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Original Contribution

Predictors for under-prescribing antibiotics in children with respiratory infections requiring antibiotics☆,☆☆,★

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ABSTRACT

Background/objective: Previous studies showed variability in the use of diagnostic and therapeutic resources for children with febrile acute respiratory tract infections (ARTI), including antibiotics. Unnecessary antibiotic use has important public and individual health outcomes, but missed antibiotic prescribing also has important consequences. We sought to determine factors associated with antibiotic prescribing in pediatric ARTI, specifically those with pneumonia.
Methods: We assessed national trends in the evaluation and treatment of ARTI for pediatric emergency department (ED) patients by analyzing the National Hospital Ambulatory Medical Care Survey from 2002 to 2013. We identified ED patients aged ≤18 with a reason for visit of ARTI, and created 4 diagnostic categories: pneumonia, ARTI where antibiotics are typically indicated, ARTI where antibiotics are typically not indicated, and "other" diagnoses. Our primary outcome was factors associated with the administration or prescription of antibiotics. A multivariate logistic regression model was fit to identify risk factors for underuse of antibiotics when they were indicated.
Results: We analyzed 6461 visits, of which 10.2% of the population had a final diagnosis of pneumonia and 86% received antibiotics. 41.5% of patients were diagnosed with an ARTI requiring antibiotics, of which 53.8% received antibiotics. 26.6% were diagnosed with ARTI not requiring antibiotics, of which 36.0% received antibiotics. Black race was a predictor for the underuse of antibiotics in ARTIs that require antibiotics (OR: 0.72; 95% CI: 0.58–0.90).
Conclusions: For pediatric patients presenting to the ED with pneumonia and ARTI requiring antibiotics, we found that black race was an independent predictor of antibiotic underuse.

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1. Introduction

1.1. Background

Acute respiratory tract infections (ARTIs) represent the most common presentation and reason for admission in acute pediatric illness evaluated in ambulatory settings in the United States (US) [1,2]. It is difficult to distinguish viral versus bacterial ARTI because cough and fever are nonspecific symptoms that occur commonly in both diagnoses [3]. Diagnostic testing, including laboratory testing and chest radiography, have shown inadequate accuracy in distinguishing bacterial from a viral infection [4,5]. As a result, ARTIs account for >70% of antibiotics prescriptions in ambulatory pediatric patients [6], even though the majority are from viral infections [7,8]. Given the high volume of patients with ARTIs presenting to ambulatory centers, and the wide variability in physician practice styles [4,9], ARTIs provide an exceptional opportunity to examine factors associated with antibiotic treatment.

1.2. Significance

Antibiotics are the most frequently prescribed medications to children [10]. Antibiotic prescribing is a modifiable behavior that is influenced by factors related to the patient, hospital, and clinical presentation [11]. Previous literature has shown unnecessary use of broad-spectrum antibiotic prescribing for pediatric ARTI [6,12]. National organizations, such as the Center for Disease Control, the American

Abbreviations: ARTI, acute respiratory tract infection; CAP, community acquired pneumonia; CBC, complete blood count; CDC, Centers for Disease Control; CI, confidence interval; CXR, chest radiography; ED, emergency department; ICD-9-CM, International Classification of Diseases, 9th Revision, Clinical Modification; MSA, metropolitan statistical area; NHAMCS, National Hospital Ambulatory Medical Care Survey; OR, odds ratio; US, United States.

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Academy of Pediatrics and the Infectious Diseases Society of America, have made an effort to decrease the use of unnecessary antibiotics in patients with acute respiratory infections in order to reduce avoidable drug related adverse events, antibiotic resistance, and excess medical costs [3,6,8].

Yet, prior national surveys have also shown that 14–28% of children with an antibiotic-requiring ARTI were not given antibiotics [6,12]. Missed treatment of antibiotic-requiring diagnoses can result in additional medical care and progression of illness to serious sequelae [13, 14]. Thus, it appears that healthcare providers may both over- and under-prescribe antibiotics for children with ARTIs, such as pneumonia. Previous literature has evaluated patient, clinician, and community characteristics to determine associations with over-prescribing patterns with patients suggestive of pneumonia [15-17]. We wished to understand the extent and factors associated with the under-prescribing of antibiotics in the emergency department (ED).

Community acquired pneumonia (CAP) is a leading diagnosis requiring hospitalization among children in the United States, [18,19] representing approximately half of all pediatric hospitalizations. CAP is a serious pediatric infection and causes significant complications such as empyema, respiratory distress, and sepsis [19]. Our goal was to simulate the experience of the patient with suspected pneumonia, those patients with fever and cough, and understand the care that they received in US emergency departments (EDs), beginning with the reason for visit, through their evaluation, diagnosis, and disposition.

Much of our current literature body has sought to identify a patient population that does not require antibiotics, however, we sought to assemble a cohort of ARTI patients that had the potential for serious bacterial illness if antibiotic treatment was missed. CAP represents a patient population in which missed antibiotics is a serious concern.

