

# Unnecessary Antibiotics for Acute Respiratory Tract Infections: Association With Care Setting and Patient Demographics

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**Background.** Up to 40% of antibiotics are prescribed unnecessarily for acute respiratory tract infections (ARTIs). We sought to define factors associated with antibiotic overprescribing of ARTIs to inform efforts to improve practice.

**Methods.** We conducted a retrospective analysis of ARTI visits between 2006 and 2010 from the National Ambulatory Medical Care Survey and the National Hospital Ambulatory Medical Care Survey. Those surveys provide a representative sample of US visits to community-based physicians and to hospital-based emergency departments (EDs) and outpatient practices. Patient factors (age, sex, race, underlying lung disease, tobacco use, insurance), physician specialty, practice demographics (percentage poverty, median household income, percentage with a Bachelor's Degree, urban-rural status, geographic region), and care setting (ED, hospital, or community-based practice) were evaluated as predictors of antibiotic overprescribing for ARTIs.

**Results.** Hospital and community-practice visits had more antibiotic overprescribing than ED visits (odds ratio [OR] = 1.64 and 95% confidence interval [CI], 1.27–2.12 and OR = 1.59 and 95% CI, 1.26–2.01, respectively). Care setting had significant interactions with geographic region and urban and rural location. The quartile with the lowest percentage of college-educated residents had significantly greater overprescribing (adjusted OR = 1.41; 95% CI, 1.07–1.86) than the highest quartile. Current tobacco users were overprescribed more often than nonsmokers (OR = 1.71; 95% CI, 1.38–2.12). Patient age, insurance, and provider specialty were other significant predictors.

**Conclusions.** Tobacco use and a lower grouped rate of college education were associated with overprescribing and may reflect poor health literacy. A focus on educating the patient may be an effective approach to stewardship.

**Keywords.** acute respiratory tract infections; antibiotic stewardship; inappropriate antibiotic prescribing.

In the ambulatory care setting, up to 40% of antibiotics are prescribed unnecessarily for viral respiratory tract infections (eg, acute bronchitis, nonspecific upper respiratory tract infections, and the common cold) [1, 2]. Excessive antibiotic use promotes the emergence, persistence, and transmission of antibiotic-resistant bacteria [3–5] while increasing healthcare costs [6]. Patients unnecessarily prescribed antibiotics for acute respiratory tract infections (ARTIs) are put at risk for adverse drug effects such as allergic reactions or *Clostridium difficile* infection [7]. Despite efforts to improve prescribing, inappropriate use remains commonplace. Further characterization of antibiotic prescribing for ARTIs in ambulatory settings is important to identify predictors of overprescribing.

The National Ambulatory Medical Care Survey (NAMCS) and the National Hospital Ambulatory Medical Care Survey (NHAMCS) provide patient encounter data that can be used to examine ARTI antibiotic prescribing for community-based office practices (“community practice”), hospital-based outpatient practices (“hospital practice”), and emergency departments (EDs). In 2006, those surveys added information not previously available on poverty, higher education, and median income of the practice population [8]. We evaluated ARTI antibiotic prescribing with the objective of providing researchers and policymakers data upon which to develop and advocate for better antimicrobial stewardship approaches. The principal goals were to update existing analyses with more recent survey years and to determine factors associated with inappropriate ARTI antibiotic prescribing, including the new variables on poverty and education, in the context of care setting and region of the country.

## METHODS

We performed a retrospective analysis of NAMCS and NHAMCS data between 2006 and 2010. The NAMCS is a survey of a nationally representative sample of visits to nonfederal office-based and community health center-based physicians,

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whereas the NHAMCS is a survey of visits to emergency rooms and outpatient practices from a national sample of hospitals. Both surveys, conducted annually by the National Center for Health Statistics (NCHS) at the Centers for Disease Control and Prevention, use a multistage probability design based on geographically defined primary sampling units. The NAMCS focuses on participating physicians within those units and visits seen by those physicians during a 1-week survey period each year, whereas NHAMCS uses hospitals within those areas, the clinics and EDs within those hospitals, and visits during an annual survey period of 4 weeks. All data are publicly available and fully deidentified; the study was classified as exempt by the Boston University Medical Campus Institutional Review Board.

