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MAJOR ARTICLE

Parenteral Antibiotic Use Among Ambulatory Children in United States Children's Hospital Emergency Departments

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Background. Despite increasing recognition of the importance of optimal antibiotic selection and expansion of antimicrobial stewardship activities to ambulatory settings, few studies have examined the frequency of parenteral antibiotic use among ambulatory children. We assessed the prevalence and patterns of parenteral antibiotic administration among ambulatory children in pediatric emergency departments (EDs).

Methods. We conducted a cross-sectional assessment of parenteral antibiotic use among ambulatory children aged 0–18 years in 49 US children's hospital EDs in 2018. We assessed the prevalence rates of parenteral antibiotic use and stratified these by patient-, clinic-, and hospital-level characteristics. We also assessed the prevalence of use of specific antibiotics by age and diagnosis category. Among encounters associated with an infection diagnosis, we identified factors associated with parenteral antibiotic use using multivariable logistic regression.

Results. Among 3 452 011 ambulatory ED encounters in 2018, parenteral antibiotics were administered in 62 648 (1.8%). The highest proportion of parenteral antibiotic use occurred in the 15–18-year age group (3.3%) and among encounters in children with complex chronic conditions (8.9%) and with primary diagnoses of neoplasms (36%). Ceftriaxone was the most commonly administered parenteral antibiotic (61%). In multivariable analysis, several factors including age ≤2 months, White race, private insurance, complex chronic conditions, digestive and genitourinary system diseases, and encounters attributed to emergency medicine providers were significantly associated with higher odds of parenteral antibiotic use.

Conclusions. This study demonstrates substantial variability in the frequency of parenteral antibiotic administration by age and diagnosis in the ambulatory ED setting and highlights potential opportunities to target stewardship activities.

Keywords. ambulatory children; antibiotic use; emergency department; parenteral antibiotics; pediatric.

Infections are among the most common indications for emergency department (ED) visits in children, and antibiotics are commonly prescribed among the >28 million annual pediatric ED visits in the United States [1–4]. Respiratory illnesses account for more than two-thirds of antibiotic prescriptions in ambulatory children [5]. Yet, many of these prescriptions are not in accordance with national guidelines for management of these conditions [2]. Antibiotic use in health care settings is among the primary drivers of antibiotic resistance and is also associated with adverse drug events, such as allergic reactions, *Clostridioides difficile* infections, and increased health care costs [6, 7].

A study of US pediatric ED visits found that between 2009 and 2014, antibiotics were prescribed in 23% of encounters, and 32% of prescriptions were for conditions for which antibiotics are generally not indicated [3]. Compared with dedicated pediatric EDs, pediatric visits in nonpediatric EDs had a lower frequency of guideline-concordant prescribing for certain respiratory conditions [3]. These assessments largely focused on overall antibiotic prescribing, but few studies have distinguished the use of oral vs parenteral antibiotics. In contrast to oral antibiotics, guideline-concordant indications for use of parenteral (intravenous [IV] or intramuscular [IM]) antibiotic therapy in common infectious conditions among children and adolescents who do not require hospitalization are very few except in certain circumstances, such as use of IM penicillin G for group A streptococcal pharyngitis [8], use of IM ceftriaxone in children with otitis media who have failed oral antibiotics or experience recurrence of otitis media within 2 weeks of a prior treatment course [9], and use of ceftriaxone for uncomplicated gonococcal infections [10]. Third-generation cephalosporins, such as ceftriaxone, are broad-spectrum antibiotics and are frequently prescribed in pediatrics despite a lack of first-line indications [11]. Preserving the use of such agents to treat serious

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and resistant bacterial infections [12] and reducing unnecessary broad-spectrum and parenteral antibiotic use are key to optimizing treatment of infectious conditions and to minimizing the risk of antibiotic-associated adverse events and development of antibiotic resistance.

Despite increasing recognition of the importance of optimal antibiotic selection and expansion of antimicrobial stewardship activities to ambulatory settings, few studies have examined the prevalence of parenteral antibiotic use among children who are treated in the ED. Using data from a large administrative database of freestanding children's hospitals, we assessed the prevalence and patterns of parenteral antibiotic administration among children discharged from the ED and examined factors associated with this practice.

METHODS

Study Design and Data Source

We conducted an observational cross-sectional study of parenteral antibiotic use among children who were evaluated in and discharged from EDs in hospitals that participate in the Children's Hospital Association's Pediatric Health Information System (PHIS). We assessed the prevalence of parenteral antibiotic use, and we assessed factors associated with parenteral antibiotic use, including patient demographic and clinical characteristics, primary diagnosis category associated with each encounter, and encounter- and hospital-level characteristics.

Data for this study were obtained from PHIS, an administrative database that contains detailed ED, inpatient, ambulatory surgery, and observation encounter–level data from over 50 not-for-profit, tertiary care freestanding children's hospitals in the urban United States. PHIS data contain detailed information for each ED encounter, including patient demographic information, associated diagnoses, medications administered, procedures, and laboratory tests. Data are maintained by the Children's Hospital Association, participating hospitals, and Truven Health Analytics. Children are assigned unique study identifiers to allow for linking across encounters within a hospital while preserving the privacy of their personal information.

