






## Original Article

# Patterns of inpatient antibiotic utilization by race and ethnicity at US children's hospitals

Bethany A. Wattles PharmD, MHA<sup>1</sup> , Jeffrey I. Campbell MD, MPH<sup>2</sup>, Theresa Kluthe MS<sup>3</sup> , Yana B. Feygin PhD, MS<sup>3</sup> , Kahir Jawad MD, MPH, PhD<sup>3</sup>, Michelle D. Stevenson MD, MS<sup>1,3</sup>, Deborah Winders Davis PhD<sup>1,3</sup> , Jennifer Porter MD<sup>1,3</sup>, V. Faye Jones MD, PhD, MSPH<sup>1</sup>, Matt Hall PhD<sup>4</sup> and Michael J. Smith MD, MSCE<sup>5</sup> 

<sup>1</sup>Department of Pediatrics, University of Louisville School of Medicine, Louisville, KY, USA, <sup>2</sup>Department of Pediatrics, Boston Medical Center, Boston, MA, USA, <sup>3</sup>Norton Children's Research Institute affiliated with the University of Louisville School of Medicine, Louisville, KY, USA, <sup>4</sup>Children's Hospital Association, Lenexa, KS, USA and <sup>5</sup>Department of Pediatrics, Duke University Medical Center, Durham, NC, USA

## Abstract

**Background and Objectives:** Racial and ethnic variations in antibiotic utilization are well-reported in outpatient settings but little is known about inpatient settings. Our objective was to describe national inpatient antibiotic utilization among children by race and ethnicity.

**Methods:** This study included hospital visit data from the Pediatric Health Information System between 01/01/2022 and 12/31/2022 for patients <20 years. Primary outcomes were the percentage of hospitalization encounters that received an antibiotic and antibiotic days of therapy (DOT) per 1000 patient days. Mixed-effect regression models were used to determine the association of race-ethnicity with outcomes, adjusting for covariates.

**Results:** There were 846,530 hospitalizations. 45.2% of children were Non-Hispanic (NH) White, 27.1% were Hispanic, 19.2% were NH Black, 4.5% were NH Other, 3.5% were NH Asian, 0.3% were NH Native Hawaiian/Other Pacific Islander (NHPI) and 0.2% were NH American Indian. Adjusting for covariates, NH Black children had lower odds of receiving antibiotics compared to NH White children (aOR 0.96, 95%CI 0.94–0.97), while NH NHPI had higher odds of receiving antibiotics (aOR 1.16, 95%CI 1.05–1.29). Children who were Hispanic, NH Asian, NH American Indian, and children who were NH Other received antibiotic DOT compared to NH White children, while NH NHPI children received more antibiotic DOT.

**Conclusions:** Antibiotic utilization in children's hospitals differs by race and ethnicity. Hospitals should assess policies and practices that may contribute to disparities in treatment; antibiotic stewardship programs may play an important role in promoting inpatient pharmaco-equity. Additional research is needed to examine individual diagnoses, clinical outcomes, and drivers of variation.

(Received 15 April 2024; accepted 26 August 2024)

## Introduction

Pharmaco-equity is defined as the goal of ensuring that all individuals, regardless of race, ethnicity, and socioeconomic status, have access to the highest-quality medications required to manage their health needs. Pharmaco-equity is increasingly recognized as a priority to reduce health disparities.<sup>14</sup> Antibiotics are the most commonly prescribed class of medications to children<sup>15</sup> and are crucial in the management of infections. Racial and ethnic variations in antibiotic prescribing to children are well-reported in outpatient, emergency department, and urgent care settings.<sup>1–6</sup> In studies evaluating ambulatory prescribing data, White children consistently receive more antibiotics than children of other races or ethnicities, both at a population level<sup>2,7,8</sup> and within healthcare systems.<sup>1,5,6</sup>

Because race is a social construct with no biological meaning,<sup>9</sup> these differences likely reflect non-clinical factors and potential inequities in over or under utilization. Although demographic and between-hospital variations in antibiotic utilization are reported in pediatric outpatient settings,<sup>10,11</sup> little is known about racial and ethnic patterns of antibiotic utilization in inpatient settings. In a recent scoping review examining race and antibiotic prescribing, only one of 61 eligible studies was conducted in an acute care setting.<sup>12</sup> The study, an evaluation of adults with skin and soft tissue infections, found that race was associated with differential management.<sup>13</sup> The authors of the review provide a framework of factors contributing to health inequities in antibiotic prescribing in the United States (US), including national, community, healthcare, and individual factors.<sup>12</sup>

The frequency of antibiotic prescribing in hospitalized children, and the gap in literature on racial and ethnic differences in inpatient antibiotic prescribing, makes this an important area to study inequities. Identifying variations and inequities in treatment is an important step toward understanding downstream racial and ethnic disparities in health outcomes during and after

**Corresponding author:** Michael J. Smith; Email: [michael.j.smith@duke.edu](mailto:michael.j.smith@duke.edu)

**Cite this article:** Wattles BA, Campbell JI, Kluthe T, *et al.* Patterns of inpatient antibiotic utilization by race and ethnicity at US children's hospitals. *Infect Control Hosp Epidemiol* 2024. doi: 10.1017/ice.2024.168



hospitalization. Our objective was to provide a broad overview of national inpatient antibiotic utilization among children by race and ethnicity. We hypothesized that there would be racial and ethnic variations in antibiotic prescribing to children in hospital settings. The aforementioned framework<sup>12</sup> guided variable selection for our study.

## Methods

### Data source

This study was a retrospective, observational, cross-sectional study of the Pediatric Health Information System (PHIS), an administrative database managed by Children's Hospital Association (Lenexa, KS) that contains data from 46 tertiary referral children's hospitals in the US. The database captures demographics, diagnoses and procedures (using the *International Classification of Diseases version 10*), and daily billing data for all inpatient, observation, emergency room, and ambulatory surgery centers at participating hospitals. The study was reviewed by the University of Louisville Institutional Review Board and classified as Non-Human Subjects Research.

### Study population

We collected hospitalization (inpatient and observation) data for all patients <20 years old who were admitted to a participating PHIS hospital between January 1, 2022 and December 31, 2022. All patients with an inpatient hospitalization encounter within these age limits and timeframes were included. Data were analyzed at the individual-visit level, meaning that patients could have more than one included visit within the study period.

### Exposure

The exposure of interest was patient race and ethnicity. Race and ethnicity in PHIS are submitted by hospitals based on local hospital collection practices (e.g., parent/guardian self-report, assignment at registration) and categorized separately as race (White, Black, Asian, Native Hawaiian or Other Pacific Islander, American Indian or Alaska Native, other) and ethnicity (Hispanic or Latino, not Hispanic or Latino (NH)). We combined race and ethnicity variables to create the following mutually exclusive categories: Hispanic (including any race), NH American Indian, NH Asian, NH Black, NH Native Hawaiian and Other Pacific Islander, NH White, and NH Other (including a non-listed race, more than one race, or missing race and ethnicity). Visits with an unassigned ethnicity were recategorized as NH and then classified by race. The majority group (NH White) was used as the reference group in comparison analyses, though we note that race is a social construct and does not imply that the majority group represents the preferred standard of care. In certain stratified analyses, NH American Indian, NH Asian, NH Native Hawaiian and Other Pacific Islander and NH Other were combined as "NH Other" due to low sample sizes, though our intention is not to imply that these groups experience the same potential social and structural drivers of differential antibiotic utilization.