1.3. Goals

Our objective was to conduct an analysis of pediatric patients with febrile ARTI, an area where there is known physician practice variation in US EDs [4,9]. We sought to understand the rate of antibiotic use for pediatric patients with ARTI requiring antibiotics and those diagnoses that did not. Likewise, we sought to characterize patient and hospital factors associated with antibiotic use in pediatric ARTI.

2. Methods

2.1. Study design

We performed a cross-sectional, secondary analysis of publically available and de-identified data from the National Hospital Ambulatory Medical Care Survey (NHAMCS) for years 2002 to 2013. The NHAMCS is a national probability sample of US ED and outpatient visits conducted annually by the Centers for Disease Control and Prevention's National Center for Health Statistics (CDC/NCHS). Detailed information about the NHAMCS methodology is available through the CDC/NCHS [20]; importantly, their multistage sample approach provides nationally representative estimates of ED visits and relevant information on patient and hospital characteristics, including reasons for visits. Our institutional review board designated this study as exempt from review; NHAMCS itself has been approved by the NCHS Research Ethics Review Board.

2.2. Selection of participants

We defined a pediatric febrile ARTI case as all pediatric (≤18 years) ED visits where any of the three patient "reasons for visit" included at least one respiratory complaint and either a complaint of fever or had a documented fever in the triage vital signs. The NHAMCS data abstraction form includes three patient "reason for visit" fields, coded based on a standardized sourcebook (the *Reason for Visit Classification for Ambulatory Care*) used in NCHS studies [20]. Respiratory reasons for visit included: cough, abnormalities of sputum, hemoptysis, shortness of breath, labored breathing, dyspnea, or breathing problems. Fever reasons for visit included: chills, fever, or feeling hot and/or cold. We additionally included any child with a triage temperature ≥100.4 °F. We excluded any child with a diagnosis of an underlying congenital, mental/developmental, or otherwise severe chronic medical condition as has been described previously [21,22]. For details of our coding scheme of reason for visit from within NHAMCS, please see Appendix Table A.1.

2.3. Creation of 4 diagnostic categories

We created subgroups using *International Classification of Diseases, 9th Revision, Clinical Modification* (ICD-9-CM) diagnosis based on previously published schemes [6,23]. Our coding scheme for ICD-9-CM codes is also available in Appendix Table A.1. The four subgroups included bacterial pneumonia [24], ARTI requiring antibiotics (e.g., otitis media, acute sinusitis, pharyngitis), ARTI not requiring antibiotics (e.g., nasopharyngitis, bronchitis, viral pneumonia, influenza), and other (e.g., asthma, allergy, chronic sinusitis, chronic bronchitis) (Appendix Fig. A.1). The creation of subgroups is based on prior research [6] and intended to identify those patients in whom antibiotics are typically indicated (pneumonia and ARTI requiring antibiotics) and those patients in who antibiotics are typically not indicated (ARTI not requiring antibiotics and other). Because NHAMCS collects up to three ICD-9-CM codes per visit, if a child had more than one ICD-9-CM that fell into more than one diagnostic category, we coded the diagnostic category variable according to the following hierarchy: 1) pneumonia, 2) ARTI with antibiotics, 3) ARTI without antibiotics, followed by 4) other diagnoses. For example, if "pneumonia, organism NOS" was entered as a diagnosis in one of the three ICD-9-CM diagnostic codes, the patient was categorized into the pneumonia sub-category.

2.4. Data collection

We collected the following data for each child: demographics (age, sex, race/ethnicity, and insurance status), plain X-ray use, complete blood count (CBC) testing, antibiotic use, as well as ED characteristics (pediatric vs. non-pediatric and academic vs. nonacademic), geographic location (US region and urban area), and hospital admission. We combined patients transferred to another facility with those who were hospitalized as we assumed that this was to receive a higher level of care or more specialized care (e.g., further observation, consultation with a pediatrician, obtaining pediatric-specific imaging, or for hospitalization). Age categories were designated as younger than 1 year, 1 to 5 years, 6 to 10 years, and 11–18 years. Urban areas were defined according to the US Census Bureau's metropolitan statistical area (MSA) designation. Pediatric EDs were defined as 50% or more of visits by patients under age 21 years, and academic EDs as facilities in which 25% or more patients were evaluated by a resident physician [25]. Our primary outcome was administration or prescription of antibiotics. We used the Multum Lexicon coding within NHAMCS to identify medications that were antibiotics [12].