Ethics and Patient Consent Statement

This study of existing, deidentified patient data does not include factors necessitating patient consent and was considered exempt from further review by the Vanderbilt University Medical Center Institutional Review Board.

Study Population

We included any ED encounter in a PHIS-participating hospital from January 1, 2018, to December 31, 2018, in children 0 to 18 years of age who were discharged directly from the ED without being admitted under "observation" status. We identified ED encounters using the PHIS Clinical Transaction Classification (CTC) system, a proprietary system used by the PHIS to categorize hospital billing for clinical, pharmacy, and other services. We considered an ambulatory ED encounter to represent any encounter associated with an ED CTC code corresponding to any level of service (Supplementary Table 1) and associated with a discharge status of "emergency department," the PHIS designation indicating that the patient was evaluated and discharged from the ED. We also identified the specialty training of the attending provider of record for the encounter, as available.

Sociodemographic Information From Children

We characterized sociodemographic information of children associated with each ED encounter, including age, gender, race, insurance payor status, and the presence of at least 1 complex chronic condition (CCC), defined using a validated method for characterizing coded diagnosis-based pediatric complex chronic conditions, represented by 11 categories: neuromuscular, cardiovascular, respiratory, renal, gastrointestinal, hematologic or immunologic, metabolic, malignancy, genetic or other congenital defect conditions, premature, and neonatal [13].

Diagnostic Categories

For each encounter, we identified the primary diagnosis using International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM), diagnosis codes, and these were classified into 1 of 21 system-based groups (Supplementary Table 2). We further subclassified encounters associated with ICD-10-CM codes that are considered consistent with "infection diagnoses" as the primary diagnosis using Agency for Healthcare Research and Quality pediatric quality indicators [14, 15].

Parenteral Antibiotic Use

We defined parenteral antibiotic administration as the administration of an IV or IM antibiotic during an individual ED encounter using billing codes associated with each individual antibiotic. A comprehensive list of parenteral antibiotics included is shown in Supplementary Table 3.

Hospital-Level Assessments

Hospital-level variables of interest included geographic/census region of hospital (Northeast, South, Midwest, West), type of hospital (academic/teaching hospital or community/nonteaching hospital), insurance payor mix, ED patient volume (number of visits), and case mix index (CMI), a widely used surrogate for severity of illness and risk of mortality that represents the clinical complexity of the patient population of each individual hospital [16]. In PHIS, CMI is based on All Patients Redefined Diagnosis-Related Groups (APR-DRG) categories and severity levels and is calculated as the ratio of the average charge for encounters in a particular APR-DRG category/severity level combination to the average charge for all encounters included in the PHIS database.

Statistical Analysis

We reported the overall number of eligible ED encounters and the number and proportion of these encounters that resulted in administration of a parenteral antibiotic and stratified this information according to sociodemographic characteristics of patients including age, gender, race, insurance payor, and calendar month. We also reported the prevalence of parenteral antibiotic use overall for each clinical diagnosis group and ranked the most commonly administered parenteral antibiotics for each group. Among encounters associated with an ICD-10-CM "infection diagnosis" code [15], we identified factors associated with parenteral antibiotic use using multivariable logistic regression and accounted for clustering within hospitals using a random intercept for each hospital. Potential associated factors included age, gender, race, insurance payor, presence of a CCC, provider subspecialty, calendar month, diagnostic category, and transfer status from an outside facility. For each hospital, we reported CMI and calculated the number of ambulatory ED visits and proportion of ED visits with parenteral antibiotic use. At the hospital level, we examined the association of hospital CMI and ambulatory ED parenteral antibiotic use using Pearson's correlation.

RESULTS

Overview of Parenteral Antibiotic Use in the Study Population

Among 49 hospitals contributing complete data for the study period, 3 452 011 ambulatory ED encounters occurred among 2 417 609 individual children (Table 1). In 3 448 506 (99.9%) of these encounters, patients were evaluated in the ED and discharged on the same calendar day. Parenteral antibiotics were administered in 62 648 (1.8%) ambulatory ED encounters. In the 62 648 encounters associated with parenteral antibiotics, 66 056 parenteral antibiotic administrations occurred. The proportion of ED encounters associated with parenteral antibiotic use was highest among adolescents (3.3% 15–18-year age group). The proportion of encounters associated with parenteral antibiotic use was similar across racial categories, although it was lowest (1.6%) among Hispanic children. Among children with a CCC, the proportion of ambulatory ED encounters associated with parenteral antibiotic use was 8.9%. The proportion of encounters associated with parenteral antibiotics was higher among emergency medicine providers (2.0%), which included subspecialists in pediatric emergency medicine, compared with pediatrics (1.5%) or "other" (1.4%) types of providers. Among 630 480 encounters associated with an infection diagnosis code, 33 156 (5.3%) were associated with parenteral antibiotic use.