### Covariates

Other covariates included age at admission, sex, rural-urban continuum area based on each patient's residential zip code (metropolitan, micropolitan, or rural),<sup>16</sup> diagnosis antibiotic frequency, hospital region (Midwest, Northeast, South, West),

Child Opportunity Index (COI version 2.0) (classified as very low, low, moderate, high or very high opportunity areas),<sup>17</sup> payor (government, private, other), Pediatric Medical Complexity Algorithm (PMCA) (no chronic condition, chronic condition, complex chronic condition),<sup>18</sup> inpatient unit (NICU or PICU vs. non-ICU), and Hospitalization Resource Intensity Scores for Kids (H-RISK). To represent the likelihood that a patient's diagnosis was associated with antibiotic administration, we determined the proportion of inpatient encounters associated with each All Patients Refined Diagnosis Related Group (APR-DRG) (3M Health, version 38) for which an antibiotic was prescribed. APR-DRGs for which >75% of inpatient encounters were prescribed antibiotics were labeled as "very high frequency", >50%–75% as "high frequency", >25%–50% as "intermediate frequency", and 0%–25% as "low frequency" (eTable 1). The COI is an index of neighborhood resources and conditions that help children develop in a healthy way<sup>17</sup> and is classified based on residential zip code in PHIS. The COI combines the 3 subdomains of education, health-environment, and social-economic indices. H-RISK is a surrogate for severity of illness and is calculated by assigning cost-based relative weights to each APR-DRG and severity of illness level, enabling comparison of severity across APR-DRGs.<sup>19</sup>

We also chose five diagnostic groups—categorized by infection-related APR-DRG categories—to stratify for a secondary analysis: infections of the upper respiratory tract; bronchiolitis and respiratory syncytial virus (RSV) pneumonia; other pneumonia; cellulitis and other skin infections; and septicemia and disseminated infections.

### Outcomes

The primary outcome was antibiotic use, which was measured (1) as the percentage of all hospitalizations that received an antibiotic, and (2) as days of therapy (DOT) per 1000 patient days. Antibiotic prescriptions were identified using billing data. Secondary outcomes included length of stay (LOS) in days, days of broad-spectrum antibiotic therapy per 1000 patient days ("Broad DOT"), and intravenous (IV) DOT per 1000 patient days ("IV DOT"). Broad-spectrum antibiotics were classified using previously published studies<sup>10,11,21</sup> and author consensus (eTable 2). DOT was calculated such that multiple antibiotics on the same calendar day each counted individually as a "day of therapy"; thus, DOT could exceed LOS for a given encounter.

### Statistical analysis

We summarized visit characteristics, stratified by child race and ethnicity. Additional descriptive analyses were performed for percent of antibiotic visits by hospital, DOT outcomes, and outcomes by APR-DRGs of interest, all stratified by race and ethnicity. Outcomes by hospital and APR-DRGs were risk-adjusted using mean H-RISK scores for each racial-ethnic group within the individual hospital or diagnosis group. Pairwise chi-square tests were used to compare outcomes stratified by APR-DRGs of interest.

Mixed-effect logistic regression models were used to assess the likelihood of receiving an antibiotic, overall and stratified by race-ethnicity, after adjusting for covariates and accounting for clustering by hospital using random intercepts. A quasi-Poisson mixed-effect regression with a log-link was used to model antibiotic DOT, using LOS as the offset, and clustering by hospital using random intercepts. All regression models controlled for all covariates. Collinearity was assessed between all variables. To

address the impact of variations in NICU or newborn nursery visits within our sample, we performed a sensitivity analysis excluding children less than 2 months of age. Analyses were conducted using R version 4.2.3 (2023-03-15 ucrt).

## Results

There were 846,530 pediatric hospitalizations included in the analysis. Demographic characteristics and percentage of antibiotic visits for the overall study sample and stratified by race and ethnicity are presented in Table 1. Most hospitalizations were for NH White (45.2%) children, followed by Hispanic (27.1%), NH Black (19.2%), NH Other (4.5%), and NH Asian (3.5%) children. Children identified as NH NHPI and NH American Indian represented 2,665 (0.3%) and 2,054 (0.2%) visits, respectively. There were 15,672 visits (1.9%) with missing race and ethnicity variables, who were included in the NH Other category. The median length of stay was 2 days (IQR 1–4) for the study sample and across all racial-ethnic groups.

Overall, 41.6% of hospitalizations included an antibiotic. The percentage of antibiotic visits ranged from 38.4% in NH Black children to 47.5% in NH NHPI children. Compared to NH White children, who had an antibiotic visit rate of 42.4%, Hispanic children had a higher antibiotic visit rate (42.9%,  $P < .001$ ) and NH Black children had a lower rate (38.4%,  $P < .001$ ). Among children prescribed an antibiotic, NH Black children had a higher rate of broad-spectrum antibiotic visits (72.9%) compared to NH White children (71.2%,  $P < .001$ ). Among NH White children, antibiotic visits decreased with increasing COI, but a reverse relationship was observed for NH Black children. H-RISK-adjusted variations in antibiotic visits by race and ethnicity across and within individual hospitals are shown in Figure 1.

The H-RISK-adjusted distribution of DOT per 1000 patient days, IV DOT, and broad-spectrum DOT stratified by racial-ethnic groups are shown in Figure 2. In general, compared to patients who were NH White, patients who were NH Black, NH Other, and NH Asian received fewer DOT, IV DOT, and broad-spectrum DOT, and patients who were NH NHPI received more DOT, IV DOT, and broad-spectrum DOT.

## Adjusted outcomes

Adjusted odds of receiving an antibiotic and incident rate ratios of antibiotic DOT are shown in Figure 3, and presented in eTable 3. Adjusting for all covariates, NH Black children had lower odds of an antibiotic visit compared to NH White children (aOR 0.96 [95% CI 0.94–0.97]), while NH NHPI had higher odds of an antibiotic visit (aOR 1.16 [95% CI 1.05–1.29]). Compared to NH White children, NH NHPI children received more antibiotic DOT (adjusted incident rate ratio [aIRR] 1.06 [95% CI 1.04–1.08]), while patients who were Hispanic (aIRR 0.99 [95% CI 0.99–0.99]), NH Other (aIRR 0.97 [95% CI 0.96–0.98]), NH Asian (aIRR 0.94 [95% CI 0.93–0.94]), and NH American Indian (aIRR 0.99 [95% CI 0.98–0.99]) received fewer antibiotic DOT (Figure 3, eTable 4). A sensitivity analysis excluding infants <2 months old revealed similar findings (eTable 5).