2.5. Data analysis

We reported survey-weighted proportions and 95% confidence intervals (CIs) of patient and ED characteristics, both for the entire cohort, and stratified by diagnostic category. A multivariable logistic regression model was then used to estimate adjusted odds ratios (ORs) and associated 95% CIs for factors associated with antibiotic use. Covariates included age category, sex, race/ethnicity, insurance status, ED characteristics, triage acuity, and diagnostic category. Our goal was to isolate the effects of demographic and clinical characteristics and not to establish a parsimonious prediction model, so we specified that all a prior defined study variables remain in the model regardless of statistical significance. We conducted a sensitivity analysis by constructing a second multivariable logistic regression model restricted to the diagnostic categories in which antibiotics are indicated: pneumonia and ARTI requiring antibiotics. Statistical analysis was performed using Stata 13 (StataCorp, College Station, TX), and to account for the complex sampling design, we used the *svy* command and the NCHS-assigned patient weights according to NHAMCS specifications to produce national estimates.

3. Results

3.1. Characteristics of the study population

During the 12 survey years (2002 to 2013), there were 100,728 ED visits by children 18 years old or younger captured in NHAMCS, representing an estimated 366,201,824 visits in the United States. When accounting for the survey methodology, febrile ARTI visits accounted for 6.6% (95% CI: 6.2–6.9%) of these pediatric visits, excluding those with chronic illness and conditions. Using survey weights and averaging over our study period, we estimated an average of 2,000,978 febrile ARTI visits were made annually to US EDs. In our analysis, the majority of patients were between the ages of 1–5 years old, 56.0% (95% CI: 54.9–58.0%), insured via Medicaid 58.3% (95% CI: 54.5–59.5%), male 53.6% (95% CI: 52.6–55.6%), and evaluated in an urban ED (MSA) 88.0% (95% CI, 77.8–89.8%), (Table 1). Of patients with febrile respiratory illness who presented to the ED, approximately half (51.7%) were diagnosed with a condition requiring antibiotics, however 37.1% of these patients did not receive antibiotics.

Of the four diagnostic categories, ARTI requiring antibiotics was the largest group, followed by ARTI not requiring antibiotics, other, and pneumonia (Table 1). Overall, the patient and ED characteristics were similar across each of the diagnostic subcategories (Table 2). Of the four sub-cohorts, 10.2% of the population had a final diagnosis of pneumonia, of which 85.6% received antibiotics. 41.5% of patients were diagnosed with ARTI requiring antibiotics, of which 53.8% received antibiotics. 26.6% were diagnosed with ARTI not requiring antibiotics, of which 36.0% received antibiotics. The most common diagnosis in the pneumonia subcategory was "pneumonia, organism NOS" of which 86.0% received antibiotics (Appendix Table A.2). In the ARTI requiring antibiotics subcategory, the two most common diagnoses were "acute URI, NOS" and "otitis media, NOS" of which 26.0% and 88.4% received antibiotics respectively.

3.2. Evaluation and treatment

The evaluation and treatment of pediatric patients with febrile ARTIs is described at the bottom of Table 2. When compared to the ARTI requiring antibiotics, ARTI not requiring antibiotics, and other diagnoses, those diagnosed with pneumonia were significantly more likely to have a fever, CBC, chest radiography (CXR), antibiotic use, and hospitalization. The evaluation of ARTI requiring antibiotics was similar to the other subcategories. Of those diagnosed with pneumonia, 85.6% were given antibiotics, as compared to 53.8% diagnosed with an ARTI requiring antibiotics. Thus, 14.4% diagnosed with pneumonia and 46.2% diagnosed with ARTI requiring antibiotics did not receive antibiotics. Also of note, a substantial minority of patients in the ARTI not requiring antibiotics category actually received antibiotics.

Table 1
Cohort demographics of a nationally representative sample of pediatric patients presenting to the ED for fever and cough, 2002–2013.

	Unweighted number of observations (n = 6461)	Weighted % (95% CI)
Patient characteristics		
Age category (years)		
<1	1341	20.8 (18.6–21.5)
1–5	3620	56.0 (54.9–58.0)
6–10	906	14.0 (13.2–15.4)
11–18	594	9.2 (8.2–10.6)
Sex		
Female	2998	46.4 (44.4–47.4)
Male	3463	53.6 (52.6–55.6)
Race/ethnicity		
White/non-Hispanic	2532	39.7 (38.3–45.7)
Black/non-Hispanic	1525	23.9 (20.0–26.4)
Hispanic	1938	30.4 (26.5–33.9)
Other	391	6.1 (3.9–6.2)
Insurance status		
Private	1764	27.8 (26.4–31.0)
Medicare	69	1.1 (0.8–1.7)
Medicaid	3694	58.3 (54.5–59.5)
Self-pay/none	493	7.8 (7.2–9.4)
Other/unknown	320	5.1 (3.7–6.5)
Hospital characteristics		
ED traits		
Academic	587	9.1 (5.2–9.0)
Pediatric focused	676	10.5 (6.2–10.8)
Region		
Northeast	1378	21.3 (11.8–17.6)
Midwest	1249	19.3 (13.6–22.0)
South	2388	37.0 (39.2–52.2)
West	1446	22.4 (17.5–28.3)
Urban		
MSA	5329	88.0 (77.8–89.8)
Clinical characteristics		
Triage acuity		
Immediate/emergent	607	10.8 (8.7–12.0)
Urgent	2102	37.4 (33.6–39.3)
Semi-urgent	1571	28.0 (26.7–33.2)
Non-urgent	546	9.7 (8.7–13.5)
Unknown/no-triage	795	14.1 (10.4–15.1)
Symptoms and management		
Fever	3766	59.4 (54.4–59.0)
CBC obtained	1010	15.6 (13.2–15.8)
X-ray obtained	2344	36.3 (33.2–38.1)
Antibiotics prescribed	2918	45.2 (43.7–47.8)
Admission/transfer	335	5.3 (4.1–5.8)
Diagnostic categories		
Pneumonia	657	10.2 (8.6–10.7)
ARTI requiring antibiotics	2683	41.5 (37.8–42.7)
ARTI not requiring antibiotics	1716	26.6 (26.1–29.8)
Other	1405	21.8 (20.5–24.0)