Preferred Parenteral Antibiotics

Overall, the most common parenteral antibiotic administered was ceftriaxone (40 508/66 056 parenteral antibiotic administrations; 61.3%), followed by penicillin G (7869/66 056; 11.2%), clindamycin (5019/66 056; 7.6%), cefazolin (3726/66 056; 5.6%), ampicillin/sulbactam (2245/66 056; 3.4%), cefepime (1687/66 056; 2.6%), ampicillin (1108/66 056; 1.7%), piperacillin/tazobactam (620/66 056; 0.9%), vancomycin (618/66 056; 0.9%), and metronidazole (541/66 056; 0.8%).

Table 1. Sociodemographic Characteristics of Children and Encounter Characteristics for Ambulatory ED Visits in Which Parenteral Antibiotics Were Administered From 49 Children's Hospital EDs Included in the PHIS Network

	Ambulatory ED Encounters, No. (Column %)	Parenteral Antibiotics, No. (Row %)
ED visits, No.	3 452 011	62 648 (1.8)
Individual children, No.	2 417 609	55 919 (2.3)
Age group		
<2 mo	126 059 (3.7)	2040 (1.6)
3 mo–<1 y	386 321 (11.2)	5877 (1.5)
1–4 y	1 219 319 (35.3)	19 844 (1.6)
5–9 y	790 537 (22.9)	14 511 (1.8)
0–14 y	583 464 (16.9)	8969 (1.5)
15–18 y	346 311 (10)	11 407 (3.3)
Gender		
Female	1 649 110 (47.8)	33 120 (2)
Male	1 802 901 (52.2)	29 528 (1.6)
Race		
White	1 207 804 (35)	23 141 (1.9)
Black	882 901 (25.6)	16 590 (1.9)
Hispanic	975 640 (28.3)	15 960 (1.6)
Asian	90 522 (2.6)	1553 (1.7)
Other	295 144 (8.5)	5404 (1.8)
Complex chronic condition	128 198 (3.7)	11 455 (8.9)
Insurance payor		
Government/public	2 126 999 (61.6)	35 525 (1.7)
Private	961 364 (27.8)	19 286 (2)
Other	363 648 (10.5)	7837 (2.2)
Provider subspecialty		
Emergency medicine[a]	2 146 843 (72.9)	45 019 (2.1)
Pediatrics	388 162 (13.2)	7094 (1.8)
Unknown	151 966 (5.2)	2631 (1.7)
Other	256 319 (8.7)	4214 (1.6)
Primary infection diagnosis	630 480 (18.3)	33 156 (5.3)
Discharge month		
January	347 635 (10.1)	5969 (1.7)
February	332 368 (9.6)	5739 (1.7)
March	299 767 (8.7)	5596 (1.9)
April	279 694 (8.1)	5449 (1.9)
May	289 993 (8.4)	5492 (1.9)
June	241 190 (7)	4667 (1.9)
July	235 832 (6.8)	4682 (2)
August	248 260 (7.2)	4299 (1.7)
September	275 763 (8)	4663 (1.7)
October	289 341 (8.4)	4995 (1.7)
November	286 982 (8.3)	5043 (1.8)
December	325 186 (9.4)	6054 (1.9)

Abbreviations: ED, emergency department; PHIS, Pediatric Health Information System.
[a]Includes subspecialty-trained pediatric emergency medicine providers.

Variation Across Clinical Conditions

The antibiotics most commonly administered for each clinical condition listed as the primary diagnosis for each encounter

are listed in Table 2, ranked by diagnostic categories with the highest proportion of encounters associated with parenteral antibiotic administration. According to clinical condition, ambulatory ED encounters associated with the "neoplasms" or "diseases of blood/immunity" diagnostic codes were associated with the highest proportion of parenteral antibiotic

Table 2. Prevalence and Type of Parenteral Antibiotic Administration for Common Clinical Conditions Listed as the Primary Diagnosis Among Ambulatory Children in Children's Hospital EDs, Ranked From Highest to Lowest Proportion of Encounters Associated With Parenteral Antibiotic Administration

Clinical Condition	ED Encounters, No. (% of Total)	Encounters Receiving Parenteral Antibiotics, No. (Row %)	Top 2 Antibiotics Most Commonly Administered (% Within Category)
Neoplasms	3252 (<0.1)	1172 (36.0)	
			Ceftriaxone (59.2)
			Cefepime (17.1)
Diseases of blood/immunity	13 083 (0.4)	3422 (26.2)	
			Ceftriaxone (87.2)
			Cefepime (5.1)
Diseases of the genitourinary system	81 616 (2.4)	8556 (10.5)	
			Ceftriaxone (89.9)
			Cefazolin (4.6)
Pregnancy, childbirth, puerperium	2275 (0.07)	97 (4.3)	
			Ceftriaxone (82.5)
			Azithromycin (2.9)
Diseases of the circulatory system	11 292 (0.3)	342 (3.0)	
			Clindamycin (51.3)
			Ceftriaxone (23.8)
Endocrine, nutritional, metabolic	20 410 (0.6)	594 (2.9)	
			Ceftriaxone (70.1)
			Penicillin G (14.0)
Diseases of ear/mastoid	204 643 (5.9)	5251 (2.6)	
			Ceftriaxone (94.2)
			Clindamycin (1.7)
Congenital/chromosomal	4767 (0.1)	114 (2.4)	
			Ceftriaxone (60.5)
			Cefazolin (10.5)
Diseases of skin/subcutaneous tissue	142 208 (4.1)	3163 (2.2)	
			Clindamycin (68.2)
			Ceftriaxone (13.7)
Diseases of the respiratory system	769 512 (22.3)	14 587 (1.9)	
			Penicillin G (43.0) Ceftriaxone (42.9)
Symptoms/signs not elsewhere classified	723 773 (21.0)	11 226 (1.6)	
			Ceftriaxone (77.4)
			Cefepime (5.8)
Certain infectious and parasitic diseases	241 012 (7.0)	2774 (1.2)	
			Ceftriaxone (74.8)
			Penicillin G (13.4)
Factors influencing health status	83 962 (2.4)	984 (1.2)	
			Ceftriaxone (85.0)
			Cefazolin (3.3)
Diseases of the digestive system	191 392 (5.5)	2162 (1.1)	
			Ceftriaxone (35.5)
			Clindamycin (16.1)
Injury/poisoning	698 079 (20.2)	6851 (1.0)	
			Cefazolin (40.7)
			Ceftriaxone (27.8)
Certain perinatal conditions	25 414 (0.7)	236 (0.9)	
			Ampicillin (40.2)
			Ceftriaxone (16.9)
External causes of morbidity	132 (<0.1)	1 (0.8)	