## Diagnoses of interest

The most common infectious diagnoses identified by APR-DRGs were bronchiolitis and RSV pneumonia ( $n = 44,930$ ), infections of the upper respiratory tract ( $n = 18,823$ ), other pneumonia ( $n = 17,220$ ), cellulitis and skin infections ( $n = 8,221$ ), and

septicemia and disseminated infections ( $n = 8,067$ ). Collectively, these APR-DRGs account for 11.5% of all hospitalizations. H-RISK-adjusted variations in antibiotic use by race-ethnicity and diagnoses are shown in Figure 4, using a composite “NH Other” category due to limited representation of several racial and ethnic groups in encounters with these APR-DRG codes. Trends across racial and ethnic groups within diagnoses were similar in a risk-adjusted analysis; however, trends in antibiotic variations were not consistent across diagnoses. Additional unadjusted outcomes by diagnosis group, including DOT and H-RISK, are provided in eTable 6.

## Discussion

Our analysis of more than 800,000 hospitalizations in tertiary children’s hospitals across the US in 2022 found that antibiotic visits were lower in NH Black children compared to NH White children and that antibiotic DOT varied by race and ethnicity. These differences persisted after controlling for covariates, including socioeconomic status, illness severity, and the presence of chronic conditions. These findings are important for hospital and antimicrobial stewardship program leadership seeking to improve pharmaco-equity for hospitalized children.

Our study was not designed to determine whether racial variations in antibiotic utilization represent *health disparities* (preventable differences in the burden of disease or opportunities to achieve optimal health), or *health inequities* (particular types of health disparities that stem from unfair and unjust systems, policies, and practices and limit access to the opportunities and resources needed to live the healthiest life possible).<sup>12</sup> Health disparities are complex and represent multiple domains and levels of influence.<sup>22</sup> Differential access to care or medications is a common driver of health disparities.<sup>14</sup> Our study identified variations in treatment within the hospital visit, and differential access and utilization of antibiotics within hospitals may be a source of differential health outcomes. A variety of mechanisms plausibly lead to these observed differences, including structural racism and its effects on pre-hospital conditions and illness severity, implicit biases on the part of care teams, disparate access to subspecialty care, and differences in communication between caregivers and clinical teams.

To assess the intersectionality of race and socioeconomic status, we explored outcomes by COI. In unadjusted analyses, racial variations in antibiotic utilization between NH Black and NH White children remained across all COI levels. In our unadjusted analysis, the direction of antibiotic visit trends by COI was opposite in NH White and NH Black children, possibly suggesting that area opportunity and socioeconomic status affect care access and utilization in different ways for these populations. Similar findings were reported in an analysis of outpatient antibiotic prescribing.<sup>5</sup> In adjusted models, we did not find an independent association between COI and odds of receiving an antibiotic, suggesting that this area-based composite marker of socioeconomic status contributes less to inpatient antibiotic utilization than patients’ demographic characteristics and insurance status—a more direct marker of socioeconomic status.

In an exploratory analysis of select diagnoses, we found that racial and ethnic variations and directions of variations in antibiotic utilization are not consistent across diagnoses. The most common APR-DRG in our study, bronchiolitis and RSV pneumonia, demonstrates similar patterns of racial and ethnic differences in antibiotic utilization as another study using PHIS