3.3. Predictors of underuse of antibiotics

The multivariate logistic regression model (Table 3) indicated that there were patient and hospital characteristics, along with diagnostic subcategories, that were associated with decreased antibiotic use among children presenting with EDs with ARTI. Children aged 1–5 years had higher rates of antibiotic prescribing. Black race, children evaluated in a pediatric-focused ED, and those seen in the Northeast were less likely to receive antibiotics. Age, gender, insurance status, urban centers and triage acuity were not associated with antibiotic prescribing. Children diagnosed with pneumonia or an ARTI requiring antibiotics had higher rates of antibiotic prescription; the pneumonia subcategory had the strongest association (OR: 9.97; 95% CI: 6.68–14.88). Black race was associated with decreased use (OR: 0.72; 95% CI: 0.58–0.90) independent of other variables in the

Table 2
Univariate associations of clinical and outcome variables in sub-cohorts of ARTI, n = 6461.

	Pneumonia cohort	ARTI requiring antibiotics cohort	ARTI not requiring antibiotics cohort	Other
Patient characteristics				
Age category (years)				
<1	17.4 (13.8–21.9)	21.6 (19.2–24.2)	19.1 (16.7–21.8)	19.2 (16.5–22.3)
1–5	62.4 (57.4–67.2)	56.3 (53.9–58.6)	55.6 (52.5–58.6)	55.1 (51.8–58.5)
6–10	10.3 (7.9–13.3)	13.0 (11.5–14.6)	16.0 (13.7–18.5)	16.2 (13.9–18.8)
11–18	9.9 (7.1–13.6)	9.1 (7.4–11.2)	9.3 (7.6–11.4)	9.4 (7.7–11.5)
Sex				
Female	44.0 (38.8–49.4)	44.6 (42.1–47.0)	47.6 (44.4–50.7)	47.1 (43.6–50.6)
Male	56.0 (50.6–61.2)	55.4 (53.0–57.9)	52.4 (49.3–55.6)	52.9 (49.4–56.4)
Race/ethnicity				
White/non-Hispanic	40.7 (35.0–46.7)	44.7 (40.1–49.4)	42.1 (37.4–46.9)	37.4 (32.8–42.3)
Black/non-Hispanic	20.7 (15.6–27.0)	21.9 (19.0–25.1)	23.6 (19.4–28.3)	25.5 (21.4–30.1)
Hispanic	33.2 (27.6–39.2)	29.5 (25.2–34.2)	28.6 (24.5–33.2)	31.6 (26.8–36.8)
Other	5.4 (3.4–8.4)	3.9 (2.9–5.4)	5.7 (4.2–7.6)	5.5 (4.1–7.4)
Insurance status				
Private	32.3 (27.2–37.9)	27.4 (24.6–30.3)	31.0 (27.0–35.3)	26.2 (22.2–30.7)
Medicare	1.9 (0.6–6.3)	1.0 (0.5–1.7)	1.1 (0.6–2.1)	1.3 (0.7–2.4)
Medicaid	53.5 (47.9–59.1)	57.6 (54.6–60.6)	57.6 (53.4–61.7)	56.7 (51.8–61.4)
Self-pay/none	7.6 (5.0–11.3)	9.1 (7.3–11.3)	6.9 (5.5–8.7)	8.6 (6.8–10.8)
Other/unknown	4.7 (3.0–7.2)	4.9 (3.7–6.4)	3.3 (2.3–4.9)	7.2 (3.9–12.6)
Hospital characteristics				
ED traits				
Academic	7.9 (5.3–11.6)	7.7 (5.9–9.9)	4.0 (2.5–6.4)	8.6 (5.6–12.9)
Pediatric focused	9.3 (6.3–13.7)	10.7 (7.8–14.6)	3.4 (2.2–5.0)	9.2 (6.7–12.5)
Region				
Northeast	18.0 (13.2–24.0)	15.9 (12.9–19.6)	11.7 (8.9–15.0)	14.0 (10.9–17.9)
Midwest	16.4 (12.1–21.7)	17.8 (13.9–22.5)	17.0 (12.8–22.2)	17.7 (12.6–24.4)
South	38.1 (30.7–46.0)	45.8 (38.6–53.1)	47.4 (40.1–54.8)	46.4 (38.9–54.0)
West	27.6 (20.6–36.0)	20.5 (16.0–26.0)	23.9 (17.9–31.2)	21.9 (16.1–29.0)
Urban				
MSA	86.6 (78.9–91.8)	83.3 (76.3–88.5)	83.2 (74.9–89.2)	88.4 (80.5–93.3)
Clinical characteristics				
Triage acuity				
Immediate/emergent	16.8 (12.9–21.7)	9.3 (7.6–11.3)	8.4 (56.0–11.6)	11.3 (8.9–14.2)
Urgent	44.2 (38.8–49.8)	33.8 (30.4–37.3)	36.6 (32.8–40.6)	37.8 (32.5–43.4)
Semi-urgent	21.2 (17.0–26.1)	30.9 (27.3–34.8)	34.2 (29.5–39.3)	26.6 (22.3–31.3)
Non-urgent	6.9 (4.4–10.8)	12.1 (9.0–16.1)	10.8 (8.1–14.2)	10.3 (7.7–13.6)
Unknown/no-triage	10.8 (7.9–14.5)	13.8 (11.1–17.1)	10.0 (7.7–13.0)	14.0 (9.9–19.4)
Symptoms and management				
Fever	70.9 (65.2–76.1)	55.6 (52.8–58.3)	53.9 (50.4–57.3)	55.9 (51.0–60.7)
CBC obtained	37.3 (31.6–43.4)	10.2 (8.6–12.0)	10.7 (8.8–13.1)	16.9 (14.5–20.0)
X-ray obtained	86.4 (81.5–90.2)	25.2 (22.4–28.1)	35.1 (31.5–38.8)	33.1 (29.4–37.1)
Antibiotics prescribed	85.6 (81.2–89.2)	53.8 (50.5–57.0)	36.0 (32.7–39.5)	26.2 (23.0–29.7)
Admission/transfer	22.4 (18.3–27.2)	2.2 (1.6–3.2)	1.9 (1.3–3.0)	5.8 (4.4–7.6)