Up to 3 diagnoses are recorded per visit using the *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes. Visits that received both an ICD-9-CM code for an ARTI for which antibiotics are not typically indicated and documentation of an antibiotic prescription were categorized as inappropriate (overprescribed). The diagnoses of acute nonsuppurative otitis media (ICD-9-CM 381), acute nasopharyngitis, and acute upper respiratory tract infection of multiple or unspecified sites (ICD-9-CM 460, 465), acute pharyngitis, tonsillitis, laryngitis and tracheitis (ICD-9-CM 462, 463, 464), acute or unspecified bronchitis and bronchiolitis (ICD-9-CM 466, 490), viral pneumonia (ICD-9-CM 480), influenza (ICD-9-CM 487), and pleurisy (ICD-9-CM 511) were ARTIs included for which antibiotics are not usually indicated. If there was no record of an antibiotic being prescribed, the visits were considered appropriate. We also included ARTI visits for which an antibiotic might be indicated, and we labeled those appropriate if an antibiotic was given. The diagnoses of streptococcal sore throat (ICD-9-CM 034), acute suppurative otitis media or mastoiditis (ICD-9-CM 382 383), acute sinusitis (ICD-9-CM 461), peritonsillar abscess (ICD-9-CM 475), bacterial pneumonias (ICD-9-CM 481–483 486), and empyema or lung abscess (ICD-9-CM 501 513) were ARTIs for which an antibiotic might appropriately be indicated. Streptococcal sore throat is the primary indication for pharyngitis treatment and has a unique code. For the analysis, other pharyngitis codes were classified as ARTIs for which antibiotics are not indicated. Visits with more than 1 ARTI code were excluded. We compared visits where an antibiotic was inappropriately prescribed to visits where the antibiotic prescribing decision was labeled appropriate.

Up to 8 medications can be listed for each visit. Antibiotics were classified according to a system developed at NCHS and a unique generic drug code from Multum's Lexicon Drug Database [9]. Antibiotic use was defined as prescription of any of the following oral agents: penicillins, cephalosporins, macrolides, fluoroquinolones, tetracyclines, sulfonamides including trimethoprim-sulfamethoxazole, and lincosamides.

The variables of interest included patient age, sex, race, chronic pulmonary disease (emphysema, chronic bronchitis),

use of tobacco (current, not current, unknown, never used tobacco), insurance (private, Medicaid, Medicare, out-of-pocket, unknown), physician specialty (general practice, eg, primary care pediatricians, internists and family medicine practitioners, medical subspecialty, surgical subspecialty), housing status (private residence, nursing home, homeless, other), practice location (US Census geographic regions Northeast, South, Midwest, West), and visit care setting (ED, hospital practice, community practice). Race was included because it has been linked with antibiotic prescribing in other studies [10]. Variables for population quartiles using the patient's zip code as the level of aggregation for percentage poverty, median household income, and percentage of adults with a Bachelor's Degree or higher were developed in 2006 and made available for public use. In addition, in 2006, a new NCHS Urban-Rural classification scheme was added using a 5-tiered measure of residential status, which we grouped into urban, suburban, and rural tiers. We used the Elixhauser comorbidity index [11] to control for patient complexity and case-mix, which has been adapted for studies with outpatient data [12, 13]. We determined variables predictive of the primary outcome of interest—inappropriate antibiotic prescribing for ARTIs.

#### Statistical Analysis

We applied individual-level weights, clustering, and stratification to the analysis to adjust for nonresponse and account for the complex survey design of the database. First, unweighted frequencies and weighted percentages were calculated for the overall sample. Second, we evaluated the unadjusted association between the outcome (inappropriate vs appropriate prescription) and each independent variable. Third, multivariable logistic regression analyzed the relationship between the outcome and the main exposure (care setting), controlling for demographic, regional, and clinical characteristics (Model I). We estimated odds ratios (ORs) and 95% confidence intervals (CIs) for both unadjusted and adjusted assessments. Finally, we examined a series of interactions—most involving care setting—with the other main effects in the model. Interactions that improved the goodness of fit, or those that could be relevant for policymakers, were tested. There were no statistically significant interactions between race and care setting, poverty and care setting, tobacco use, and poverty or tobacco use and education. However, there were significant interactions between care setting and both geographic region and residential status. Those interactions were included in Model II. All estimates were considered statistically significant at  $P < .05$ . For those variables that carried at least 5% of data incompleteness, we imputed missing values, accounting for the complex data structure. This approach involves imputing multiple, plausible sets of missing values in the incomplete dataset resulting in several completed data sets. This multiple imputation approach allows us to obtain valid point and interval estimates under a fairly general set of

conditions [14]. For goodness of fit, we evaluated the c-statistic value (area under the curve) to estimate discrimination accuracy and the Hosmer-Lemeshow test to assess how well the data fit the model in terms of calibration. The accuracy of the estimates between antibiotic use and the covariates described in results were tested using the Bootstrap inference method (10 000 bootstrap samples), applying techniques described elsewhere [15]. The *P* values between antibiotic use and the covariates remained stable (data not shown). All analyses were conducted in SAS statistical software package (version 9.3; SAS Institute Inc., Cary, NC) using methods appropriate for the analysis of complex sample survey data (“PROC SURVEY” procedures).

## RESULTS

Table 1 contains baseline characteristics for ARTI visits by care setting. Overall, the population was young (88.2% were 45 years of age or younger), white, and urban. Few patients had chronic pulmonary disease. Table 2 shows ARTI visits by care setting

and antibiotic use. There were fewer antibiotic prescriptions for ARTIs in the ED (51%) than in the community practices (60%) or hospital practices (56%). The ED had a greater proportion of ARTI visits for bronchitis, bronchiolitis, and pharyngitis than seen in community practice and hospital practice; ED prescribed fewer antibiotics for bronchitis than hospital practices.