**Table 1.** Unadjusted visit demographics and antibiotic visits by race and ethnicity

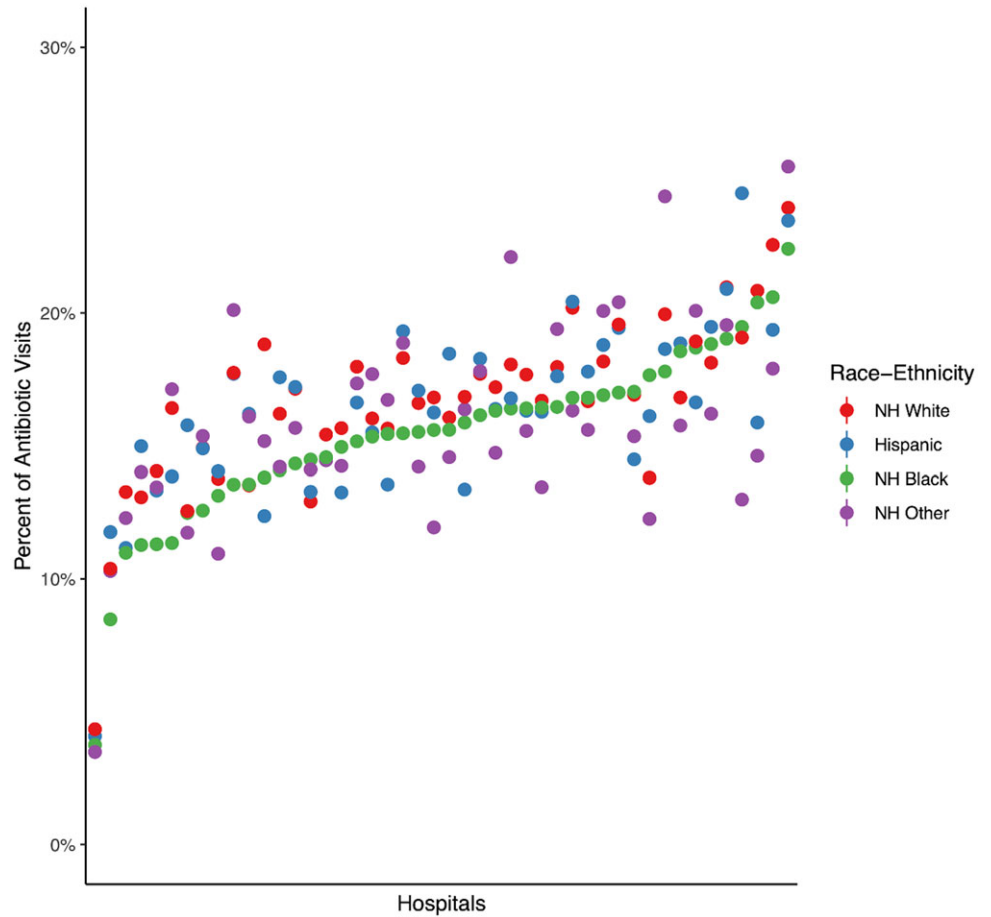
|   | All visits           |                  | NH White             |                  | Hispanic             |                  | NH Black             |                  | NH Other             |                  | NH Asian             |                  | NH Native Hawaiian/<br>Other Pacific Islander |                  | NH American Indian   |                     |
|---|----------------------|------------------|----------------------|------------------|----------------------|------------------|----------------------|------------------|----------------------|------------------|----------------------|------------------|---|------------------|----------------------|---------------------|
|   | All visits,<br>n (%) | Abx Visits,<br>% | All visits,<br>n (%) | Abx Visits,<br>% | All visits,<br>n (%) | Abx Visits,<br>% | All visits,<br>n (%) | Abx Visits,<br>% | All visits,<br>n (%) | Abx Visits,<br>% | All visits,<br>n (%) | Abx Visits,<br>% | All visits,<br>n (%)                          | Abx<br>Visits, % | All visits,<br>n (%) | Abx<br>Visits,<br>% |
| <b>No. (%)</b>  | 846530               | 352353 (41.6)    | 382541 (45.2)        | 162297 (42.4)    | 229174 (27.1)        | 98306 (42.9)     | 162327 (19.2)        | 62320 (38.4)     | 37835 (4.5)          | 15241 (40.3)     | 29934 (3.5)          | 11999 (40.1)     | 2665 (0.3)                                    | 1266 (47.5)      | 2054 (0.2)           | 924 (45)            |
| <b>Broad Spectrum<br/>Visits<sup>1</sup></b>                  | 254799 (72.3)        | /                | 115525 (71.2)        | /                | 72322 (73.6)         | /                | 45416 (72.9)         | /                | 11219 (73.6)         | /                | 8765 (73.0)          | /                | 909 (71.8)                                    | /                | 643 (69.6)           | /                   |
| <b>Age</b>  |                      |                  |                      |                  |                      |                  |                      |                  |                      |                  |                      |                  |   |                  |                      |                     |
| < 2 mo  | 164625 (19.4)        | 30.1             | 67956 (17.8)         | 32.8             | 48283 (21.1)         | 28.9             | 28270 (17.4)         | 30.0             | 10669 (28.2)         | 27.3             | 8650 (28.9)          | 19.0             | 480 (18.0)                                    | 31.5             | 317 (15.4)           | 39.4                |
| 2 mo to < 1y  | 97502 (11.5)         | 40.8             | 44201 (11.6)         | 41.1             | 27770 (12.1)         | 41.3             | 17735 (10.9)         | 37.8             | 4317 (11.4)          | 41.6             | 2848 (9.5)           | 45.3             | 392 (14.7)                                    | 52.0             | 239 (11.6)           | 43.9                |
| 1 to 4y   | 206036 (24.3)        | 43.2             | 91781 (24.0)         | 43.6             | 55996 (24.4)         | 44.7             | 41044 (25.3)         | 39.9             | 8719 (23.0)          | 43.4             | 7260 (24.3)          | 45.3             | 694 (26.0)                                    | 50.0             | 542 (26.4)           | 47.0                |
| 5 to 11y  | 174669 (20.6)        | 48.3             | 80568 (21.1)         | 49.0             | 46326 (20.2)         | 51.6             | 34172 (21.1)         | 40.6             | 6890 (18.2)          | 50.3             | 5762 (19.2)          | 54.1             | 497 (18.6)                                    | 53.7             | 454 (22.1)           | 50.7                |
| 12 to 19y   | 203698 (24.1)        | 44.0             | 98035 (25.6)         | 43.2             | 50799 (22.2)         | 47.1             | 41106 (25.3)         | 41.1             | 7240 (19.1)          | 45.4             | 5414 (18.1)          | 49.1             | 602 (22.6)                                    | 49.3             | 502 (24.4)           | 41.6                |
| <b>Sex</b>  |                      |                  |                      |                  |                      |                  |                      |                  |                      |                  |                      |                  |   |                  |                      |                     |
| Male  | 451345 (53.3)        | 42.1             | 202491 (52.9)        | 43.2             | 123070 (53.7)        | 43.1             | 86862 (53.5)         | 38.6             | 20193 (53.4)         | 40.7             | 16169 (54.0)         | 40.4             | 1469 (55.1)                                   | 48.9             | 1091 (53.1)          | 46.1                |
| Female  | 394877 (46.7)        | 41.0             | 179953 (47.1)        | 41.5             | 105998 (46.3)        | 42.6             | 75380 (46.5)         | 38.1             | 17628 (46.6)         | 39.7             | 13759 (46.0)         | 39.7             | 1196 (44.9)                                   | 45.8             | 963 (46.9)           | 43.7                |
| <b>RUCA</b>   |                      |                  |                      |                  |                      |                  |                      |                  |                      |                  |                      |                  |   |                  |                      |                     |
| Metropolitan  | 732767 (86.6)        | 40.8             | 302853 (79.2)        | 41.4             | 209612 (91.5)        | 42.3             | 152426 (93.9)        | 38.0             | 34649 (91.6)         | 39.7             | 29260 (97.7)         | 39.7             | 2418 (90.7)                                   | 46.4             | 1549 (75.4)          | 43.1                |
| Micropolitan  | 63003 (7.4)          | 45.6             | 42159 (11.0)         | 45.0             | 12310 (5.4)          | 48.8             | 5893 (3.6)           | 42.9             | 1849 (4.9)           | 44.9             | 458 (1.5)            | 53.5             | 148 (5.6)                                     | 51.4             | 186 (9.1)            | 43.0                |
| Rural   | 50760 (6.0)          | 48.1             | 37529 (9.8)          | 47.8             | 7252 (3.2)           | 49.6             | 4008 (2.5)           | 46.1             | 1337 (3.5)           | 48.2             | 216 (0.7)            | 62.5             | 99 (3.7)                                      | 68.7             | 319 (15.5)           | 55.5                |
| <b>Antibiotic<br/>frequency for<br/>diagnosis<sup>2</sup></b> |                      |                  |                      |                  |                      |                  |                      |                  |                      |                  |                      |                  |   |                  |                      |                     |
| Very high   | 184424 (21.8)        | NA               | 87938 (23.0)         | NA               | 53312 (21.8)         | NA               | 27553 (13.5)         | NA               | 8052 (21.3)          | NA               | 6361 (21.3)          | NA               | 716 (26.9)                                    | NA               | 492 (24.0)           | NA                  |
| High  | 79558 (9.4)          | NA               | 35106 (9.2)          | NA               | 35106 (14.3)         | NA               | 19473 (9.6)          | NA               | 3217 (8.5)           | NA               | 2226 (7.4)           | NA               | 212 (8.0)                                     | NA               | 209 (10.2)           | NA                  |
| Intermediate  | 248489 (29.4)        | NA               | 112571 (29.4)        | NA               | 69481 (28.4)         | NA               | 69481 (34.2)         | NA               | 10529 (27.8)         | NA               | 8579 (28.7)          | NA               | 859 (32.2)                                    | NA               | 689 (33.5)           | NA                  |
| Low   | 334056 (39.5)        | NA               | 146925 (38.4)        | NA               | 86907 (35.5)         | NA               | 86907 (42.7)         | NA               | 16037 (42.4)         | NA               | 12768 (42.7)         | NA               | 878 (32.9)                                    | NA               | 664 (32.3)           | NA                  |