Table 2. Continued

Clinical Condition	ED Encounters, No. (% of Total)	Encounters Receiving Parenteral Antibiotics, No. (Row %)	Top 2 Antibiotics Most Commonly Administered (% Within Category)
			Penicillin G (100)
Diseases of nervous system	38 116 (1.1)	264 (0.7)	
			Ceftriaxone (64.1)
			Vancomycin (8.2)
Diseases of eye/adnexa	59 049 (1.7)	273 (0.5)	
			Ceftriaxone (46.6)
			Clindamycin (26.2)
Mental, behavioral, neurodevelopmental	48 450 (1.4)	204 (0.4)	
			Ceftriaxone (91.7)
			Penicillin G (2.9)
Diseases of musculoskeletal/connective	89 574 (2.6)	375 (0.4)	
			Ceftriaxone (45.5)
			Clindamycin (23.7)

Abbreviation: ED, emergency department.

administration (1172/3252; 36.0%; and 3422/13 083; 26.2%; respectively), although these conditions combined comprised only 16 335 (0.47%) of the study ambulatory ED encounters (Table 2, Figure 1). "Diseases of the genitourinary system," comprising 81 616 (2.4%) of the ambulatory ED encounters, were associated with parenteral antibiotic use in 10.5% of encounters. The remaining clinical conditions were associated with parenteral antibiotic use in 0.4%–4.3% of ambulatory ED encounters. The diagnostic categories most frequently associated with parenteral antibiotic use and most commonly administered antibiotics among encounters associated with parenteral antibiotic use stratified by age group are listed in Table 3.

Factors Associated With Parenteral Antibiotic Use Among Children With Infection Diagnoses

In our multivariable regression analysis, among encounters associated with an "infection diagnosis," compared with age 15–18 years, age ≤2 months was associated with higher odds (adjusted odds ratio [OR], 1.34; 95% CI, 1.23–1.46) of parenteral antibiotic administration, while the other age groups were associated with lower odds of parenteral antibiotic administration (Figure 2). Females had similar odds of parenteral antibiotic administration (OR, 1.01; 95% CI, 0.98–1.03) compared with males. Compared with children in the "White" race group category, encounters among children from the Black (OR, 0.87; 95% CI, 0.84–0.90) and Hispanic (OR, 0.79; 95% CI, 0.76–0.81) race groups were associated with lower odds of parenteral antibiotic administration. Children with public insurance had lower odds of receiving parenteral antibiotics (OR, 0.76; 95% CI, 0.74–0.78) than those who were privately insured. The presence of a CCC was associated with higher odds of parenteral antibiotic administration (OR, 3.11; 95% CI, 2.97–3.26). Compared with emergency medicine providers, encounters associated with "pediatrics" or "other" specialty types were associated with lower odds of parenteral antibiotic administration (pediatrics: OR, 0.79; 95% CI, 0.76–0.82; other: OR, 0.59; 95% CI, 0.56–0.61). Compared with December (reference), encounters in April were associated with higher odds of parenteral antibiotic administration (OR, 1.10; 95% CI, 1.04–1.16), while other months were associated with similar or lower odds of parenteral antibiotic administration. While comprising only 5.5% of all encounters and 1% of encounters associated with parenteral antibiotic use, in multivariable regression, "diseases of the digestive system" was associated with increased odds of parenteral antibiotic use compared with the reference, "diseases of the respiratory system." The most common conditions associated with parenteral antibiotic use within this category were unspecified acute appendicitis (ICD-10-CM K3580, 21.8%), periapical abscess (ICD-10-CM K047, 16.8%), noninfective gastroenteritis and colitis, unspecified (ICD-10-CM K529, 11.2%), and constipation, unspecified (ICD-10-CM, 9.8%). "Diseases of the genitourinary system" was also significantly associated with increased odds of parenteral antibiotic use compared with the reference in multivariable analysis.