Table 3 shows overall *P* values for predictors of inappropriate antibiotic prescribing in Model I and Model II. Factors significantly associated with antibiotic prescribing in Model I included care setting, age group, poverty, education, insurance type, tobacco use, and provider specialty. In Model II, after inclusion of interaction variables, geographic region and residential status became significant, but it was otherwise similar to Model I.

Table 4 shows the relationship within predictors of inappropriate overprescribing by categories or quartiles. Income and Medicaid insurance were significant in the unadjusted model only. In the adjusted model, patients younger than 18 years of age or older than 45 years of age had a 45% (OR = 0.55; 95% CI,

**Table 1. Baseline Characteristics of Visits for Acute Respiratory Tract Infections<sup>a</sup>**

Characteristics	Community Practice n = 5653	Hospital Practice n = 4901	Emergency Department n = 10 067
<b>Age group, n (%)</b>			
0–17 years	2796 (49.8)	2294 (44.1)	3885 (46.8)
18–45 years	2236 (38.4)	2203 (46.3)	4702 (46.8)
46 years and above	621 (11.8)	404 (9.6)	1480 (14.5)
<b>Region, n (%)</b>			
Northeast	1054 (18.5)	668 (12.2)	2040 (15.8)
West	1223 (17.0)	857 (15.9)	1819 (18.1)
Midwest	1362 (21.5)	1852 (42.8)	3971 (21.1)
South	2014 (43.0)	1524 (29.2)	3971 (45.0)
<b>Residential status, n (%)</b>			
Rural	1213 (20.6)	1554 (36.2)	2268 (27.4)
Suburban	1436 (26.2)	1249 (27.6)	2675 (24.0)
Urban	3004 (53.2)	2098 (36.1)	5124 (48.6)
<b>Gender n (%)</b>			
Male	2540 (44.4)	2061 (41.1)	4601 (45.3)
Female	3113 (55.6)	2840 (58.9)	5466 (54.7)
<b>Ethnicity/Race, n (%)</b>			
Hispanic	820 (13.6)	659 (13.4)	1571 (15.6)
Non-Hispanic Black	875 (15.6)	817 (16.7)	1957 (19.4)
Non-Hispanic Other	266 (4.8)	220 (4.7)	423 (3.9)
Non-Hispanic White	3692 (66.0)	3205 (65.2)	6116 (61.1)
<b>Poverty, n (%)</b>			
Quartile 1 (<5.00%)	1254 (24.1)	1018 (20.2)	1411 (13.2)
Quartile 2 (5.00%–9.99%)	1690 (30.9)	1314 (27.7)	2628 (25.5)
Quartile 3 (10.00%–19.99%)	1795 (30.7)	1729 (36.4)	3669 (37.1)
Quartile 4 (20.00% or more)	914 (14.3)	840 (15.7)	2359 (24.2)
<b>Education, n (%)</b>			
Quartile 1 (<2.84%)	1415 (25.6)	1446 (31.1)	3226 (33.8)
Quartile 2 (2.84%–19.66%)	1350 (23.0)	1295 (25.9)	2600 (26.3)
Quartile 3 (19.67%–31.68%)	1464 (24.9)	1092 (22.5)	2287 (22.2)
Quartile 4 (31.69% or more)	1424 (26.5)	1068 (20.5)	1954 (17.8)
<b>Comorbidity</b>			
Chronic Pulmonary Disease	142 (2.3)	89 (1.3)	170 (1.5)

Abbreviations: n, unweighted number of visits; %, weighted percentage of visits.

<sup>a</sup> Unweighted number of visits = 20 621; weighted number of visits = 289 472 321.

**Table 2. Antibiotic Prescribing for Acute Respiratory Tract Infections by Care Setting**

Type of Infection (ICD-9-CM codes)	Number of Cases No. (%)	Community Practice		Hospital Practice		Emergency Department	
		Visits No. (%)	Antibiotic Prescribed No. (%)	Visits No. (%)	Antibiotic Prescribed No. (%)	Visits No. (%)	Antibiotic Prescribed No. (%)
Otitis/ear infection (381)	2254 (14.7)	800 (31.0)	89 (10.7)	723 (28.0)	610 (75.9)	731 (28.3)	63 (8.9)
Nonspecific URI/cold (460 465)	49 (3.1)	31 (61.2)	20 (71.0)	10 (20.4)	1 (1.6)	8 (16.3)	2 (26.0)
Pharyngitis (462–464)	5192 (33.9)	2120 (29.9)	1050 (48.2)	1840 (25.9)	975 (55.3)	3140 (47.9)	1599 (53.1)
Bronchiolitis (490)	3760 (24.5)	1129 (29.8)	750 (67.2)	934 (24.7)	703 (78.7)	1697 (45.1)	1118 (65.9)
Bronchitis (466)	2630 (15.0)	682 (25.9)	433 (62.1)	575 (21.9)	389 (70.7)	1373 (52.2)	811 (61.3)
Miscellaneous (480 487 511)	1442 (9.4)	349 (24.20)	68 (22.7)	298 (20.7)	48 (18.6)	795 (55.1)	132 (17.3)
Total	15 327 (100.0)	5111 (29.1)	2410 (60.0)	4380 (24.9)	2726 (56.0)	7744 (44.1)	3725 (51.0)

Abbreviations: ICD-9-CM, *International Classification of Diseases, Ninth Revision, Clinical Modification*; No., unweighted number of visits; URI, upper respiratory infection; %, weighted percentage of visits.