| Region                       |               |             |               |             |               |             |               |            |              |             |              |             |             |             |             |            |
|------------------------------|---------------|-------------|---------------|-------------|---------------|-------------|---------------|------------|--------------|-------------|--------------|-------------|-------------|-------------|-------------|------------|
| Midwest                      | 233833 (27.6) | 42.4        | 132227 (34.6) | 43.6        | 39512 (17.2)  | 42.9        | 47485 (29.3)  | 38.3       | 7120 (18.8)  | 42.3        | 6675 (22.3)  | 43.5        | 364 (13.7)  | 45.3        | 450 (21.9)  | 47.1       |
| Northeast                    | 105477 (12.5) | 43.3        | 49549 (13.0)  | 44.7        | 26576 (11.6)  | 43.7        | 18576 (11.4)  | 36.6       | 7508 (19.8)  | 48.4        | 2985 (10.0)  | 47.2        | 62 (2.3)    | 38.7        | 221 (10.8)  | 45.7       |
| South                        | 370510 (43.8) | 39.9        | 153196 (40.0) | 40.1        | 101084 (44.1) | 41.8        | 88841 (54.7)  | 38.9       | 14600 (38.6) | 33.2        | 10801 (36.1) | 37.3        | 1139 (42.7) | 47.9        | 849 (41.3)  | 37.8       |
| West                         | 136710 (16.1) | 43.6        | 47569 (12.4)  | 44.3        | 62002 (27.1)  | 44.3        | 7425 (4.6)    | 37.9       | 8607 (22.7)  | 43.5        | 9473 (31.6)  | 38.6        | 1100 (41.3) | 48.3        | 534 (26.0)  | 54.3       |
| Child Opportunity Index      |               |             |               |             |               |             |               |            |              |             |              |             |             |             |             |            |
| Very Low                     | 182031 (21.6) | 40.8        | 36029 (9.4)   | 42.8        | 64215 (28.1)  | 42.9        | 70518 (43.5)  | 37.9       | 7645 (20.5)  | 40.6        | 2946 (9.9)   | 42.0        | 249 (9.5)   | 51.8        | 429 (21.0)  | 51.7       |
| Low                          | 166953 (19.8) | 42.0        | 70603 (18.5)  | 42.8        | 52768 (23.1)  | 43.6        | 32285 (19.9)  | 38.3       | 6857 (18.4)  | 37.7        | 3458 (11.6)  | 43.3        | 581 (22.1)  | 52.2        | 401 (19.6)  | 41.4       |
| Moderate                     | 168400 (20.0) | 42.1        | 83368 (21.8)  | 42.9        | 46520 (20.4)  | 42.9        | 25731 (15.9)  | 38.7       | 7345 (19.7)  | 40.4        | 4421 (14.8)  | 40.8        | 576 (21.9)  | 46.4        | 439 (21.5)  | 46.5       |
| High                         | 155727 (18.5) | 42.1        | 86755 (22.7)  | 42.6        | 35869 (15.7)  | 43.1        | 19607 (12.1)  | 39.3       | 6734 (18.1)  | 40.0        | 5771 (19.3)  | 40.0        | 620 (23.6)  | 48.1        | 371 (18.2)  | 39.1       |
| Very High                    | 170735 (20.2) | 40.9        | 105078 (27.5) | 41.4        | 28912 (12.7)  | 40.8        | 13866 (8.6)   | 39.3       | 8632 (23.2)  | 40.6        | 13238 (44.4) | 38.5        | 605 (23.0)  | 41.0        | 404 (19.8)  | 44.3       |
| Payor                        |               |             |               |             |               |             |               |            |              |             |              |             |             |             |             |            |
| Government                   | 450979 (53.3) | 41.4        | 145285 (38.0) | 42.7        | 153354 (66.9) | 42.7        | 120147 (74.0) | 38.4       | 19304 (51.0) | 39.2        | 10130 (33.8) | 42.3        | 1514 (56.8) | 49.7        | 1245 (60.6) | 46.0       |
| Private                      | 363693 (43.0) | 41.4        | 225997 (59.1) | 42.1        | 65742 (28.7)  | 42.1        | 35828 (22.1)  | 38.3       | 15680 (41.4) | 38.7        | 18593 (62.1) | 38.1        | 1089 (40.9) | 44.1        | 764 (37.2)  | 43.6       |
| Other                        | 31858 (3.8)   | 47.6        | 11259 (2.9)   | 46.5        | 10078 (4.4)   | 50.9        | 6352 (3.9)    | 39.7       | 2851 (7.5)   | 56.3        | 1211 (4.0)   | 51.9        | 62 (2.3)    | 54.8        | 45 (2.2)    | 40.0       |
| PMCA                         |               |             |               |             |               |             |               |            |              |             |              |             |             |             |             |            |
| No CC                        | 346657 (41.0) | 36.0        | 152557 (39.9) | 37.3        | 102637 (44.8) | 37.8        | 57519 (35.4)  | 32.3       | 17527 (46.3) | 31.7        | 14542 (48.6) | 30.0        | 1101 (41.3) | 43.1        | 774 (37.7)  | 38.9       |
| CC                           | 200545 (23.7) | 33.0        | 90285 (23.6)  | 34.3        | 50827 (22.2)  | 34.6        | 44207 (27.2)  | 27.3       | 8280 (21.9)  | 34.9        | 5832 (19.5)  | 38.1        | 606 (22.7)  | 38.6        | 508 (24.7)  | 33.9       |
| Complex CC                   | 299328 (35.4) | 53.9        | 139699 (36.5) | 53.3        | 75710 (33.0)  | 55.4        | 60601 (37.3)  | 52.3       | 12028 (31.8) | 56.5        | 9560 (31.9)  | 56.7        | 958 (35.9)  | 58.2        | 772 (37.6)  | 58.4       |
| <b>H-RISK</b><br>(mean (SD)) | 2.52 (5.28)   | 4.37 (7.54) | 2.53 (5.16)   | 4.31 (7.31) | 2.5 (5.28)    | 4.27 (7.46) | 2.45 (5.35)   | 4.45 (7.9) | 2.8 (6.03)   | 5.16 (8.67) | 2.45 (5.38)  | 4.47 (7.81) | 2.97 (5.67) | 4.75 (7.49) | 2.96 (5.64) | 4.88 (7.7) |

