

Antibiotic Utilization for Acute Respiratory Tract Infections in U.S. Emergency Departments

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Inappropriate use of antibiotics for acute respiratory tract infections (ARTIs) has decreased in many outpatient settings. For patients presenting to U.S. emergency departments (EDs) with ARTIs, antibiotic utilization patterns are unclear. We conducted a retrospective cohort study of ED patients from 2001 to 2010 using data from the National Hospital Ambulatory Medical Care Survey (NHAMCS). We identified patients presenting to U.S. EDs with ARTIs and calculated rates of antibiotic utilization. Diagnoses were classified as antibiotic appropriate (otitis media, sinusitis, pharyngitis, tonsillitis, and nonviral pneumonia) or antibiotic inappropriate (nasopharyngitis, unspecified upper respiratory tract infection, bronchitis or bronchiolitis, viral pneumonia, and influenza). There were 126 million ED visits with a diagnosis of ARTI, and antibiotics were prescribed in 61%. Between 2001 and 2010, antibiotic utilization decreased for patients aged <5 presenting with antibiotic-inappropriate ARTI (rate ratio [RR], 0.94; confidence interval [CI], 0.88 to 1.00). Utilization also decreased significantly for antibiotic-inappropriate ARTI patients aged 5 to 19 years (RR, 0.89; CI, 0.85 to 0.94). Utilization remained stable for antibiotic-inappropriate ARTI among adult patients aged 20 to 64 years (RR, 0.99; CI, 0.97 to 1.01). Among adults, rates of quinolone use for ARTI increased significantly from 83 per 1,000 visits in 2001 to 2002 to 105 per 1,000 in 2009 to 2010 (RR, 1.08; CI, 1.03 to 1.14). Although significant progress has been made toward reduction of antibiotic utilization for pediatric patients with ARTI, the proportion of adult ARTI patients receiving antibiotics in U.S. EDs is inappropriately high. Institution of measures to reduce inappropriate antibiotic use in the ED setting is warranted.

Acute respiratory tract infections (ARTIs) such as bronchitis, sinusitis, and rhinitis account for almost 10% of ambulatory care visits in the United States (1). While many of these infections are caused by viruses, clinicians prescribe antibiotics for over half of the visits for these conditions (1, 2). This inappropriate antibiotic use is potentially harmful to the community, fostering the growth of antimicrobial-resistant organisms (3). Other potential consequences include antibiotic-related adverse effects, such as *Clostridium difficile*-associated disease, antibiotic-associated diarrhea, and allergic reactions (4–6). Over the past decade, multiple campaigns and interventions have sought to curtail the use of inappropriate antibiotics for ARTIs, focused primarily on outpatient visits. There is evidence of improvement, with ARTI antibiotic prescription rates decreasing among young children and reduction of rates of broad-spectrum antimicrobial use in older persons (1, 2, 7, 8).

Much less is known about patterns of antibiotic use for ARTIs among persons visiting emergency departments (EDs). ED use in the United States has increased over the past decade, and Americans rely increasingly on EDs for a wide range of medical conditions due to a combination of barriers to primary care access (9, 10). As a result, the ED has become a common site of care for nonemergent conditions, including ARTIs, particularly among socioeconomically disadvantaged individuals.

We sought to characterize antibiotic utilization for ARTIs treated in U.S. emergency departments with the use of national surveillance data.

MATERIALS AND METHODS

Study design and data source. We analyzed 2001-to-2010 data from the National Hospital Ambulatory Medical Care Survey (NHAMCS). The

study was approved by the Institutional Review Board of the University of Alabama at Birmingham.

Operated by the National Center for Health Statistics, NHAMCS is a national probability sample characterizing ED (NHAMCS-ED) and outpatient clinic visits at hospitals across the United States (11). Using a four-stage probability design, NHAMCS-ED samples geographically defined areas, hospitals within these areas, emergency service areas within the emergency departments of the hospitals, and patient visits to the emergency service areas. For an assigned 4-week period, the studies systematically selected all patients from selected facilities. The National Center for Health Statistics (NCHS) works with each hospital and clinic to abstract clinical data from selected charts.

Inclusion criteria. For each visit, NHAMCS reports up to three diagnoses, classified using codes from the *International Classification of Diseases, 9th Revision* (ICD-9). We examined presentation to the ED with ARTI, including otitis media, sinusitis, pharyngitis, tonsillitis, nonviral pneumonia, nasopharyngitis, unspecified upper respiratory tract infection (URI), bronchitis or bronchiolitis, viral pneumonia, and influenza (ICD-9 381.0 to 381.4, 382, 460 to 463, 465 to 466, 480 to 488, 490). We further classified ARTIs as antibiotic appropriate (otitis media [381.0 to 381.4, 382], sinusitis [461], pharyngitis [462]), tonsillitis [463], and nonviral pneumonia [481 to 486]) or antibiotic inappropriate (nasopharyngitis [460], unspecified URI [465], bronchitis or bronchiolitis [466, 490], viral pneumonia [480], and influenza [487, 488]). We included only ICD-9 codes representing infections identified as acute.

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Exclusion criteria. In defining ARTI, we excluded any visit that resulted in admission to the hospital from the ED. When examining utilization for ARTI where use was deemed inappropriate, we excluded patients with additional diagnoses for antibiotic-appropriate ARTIs, those with a diagnosis of urinary tract infection (ICD-9 595.0, 595.9, 599.0), and patients with a diagnosis of soft tissue infection (680 to 682) (1). There were no exclusions based on age.