Hospital-Level Assessment

Forty-seven of 49 (96%) hospitals contributing data to this analysis were academic teaching hospitals. The prevalence rates of parenteral antibiotic use among the 2 nonteaching hospitals were 2.1% and 3.0% in 169 628 combined encounters. The proportion of ambulatory ED encounters associated with parenteral antibiotic use was higher in the South (29 164/1 252 707, 2.3%, n = 19 hospitals) compared with the Midwest (14 829/1 092 666, 1.4, n = 14), Northeast (6361/337 921, 1.9%, n = 6), and West (12 294/768 717, 1.6%, n = 10). Among hospitals, the prevalence of parenteral antibiotic use ranged from 0.6% to 4.5%. There was no significant correlation between hospital median CMI and the proportion of visits associated with parenteral antibiotic use (Pearson correlation coefficient = .13, $P = .38$) (Supplementary Figure 1).

DISCUSSION

We found that parenteral antibiotics were administered in 1.8% of the >3 million ambulatory ED encounters captured in 49 pediatric EDs associated with PHIS-participating freestanding children's hospitals in 2018. In multivariable analysis, several factors were significantly associated with increased odds of

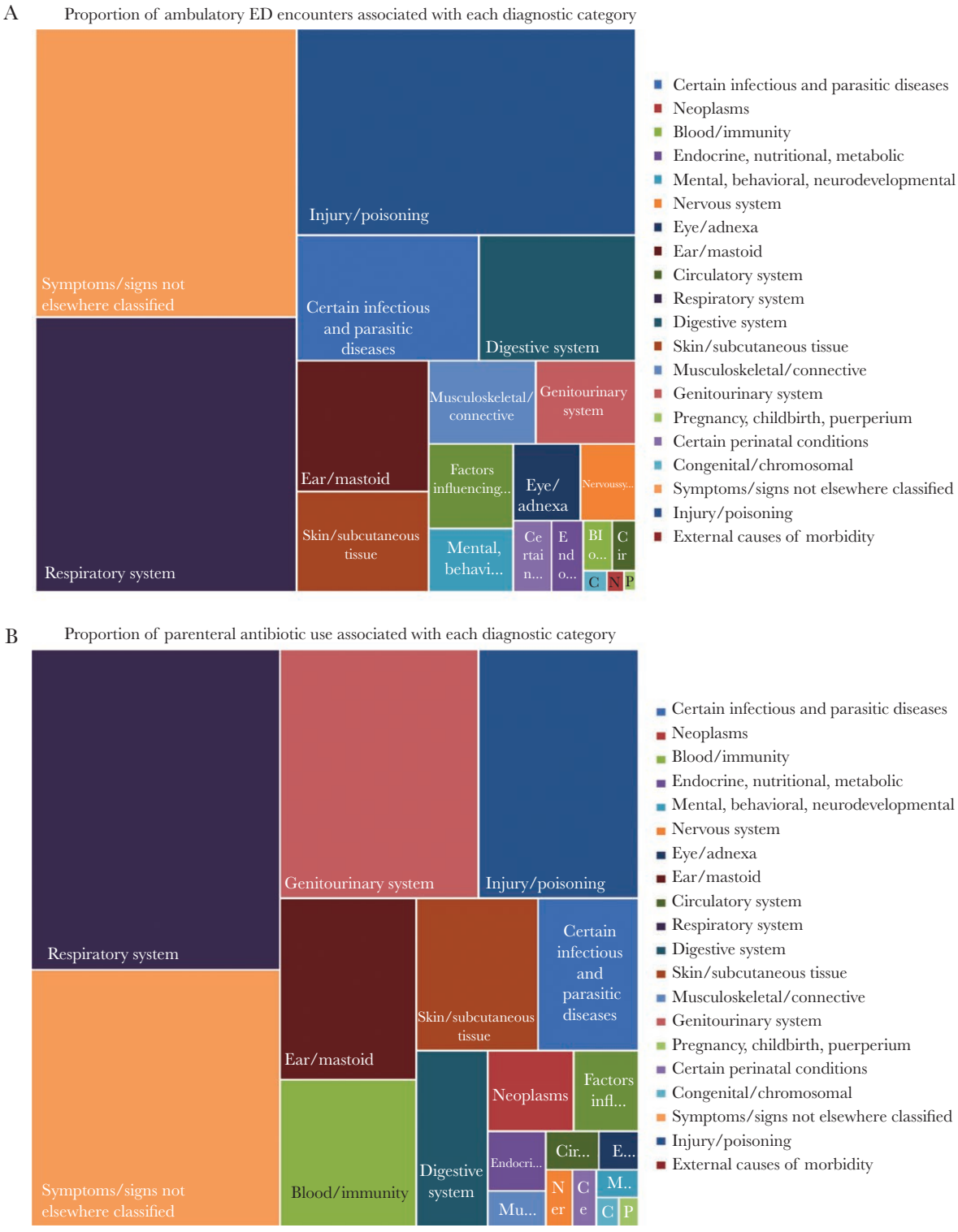

Figure 1. Proportional representation of (A) primary diagnosis diagnostic categories associated with 3 452 011 total encounters and (B) each diagnostic category's contribution to overall frequency of parenteral antibiotic use among 62 648 encounters associated with parenteral antibiotics. Each diagnostic category is labeled with a distinct color that is consistent between panels A and B. Abbreviation: ED, emergency department.