.46–.65) and 37% (OR = 0.63; 95% CI, .47–.86) reduction in the odds of receiving an inappropriate antibiotic, respectively, than patients 18 to 45 years. Inappropriate prescribing was also less likely in patients older than 64 years of age (data not shown). Although the association with the quartile of poverty was significant (Table 3), the individual estimates between the poorer and richer quartiles were not significantly different. The quartile with the lowest percentage of college-educated residents had significantly greater inappropriate prescribing (OR = 1.41; 95% CI, 1.07–1.86) than the highest quartile. Patients who paid out-of-pocket for visits were more likely to inappropriately receive an antibiotic compared with privately insured patients (OR = 1.45; 95% CI, 1.17–1.81). Chronic pulmonary disease was not associated with greater overprescribing (data not shown). However, visits for current tobacco users were associated with inappropriate antibiotic prescribing more often than

encounters for patients who were not current tobacco users (OR = 1.71; 95% CI, 1.38–2.12). General practice physicians were significantly more likely to overprescribe than medical or surgical subspecialists.

Care setting was significantly associated with prescribing; hospital practice and community practice visits were more likely than ED visits to be associated with an inappropriate antibiotic prescription (OR = 1.64 and 95% CI, 1.27–2.12 and OR = 1.59 and 95% CI, 1.26–2.01, respectively). When examining geographic region and care setting (Table 5), ED and hospital practice encounters were less likely to result in overprescription of antibiotics than community practice encounters in the Northeast (OR = 0.66 and 95% CI, .50–.87 and OR = 0.70 and 95% CI, .51–.96, respectively). In contrast, in the Midwest, hospital practices were more likely to inappropriately prescribe when compared with community practices (OR = 1.50; 95% CI, 1.10–2.25) or the ED. Southern EDs were less likely to overprescribe than hospital practices (OR = 0.65; 95% CI, .48–.86). The interaction between care setting and residential status (Table 5) demonstrates EDs were less likely to overprescribe for ARTI visits in urban and rural settings when compared with hospital practice (OR = 0.73 and 95% CI, .54–.98 and OR = 0.58 and 95% CI, .44–.77, respectively). In rural areas, hospital practices were also more likely to overprescribe than community practices (OR = 1.42; 95% CI, 1.02–1.99).

**DISCUSSION**

Understanding the factors associated with ARTI antibiotic prescribing is essential to the design of stewardship interventions. Our study adds to that understanding in 2 important ways. First, we included care setting in our models, a factor that significantly impacted prescribing. Second, we had the opportunity to include newly added survey variables on higher education, poverty, and income using zip code as the level of aggregation, as well as rural-urban setting, which enriches our knowledge of how the community of patients treated by a physician affects prescribing. Unlike prior studies, geographic region [16–18],

**Table 3. Overall P Values for Variables Associated With Antibiotic Overprescription for Acute Respiratory Tract Infections**

Predictors	Model I <sup>a</sup> $\chi^2$ (P Value)	Model II <sup>a</sup> $\chi^2$ (P Value)
Setting	<b>13.30 (.001)</b>	<b>7.94 (.01)</b>
Geographic region <sup>b</sup>	6.11 (.10)	<b>6.98 (.01)</b>
Residential status <sup>b</sup>	0.90 (.62)	<b>3.20 (.001)</b>
Age group	<b>53.40 (&lt;.001)</b>	<b>54.00 (&lt;.001)</b>
Gender	0.30 (.56)	0.30 (.57)
Ethnicity/race	3.20 (.36)	3.30 (.35)
Poverty	<b>8.40 (.03)</b>	<b>7.90 (.04)</b>
Education	<b>14.00 (.002)</b>	<b>13.30 (.004)</b>
Income	1.80 (.61)	1.65 (.64)
Insurance type	<b>17.30 (.001)</b>	<b>17.00 (.001)</b>
Tobacco use	<b>29.39 (&lt;.001)</b>	<b>29.90 (&lt;.001)</b>
Provider specialty	<b>15.00 (&lt;.001)</b>	<b>14.80 (&lt;.001)</b>
Elixhauser comorbidity index	0.19 (.65)	0.22 (.63)

Bold value indicates statistically significant results.

<sup>a</sup> Model I includes all the main effects studied; Model II includes the main effects and the interaction of care setting/geographic region and care setting/residential status. c-statistic: Model I = 0.621, Model II = 0.641.

<sup>b</sup> Geographic region and residential status (urban, suburban, rural) were significant in Model II when the interaction variables were included.