Outcomes. The primary outcome was antibiotic utilization in the ED. We determined medications from specific drug class identification codes specified by the National Center for Health Statistics, using the most recent NHAMCS medication classification system (Lexicon Plus; Cerner Multum, Inc.) (12). For each visit, NHAMCS reported up to eight medications, either prescribed or administered during treatment. We identified the use of antibiotics and categorized these as penicillins, cephalosporins, macrolides, sulfonamides and lincomycin derivatives, quinolones, or other (carbapenams, aminoglycosides, glycolcyclines, glycopeptides, leprostatics, urinary anti-infectives, and miscellaneous).

Statistical analysis and rate calculations. We incorporated sampling design and weight variables to calculate nationally weighted estimates and their corresponding 95% confidence intervals (CI), accounting for the complex survey design. We used ultimate cluster design (single-stage sampling) in variance calculations, making use of “masked” stratum and primary sampling unit identifiers provided with the NHAMCS public-use data sets (13). Prior efforts have demonstrated that variance estimates calculated using these methods are conservative (14, 15).

For the study period 2001 to 2010, we calculated secular rates in 2-year intervals. In order to assess trends in overall ED use, we calculated population-based rates (per 1,000) using age-specific U.S. Census Bureau population estimates, including population estimates in the denominator and weighted visit counts in the numerator (data not shown) (16). We also determined visit-based rates (per 1,000 visits) for each 2-year interval, including the weighted number of observations of patients receiving antibiotics or an ARTI diagnosis in the numerator, and the total weighted number of visits in the denominator. Results were stratified on the basis of age using available census groups (<5, 5 to 19, 20 to 64, and ≥65 years of age) (16).

To determine secular trends in antibiotic utilization, we fit binomial generalized linear models with a logarithmic link function, incorporating the year interval as a continuous variable and calculating the corresponding rate ratios (RRs). Performing the analysis in this manner provided a more accurate estimate of true RRs than calculation of odds ratios using logistic regression, as neither ARTI diagnosis nor antibiotic utilization represented a rare outcome. All analyses were conducted using Stata v.12.1 (Stata, College Station, TX).

RESULTS

Visit characteristics. During the study period (2001 to 2010), there were 126 million ED visits with a diagnosis of ARTI. The mean age of ARTI patients was 21.1 years (95% CI, 20.5 to 21.7), and the majority of patients were female (54.2%) and white (69.4%). Children less than 5 years of age accounted for the highest percentage of ARTI visits (34.3%). Disproportionate percentages of ARTI patients were black (26.6%), uninsured (14.3%), or insured by Medicaid (39.8%).

Rates of acute respiratory tract infection. ARTIs accounted for 12.2% of ED visits (rate, 122 per 1,000 visits). The most common infections were unspecified URI, otitis media, and bronchitis or bronchiolitis (Table 1). There was a decrease in the rate of otitis media (rate ratio [RR], 0.91; 95% CI, 0.89 to 0.94) and an increase in the rate of influenza (RR, 1.27; 95% CI, 1.16 to 1.39) over the study period. The overall rate of ARTI decreased from 135 to 122 per 1,000 ED visits (RR, 0.97; CI, 0.95 to 0.99) during the study period; this reduction was limited to antibiotic-appropriate ARTIs.

TABLE 1 Emergency department acute respiratory tract infection visits and rates, 2001 to 2010^a

ARTI type	All ED visits 2001–2010		
	Annual no. of visits (1,000s) (n = 103,159)	Rate (per 1,000 ED visits) (95% CI)	% patients receiving antibiotics (95% CI)
Any ARTI diagnosis	12,610	122 (118–126)	61.1 (59.7–62.5)
ARTI diagnosis (antibiotic appropriate)	6,977	68 (65–70)	76.5 (75.2–77.8)
Otitis media	3,052	30 (28–31)	83.7 (82.2–85.1)
Sinusitis	348	3 (3–4)	84.0 (80.3–87.1)
Pharyngitis	2,315	22 (21–24)	63.9 (61.4–66.3)
Tonsillitis	405	4 (3–4)	80.1 (76.7–83.1)
Nonviral pneumonia (bacterial or unspecified organism)	1,199	12 (11–12)	81.8 (79.5–84.0)
ARTI diagnosis (antibiotic inappropriate)	6,681	65 (62–67)	47.9 (46.0–49.8)
Acute nasopharyngitis	102	1 (1–1)	29.5 (23.9–35.8)
Unspecified upper respiratory tract infection	3,434	33 (32–35)	36.7 (34.5–38.9)
Bronchitis or bronchiolitis	2,889	28 (27–29)	67.4 (65.2–69.6)
Viral pneumonia	16	0.2 (0.1–0.2)	63.4 (44.5–78.9)
Influenza	491	5 (4–5)	18.6 (15.6–22.1)

^a Data exclude all visits resulting in admission to the hospital. All percentages reported are row percentages. ARTI, acute respiratory tract infection; CI, confidence interval; ED, emergency department.

Children <5 years of age had the highest rate of ARTI visits (354 per 1,000 ED visits) among all age groups (Table 2). Among the members of this age group, the rate of ARTI decreased for antibiotic-appropriate infections but not for antibiotic-inappropriate infections (Table 2 and Fig. 1). The most common infection was otitis media, accounting for 43.4% (CI, 41.9 to 45.0) of all ARTI visits, followed by unspecified URI (38.4%; CI, 36.8 to 39.9%). The ARTI rate for those aged 5 to 19 years was 147 per 1,000 visits (Table 2). There was a significant decrease in the rate of antibiotic-appropriate ARTI and an increase in the rate of antibiotic-inappropriate ARTI during the study period (Table 2 and Fig. 1). Among those aged 5 to 19 years, pharyngitis was the most common infection (30.1%; CI, 28.8 to 31.6), followed by unspecified URI (25.8%; CI, 24.3 to 27.5) and otitis media (22.4%; CI, 20.9 to 23.9).

