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.
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 lincosycin derivatives, quinolones, or other (carbapenams, aminoglycosides, glycyclines, glycopeptides, lerpotistics, 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 percent 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>
<thead>
<tr>
<th>ARTI type</th>
<th>Annual no. of visits (n = 103,159)</th>
<th>Rate (per 1,000 ED visits) (95% CI)</th>
<th>% patients receiving antibiotics (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any ARTI diagnosis</td>
<td>12,610</td>
<td>122 (118–126)</td>
<td>61.9 (59.7–62.5)</td>
</tr>
<tr>
<td>ARTI diagnosis (antibiotic appropriate)</td>
<td>6,977</td>
<td>68 (65–70)</td>
<td>76.5 (75.2–77.8)</td>
</tr>
<tr>
<td>Otitis media</td>
<td>3,052</td>
<td>30 (28–31)</td>
<td>83.7 (82.2–85.1)</td>
</tr>
<tr>
<td>Sinusitis</td>
<td>348</td>
<td>3 (3–4)</td>
<td>84.0 (80.3–87.1)</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>2,315</td>
<td>22 (21–24)</td>
<td>63.9 (61.4–66.3)</td>
</tr>
<tr>
<td>Tonsillitis</td>
<td>405</td>
<td>4 (3–4)</td>
<td>80.1 (76.7–83.1)</td>
</tr>
<tr>
<td>Nonviral pneumonia (bacterial or unspecified organism)</td>
<td>1,199</td>
<td>12 (11–12)</td>
<td>81.8 (79.5–84.0)</td>
</tr>
</tbody>
</table>

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)

* 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).
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 visits 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-
urate 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-
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.

![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.](http://aac.asm.org/)

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1455

on August 29, 2017 by guest

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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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**REFERENCES**


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.