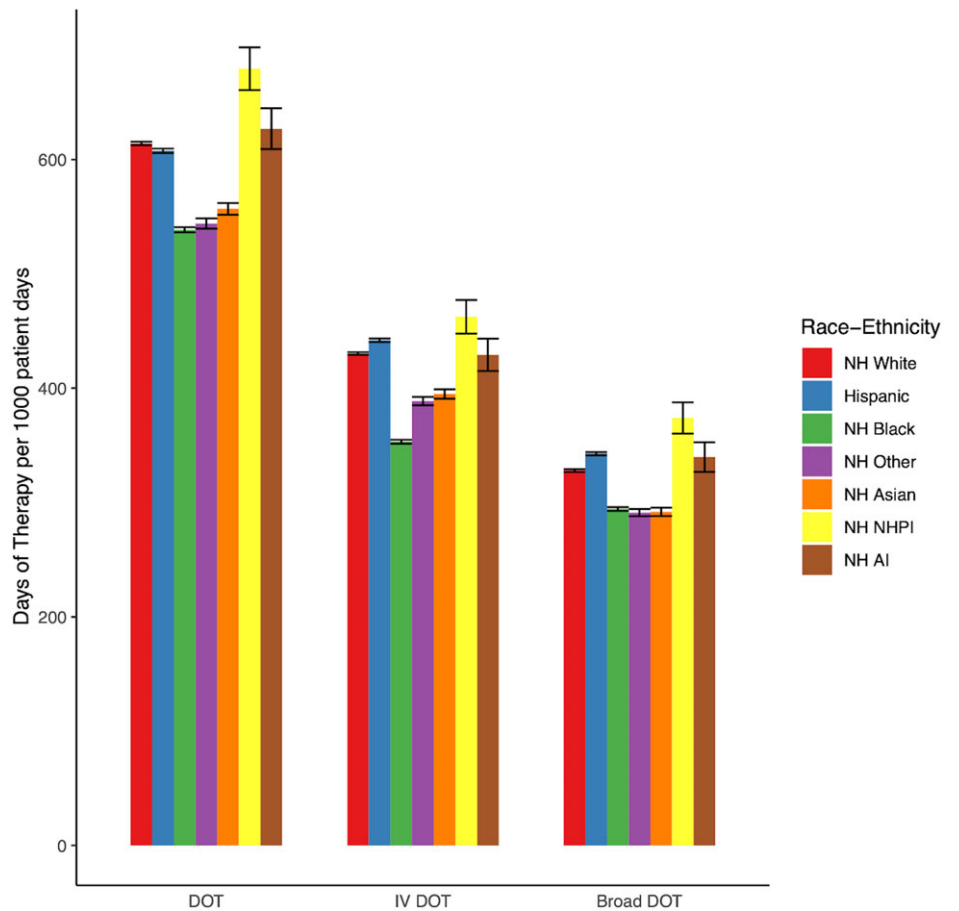
NH, Non-Hispanic; Child Opportunity Index (a neighborhood measure of resources and conditions for healthy development) was assigned using patient zip code; CC, chronic condition.

<sup>1</sup>Broad spectrum visit percentages are the proportion of antibiotic visits that included at least one order for a broad-spectrum antibiotic.

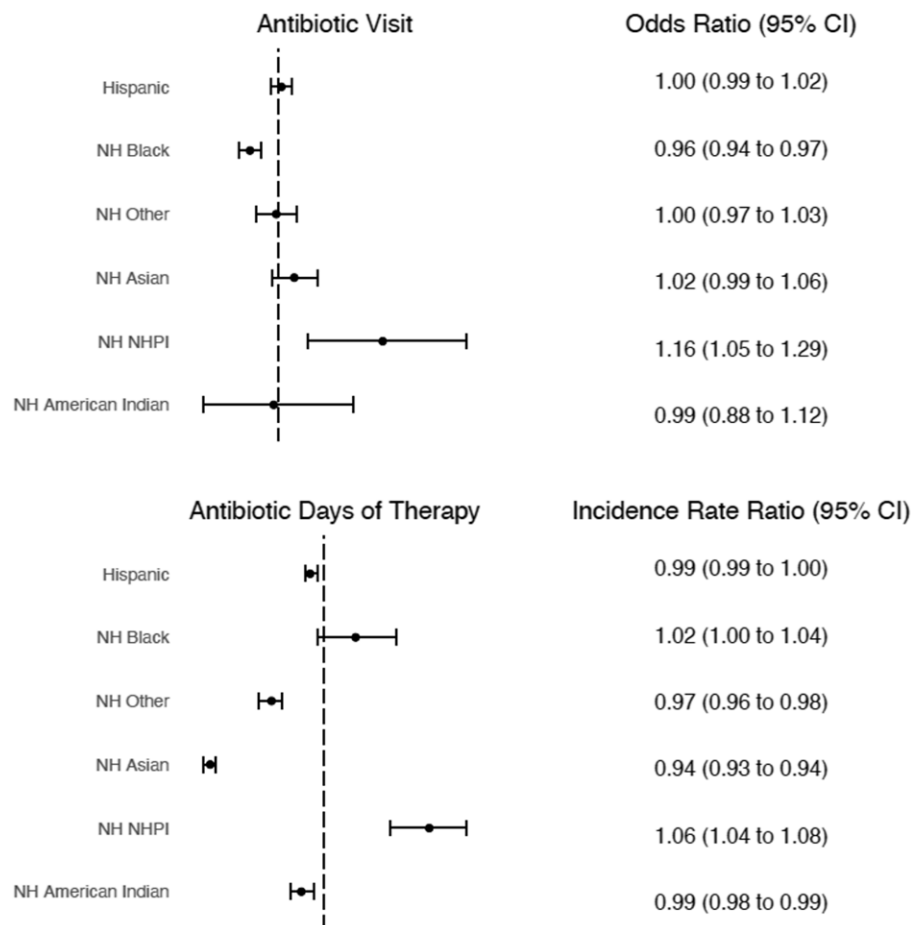
<sup>2</sup>Antibiotic frequency for diagnosis is the proportion of encounters with a given APR-DRG code received inpatient antibiotics. "Very high" refers to APR-DRG codes for which >75% of encounters were associated with an antibiotic. "High" refers to APR-DRG codes for which >50%–75% of encounters were associated with an antibiotic. "Intermediate" refers to APR-DRG codes for which >25%–50% of encounters were associated with an antibiotic. "Low" refers to APR-DRG codes for which 0%–25% of encounters were associated with an antibiotic.



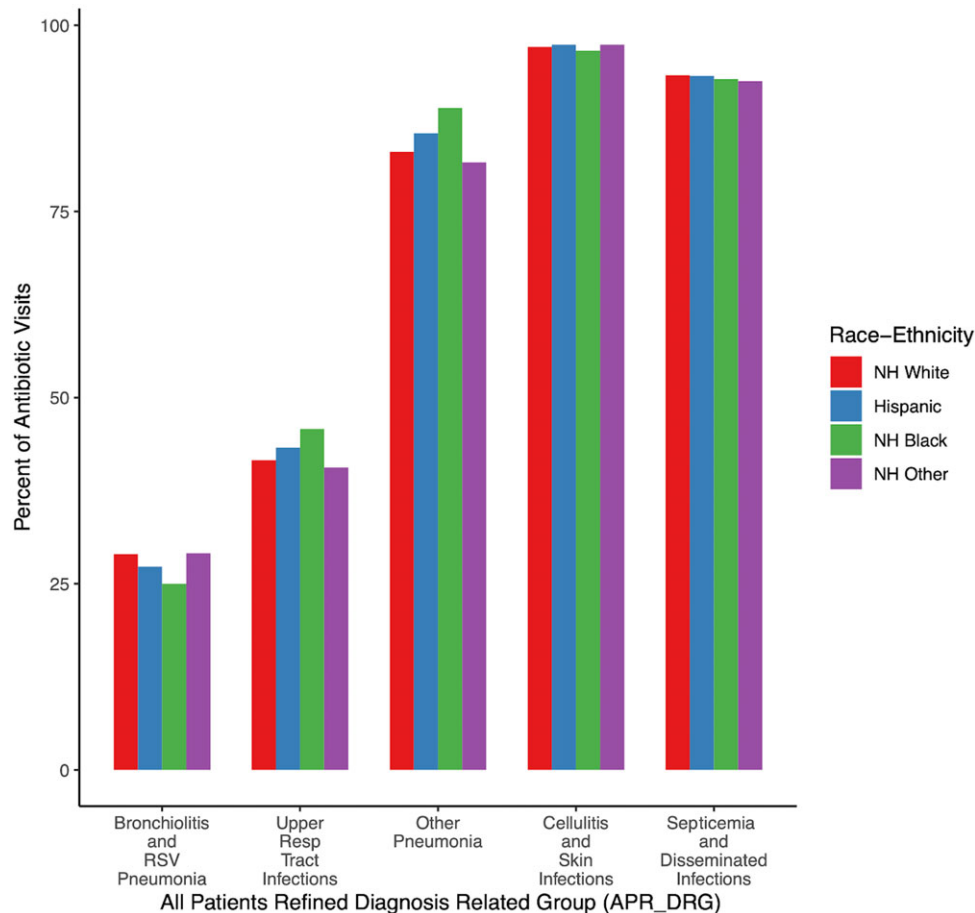
**Figure 1.** Hospitalization Resource Intensity Scores for Kids (H-RISK)-adjusted racial and ethnic variations by individual hospital. Adjusted by case mix index (using mean H-RISK for each racial-ethnic group within each hospital). Hospitals are ordered by percent of antibiotic visits for NH Black children (lowest to highest). The outlier hospital with <10% of visits including an antibiotic had >50% of visits in children ages <2 months.