For those aged 20 years or older, the ARTI rate was 76 per 1,000 visits, lowest among all age groups. From 2001 to 2010, the rate of antibiotic-appropriate ARTI decreased for those aged 20 to 64 but remained stable for those 65 or older (Table 2; Fig. 1). For adult patients aged 20 to 64, the most common ARTIs were bronchitis or bronchiolitis (34.5%; CI, 33.1 to 35.9) and pharyngitis (21.2%; CI, 20.2 to 22.2). Among patients aged 65 or older, the most common ARTIs were bronchitis or bronchiolitis (41.1%; CI, 38.0 to 44.2) and nonviral pneumonia (32.8%; CI, 30.0 to 35.7).

Rates of antibiotic utilization. Antibiotics were administered during treatment or prescribed at discharge in 61.1% of all ARTI ED visits. Overall, during the study period, ARTI antibiotic utilization decreased significantly from 621 to 577 per 1,000 ED visits (RR, 0.98; CI, 0.97 to 0.99). For antibiotic-appropriate ARTI, utilization was stable. However, for antibiotic-inappropriate ARTI, utilization decreased (RR, 0.96; CI, 0.94 to 0.98).

TABLE 2 ED visit rates for acute respiratory tract infections by age group and time interval^a

Visit category and age group of patients (yr)	Entire study period (2001–2010)		Rate (per 1,000 ED visits)		Rate ratio for 2001–2010 (95% CI) ^b
	Annual no. of visits (1,000s) (n = 103,159)	Rate (per 1,000 ED visits) (95% CI)	2001–2002	2009–2010	
All ARTI visits					
<5	4,332	354 (343–365)	385	338	0.97 (0.95–0.99) ^c
5–19	2,764	147 (141–153)	166	160	0.99 (0.96–1.02)
20–64	4,846	79 (77–82)	88	78	0.97 (0.95–0.99) ^c
65+	669	60 (56–64)	63	57	0.97 (0.93–1.01)
ARTI visits (antibiotic appropriate)					
<5	2,560	209 (200–218)	244	188	0.94 (0.92–0.96) ^c
5–19	1,744	93 (88–97)	112	91	0.95 (0.92–0.98) ^c
20–64	2,363	39 (37–40)	42	36	0.96 (0.94–0.99) ^c
65+	310	28 (25–31)	29	30	0.98 (0.93–1.04)
Antibiotics in ARTI visits (antibiotic appropriate)					
<5	2,098	820 (804–834)	805	800	1.00 (0.99–1.01)
5–19	1,257	721 (698–742)	745	708	0.99 (0.97–1.01)
20–64	1,758	744 (726–761)	700	763	1.02 (1.00–1.03) ^c
65+	226	730 (685–770)	677	759	1.03 (0.99–1.07)
ARTI visits (antibiotic inappropriate)					
<5	2,300	188 (180–196)	194	187	1.00 (0.97–1.02)
5–19	1,220	65 (61–69)	67	80	1.05 (1.00–1.10) ^c
20–64	2,767	45 (44–47)	50	47	0.98 (0.96–1.01)
65+	394	35 (32–38)	39	30	0.95 (0.90–1.00) ^c
Antibiotics in ARTI visits (antibiotic inappropriate) ^d					
<5	413	234 (212–258)	261	203	0.94 (0.88–1.00) ^c
5–19	366	363 (335–392)	444	275	0.89 (0.85–0.94) ^c
20–64	1,310	535 (512–559)	535	500	0.99 (0.97–1.01)
65+	218	625 (583–664)	595	666	1.03 (0.99–1.07)

^a Data exclude all visits resulting in admission to the hospital. ARTI, acute respiratory tract infection; CI, confidence interval; ED, emergency department.

^b Trend analysis using generalized linear models, examining the rate of ARI diagnosis or antibiotic utilization over the ten-year study period. A rate ratio of >1 indicates an increasing trend, and <1 indicates a decreasing trend.

^c Indicates a trend which achieved significance at the 0.05 level.

^d Excludes visits with an additional diagnosis of ARTI (for which antibiotic use is appropriate), urinary tract infection, and soft tissue infection.

Overall antibiotic utilization was lowest among ARTI patients aged <5 years (581 per 1,000 visits; CI, 563 to 600). There was no change in antibiotic utilization for antibiotic-appropriate ARTI patients in this age group (Table 2). For antibiotic-inappropriate ARTI, there was a significant decrease (Table 2). Penicillins accounted for over half of all antibiotics given (Table 3). Among patients 5 to 19 years of age, there was no change in utilization for antibiotic-appropriate ARTI (Table 2). In contrast, for antibiotic-inappropriate ARTI, there was a significant decrease in use, with rates falling from 444 per 1,000 visits in 2001 to 2002 to 275 per 1,000 in 2009 to 2010 (RR, 0.89; CI, 0.85 to 0.94). Penicillins and cephalosporins accounted for greater than 50% of antibiotics prescribed to patients aged 5 to 19 years (Table 3).