Note: data are presented as survey weighted % (95% CI).

model. In a post-hoc analysis, we included only those diagnostic categories requiring antibiotics (pneumonia, ARTI requiring antibiotics), and black race remained a predictor of decreased antibiotic use (Appendix Table A.3). Hospital region also was a statistically significant predictor of underuse in those with pneumonia or ARTI requiring antibiotics.

4. Discussion

We used the NHAMCS survey to examine rates of antibiotic use in pediatric patients presenting to EDs with a presenting complaint of febrile ARTI. Between 1997 and 2007 there was an estimated 25 million ED visits a year by children younger than 18 years old [26]. Respiratory conditions are the most common cause for presentation and admission [27]. We identified predictors of antibiotic use in different diagnostic subgroups, those that should receive antibiotics, such as pneumonia and ARTIs requiring antibiotics, and those that did not require antibiotics (see Appendix Table A.1). Approximately 52% of children with ARTI required antibiotics, which is in contrast to previous pediatric ARTI literature that found the majority of patients had viral illness not requiring antibiotics [28]. We found that there was a substantial proportion of children diagnosed with pneumonia or ARTI requiring antibiotics that did not receive antibiotics (14.4% and 46.2%, respectively). It is likely that our study population differs from previous literature as it includes patients selected by presenting complaint instead of final diagnosis. By selecting a cohort of patients on the basis of presenting complaints (respiratory symptoms and fever), instead of final diagnosis, we were better able to evaluate physician behavior from a real-world perspective. Likewise, we chose to concentrate on reason for visit coding that focused on patients with lower respiratory symptoms to better characterize patients with the potential for pneumonia.

Fever and cough are two of the most common symptoms suggestive of pneumonia in pediatric patients presenting to EDs in the United States [29,30]. The majority of pediatric patients presenting with cough and/or fever have more benign conditions such as uncomplicated self-limiting ARTI. Because of the non-specific nature of fever and cough, only a small proportion (10%) of those children presenting with these complaints received a diagnosis of pneumonia, whereas the majority of the cohort was diagnosed with a variety of diagnoses, some of which required antibiotics. This mirrors the diagnostic uncertainty in clinical practice. Furthermore, we sought to examine patient and hospital-related variables related to antibiotics prescribing practices.

We found that black race is independently associated with failure to prescribe antibiotics in those diagnosed with pneumonia and ARTIs requiring antibiotics. In our multivariable model, black children were 30% less likely to receive antibiotics when they were indicated, which raises the possibility of a racial disparity. It is unclear why black patients did

Table 3
Proportions of factors and multivariate odds ratios for predictors of antibiotics use among children who present to the ED with fever and cough, 2002–2013.