**Table 4. Associations With Inappropriate Antibiotic Prescription for Acute Respiratory Tract Infections**

Predictors	Unadjusted OR (95% CI)	Model I <sup>a</sup> OR (95% CI)
<b>Setting</b>		
Hospital Practice	<b>1.38 (1.14–1.66)<sup>b</sup></b>	<b>1.64 (1.27–2.12)<sup>c</sup></b>
Community Practice	<b>1.25 (1.10–1.41)<sup>d</sup></b>	<b>1.59 (1.26–2.01)<sup>d</sup></b>
Emergency Department	Referent	Referent
<b>Age group</b>		
0–17	<b>0.50 (.43–.58)<sup>b</sup></b>	<b>0.55 (.46–.65)<sup>b</sup></b>
18–45	Referent	Referent
46 and above	<b>0.60 (.49–.73)<sup>b</sup></b>	<b>0.63 (.47–.86)<sup>b</sup></b>
<b>Poverty</b>		
Quartile 1 (<5.00%)	0.81 (.65–1.00)	0.96 (.63–1.45)
Quartile 2 (5.00%–9.99%)	<b>0.71 (.58–.87)<sup>b</sup></b>	0.74 (.51–1.06)
Quartile 3 (10.00%–19.99%)	<b>0.92 (.77–1.11)<sup>d</sup></b>	0.90 (.67–1.20)
Quartile 4 (20.00% or more)	Referent	Referent
<b>Education</b>		
Quartile 1 (<12.84%)	<b>1.40 (1.14–1.71)<sup>c</sup></b>	<b>1.41 (1.07–1.86)<sup>c</sup></b>
Quartile 2 (12.84%–19.66%)	1.09 (.92–1.29)	1.14 (.89–1.47)
Quartile 3 (19.67%–31.68%)	0.90 (.76–1.07)	0.92 (.73–1.15)
Quartile 4 (31.69% or more)	Referent	Referent
<b>Income</b>		
Quartile 1 (Below \$32 793)	<b>1.30 (1.10–1.54)<sup>c</sup></b>	0.97 (.66–1.44)
Quartile 2 (\$32 794–\$40 626)	<b>1.22 (1.01–1.48)<sup>d</sup></b>	1.13 (.84–1.54)
Quartile 3 (\$40 627–\$52 387)	1.00 (.83–1.20)	1.05 (.82–1.34)
Quartile 4 (\$52 388 or more)	Referent	Referent
<b>Insurance Type</b>		
Medicaid	<b>0.82 (.69–0.98)<sup>d</sup></b>	0.86 (.70–1.07)
Medicare	0.95 (.76–1.19)	1.03 (.73–1.47)
Out-of-Pocket	<b>1.54 (1.29–1.82)<sup>b</sup></b>	<b>1.45 (1.17–1.81)<sup>c</sup></b>
Private Insurance	Referent	Referent
<b>Tobacco Use</b>		
Current User	<b>2.13 (1.76–2.59)<sup>b</sup></b>	<b>1.71 (1.38–2.12)<sup>b</sup></b>
Not Current User	Referent	Referent
<b>Provider Specialty</b>		
Medical Specialty	<b>0.72 (.58–.89)<sup>c</sup></b>	<b>0.60 (.43–.84)<sup>c</sup></b>
Surgical Specialty	<b>0.82 (.71–.95)<sup>c</sup></b>	<b>0.69 (.56–.85)<sup>c</sup></b>
General Practice	Referent	Referent

Bold value indicates statistically significant results.

Abbreviations: CI, confidence interval; OR, odds ratio.

<sup>a</sup> Model I includes all the main effects of the model including region, residential status, gender, and race, which had no significant associations and are excluded from this table.

<sup>b</sup> Significance at  $P < .01$ .

<sup>c</sup> Significance at  $P < .001$ .

<sup>d</sup> Significance at  $P < .05$ .

rural setting [19, 20], and patient gender and race [10, 16, 18, 20, 21] did not have significant associations with ARTI antibiotic overprescribing when care setting and the new survey variables were included. Other significant associations with prescribing, eg, provider specialty, have been previously described and were also evident in our analysis [18, 19, 21].

Although inappropriate overprescribing was high for patients treated in EDs [22], it was significantly lower compared with other care settings including community practices. This may be because ED physicians are less likely to prescribe antibiotics

to improve patient satisfaction with the visit in contrast to office-based physicians, who have an ongoing relationship with the patient [23–25]. Prior studies have demonstrated significantly more resource use for cases of infectious disease in the ED than in community practice [26]. It is possible that ED providers may prescribe more appropriately because there is ready availability of point-of-care testing such as chest x-rays and complete blood counts; however, it is not clear whether this actually translates into better care.