Table 3. Diagnostic Categories Associated With the Highest Number of Parenteral Antibiotic Administrations and the Most Commonly Administered Antibiotics Among Encounters Associated With Parenteral Antibiotic Administration, by Age Group, Among Ambulatory Children in US Pediatric Emergency Departments

Age Group	Top 3 Diagnostic Categories Associated With Most Parenteral Antibiotic Administrations (No. of Encounters With Parenteral Antibiotic Administration/Total Encounters for Each Category; %)	Most Commonly Administered Antibiotics (No./No. of Encounters With Antibiotic Use; %)
≤2 mo	Symptoms/signs not elsewhere classified (820/36 151; 2.3) Diseases of the genitourinary system (403/1662; 24.2) Diseases of the respiratory system (249/24 727; 1.0)	Ceftriaxone (1674/2040; 82.0) Ampicillin (290/2040; 14.2) Ceftazidime (85/2040; 4.2)
3 mo–1 y	Symptoms/signs not elsewhere classified (1364/86 749; 1.6) Diseases of ear/mastoid (1183/35 641; 3.3) Diseases of the genitourinary system (1164/5983; 19.5)	Ceftriaxone (5348/5877; 91.0) Clindamycin (240/5877; 4.1) Cefazolin (66/5877; 1.1)
1–4 y	Diseases of the respiratory system (4898/311 921; 1.6) Symptoms/signs not elsewhere classified (3688/236 135; 1.6) Diseases of ear/mastoid (3245/104 124; 3.1)	Ceftriaxone (13 551/19 844; 68.3) Penicillin G (2187/19 844; 11.0) Clindamycin (1466/19 844; 7.4)
5–9 y	Diseases of the respiratory system (4967/181 810; 2.7) Symptoms/signs not elsewhere classified (2333/157 397; 1.5) Injury/poisoning (1564/179 041; 0.9)	Ceftriaxone (6940/14 511; 47.8) Penicillin G (3636/14 511; 25.1) Clindamycin (1332/14 511; 9.2)
10–14 y	Diseases of the respiratory system (2114/84 838; 2.7) Injury/poisoning (1885/172 006; 1.1) Symptoms/signs not elsewhere classified (1146/123 943; 0.9)	Ceftriaxone (4499/8969; 50.2) Penicillin G (1369/8969; 15.3) Clindamycin (1056/8969; 11.8)
15–18 y	Diseases of the genitourinary system (3302/16 700; 19.8) Symptoms/signs not elsewhere classified (1875/83 398; 2.2) Injury/poisoning (1491/84 731; 1.8)	Ceftriaxone (8496/11 407; 74.5) Clindamycin (877/11 407; 7.7) Penicillin G (652/11 407; 5.7)

parenteral antibiotic administration, including age ≤2 months, white race, private insurance payor, presence of a CCC, encounters associated with emergency medicine providers, and encounters associated with genitourinary and digestive system diseases. The frequency of parenteral antibiotic administration also varied significantly by calendar month, which may reflect some seasonal variability in patterns of presenting ED conditions [17]. Ceftriaxone, for which few first-line pediatric indications exist, was the most commonly administered parenteral antibiotic, highlighting a potential stewardship target. The frequency of administration of ceftriaxone and other antibiotic types varied by age group and clinical condition. Substantial variability was seen in parenteral antibiotic administration frequency across hospitals, with a >7-fold difference between the lowest and highest prescribing hospitals, which did not correlate with hospital CMI.

Of the 21 diagnostic categories, encounters associated with a primary diagnosis code included in the "diseases of the genitourinary system" category had among the highest proportions of parenteral antibiotic use (10.5%). Although the specific diagnostic codes within these categories were not examined, much of this use may be attributable to urinary tract infections (UTIs), especially among the younger age groups, in which these infections occur commonly [18, 19]. While clinical practice guidelines for UTI management in young children endorse oral antibiotic therapy in most cases, parenteral therapy may be used in patients whom clinicians judge to be "toxic"-appearing or those who are unable to retain oral medications [19]. However, a recent retrospective assessment of patients 29 days to 2 years of age in an ambulatory ED setting in the PHIS network found that children diagnosed with a UTI who received parenteral antibiotics before ED discharge (36%) had similar rates of revisits leading to admission as those who did not receive parenteral antibiotics, thus supporting the use of oral antibiotics for most children with UTI, and potentially identifying a high-yield target for stewardship efforts [20].

By age group, the highest proportion of parenteral antibiotic administration was observed in older adolescents (15–18 years; 3.3%). In this group, encounters with a primary diagnosis code consistent with "diseases of the genitourinary system" contributed the highest frequency of parenteral antibiotic administration, accounting for 3302/8496 (39%) parenteral antibiotic administrations in this age group. While UTI may also be a frequent genitourinary diagnosis in females in this age group, pelvic and/or genital inflammatory disorders, for which empiric ceftriaxone use is guideline-concordant, are included within this category and may represent more prevalent diagnoses in this age group compared with younger age groups. Of note, specific diagnostic codes for gonococcal infections, for which the use of ceftriaxone is concordant with guidelines for first-line therapy, are not included within the ICD-10-CM "diseases of the genitourinary system" category, but rather the "certain infectious and parasitic diseases" diagnostic category.