**Figure 2.** Days of therapy by race-ethnicity. NH NHPI = Non-Hispanic Native Hawaiian/other Pacific Islander; NH AI = Non-Hispanic American Indian. Error bars represent standard error of the mean.



**Figure 3.** Mixed-effects multivariable regression models. Reference group = NH White. Models control for age, sex, RUCA, COI, antibiotic frequency, region, payor, PMCA, location, and H-RISK, and account for clustering by hospital. No collinearity was found among covariates.



**Figure 4.** Hospitalization Resource Intensity Scores for Kids-adjusted racial-ethnic stratification of antibiotic visits by diagnosis. The following categories were combined as “NH Other” due to small sample sizes: NH Other, NH Asian, NH Native Hawaiian/Pacific Islander, NH American Indian.

data that evaluated disparities in bronchiolitis management.<sup>23</sup> Studies in outpatient settings consistently report higher variability in antibiotic utilization by race and ethnicity for indications in which antibiotics are not always indicated.<sup>24–26</sup> Similarly, we report higher variability (though inconsistent directions of variability) in antibiotic visits for bronchiolitis and RSV pneumonia, infections of the upper respiratory tract, and other pneumonia. As in outpatient settings, these findings suggest that racial and ethnic differences were more pronounced for conditions in which antibiotic use was not always indicated. Stewardship programs seeking to ensure appropriate use or avoidance of antibiotics for specific diagnoses (e.g., RSV bronchiolitis) may directly influence pharmaco-equity through standardization of antibiotic policies. Furthermore, stewardship programs that track and report differences in inpatient prescribing by race and ethnicity may counteract the potential for unconscious biases to lead to differential antibiotic treatment plans for hospitalized children. Notably, an examination of diagnosis-specific antibiotic utilization and appropriateness was beyond the scope of our analysis; such analyses for key diseases in which antibiotics are often over- or under-utilized could reveal specific areas for equity-oriented stewardship interventions.

Over the past decade, stewardship programs have successfully reduced antibiotic utilization,<sup>30</sup> with the intent of decreasing unnecessary use and the subsequent development of antimicrobial resistance. However, without careful consideration of health equity principles, well-meaning efforts could increase disparities in treatment among vulnerable, racial and ethnic minority populations. In a recent review, Cichon and colleagues outline the following guidance, “Interventions to reimagine antimicrobial stewardship through a lens of equity”: (1) Improved access to antimicrobial stewardship; (2) Reduction in antimicrobial prescribing disparities; (3) Public health campaigns; and (4) Representation in decision-making.<sup>31</sup> Our findings confirm the opportunity for stewardship programs to stratify antibiotic use data by race and ethnicity as reported by the patient. In partnership with local health equity collaborators, hospital stewardship programs are well-positioned to address racial and ethnic inequities through their broad reach across service lines, collaborative efforts with quality improvement, and influential reporting to hospital administrators.

As a broad overview of patterns of inpatient antibiotic prescribing in pediatric settings, our analyses highlight questions that should be investigated in further studies. First, we did not aim to determine drivers of antibiotic utilization variations. It is possible that racial and ethnic differences in inpatient antibiotic utilization are pronounced for key diagnoses that may, but do not always, merit antibiotics (e.g., children admitted with asthma exacerbations in the setting of possible lower respiratory tract infections). Second, condition-specific studies are important to examine racial and ethnic differences in the appropriateness of antibiotic utilization. Alignment of specific antibiotics with specific diagnoses—and racial and ethnic differences in appropriate alignment—should be the focus of future diagnosis-specific investigation to identify differences amenable to antibiotic stewardship interventions. Third, future work could study differences among diagnoses for which there are national guidelines to determine differences in guideline adherence. Fourth, mixed-methods studies, with input from patients and families, could evaluate hypotheses about drivers and the impact of racial variations in antibiotic utilization.

Our study has several limitations. First, our data were obtained from an administrative and billing database and do not include

detailed clinical information about patient encounters. We were unable to assess the appropriateness of antibiotic utilization, the accuracy of the assigned APR-DRGs or association of the antibiotic with the assigned APR-DRG. Second, as a large database, there may be incomplete data and errors in billing coding. Moreover, reporting of race and ethnicity within the dataset is not consistent across included hospitals and does not precisely capture multi-racial and ethnic backgrounds. Third, PHIS only includes data from freestanding US children’s hospitals and is not nationally representative. Therefore, findings may not be generalizable. Fourth, we elected to present relative likelihood of receiving an antibiotic and results of regression models as odds ratios to facilitate comparison with other equity literature. Notably, odds ratios may overestimate relative risk when outcomes are relatively common; thus, the magnitude of effect estimates from our logistic regression analysis should be considered illustrative. Fifth, although we identified significant associations between race and ethnicity and antibiotic utilization, as a retrospective cross-sectional analysis, we are unable to assess causality in these relationships. Recognizing that race and ethnicity are social constructs, future studies should explore social determinants of health, provider bias, and other potential aspects of structural racism and discrimination as potential drivers of variation in antibiotic utilization. Finally, it is important to be cautious in interpreting findings for groups representing a smaller proportion of our sample (NH Asian, NH Native Hawaiian/Other Pacific Islander, and NH American Indian).

## Conclusion

Inpatient antibiotic utilization in US children’s hospitals differs by race and ethnicity and diagnosis. Inpatient antimicrobial stewardship programs could stratify local antibiotic use data by race and ethnicity. This type of stratification would shed further light on how differences in antibiotic utilization may contribute to inequities in hospitalization outcomes. Additional research is needed to examine differences by individual diagnoses, clinical outcomes, and drivers of variation.