Both urban-rural visit location and region of the country had statistically significant interactions with visit care setting. The role of residential status has been inconsistent in prior studies [16, 20]; this may be due to those interactions. Region of the country was only significant in our analysis when the interaction with care setting was included, and this result is different from other published data [16, 18]. For example, hospital practice was associated with less overprescribing in the Northeast but greater overprescribing in the Midwest. A recent study suggested stewardship interventions should target the southern United States, but it did not consider care setting [18]. Without recognition and resolution of local characteristics, a regional or national stewardship initiative for physicians will less likely be successful. In contrast, several patient-related factors were significantly associated with antimicrobial prescribing and had no interactions with care setting.

Out-of-pocket payment for care, which is typically due to being uninsured, was associated with overprescribing. For uninsured patients, who must pay for all medications, antibiotics may appear a less expensive route than purchasing products for symptomatic relief (eg, acetaminophen, diphenhydramine), especially given recent promotions for “free antibiotics” by large pharmacy retail chains—an action denounced by public health experts [27]. Many state Medicaid programs provide coverage for over-the-counter (OTC) medications [28]. Medicaid patients were less likely to be given antibiotics in the unadjusted model. Further investigation of the impact of payment source and coverage for OTC medications can be assessed to determine how it drives prescribing.

Factors that have been linked with low health literacy were associated with antibiotic overprescribing in our study. For example, tobacco use was associated with inappropriate antibiotic prescribing for ARTIs, consistent with other studies [29]. In addition, patient populations with fewer college-educated residents were significantly more likely to be overprescribed antibiotics. Educational advancement has been shown to be a determinant for good health outcomes [30]. An impoverished population has fewer opportunities to attend college, are more likely to use tobacco, and likely to have low health literacy [31–33]. In addition, there is strong evidence of an association between health literacy and smoking cessation [34].

A coordinated effort to educate patients, particularly those with lower health literacy, about appropriate indications for

**Table 5. Antibiotic Overprescription for Acute Respiratory Tract Infections: Interactions Between Setting, Region, and Residential Status (Model II<sup>a</sup>)**

Region	Northeast OR (95% CI)	West OR (95% CI)	Midwest OR (95% CI)	South OR (95% CI)
<b>Setting</b>				
ED vs Hospital Practice	0.93 (.73–1.20)	0.75 (.56–1.01)	<b>0.59 (.41–.86)<sup>b</sup></b>	<b>0.65 (.48–.86)<sup>b</sup></b>
ED vs Community Practice	<b>0.66 (.50–.87)<sup>b</sup></b>	0.93 (.64–1.35)	0.89 (.69–1.15)	0.90 (.71–1.13)
Hospital vs Community Practice	<b>0.70 (.51–.96)<sup>c</sup></b>	1.24 (.92–1.67)	<b>1.50 (1.10–2.25)<sup>c</sup></b>	1.38 (.96–1.98)
<b>Residential Status</b>				
	Urban	Suburban	Rural	
<b>Setting</b>				
ED vs Hospital Practice	<b>0.73 (.54–.98)<sup>c</sup></b>	0.88 (.64–1.19)	<b>0.58 (.44–.77)<sup>b</sup></b>	
ED vs Community Practice	0.82 (.66–1.01)	0.86 (.66–1.11)	0.83 (.61–1.13)	
Hospital vs Community Practice	1.12 (.82–1.52)	0.98 (.72–1.33)	<b>1.42 (1.02–1.99)<sup>c</sup></b>	

Bold value indicates statistically significant results.

Abbreviation: CI, confidence interval; ED, emergency department; OR, odds ratio.

<sup>a</sup> Controlling for setting, geographic region, residential status, age group, gender, ethnicity/race, poverty, education, income, insurance type, tobacco use, provider specialty, Elixhauser comorbidity index.

<sup>b</sup> Significance at  $P < .01$ .

<sup>c</sup> Significance at  $P < .001$ .

antibiotic treatment of ARTIs and smoking cessation should be a high public health priority. Studies that have included patient education, such as information pamphlets mailed to the home, have demonstrated that such education makes an important contribution to improved prescribing [35, 36]. Better prescribing for children and adolescents may reflect successful stewardship programs for pediatricians that have included components of parent education [10, 35]. Lower overprescribing for ARTIs has been linked to reduced visit rates [37, 38], suggesting that patients are performing their own triage before coming to their physician's office.

Innovative educational resources for the consumer and tools to help them decide when they should see their doctor should be developed. Internet-based training has been successful in Europe [39] but has not been adequately explored in the United States where electronic interventions have focused on decision support for healthcare providers [40]. Utilizing technology to educate 18- to 45-year-olds, the most overprescribed group in our analysis, may be particularly useful given that groups' familiarity with both the internet and other social media. This approach has been successful for patients with other diagnoses such as diabetes [41]. However, because less health-literate patients may also be less computer literate or lack internet access, that barrier must first be carefully assessed [42].