Among the 3 month–1 year and 1–4-year-old age groups, "diseases of the ear/mastoid" were among the most common indications for parenteral antibiotic use, consistent with the high frequency of recurrent/refractory otitis media (OM) in this age group [21, 22]. The use of ceftriaxone is potentially guideline-concordant for recurrent or refractory OM in this age group [9], although the use of administrative data did not enable detailed evaluations of the appropriateness of antibiotics for each encounter.

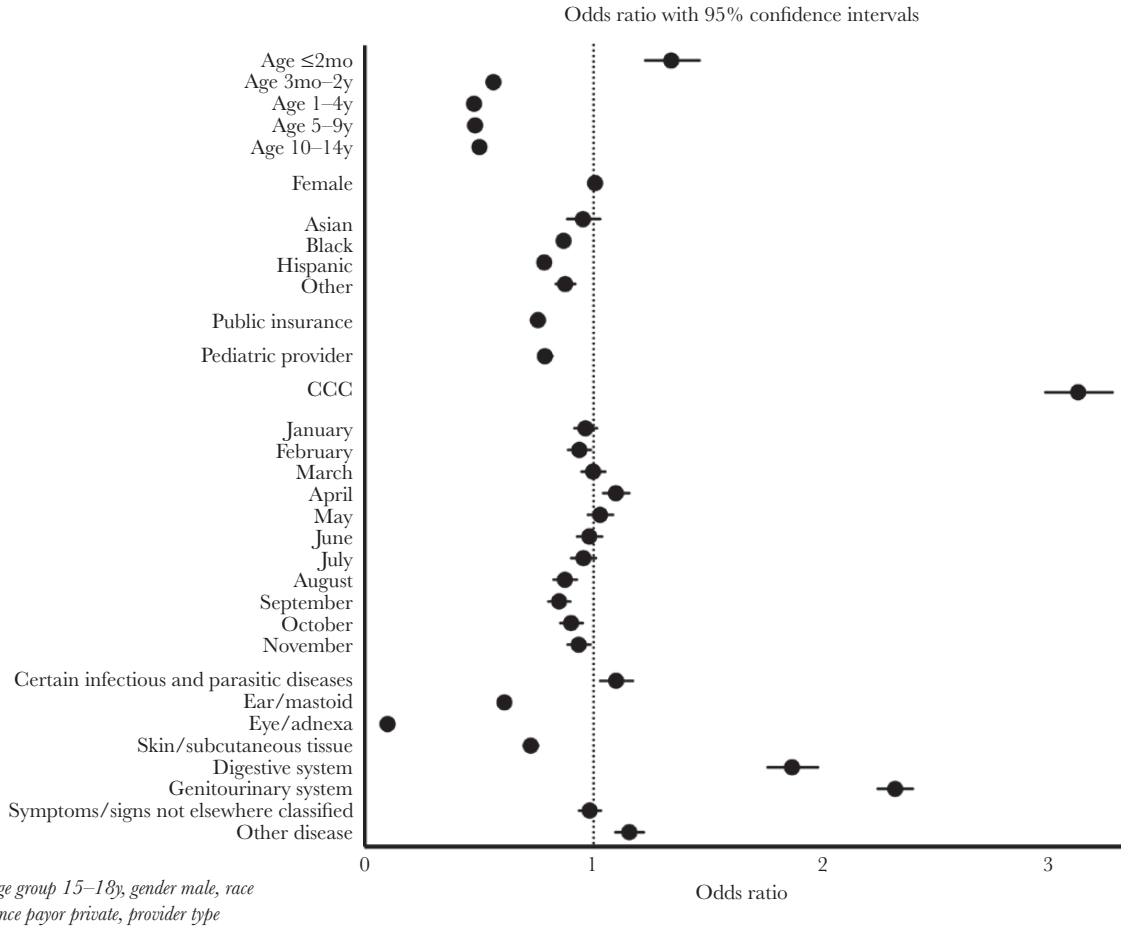

Figure 2. Proportional odds regression of parenteral antibiotic use adjusted for several sociodemographic and clinical characteristics. Circles indicate odds ratios; lines represent 95% confidence intervals. Covariates include age group, gender, race, insurance payor, provider type, presence of a complex chronic condition, calendar month, and disease category. Abbreviation: CCC, complex chronic condition.

In multivariable regression, "symptoms, signs, abnormal clinical and laboratory findings, not elsewhere classified," encompassing nonspecific febrile syndromes, were associated with likelihood of parenteral antibiotic use similar to "diseases of the respiratory system." While this category may be considered to be associated with nonspecific, less severe illnesses, it likely encompasses encounters associated with fever in children with other complicating factors such as neonatal status or immunocompromising conditions, although the contributions of specific diagnoses to the overall prevalence of parenteral antibiotic use within this category are not known.