**Supplementary material.** The supplementary material for this article can be found at <https://doi.org/10.1017/ice.2024.168>.

**Financial support.** None.

**Competing interests.** BAW, JF, KJ, and MJS received grant support from Merck, unrelated to the present study. MJS receives funding support from Pfizer for clinical trials. All other authors report no conflicts of interest relevant to this article to disclose.

## References

- Gerber JS, Prasad PA, Localio AR, *et al.* Racial differences in antibiotic prescribing by primary care pediatricians. *Pediatrics* 2013;131:677–684.
- Fleming-Dutra KE, Shapiro DJ, Hicks LA, Gerber JS, Hersh AL. Race, otitis media, and antibiotic selection. *Pediatrics* 2014;134:1059–1066.
- Goyal MK, Johnson TJ, Chamberlain JM, *et al.* Racial and ethnic differences in antibiotic use for viral illness in emergency departments. *Pediatrics*. 2017;140(2):e20170203.
- Wattles BA, Jawad KS, Feygin YF, *et al.* Quality of antibiotic prescribing to children through the coronavirus disease 2019 (COVID-19) pandemic. *Antimicrob Steward Healthc Epidemiol* 2022;2:e94.
- Wattles BA, Feygin Y, Jawad KS, *et al.* Use of the child opportunity index to examine racial variations in outpatient antibiotic prescribing to children. *J Pediatr* 2023;261:113572.



6. Nedved AC, Lee BR, Wirtz A, *et al*. Socioeconomic differences in antibiotic use for common infections in pediatric urgent-care centers—A quasi-experimental study. *Infect Control Hosp Epidemiol* 2023;44:2009–2016.
7. Wattles BA, Vidwan NK, Feygin Y, Jawad KS, Creel LM, Smith MJ. Antibiotic prescribing to Kentucky Medicaid children, 2012–2017: prescribing is higher in rural areas. *J Rural Health*. 2022;38:427–432.
8. Kilgore JT, Lanata MM, Willis JM, *et al*. Utilization of West Virginia pediatric Medicaid claims data to guide outpatient antimicrobial stewardship interventions. *J Pediatric Infect Dis Soc* 2022;11:172–176.
9. Yudell M, Roberts D, DeSalle R, Tishkoff S. Science and society. Taking race out of human genetics. *Science* 2016;351:564–565.
10. Gerber JS, Newland JG, Coffin SE, *et al*. Variability in antibiotic use at children's hospitals. *Pediatrics* 2010;126:1067–1073.
11. Griffith HG, Dantuluri K, Thurm C, *et al*. Considerable variability in antibiotic use among US children's hospitals in 2017–2018. *Infect Control Hosp Epidemiol* 2020;41:571–578.
12. Kim C, Kabbani S, Dube WC, *et al*. Health equity and antibiotic prescribing in the United States: a systematic scoping review. *Open Forum Infect Dis* 2023;10:ofad440.
13. Wurcel AG, Essien UR, Ortiz C, *et al*. Variation by race in antibiotics prescribed for hospitalized patients with skin and soft tissue infections. *JAMA Netw Open* 2021;4:e2140798.
14. Essien UR, Dusetzina SB, Gellad WF. A policy prescription for reducing health disparities—achieving pharmaco-equity. *JAMA* 2021;326:1793–1794.
15. Hales CM, Kit BK, Gu Q, Ogden CL. Trends in prescription medication use among children and adolescents—United States, 1999–2014. *JAMA* 2018;319:2009.
16. Rural-Urban Continuum Codes. Economic Research Service. <https://www.ers.usda.gov/data-products/rural-urban-continuum-codes/>. Accessed October 5, 2023.
17. Acevedo-Garcia D, Noelke C, McArdle N, *et al*. Racial and ethnic inequities in children's neighborhoods: evidence from the new child opportunity index 2.0. *Health Aff (Millwood)* 2020;39:1693–1701.
18. Simon TD, Cawthon ML, Stanford S, *et al*. Pediatric medical complexity algorithm: a new method to stratify children by medical complexity. *Pediatrics* 2014;133:e1647–54.
19. Richardson T, Rodean J, Harris M, Berry J, Gay JC, Hall M. Development of hospitalization resource intensity scores for kids (H-RISK) and comparison across pediatric populations. *J Hosp Med* 2018;13:602–608.
20. Keren R, Luan X, Localio R, *et al*. Prioritization of comparative effectiveness research topics in hospital pediatrics. *Arch Pediatr Adolesc Med* 2012;166:1155–1164.
21. Gerber JS, Hersh AL, Kronman MP, Newland JG, Ross RK, Metjian TA. Development and application of an antibiotic spectrum index for benchmarking antibiotic selection patterns across hospitals. *Infect Control Hosp Epidemiol* 2017;38:993–997.
22. National Institute on Minority Health and Health Disparities (NIMHD). NIMHD Minority Health and Health Disparities Research Framework. Published 2022. <https://nimhd.nih.gov/about/overview/research-framework/>. Accessed May 31, 2023.
23. Honcoop AC, Poitevien P, Kerns E, Alverson B, McCulloh RJ. Racial and ethnic disparities in bronchiolitis management in freestanding children's hospitals. *Acad Emerg Med* 2021;28:1043–1050.
24. Fleming-Dutra KE, Hersh AL, Shapiro DJ, *et al*. Prevalence of inappropriate antibiotic prescriptions among US ambulatory care visits, 2010–2011. *Obstet Gynecol Surv* 2016;71:509–510.
25. Wattles BA, Jawad KS, Feygin Y, *et al*. Inappropriate outpatient antibiotic use in children insured by Kentucky Medicaid. *Infect Control Hosp Epidemiol* 2022;43:582–588.
26. El Feghaly RE, Herigon JC, Kronman MP, *et al*. Benchmarking of outpatient pediatric antibiotic prescribing: results of a multicenter collaborative. *J Pediatric Infect Dis Soc* 2023;12:364–371.
27. Mitchell HK, Reddy A, Montoya-Williams D, Harhay M, Fowler JC, Yehya N. Hospital outcomes for children with severe sepsis in the USA by race or ethnicity and insurance status: a population-based, retrospective cohort study. *Lancet Child Adolesc Health* 2021;5:103–112.
28. Moorthy GS, Young RR, Smith MJ, White MJ, Hong H, Kelly MS. Racial inequities in sepsis mortality among children in the United States. *Pediatr Infect Dis J* 2023;42:361–367.
29. Parente VM, Reid HW, Robles J, *et al*. Racial and ethnic differences in communication quality during family-centered rounds. *Pediatrics* 2022;150(6):e2021055227.
30. Zay Ya K, Win PTN, Bielicki J, Lambiris M, Fink G. Association between antimicrobial stewardship programs and antibiotic use globally: A systematic review and meta-analysis. *JAMA Netw Open* 2023;6:e2253806.
31. Cichon CJ, Green EC, Hilker E, Marcelin JR. Inclusion, diversity, access, and equity in antimicrobial stewardship: where we are and where we are headed. *Curr Opin Infect Dis* 2023;36:281–287.