This study has several limitations. The potential for sampling bias exists, although the design of the surveys minimizes this limitation. A secondary database does not allow for determination of differences in physicians coding and reasons for prescribing. However, because we grouped ARTIs, we minimized those differences for our main analyses. We did not limit visits to those where an ARTI was the primary diagnosis. Because only 3 visit diagnoses are included in NAMCS and NHAMCS surveys, and ARTIs are self-limited infections, we thought it likely an ARTI

was current if listed. We could not determine whether an antibiotic prescribed was for the ARTI or another infection. However, other common infectious diseases, including urinary tract or skin and soft tissue infections, were present in less than 0.1% of the ARTI visits. It is still possible that we overestimated inappropriate antibiotic prescribing for ARTIs. Nevertheless, because we used a conservative analytic approach for our definition of appropriate care, a strength of our study, we minimized that limitation. We included both ARTIs that should and should not get antibiotics, thus creating a more complete picture of those clinicians who appropriately decide when to withhold and when to prescribe an antibiotic.

## CONCLUSIONS

In conclusion, prescribing for ARTIs remains suboptimal. Although many important factors are associated with inappropriate prescribing, markers that may reflect poor health literacy—tobacco use and lower rates of higher education—are also associated with overprescribing. A focus on educating the patient may be as, or more, effective as a focus on the provider, particularly if the provider believes that he or she is responding to patient preferences. A concentrated effort to educate and involve patients in the treatment decisions for ARTIs should be a healthcare priority as a way to stem inappropriate antibiotic use.

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## References

1. McCaig LF, Hughes JM. Trends in antimicrobial drug prescribing among office-based physicians in the United States. *JAMA* 1995; 273:214–9.
2. Grijalva CG, Nuorti JP, Griffin MR. Antibiotic prescription rates for acute respiratory tract infections in US ambulatory settings. *JAMA* 2009; 302:758–66.