Patients aged 65 years of age or older had the highest overall rate of antibiotic use (676 per 1,000 visits; CI, 643 to 707) (Fig. 1). Among those 20 to 64 years of age, for visits with a diagnosis of antibiotic-appropriate ARTI, there was an increase in antibiotic use. No increase was observed for those 65 or older (Table 2). Antibiotic utilization remained stable for antibiotic-inappropriate ARTI among adult patients aged 20 to 64 years, with a rate of 535 per 1,000 visits in 2001 to 2002 and a rate of 500 per 1,000 in 2009 to 2010 (RR, 0.99; CI, 0.97 to 1.01). A nonsignificant increase

was observed those aged 65 or older, with the rate of utilization rising from 595 per 1,000 visits in 2001 to 2002 to 666 per 1,000 in 2009 to 2010 (RR, 1.03; CI, 0.99 to 1.07). Cephalosporins and quinolones accounted for the majority (50.2%) of antibiotics given among patients aged 20 years or older, with rates of quinolone use for ARTI increasing significantly from 83 per 1,000 visits in 2001 to 2002 to 105 per 1,000 in 2009 to 2010 (RR, 1.08; CI, 1.03 to 1.14). Among adult patients presenting with antibiotic-inappropriate ARTI, utilization was highest for unspecified upper respiratory tract infection, bronchitis/bronchiolitis, and viral pneumonia (Fig. 2).

DISCUSSION

Over the ten-year study period (2001 to 2010), there were more than 12 million annual ED visits for ARTI, with antibiotics used in the majority of these visits. While we observed a decrease in ARTI antibiotic use among patients aged ≤19 years, we observed no decrease in ARTI antibiotic utilization among adult patients, even for those ARTIs where antibiotics are not routinely indicated. Among antibiotic-appropriate ARTI visits, utilization was generally stable, with only three-quarters of patients receiving antibiotics. These results highlight the urgent need to reduce inappropri-

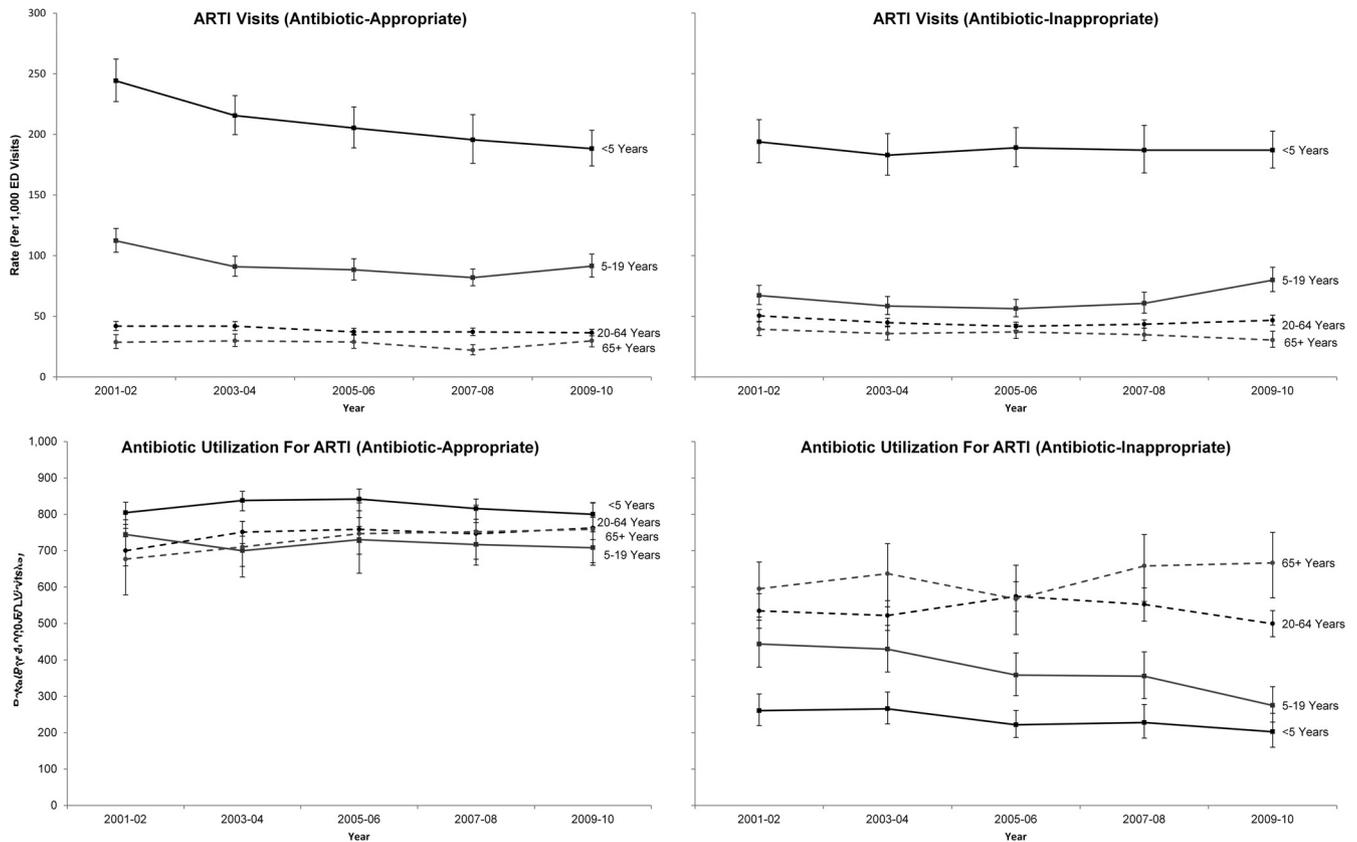


FIG 1 Visit-based rates of ARTI ED visits and antibiotic utilization by infection type, year interval, and age group, 2001 to 2010. Data exclude all visits resulting in hospital admission. For ARTI where antibiotic use was deemed inappropriate, visits with an additional diagnosis of ARTI where antibiotic use was appropriate, UTI, or soft tissue infection are also excluded. For rate calculations, weighted visit counts with a diagnosis of ARTI or those receiving antibiotics were included in the numerator and the total number of visits over the 2-year interval for each age group was included in the denominator. Error bars represent 95% confidence interval limits. ED, emergency department; ARTI, acute respiratory tract infection; UTI, urinary tract infection.

ate use of ARTIs in the ED setting and provide better treatment for those who could benefit from antibiotic therapy.