	Receiving antibiotics % (95% CI)	Odds ratio[a] (95% CI)
Age category (years)		
<1	41.1 (37.8–44.4)	Ref
1–5	48.2 (45.5–50.9)	1.26 (1.07–1.48)
6–10	42.3 (38.2–46.5)	1.18 (0.93–1.50)
11–18	46.5 (41.2–51.9)	1.17 (0.97–1.51)
Sex		
Female	45.2 (42.9–47.7)	Ref
Male	46.2 (43.5–49.0)	0.96 (0.83–1.11)
Race/ethnicity		
White/non-Hispanic	49.1 (46.0–52.2)	Ref
Black/non-Hispanic	42.3 (38.6–46.1)	0.72 (0.58–0.90)
Hispanic	44.6 (41.4–47.8)	0.88 (0.73–1.06)
Other	39.1 (32.7–45.9)	0.84 (0.61–1.16)
Insurance status		
Private	44.4 (41.1–47.7)	Ref
Medicare	47.6 (32.4–63.3)	1.27 (0.57–2.84)
Medicaid	47.0 (44.4–50.0)	1.19 (0.99–1.42)
Self-pay/none	46.8 (41.2–52.4)	1.10 (0.81–1.50)
Other/unknown	42.7 (32.5–53.6)	0.96 (0.63–1.48)
ED traits		
Non-academic	46.0 (44.0–48.1)	Ref
Academic	42.4 (34.1–51.0)	0.92 (0.64–1.33)
Non-pediatric focused	46.1 (44.1–48.2)	Ref
Pediatric focused	41.9 (36.3–47.6)	0.74 (0.58–0.93)
Geographic location		
South	50.3 (47.0–53.6)	Ref
Northeast	36.9 (33.8–40.1)	0.46 (0.36–0.58)
Midwest	43.2 (38.0–48.5)	0.68 (0.52–0.89)
West	44.4 (40.9–48.0)	0.72 (0.54–0.95)
Urban location		
Non-MSA	55.9 (50.1–61.5)	Ref
MSA	44.0 (41.7–46.3)	1.40 (0.99–1.97)
Triage acuity		
Immediate/emergent	45.9 (39.7–52.2)	Ref
Urgent	48.7 (45.0–52.4)	1.21 (0.88–1.65)
Semi-urgent	45.2 (41.7–48.9)	1.02 (0.74–1.42)
Non-urgent	42.4 (37.0–48.1)	0.89 (0.60–1.32)
Unknown/no-triage	44.2 (38.2–50.4)	1.02 (0.70–1.49)
Diagnoses		
ARTI not requiring antibiotics	36.0 (32.7–39.5)	Ref
Pneumonia	85.6 (81.2–89.2)	9.97 (6.68–14.88)
ARTI requiring antibiotics	53.8 (50.5–57.0)	2.02 (1.62–2.53)
Other	26.2 (23.0–29.7)	0.58 (0.47–0.73)

[a] Multivariate odds ratios are adjusted for: age, sex, race/ethnicity, insurance status, triage acuity, hospital type, US region, and urban/rural distinction.

not receive antibiotics at the same rate as other races, but there is a growing body of evidence showing the association of race and variability in the use of diagnostic tests, appropriate treatment, and mortality [31]. Studies using the same national sampling data have reported lower rates of broad-spectrum antibiotics prescribing to black adults [32] and a comparable trend in black children [6]. One study found that black children were less likely to receive an antibiotic prescription, but also less likely to receive an ARTI diagnosis that justified antibiotic prescribing [33]. In contrast, our study showed less antibiotic prescribing for black children, but there were comparable proportions of those diagnoses requiring antibiotics across races. This suggests that differences in physician behavior and practice patterns exist for antibiotic treatment of febrile ARTI, including for those requiring antibiotics.

Given the association between diagnosis and antibiotic prescribing, it is unclear from our study whether the diagnosis drove antibiotic prescribing or, alternatively, whether the diagnosis of an ARTI was driven by the motive for an antibiotic prescription. Pediatric-specific providers may be more aware of diagnoses requiring and not requiring antibiotics, this may account for why pediatric-specific EDs had a significant decrease in the number of patients with ARTI not requiring antibiotics. Antimicrobial prescribing is subjected to a certain degree of diagnostic uncertainty and is influenced by many factors related to the physician, the patient and the environment [11]. We found that children of various ethnicities have similar rates of ARTI requiring antibiotics, but have different rates of antibiotic treatment. Gerber et al. [33] argued that the different rates in ARTI diagnoses justified were a physician's justification for differing antibiotic prescribing practices. For example, if there was an over-prescribing practice, then there would be an increased incidence of diagnoses requiring antibiotics.