3. Fridkin SK, Steward CD, Edwards JR, et al. Surveillance of antimicrobial use and antimicrobial resistance in United States hospitals: Project ICARE Phase 2. *Clin Infect Dis* **1999**; 29:245–52.
4. Gaynes R. The impact of antimicrobial use on the emergence of antimicrobial-resistant bacteria in hospitals. *Infect Dis Clin North Am* **1997**; 11:757–65.
5. Hicks LA, Chien YW, Taylor TH Jr, et al. Outpatient antibiotic prescribing and nonsusceptible *Streptococcus pneumoniae* in the United States, 1996–2003. *Clin Infect Dis* **2011**; 53:631–9.
6. Office of Technology Assessment. Impacts of antibiotic-resistant bacteria (OTA H-629) GPO stock #052-003-01446-7, **1995**. Available at: <http://ota.fas.org/reports/9503.pdf>. Accessed 9 March 2016.
7. Srigley JA, Brooks A, Sung M, et al. Inappropriate use of antibiotics and *Clostridium difficile* infection. *Am J Infect Control* **2013**; 41:1116–8.
8. Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). National Ambulatory Medical Care Survey (NAMCS). National Hospital Ambulatory Care Survey (NHAMCS). Available at: [http://www.cdc.gov/nchs/ahcd/ahcd\\_questionnaires.htm](http://www.cdc.gov/nchs/ahcd/ahcd_questionnaires.htm). Accessed 16 April 2015.
9. Centers for Disease Control and Prevention (CDC). National Center for Health Statistics (NCHS). Ambulatory Care Drug Database System. Available at: <http://www2.cdc.gov/drugs/applicationnav1.asp>. Accessed 16 April 2015.
10. Gerber JS, Prasad PA, Fiks AG, et al. Effect of an outpatient antimicrobial stewardship intervention on broad-spectrum antibiotic prescribing by primary care pediatricians. *JAMA* **2013**; 309:2345–52.
11. Elixhauser A, Steiner C, Harris DR, Coffey RM. Comorbidity measures for use with administrative data. *Med Care* **1998**; 36:8–27.
12. Tang J, Wan JY, Bailey JE. Performance of comorbidity measures to predict stroke and death in a community-dwelling hypertensive Medicaid population. *Stroke* **2008**; 39:1938–44.
13. Carney CP, Jones L, Woolson RF. Medical comorbidity in women and men with schizophrenia: a population-based controlled study. *J Gen Intern Med* **2006**; 21:1133–7.
14. Raghunathan TE, Lepkowski JM, Van Hoewyk J, Solenberger P. A multivariate technique for multiply imputing missing values using a sequence of regression models. *Surv Methodol* **2001**; 27:85–96.
15. Cassell DL. Don't Be Loopy: Re-Sampling and Simulation the SAS® Way. *SAS Global Forum*; **2007**. Available at: <http://www2.sas.com/proceedings/forum2007/183-2007.pdf>. Accessed 16 April 2015.
16. Steinman MA, Landefeld CS, Gonzales R. Predictors of broad-spectrum antibiotic prescribing for acute respiratory tract infections in adult primary care. *JAMA* **2003**; 289:719–25.
17. Huang ES, Stafford RS. National patterns in the treatment of urinary tract infections in women by ambulatory care physicians. *Arch Intern Med* **2002**; 162:41–7.
18. Hicks LA, Bartoces MG, Roberts RM, et al. US outpatient antibiotic prescribing variation according to geography, patient population, and provider specialty in 2011. *Clin Infect Dis* **2015**; 60:1308–16.
19. Schaffner W, Ray WA, Federspiel CF. Surveillance of antibiotic prescribing in office practice. *Ann Intern Med* **1978**; 89:796–9.
20. Gonzales R, Steiner JF, Sande MA. Antibiotic prescribing for adults with colds, upper respiratory tract infections, and bronchitis by ambulatory care physicians. *JAMA* **1997**; 278:901–4.
21. Sun C, Jew S, Dasta SL. Osteopathic physicians in the United States: antibiotic prescribing practices for patients with nonspecific upper respiratory tract infections. *J Am Osteopath Assoc* **2006**; 106:450–5.
22. Donnelly JP, Baddley JQ, Wang HE. Antibiotic utilization for acute respiratory tract infections in U.S. emergency departments. *Antimicrob Agents Chemother* **2014**; 58:1451–7.
23. Ong S, Nakase J, Moran GJ, et al. Antibiotic use for emergency department patients with upper respiratory tract infections: prescribing practices, patient expectations and patient satisfaction. *Ann Emerg Med* **2007**; 50:213–20.
24. Welschen I, Kuyvenhoven M, Hoes A, Verheij T. Antibiotics for acute respiratory tract symptoms: patients' expectations, GPs' management and patient satisfaction. *Fam Practice* **2004**; 21:234–7.
25. Kermen R, Hickner J, Brody H, Hasham I. Family physicians believe the placebo effect is therapeutic but often use real drugs as placebos. *Fam Med* **2010**; 42:636–42.
26. May L, Mullins P, Pines J. Demographic and treatment patterns for infections in ambulatory settings in the United States, 2006–2010. *Acad Emerg Med* **2014**; 21:17–24.
27. Science Daily, Free antibiotics: wrong prescription for cold and flu season, experts say. Available at: <http://www.sciencedaily.com/releases/2009/01/090116111137.htm>. Accessed 16 April 2015.
28. National Pharmaceutical Council. Pharmaceutical benefits under state federal assistance programs 2003. Available at: <http://www.npcnow.org/publication/pharmaceutical-benefits-under-state-medical-assistance-programs-2003>. Accessed 16 April 2015.
29. Stone S, Gonzales R, Maselli J, Lowenstein SR. Antibiotic prescribing for patients with colds, upper respiratory tract infections, and bronchitis: a national study of hospital-based emergency departments. *Ann Emerg Med* **2000**; 36:320–7.
30. Cohen AK, Syme SL. Education: a missed opportunity for public health intervention. *Am J Public Health* **2013**; 103:997–1001.
31. Sentell T, Zhang W, Davis J, et al. The influence of community and individual health literacy on self-reported health status. *J Gen Intern Med* **2014**; 29:298–304.
32. Siahpush M, Singh GK, Jones PR, Timsina LR. Racial/ethnic and socioeconomic variations in duration of smoking: results from 2003, 2006 and 2007 tobacco use supplement of the current population survey. *J Public Health* **2010**; 32:210–8.
33. Kuipers MA, Wingen M, Stronks K, Kunst AE. Smoking initiation, continuation and prevalence in deprived urban areas compared to non-deprived urban areas in the Netherlands. *Soc Sci Med* **2013**; 87:132–7.
34. Stewart DW, Adams CE, Cano MA, et al. Associations between health literacy and established predictors of smoking cessation. *Am J Public Health* **2013**; 103:e43–9.
35. Finkelstein JA, Huang SS, Kleinman K, et al. Impact of a 16-community trial to promote judicious antibiotic use in Massachusetts. *Pediatrics* **2008**; 121:e15–23.
36. Gonzales R, Corbett KK, Leeman-Castillo BA, et al. The “minimizing antibiotic resistance in Colorado” project: impact of patient education in improving antibiotic use in private office practices. *Health Serv Res* **2005**; 40:101–16.
37. McCaig LF, Besser RE, Hughes JM. Trends in antimicrobial prescribing rates for children and adolescents. *JAMA* **2002**; 287:3096–102.
38. Gulliford M, Latinovic R, Charlton J, et al. Selective decrease in consultations and antibiotic prescribing for acute respiratory tract infections in UK primary care up to 2006. *J Public Health (Oxf)* **2009**; 31:512–20.
39. Little P, Stuart B, Francis N, et al. Effects of internet-based training on antibiotic prescribing rates for acute respiratory tract infections: a multinational, cluster, randomized, factorial, controlled trial. *Lancet* **2013**; 382:1175–82.
40. Samore MH, Bateman K, Alder SC, et al. Clinical decision support and appropriateness of antimicrobial prescribing: a randomized trial. *JAMA* **2005**; 294:2305–14.
41. Brown LL, Lustria ML, Rankins J. A review of web-assisted interventions for diabetes management: maximizing the potential for improving health outcomes. *J Diabetes Sci Technol* **2007**; 1:892–902.
42. Gibbons CM. Use of health information technology among racial and ethnic underserved communities. *Perspect Health Inf Manag* **2011**; 8:1f.