We provide current estimates of ED antibiotic utilization for ARTI treatment in the United States. To date, most analyses of ARTI antibiotic utilization have focused on outpatient settings, with few examining use in the ED (1, 17, 18). Grijalva and colleagues reported antibiotic prescribing for ARTIs in physician’s offices, outpatient clinics, and EDs during 1996 to 2006. While

those authors observed overall decreases in antibiotic utilization for patients <50 years old during the period, there were no changes in practice within EDs for all ages combined (1). Neuman and colleagues examined the use of antibiotics for the treatment of pneumonia in the ED during 1993 to 2008, finding an increase in antibiotic use concordant with Infectious Disease Society of America guidelines, as well as an increase in discordant use (19). Our results complement those from the Neuman study and pro-

TABLE 3 Antibiotic utilization by class and age group among ED patients, 2001 to 2010^a

Antibiotic class	% of all antibiotics (95% CI) for indicated age range (yr)			
	<5	5–19	20–64	65+
Penicillins	53.2 (51.7–54.6)	36.0 (34.7–37.3)	21.5 (20.7–22.2)	10.2 (9.3–11.1)
Cephalosporins	24.7 (23.5–26.0)	25.1 (23.9–26.3)	27.6 (26.7–28.5)	27.0 (25.5–28.6)
Macrolides	16.9 (15.6–18.3)	17.1 (16.1–18.2)	16.9 (16.3–17.6)	13.9 (12.7–15.2)
Sulfonamides/lincomycin derivatives	5.6 (4.9–6.4)	12.7 (11.7–13.8)	15.1 (14.2–15.9)	11.1 (10.1–12.2)
Quinolones	1.0 (0.8–1.4)	5.0 (4.5–5.4)	16.9 (16.3–17.6)	34.1 (32.3–35.9)
Tetracyclines	0.0 (NA) ^c	2.3 (1.9–2.7)	4.7 (4.3–5.1)	2.3 (1.9–2.8)
Other ^b	11.8 (11.0–12.7)	23.2 (22.0–24.4)	23.4 (22.5–24.4)	23.1 (21.6–24.7)

^a Data exclude all visits resulting in admission to the hospital. All percentages reported are column percentages. Columns do not sum to 100%, as some visits involved utilization of multiple classes of antibiotics. CI, confidence interval; ED, emergency department.

^b Includes carbapenams, aminoglycosides, glycolcyclines, glycopeptides, leprostatics, urinary anti-infectives, and miscellaneous antibiotics.

^c NA, not applicable (data represent fewer than 30 raw observations). The NCHS considers estimates based on fewer than 30 raw observations to be unreliable.

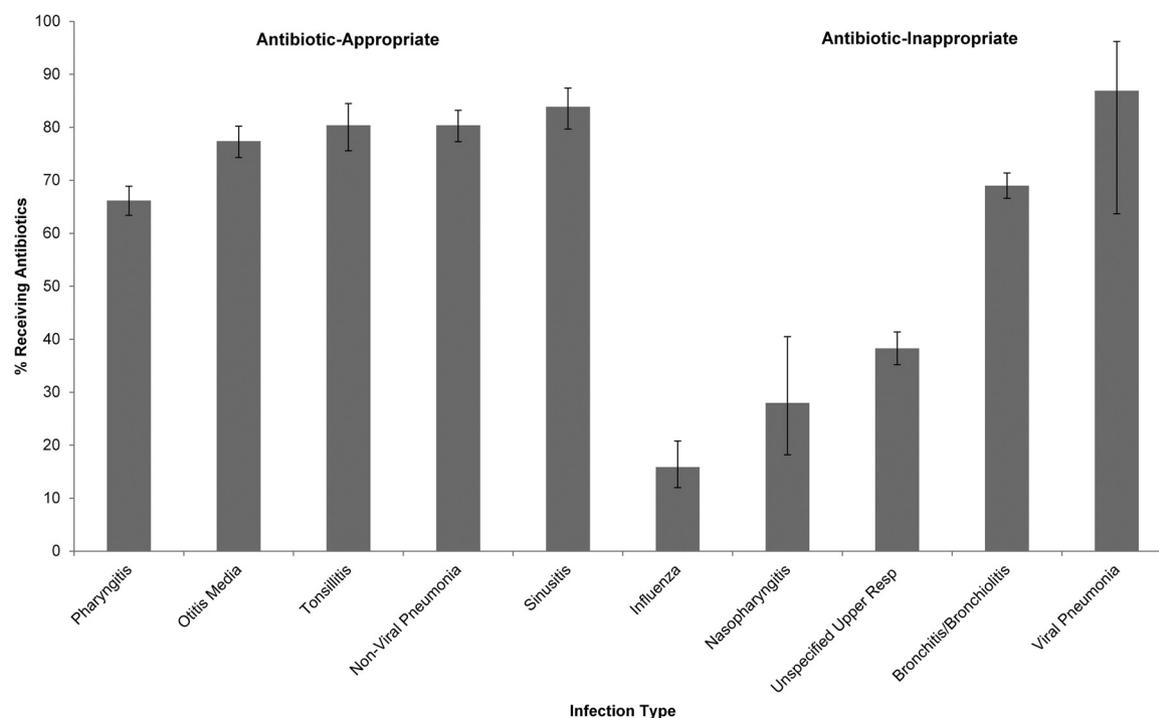


FIG 2 Percentages of adult (≥ 20 years of age) ARTI ED visits receiving antibiotics by infection type, 2001 to 2010. Data exclude all visits resulting in hospital admission. For ARTI where antibiotic use was deemed inappropriate, visits with an additional diagnosis of ARTI where antibiotic was appropriate, UTI, or soft tissue infection are also excluded. Error bars represent 95% confidence interval limits. ED, emergency department; ARTI, acute respiratory tract infection; UTI, urinary tract infection; Resp, respiratory.

vide updated estimates for ED antibiotic utilization, examining among all age groups a broader range of ARTIs.

