disease hospitalizations.

| Characteristics | OR (95% CI) | Logit aOR[a] (95% CI) |
|---|---|---|
| *Racial/Ethnic Groups* | | |
| Non-Hispanic white | 1.0 | 1.0 |
| American Indian/Alaska Native | 1.66 (1.28, 2.15) | 1.81 (1.34, 2.45) |
| Black/African American | 0.83 (0.77, 0.91) | 0.92 (0.83, 1.02) |
| Hispanic | 1.21 (1.10, 1.34) | 1.29 (1.14, 1.46) |
| Asian | 1.28 (1.08, 1.52) | 0.71 (0.53, 0.94) |
| Other | 1.02 (0.91, 1.14) | 0.91 (0.78, 1.07) |
| *Age* | | |
| <2 years | 1.0 | 1.0 |
| 2–6 years | 0.78 (0.72, 0.84) | 0.88 (0.80, 0.97) |
| >6 years | 0.20 (0.19, 0.22) | 0.23 (0.21, 0.25) |
| *Age * Race* | | |
| AI/AN * 2–6 years | | 0.85 (0.58, 1.25) |
| AI/AN * >6 years | | 0.65 (0.39, 1.08) |
| Black/African American * 2–6 years | | 0.80 (0.66, 0.95) |
| Black/African American *>6 years | | 0.82 (0.69, 0.97) |
| Hispanic * 2–6 years | | 0.77 (0.64, 0.93) |
| Hispanic * >6 years | | 0.73 (0.61, 0.87) |
| Asian * 2–6 years | | 1.43 (0.98, 2.08) |
| Asian >6 years | | 3.36 (2.16, 5.24) |
| Other * 2–6 years | | 0.83 (0.62, 1.10) |
| Other * >6 years | | 1.18 (0.92, 1.51) |
| *Sex* | | |
| Male | 1.0 | 1.0 |
| Female | 0.68 (0.65, 0.72) | 0.90 (0.86, 0.95) |
| *Chronic disease* | | |
| No Chronic Disease | 1.0 | 1.0 |
| ≥1 Chronic Disease | 0.80 (0.75, 0.84) | 0.94 (0.89, 0.99) |
| *Location*[b] | | |
| Metropolitan | 1.0 | Not included |
| Nonmetropolitan | 1.03 (0.95, 1.12) | |
| *Median Household Income* | | |
| ≥63,000 | 1.0 | 1.0 |
| 48,000–62,999 | 1.13 (1.04, 1.23) | 1.09 (1.01, 1.18) |
| 39,000–47,999 | 1.16 (1.06, 1.27) | 1.11 (1.02, 1.22) |
| ≤38,999 | 1.25 (1.14, 1.37) | 1.24 (1.14, 1.35) |

[a] Interaction was assessed for all hospitalization characteristics in a bivariate analysis with race. All covariates significantly associated with VP-ID in a main effects model were included in the final adjusted model.

[b] Metropolitan and nonmetropolitan designations are defined by 2012 NCHS Urban-Rural Classification Scheme for Counties.

### 3.3. Race/ethnicity and specific VP diseases

There were sufficient cases to conduct secondary analyses on hospitalizations for Hib, pertussis, pneumococcal, and rotavirus infection. AI/AN children had significantly greater odds of hospitalization due to pertussis and pneumococcal infection 1.76 (CI = 1.22, 2.53) and 1.78 (CI = 1.23, 2.57), respectively. There were no significant differences between AI/AN and white children for Hib and rotavirus hospitalizations; however, the point estimates were similar to other VP-IDs, 1.73 (CI = 0.96, 3.11) and 1.69 (CI = 0.73, 3.95).

### 3.4. Sensitivity analysis

A possible explanation for the observed association between AI/AN race and VP-ID is that AI/AN children present with more severe illness resulting in more frequent hospitalizations. Using a Pearson Chi-square, there appeared to be no variation in the severity of illness ($p = 0.92$) or risk of mortality ($p = 0.48$) between AI/AN and white children hospitalized for VP-ID (data not shown). Another possible explanation for our results is that patients living in rural communities are more likely to be hospitalized due to limited access to care. However, we did not find a significant association between location (metropolitan vs. nonmetropolitan) and VP-ID hospitalizations even after adjusting for race/ethnicity.

## 4. Discussion

This study suggests that AI/AN children in the general population have a higher risk of VP-ID hospitalization compared to white children. We did not find that AI/AN children present with more severe illness or that patients in a nonmetropolitan location were more likely to be admitted for VP-ID. The association of AI/AN race and VP-ID hospitalization could also be explained by increased VP-ID exposure, physiological differences in vaccine response, greater ID susceptibility, or decreased/delayed immunizations.

According to research using IHS data, AI/AN children continue to have a high burden of infectious disease morbidity and mortality compared to non-AI/AN children [19,20]. Our results suggest that the high burden of infectious disease, including vaccine-preventable diseases, extends to AI/AN children in the general population as well. The increased burden of ID among AIs has often been attributed to increased disease exposure related to poor water quality, overcrowding, and issues of low socioeconomic status (SES) [8,21]. Although these issues have primarily been studied on reservations, issues of low SES exist in the urban Indian population as well [13].

Physiological differences in vaccine response have been demonstrated in limited populations of AI/AN people. Studies have indicated lower immune response to certain formulations of Hib vaccine in Navajo, Apache, and Alaska Native children [7]. To our knowledge, these differences in vaccine response have not been universally shown across the ethnically diverse AI/AN population.

Poor healthcare continuity is associated with less consistent and timely childhood vaccinations [22]. AI children have threefold greater odds of not having a personal provider compared to white children and are less likely to have a routine care appointment within the last year [23–25]. Due to this documented disparity in healthcare access, it is conceivable that AI/AN children in the general population are under-immunized compared to white children.

Despite the large, nationally representative sample, this study is limited by the information available in the KID database. The unit of analysis is hospitalization, so it is possible that one patient contributed multiple hospitalizations. Racial misclassification of AI/AN as white is common, which may result in under reporting of

disease [13]. Immunization status is not available; as a result, any assumption of under-immunization cannot be verified.

Since many biologic targets of vaccines are not routinely tested for in outpatient settings, KID allowed us to evaluate childhood hospitalizations associated with VP-ID. There are no reported lab values in the dataset, so VP-ID diagnoses could not be confirmed. Administrative data, like ICD-9, is subject to variable reliability based on many factors including quality of information, coding experience, and electronic vs. paper record [26]. ICD-9 appears to be highly specific for VP-ID; therefore, it is likely VP-ID hospitalizations identified in KID represent true cases [27,28]. It is also possible that there is underreporting of VP-ID because there is likely decreased testing and coding for certain VP-diseases, like rotavirus.

## 5. Conclusions

We found AI/AN children have a greater burden of VP-ID hospitalizations compared to white children. Although the high burden of ID hospitalizations among AI/AN children has been described using IHS data, the incidence of VP-ID hospitalizations among the general AI/AN population, to our knowledge, has not been addressed. The disparity we observed in this study underscores the importance of developing a more comprehensive understanding of immunization coverage and ID susceptibility among AI/AN children not evaluated in an IHS setting.

## Conflict of interest

No financial disclosures were reported by the authors of this paper.

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