Our study sought to determine variables associated with appropriate antibiotic use in pediatric ARTI. Our unique cohort of patients, which utilized reason for visit code instead of final diagnosis, allowed us to examine the proportion of those patients requiring and not requiring antibiotics. Previous studies evaluating the association of race in pediatric ARTI have suggested that final diagnosis for antibiotic treatment is adjusted to accommodate treatment rendered [34,35]. For example, investigators have shown that physicians are less likely to diagnose otitis media for black versus nonblack children [33,35]. Our study found that pediatric ARTI has similar proportions of diagnoses across all races, however the frequency of antibiotic treatment differs. This raises the question of whether the observation that, when diagnosed with an ARTI requiring antibiotics - why are black children undertreated.

Variations in prescribing may reflect a wide range of factors that may be related to but not limited to patient/parent/guardian preference and physician attitudes and local practice patterns. In one study, patient preference was the leading cause for inappropriate antibiotic prescribing [34], however we are unaware of similar data for under-prescribing antibiotics. Similarly, a physician's perception of a parent/guardian's expectation for antibiotic has also been shown to influence antibiotic prescribing patterns. Likewise, physician training, including specialty training, has been shown to have varying effect on antibiotic prescribing patterns [36]. In our study, we found that hospitals in the Northeast were less likely to provide antibiotics for all diagnoses, and even for pneumonia and ARTIs requiring antibiotics. Local and regional practice variation have been found in previous reports evaluating antibiotic prescribing patterns for children [37,38]. Future studies should further evaluate patient and physician factors leading to this disparity, and evaluate if such differences in care lead to variability in clinically relevant outcomes.

A number of limitations are inherent in the analysis of such large survey databases. Primarily, the fidelity of certain NHAMCS variables or measurements may preclude ideal analyses [39]. In this study, the main outcome – antibiotic use – is captured from one of several fields noted by an abstractor. Despite this, we feel that misclassification of the outcome is not likely to be differential, and prior studies have reported antibiotic use using the NHMCS survey [6,12]. Second, important outcome variables are difficult to ascertain in this cross-sectional analyses, particularly outcomes not measured during the healthcare encounter (complications from missed diagnoses, disease severity, need for ED revisit or hospitalization, post-discharge follow-up, previous antibiotic use, or mortality). For example, NHAMCS does not allow for tracking of patients across multiple visits. Thus, we cannot comment on the effect of patient characteristics such as race on clinical outcomes in those diagnosed with pneumonia or ARTI requiring antibiotics. Third, our classification construct may lead to misclassification bias as we are unable to abstract more than ICD-9-CM coding for an ARTI need for antibiotics. However, a similar construct has been used in prior literature [6]. Finally, we must rely on assumptions regarding the accuracy of the subgroup classifications (pneumonia, ARTI requiring antibiotics, ARTI not requiring antibiotics, and other). These subgroups have been used in previous literature [6], but they are subject to many of the same limitations of other ICD-9-CM outcomes, including coding error and resolution. Likewise, our subcategory ICD-9-CM hierarchy may lead to those with non-specific codes, such as fever or viral syndromes, in those sub-categories defined within a subcategory requiring antibiotics. For example, if a patient has an ICD-9-CM diagnosis of “viral infection, NOS” but also “pneumonia, organism NOS”, that patient would be categorized into the pneumonia subcategory. We believe our hierarchy in which any syndrome requiring antibiotics in one of three diagnostic categories should be “up categorized” to an antibiotics-requiring subcategory (see Appendix Table A.2). Therefore, we cannot confirm diagnosis or appropriateness of antibiotics prescribed.

5. Conclusions

In conclusion, ARTI visits and inappropriate antibiotic use for ARTI remain important problems in pediatric patients presenting to US EDs. Our findings suggest that there are racial disparities in antibiotic treatment in children with ARTI, even after adjustment for potential confounders. This study is hypothesis generating and more research is needed to understand why such disparities exist. This could help inform the design of interventions to address and eliminate these disparities and improve upon appropriate antibiotic use.

Appendix Table A.1
Diagnostic conditions used to classify ARTI subcategories.

Subcategory	ICD-9-CM codes	Description
Pneumonia	481–486	Pneumococcal pneumonia, other bacterial pneumonia, pneumonia due to other specified organism, pneumonia in infectious disease classified elsewhere, bronchopneumonia, organism unspecified, pneumonia, organism unspecified
ARTI requiring antibiotics	034, 381–383, 461–463, 475	Sinusitis, pharyngitis, tonsillitis, otitis media, mastoiditis, streptococcal sore throat, peritonsillar abscess
ARTI not requiring antibiotics	460, 464–466, 480, 487–488, 490	Nasopharyngitis, laryngitis/tracheitis, unspecified ARTI, bronchitis, bronchiolitis, viral pneumonia, influenza
Other	460–519 (excluding those codes above); 995.3	Includes chronic sinusitis, chronic bronchitis, asthma, allergy, other respiratory conditions

Appendix Table A.2
Proportion of antibiotics received by individual diagnosis in each diagnostic subcategory.