Shapiro et al. also recently examined antibiotic use in the ambulatory care setting, reporting a utilization rate of 51% for adult ARTI visits where antibiotics are rarely indicated (20). Importantly, 80% of the antibiotics given for these ARTIs were broad spectrum (20). Our ED-specific results support these estimates, identifying a utilization rate for adult ARTI visits to the ED that was slightly higher than the rate for all ambulatory visits. Our study differed from the work by Shapiro and colleagues in that we examined a longer study period, included all ages, and provide information on trends in antibiotic utilization.

The current report confirms that EDs provide care to an increasingly larger number of patients with ARTIs. This is likely multifactorial and may result from lack of insurance, lack of primary care access, or patient preference to seek care in the ED setting (21). Our results support the hypothesis that many U.S. EDs are functioning as “safety-net” care centers, with the majority of ARTI patients being uninsured or insured by Medicaid (9, 21–23). The observed lack of change in antibiotic utilization for adult ARTI patients, especially those ARTIs for which antibiotics are not indicated, is concerning. This may indicate that efforts to curtail inappropriate antibiotic use have not been effective or have not yet been implemented for this subset of patients. Sustained antibiotic use among adult ARTI patients is likely attributable to a mixture of factors, including patient expectations and the ED environment (24). Specifically, the complexity of ARTI treatment in the ED and the difficulty of making a definitive diagnosis contribute to inappropriate use (25).

Inappropriate use of antibiotics can lead to the development of

antibiotic resistance and increase susceptibility to resistant infections (3, 26, 27). However, inappropriate use can also result in substantial morbidity and mortality in a more direct manner, placing individuals at increased risk of antibiotic-related complications. Shehab et al. estimated over 142,000 annual ED visits for complications due to antibiotic use, with nearly 80% related to allergic reactions (4). In addition, antibiotic use and the risk of *Clostridium difficile* infection have become important concerns (5, 6). Quinolone antibiotics in particular have been shown to cause significant collateral damage and toxicity (i.e., QT prolongation [prolongation of time between the start of the Q wave and the end of the T wave in the heart’s electrical cycle], drug interactions, and blood glucose fluctuation) (28, 29). For these reasons, it is important that actions are taken to reduce inappropriate use in the ED and prevent unnecessary morbidity resulting from exposure to antibiotics.

Our findings highlight opportunities for reducing inappropriate antibiotic use among adult ED ARTI patients and for optimizing treatment for antibiotic-appropriate ARTI. Antimicrobial stewardship programs (ASPs) have become a standard practice at U.S. hospitals but have focused primarily on inpatients. Recent literature highlights the success of ASPs in reducing inappropriate antibiotic use in both outpatient and inpatient settings through seminars, roundtable discussions, and personal feedback (25, 30). However, the ED has unique challenges that may not be amenable to standard ASPs. For example, emergency physicians may not be willing to stop and consult antimicrobial guidelines given the high-volume, high-acuity nature of the ED. Doctor-patient relationships in the ED are episodic, and thus ED patients may be less willing to accept emergency physician advice on antibiotic use.

Many ED patients do not have access to follow-up primary care, diminishing the options for later adjustment of ARTI care. The optimal approach to antibiotic stewardship in the ED remains unknown but could involve a combination of patient education, rapid diagnostic testing, ED-specific guidelines and treatment pathways, antibiotic order forms, or postprescription reviews (25, 30–32).

We acknowledge several important limitations of the current study. For the study period examined, NHAMCS does not provide the required information to differentiate drugs which were prescribed at discharge from those which were utilized during treatment in the ED, affecting our ability to characterize these distinct patient groups. We also could not assess the duration of treatment or readmission. An additional limitation is that NHAMCS uses a retrospective, probability-sampled design. However, the methodology of NHAMCS is rigorous, and the data set has been widely used in previous antibiotic utilization studies. We were also unable to determine whether ED visits represented readmissions by the same person. Because NHAMCS collects only three diagnoses per patient, we may have missed ARTI visits. Abstractors also may not have been consistent in the selection of diagnoses, resulting in potential misclassification.

An additional limitation is that we were unable to determine granular aspects of individual ED visits that would allow definitive judgment of appropriate antibiotic use. However, by excluding admitted patients and those with suspected bacterial infections, we were able to define a population of ARTI patients whose diagnostic codes suggest that receipt of antibiotics was likely not warranted. Of note, the NHAMCS data set does not contain sufficient information for severity adjustment and does not contain laboratory values or other measures which would allow more conclusive determination of infection severity.