Age ≤2 months was associated with the highest odds of parenteral antibiotic use in the ambulatory ED setting. The evaluation of the febrile infant <2 months of age includes assessment for invasive bacterial infection (bacteremia, UTI, and/or meningitis) and often includes hospital admission and empiric antibiotic administration. However, recent efforts have focused on identifying lower-risk infants who may be managed with fewer invasive interventions with or without oral or parenteral antibiotics in the ambulatory setting [23]. Febrile neonate evaluation is among the most common conditions managed in pediatric EDs [24], and these lower-risk infants managed in the ambulatory setting may have contributed to the parenteral antibiotic use we observed in this age group.

Encounters associated with an emergency medicine provider were associated with higher odds of parenteral antibiotic administration than pediatrics and other provider types in multivariable analysis. While there may be some misclassification of provider type, there is also likely some variation among hospitals with regards to provider type in the pediatric ED setting. In many hospitals, it may be common practice for general emergency medicine providers without pediatric subspecialty training to practice in pediatric ED settings. While some differences in approaches to management of febrile illnesses have

been reported between general emergency medicine and pediatric emergency medicine providers [25–27], this has not been consistently demonstrated [28]. However, few prior studies have assessed differences in approaches to management of infections and/or antibiotic prescribing practices among emergency medicine and pediatric providers in the ED setting. Differences in patient complexity or acuity seen by emergency medicine compared with pediatric providers in ED settings may have contributed to some of the variability we observed, although we were not able to determine the acuity of the individual encounters in this assessment. In addition to provider specialty, a number of other provider characteristics, such as degree and time since completion of training, may also be associated with antibiotic prescribing practices [29, 30], but we were not able to access detailed provider data for individual encounters.

Our finding that White race was associated with increased odds of parenteral antibiotic use is consistent with other reports that individuals of White race are more likely to be prescribed antibiotics in ambulatory settings [31–33]. Importantly, lower incidences of infectious diseases [34, 35] and infection-associated mortality [36] have also been reported among White persons in the United States compared with non-White persons. Improving the understanding of these disparities is critical to reducing the inequities in the health care system and to informing improved antimicrobial stewardship strategies.

Our study has several strengths, including detailed characterization of pediatric ED encounters with a broad range of medical conditions and a large sample size with representation of many large children's hospitals in the United States. Our study also has several limitations. Without detailed chart review and specific clinical information, we used primary discharge diagnosis codes as a surrogate for indication for antibiotic use. Certain common conditions may warrant the use of more than 1 diagnostic code. For example, febrile neutropenia may be assigned both R50.81 (fever, "symptoms, signs, abnormal clinical and laboratory findings") and D70.9 (neutropenia, "diseases of blood/immunity"). Additionally, encounters may have been associated with multiple symptoms or conditions. With access only to primary diagnosis codes and without access to detailed clinical information pertaining to the encounter, we were unable to draw inferences with regards to the indications for antibiotic use or the guideline concordance of each parenteral antibiotic administration. Even if the use of parenteral antibiotics is not guideline-concordant, such use may not be inappropriate given other clinical factors that may inform the provider's prescribing decision-making, such as ill appearance of the patient, inability to tolerate oral antibiotics, or a prior history of complicated or resistant infection. The frequency of overall antibiotic prescriptions has been shown to be higher, and guideline-discordant antibiotic use lower, among pediatric visits to nonpediatric EDs compared with dedicated pediatric EDs [3]. Our study included only pediatric EDs associated with free-standing children's hospitals; thus, our findings may underestimate the true prevalence of parenteral antibiotic use in ED visits overall. Furthermore, selection of only ambulatory ED encounters not requiring a 23-hour observation or admission likely excluded encounters associated with more complicated illnesses. Similarly, our findings may be difficult to generalize to settings outside the United States. Provider type information was extracted from discharge data; thus, potential exists for misclassification of provider to whom parenteral antibiotic administration was attributed, as multiple providers may have provided care in individual encounters. Furthermore, by reporting data from only a single 1-year period, we are unable to determine whether there may be consistent seasonal differences in parenteral antibiotic prescribing practices. Additionally, it is unclear whether there have been underlying trends in parenteral antibiotic use following enhanced ambulatory antibiotic stewardship efforts, which may vary by hospital.

CONCLUSIONS

Parenteral antibiotics were administered in approximately 1 of every 55 ambulatory pediatric ED encounters in 2018. Variability observed in parenteral antibiotic prescribing practices by patient age, provider type, and diagnostic condition highlights potential opportunities to target stewardship activities in the ED setting. Future studies should evaluate the appropriateness of parenteral antibiotics administered in the ED setting.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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Author contributions. Dr. Howard conceptualized and designed the study, drafted the initial manuscript, and reviewed and revised the manuscript. Dr. Thurm designed the study, coordinated and supervised data collection and analysis, and reviewed and revised the manuscript. Dr. Dantuluri and Ms. Griffith critically reviewed and revised the manuscript. Drs. Katz, Ward, and Banerjee critically reviewed and revised the manuscript. Dr. Grijalva conceptualized and designed the study and reviewed and revised the manuscript. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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