ICD-9 code	Diagnosis	Antibiotics received N (%)
Pneumonia		
486.0	Pneumonia, organism NOS	398/463 (86.0)
780.6	Fever	41/46 (89.1)
492.9	Bacterial pneumonia	18/19 (94.7)
ARTI requiring antibiotics		
465.9	Acute URI, NOS	199/765 (26.0)
382.9	Otitis media, NOS	572/647 (88.4)
079.99	Viral infection, NOS	38/344 (11.0)
ARTI not requiring antibiotics		
465.9	Acute URI NOS	153/511 (29.9)
490.0	Bronchitis NOS	190/264 (72.0)
780.6	Fever	98/256 (38.3)
Other		
780.6	Fever	146/455 (32.1)
079.99	Viral infection NOS	8/163 (4.9)
493.9	Asthma, unspecified	28/99 (28.3)

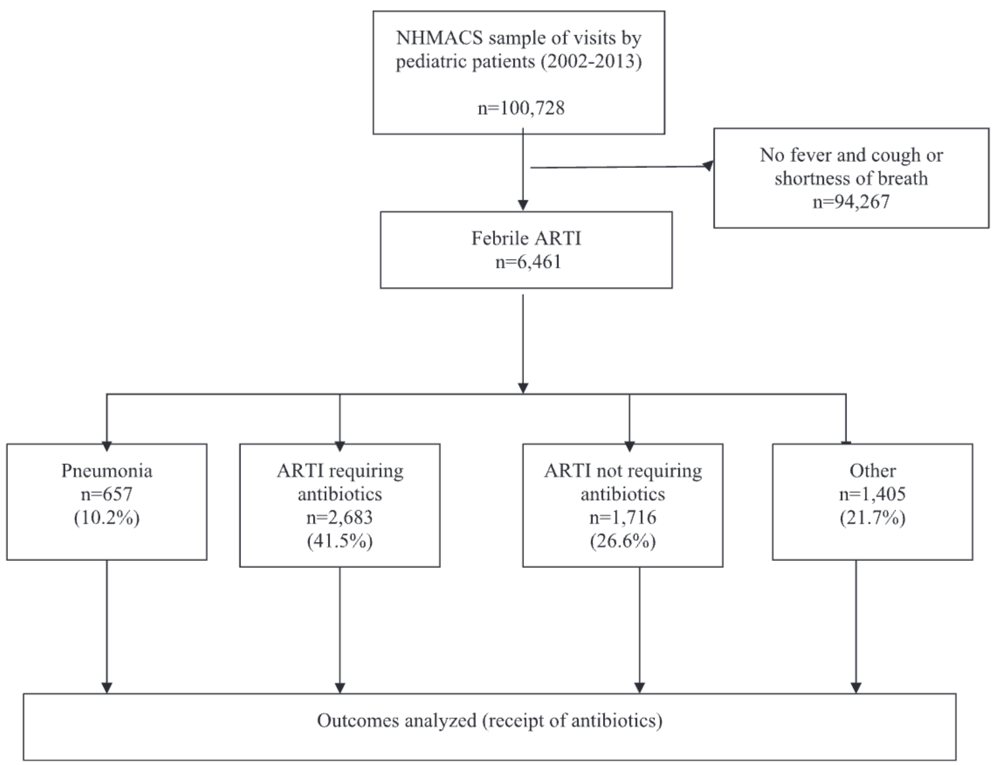
Appendix Table A.3
Odds ratios for predictors of antibiotics use among children who received a diagnosis of pneumonia or URI requiring antibiotics, 2002–2013.

	Adjusted odds ratio (95% CI)
Age category (years)	
<1	Ref
1–5	1.31 (1.04–1.67)
6–10	1.02 (0.74–1.40)
11–18	1.32 (0.91–1.92)
Sex	
Female	Ref
Male	0.92 (0.75–1.12)
Race/ethnicity	
White/non-Hispanic	Ref
Black/non-Hispanic	0.69 (0.52–0.92)
Hispanic	0.80 (0.64–1.00)
Other	0.90 (0.60–1.32)
Insurance status	
Private	Ref
Medicare	1.20 (0.44–3.33)
Medicaid	1.08 (0.85–1.37)
Self-pay/none	0.88 (0.59–1.30)
Other/unknown	0.99 (0.57–1.71)
ED traits	
Non-academic	Ref
Academic	0.92 (0.64–1.34)
Non-pediatric focused	Ref
Pediatric focused	0.71 (0.54–0.94)

(continued on next page)

Appendix Table A.3 (*continued*)

	Adjusted odds ratio (95% CI)
Geographic location	
South	Ref
Northeast	0.50 (0.37–0.66)
Midwest	0.73 (0.54–0.99)
West	0.82 (0.55–1.22)
Urban location	
Non-MSA	Ref
MSA	1.28 (0.88–1.87)
Triage acuity	
Immediate/emergent	Ref
Urgent	1.40 (0.97–2.02)
Semi-urgent	1.25 (0.86–1.82)
Non-urgent	1.06 (0.70–1.60)
Unknown/no-triage	1.02 (0.66–1.58)



Appendix Fig. A.1 Subject flow diagram.

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