Our definition of ARTI was based on ICD-9 codes, which makes it difficult to truly differentiate certain ARTIs. Due to the nature of ED care, diagnosis of these conditions is often based on nonspecific symptoms and chest radiography. Despite this limitation, NHAMCS abstractors thoroughly review patient charts prior to determining the diagnosis codes included for a given record. Differentiating bronchitis and viral pneumonia from bacterial pneumonia, or viral nasopharyngitis from bacterial rhinosinusitis, can be particularly difficult in the ED setting. In a prior study, positive predictive values of claims-based coding algorithms for pneumonia identification ranged from 72.6% to 80.8%, with sensitivity ranging from 47.8% to 66.2% and specificity ranging from 98.7% to 99.1% (33). Similar estimates were provided for other ARTIs using claims data (34). We feel that low sensitivity would result in conservative estimates of ARTI rates but would not bias our results, as there is no reason to suspect that coding practices would have changed over the study period.

In conclusion, ARTI visits and inappropriate antibiotic use for ARTI remain important problems in the ED, particularly among adult patients. Interventions to reduce inappropriate use of antibiotics which have historically targeted outpatient or inpatient settings must be expanded to the ED setting.

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of the data were performed by J.P.D., J.W.B., and H.E.W. Drafting of the manuscript was performed by J.P.D., J.W.B., and H.E.W. Critical revision of the manuscript for important intellectual content was performed by J.W.B. and H.E.W. Statistical analysis was performed by J.P.D. and H.E.W. Administrative, technical, or material support was performed by J.P.D., J.W.B., and H.E.W. Study supervision was performed by J.W.B. and H.E.W.

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REFERENCES

- Grijalva CG, Nuorti JP, Griffin MR. 2009. Antibiotic prescription rates for acute respiratory tract infections in US ambulatory settings. *JAMA* 302:758–766. <http://dx.doi.org/10.1001/jama.2009.1163>.
- Roumie CL, Halasa NB, Grijalva CG, Edwards KM, Zhu Y, Dittus RS, Griffin MR. 2005. Trends in antibiotic prescribing for adults in the United States—1995 to 2002. *J. Gen. Intern. Med.* 20:697–702. <http://dx.doi.org/10.1111/j.1525-1497.2005.0148.x>.
- Spellberg B, Guidos R, Gilbert D, Bradley J, Boucher HW, Scheld WM, Bartlett JG, Edwards J, Jr Infectious Diseases Society of America. 2008. The epidemic of antibiotic-resistant infections: a call to action for the medical community from the Infectious Diseases Society of America. *Clin. Infect. Dis.* 46:155–164. <http://dx.doi.org/10.1086/524891>.
- Shehab N, Patel PR, Srinivasan A, Budnitz DS. 2008. Emergency department visits for antibiotic-associated adverse events. *Clin. Infect. Dis.* 47:735–743. <http://dx.doi.org/10.1086/591126>.
- Owens RC, Jr, Donskey CJ, Gaynes RP, Loo VG, Muto CA. 2008. Antimicrobial-associated risk factors for *Clostridium difficile* infection. *Clin. Infect. Dis.* 46(Suppl 1):S19–S31. <http://dx.doi.org/10.1086/521859>.
- Shaughnessy MK, Amundson WH, Kuskowski MA, DeCarolis DD, Johnson JR, Drekonja DM. 2013. Unnecessary antimicrobial use in patients with current or recent *Clostridium difficile* infection. *Infect. Control Hosp. Epidemiol.* 34:109–116. <http://dx.doi.org/10.1086/669089>.
- Steinman MA, Gonzales R, Linder JA, Landefeld CS. 2003. Changing use of antibiotics in community-based outpatient practice, 1991–1999. *Ann. Intern. Med.* 138:525–533. <http://dx.doi.org/10.7326/0003-4819-138-7-200304010-00008>.
- McCaig LF, Besser RE, Hughes JM. 2002. Trends in antimicrobial prescribing rates for children and adolescents. *JAMA* 287:3096–3102. <http://dx.doi.org/10.1001/jama.287.23.3096>.
- Cheung PT, Wiler JL, Lowe RA, Ginde AA. 2012. National study of barriers to timely primary care and emergency department utilization among Medicaid beneficiaries. *Ann. Emerg. Med.* 60:4–10 e12. <http://dx.doi.org/10.1016/j.annemergmed.2012.01.035>.
- Rust G, Ye J, Baltrus P, Daniels E, Adesunloye B, Fryer GE. 2008. Practical barriers to timely primary care access: impact on adult use of emergency department services. *Arch. Intern. Med.* 168:1705–1710. <http://dx.doi.org/10.1001/archinte.168.15.1705>.
- National Center for Health Statistics, Centers for Disease Control and Prevention. 2012. Dataset documentation: National Hospital Ambulatory Medical Care Survey. National Center for Health Statistics, Centers for Disease Control and Prevention, Atlanta, GA. ftp://ftp.cdc.gov/pub/Health_Statistics/NCHS/Dataset_Documentation/NHAMCS/. Accessed 31 May 2012.
- National Center for Health Statistics, Centers for Disease Control and Prevention. 2010. Trend analysis using NAMCS and NHAMCS drug data. National Center for Health Statistics, Centers for Disease Control and Prevention, Atlanta, GA. http://www.cdc.gov/nchs/ahcd/trend_analysis.htm. Accessed 31 May 2012.
- National Center for Health Statistics, Centers for Disease Control and Prevention. 2010. NHAMCS estimation procedures. National Center for Health Statistics, Centers for Disease Control and Prevention, Atlanta, GA. http://www.cdc.gov/nchs/ahcd/ahcd_estimation_procedures.htm#nhamcs_procedures. Accessed 31 May 2012.
- Hing E, Gousen S, Shimizu I, Burt C. 2003. Guide to using masked

- design variables to estimate standard errors in public use files of the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey. *Inquiry* 40:401–415. http://dx.doi.org/10.5034/inquiryjrnl_40.4.401.
15. Wang HE, Shapiro NI, Angus DC, Yealy DM. 2007. National estimates of severe sepsis in United States emergency departments. *Crit. Care Med.* 35:1928–1936. <http://dx.doi.org/10.1097/01.CCM.0000277043.85378.C1>.
 16. US Census Bureau. 2013. Population estimates: data sets. US Census Bureau, Washington, DC. <http://www.census.gov/popest/>. Accessed 13 May 2013.
 17. Gonzales R, Malone DC, Maselli JH, Sande MA. 2001. Excessive antibiotic use for acute respiratory infections in the United States. *Clin. Infect. Dis.* 33:757–762. <http://dx.doi.org/10.1086/322627>.
 18. Centers for Disease C, Prevention. 2011. Office-related antibiotic prescribing for persons aged ≤ 14 years—United States, 1993–1994 to 2007–2008. *MMWR Morb. Mortal. Wkly. Rep.* 60:1153–1156.
 19. Neuman MI, Ting SA, Meydani A, Mansbach JM, Camargo CA, Jr. 2012. National study of antibiotic use in emergency department visits for pneumonia, 1993 through 2008. *Acad. Emerg. Med.* 19:562–568. <http://dx.doi.org/10.1111/j.1553-2712.2012.01342.x>.
 20. Shapiro DJ, Hicks LA, Pavia AT, Hersh AL. 25 July 2013. Antibiotic prescribing for adults in ambulatory care in the USA, 2007–09. *J. Antimicrob. Chemother.* <http://dx.doi.org/10.1093/jac/dkt301>.
 21. Ginde AA, Lowe RA, Wiler JL. 2012. Health insurance status change and emergency department use among US adults. *Arch. Intern. Med.* 172:642–647. <http://dx.doi.org/10.1001/archinternmed.2012.34>.
 22. Lasser KE, Kronman AC, Cabral H, Samet JH. 2012. Emergency department use by primary care patients at a safety-net hospital. *Arch. Intern. Med.* 172:278–280. <http://dx.doi.org/10.1001/archinternmed.2011.709>.
 23. Fee C, Burstin H, Maselli JH, Hsia RY. 2012. Association of emergency department length of stay with safety-net status. *JAMA* 307:476–482. <http://dx.doi.org/10.1001/jama.2012.41>.
 24. Scott JG, Cohen D, DiCicco-Bloom B, Orzano AJ, Jaen CR, Crabtree BF. 2001. Antibiotic use in acute respiratory infections and the ways patients pressure physicians for a prescription. *J. Fam. Pract.* 50:853–858.
 25. May L, Cosgrove S, L'Archeveque M, Talan DA, Payne P, Jordan J, Rothman RE. 2 November 2012. A call to action for antimicrobial stewardship in the emergency department: approaches and strategies. *Ann. Emerg. Med.* <http://dx.doi.org/10.1016/j.annemergmed.2012.09.002>.
 26. Hebert C, Weber SG. 2011. Common approaches to the control of multidrug-resistant organisms other than methicillin-resistant *Staphylococcus aureus* (MRSA). *Infect. Dis. Clin. North Am.* 25:181–200. <http://dx.doi.org/10.1016/j.idc.2010.11.006>.
 27. Weber SG, Gold HS, Hooper DC, Karchmer AW, Carmeli Y. 2003. Fluoroquinolones and the risk for methicillin-resistant *Staphylococcus aureus* in hospitalized patients. *Emerg. Infect. Dis.* 9:1415–1422. <http://dx.doi.org/10.3201/eid0911.030284>.
 28. Chou HW, Wang JL, Chang CH, Lee JJ, Shau WY, Lai MS. 2013. Risk of severe dysglycemia among diabetic patients receiving levofloxacin, ciprofloxacin, or moxifloxacin in Taiwan. *Clin. Infect. Dis.* 57:971–980. <http://dx.doi.org/10.1093/cid/cit439>.
 29. Briasoulis A, Agarwal V, Pierce WJ. 2011. QT prolongation and torsade de pointes induced by fluoroquinolones: infrequent side effects from commonly used medications. *Cardiology* 120:103–110. <http://dx.doi.org/10.1159/000334441>.
 30. Gerber JS, Prasad PA, Fiks AG, Localio AR, Grundmeier RW, Bell LM, Wasserman RC, Keren R, Zaoutis TE. 2013. Effect of an outpatient antimicrobial stewardship intervention on broad-spectrum antibiotic prescribing by primary care pediatricians: a randomized trial. *JAMA* 309:2345–2352. <http://dx.doi.org/10.1001/jama.2013.6287>.
 31. Upadhyay S, Niederman MS. 2013. Biomarkers: what is their benefit in the identification of infection, severity assessment, and management of community-acquired pneumonia? *Infect. Dis. Clin. North Am.* 27:19–31. <http://dx.doi.org/10.1016/j.idc.2012.11.003>.
 32. Schuetz P, Briel M, Mueller B. 2013. Clinical outcomes associated with procalcitonin algorithms to guide antibiotic therapy in respiratory tract infections. *JAMA* 309:717–718. <http://dx.doi.org/10.1001/jama.2013.697>.
 33. Aronsky D, Haug PJ, Lagor C, Dean NC. 2005. Accuracy of administrative data for identifying patients with pneumonia. *Am. J. Med. Qual.* 20:319–328. <http://dx.doi.org/10.1177/1062860605280358>.
 34. Cadieux G, Tamblyn R. 2008. Accuracy of physician billing claims for identifying acute respiratory infections in primary care. *Health Serv. Res.* 43:2223–2238. <http://dx.doi.org/10.1111/j.1475-6773.2008.00873.x>.