MAJOR ARTICLE

# US Outpatient Antibiotic Prescribing Variation According to Geography, Patient Population, and Provider Specialty in 2011

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**(See the Editorial Commentary by Metlay on pages 1317–8.)**

***Background.*** Appropriate antibiotic prescribing is an essential strategy to reduce the spread of antibiotic resistance. US prescribing practices have not been thoroughly characterized. We analyzed outpatient antibiotic prescribing data to identify where appropriate antibiotic prescribing interventions could have the most impact.

***Methods.*** Oral antibiotic prescriptions dispensed during 2011 were extracted from the IMS Health Xponent database. The number of prescriptions and census denominators were used to calculate prescribing rates. Prescription totals were calculated for each provider specialty. Regression modeling was used to examine the association between socioeconomic and population health factors and prescribing rates.

***Results.*** Healthcare providers prescribed 262.5 million courses of antibiotics in 2011(842 prescriptions per 1000 persons). Penicillins and macrolides were the most common antibiotic categories prescribed. The most commonly prescribed individual antibiotic agent was azithromycin. Family practitioners prescribed the most antibiotic courses (24%). The prescribing rate was higher in the South census region (931 prescriptions per 1000 persons) than in the West (647 prescriptions per 1000 persons; $P < .001$); this pattern was observed among all age groups, including children ≤2 and persons ≥65 years of age. Counties with a high proportion of obese persons, infants and children ≤2 years of age, prescribers per capita, and females were more likely to be high prescribing by multivariable analysis (adjusted odds ratio, >1.0).

***Conclusions.*** Efforts to characterize antibiotic prescribing practices should focus on the South census region and family practitioners. Further understanding of the factors leading to high prescribing among key target populations will inform appropriate prescribing interventions.

***Keywords.*** anti-bacterial agents; antibiotic; inappropriate prescribing.

The discovery of antibiotics remains one of the most important scientific advances in human health, but the proportion of infections caused by antibiotic-resistant bacteria is increasing, and new resistance patterns continue to emerge. In 2013, the Centers for Disease Control and Prevention released a report that characterized the burden of antibiotic resistance; an estimated 2 million antibiotic-resistant illnesses and 23 000 deaths occur each year in the United States [1]. Whereas the threat of antibiotic resistance continues to grow, development of new antibiotics has lagged dangerously behind [2, 3]. Minimizing the impact of antibiotic resistance requires a multifaceted approach that ensures the availability of effective antibiotics and vaccines, access to rapid and reliable diagnostics, implementation of infection prevention strategies, and appropriate antibiotic use. Antibiotic use is the most important factor contributing to the spread of resistance [4, 5]. Promoting appropriate antibiotic prescribing is an essential strategy to combat antibiotic resistance [6].

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Studies have described serious overuse and inappropriate selection of antibiotics and the need for rational antibiotic prescribing practices in virtually every healthcare setting [7–10]. The outpatient setting accounts for >60% of antibiotic expenditures in the United States [11], indicating that outpatient healthcare settings are an important part of the problem. Recent prescribing data for children suggest that there has been up to a 24% decrease in antibiotic prescribing since the 1990s, yet 58% of all antibiotic prescriptions in the outpatient setting are for respiratory infections that are predominantly viral in etiology [12, 13].

Several studies have demonstrated the success of interventions designed to improve antibiotic prescribing in ambulatory settings [14, 15]. Canadian and European studies suggest that patient socioeconomic factors, such as income and education, have an impact on antibiotic prescribing rates, but these factors have not been explored in the United States [16, 17]. In 2013, we described wide variation in antibiotic prescribing rates by US state using prescribing data from 2010 [18]. This prompted a more comprehensive analysis of outpatient antibiotic prescribing data to further characterize prescribing rates by geographic location, provider specialty, and patient population and identify where appropriate antibiotic prescribing interventions could have the most impact. We analyzed oral antibiotic prescribing data representing all outpatient US antibiotic prescriptions in 2011 to describe outpatient prescribing patterns. We explored the relationship between antibiotic prescribing and socioeconomic and population health factors. The analyses provide an evidence base to guide future selection of key target populations and geographic locations for appropriate antibiotic prescribing interventions.

## METHODS

Systemic, oral antibiotic prescriptions dispensed by US county during 2011 were extracted from the IMS Health Xponent database. IMS Health captures >70% of all outpatient prescriptions in the United States, reconciles them to wholesale deliveries, and projects to 100% coverage of all prescription activity using a patented projection method based on a comprehensive sample of patient deidentified prescription transactions, collected from pharmacies that report their entire pharmacy business to IMS Health each week. [19]. These data represent all outpatient antibiotic prescriptions, across all payers, including community pharmacies and nongovernmental mail service pharmacies. The IMS projection method standardizes these data into estimated prescription counts and uses geospatial methods to align the "estimated" prescriptions for the nonsample pharmacies to prescribers with observed prescribing behaviors for the same product in nearby sample pharmacies. The method is routinely validated at various levels of granularity by IMS Health statistical and analytic teams.

Prescription counts were summarized by drug category, provider specialty, and patient age and sex, according to the county where the prescriber was located. Antibiotics were aggregated into categories according to the Uniform System of Classification (https://www.imshealth.com/deployedfiles/ims/Global/Content/Insights/Health%20Services%20Research%20Network/USC_Classiification_Process_2011.pdf), a therapeutic classification system created by IMS Health, as follows: tetracyclines, cephalosporins and related, lincosamides, macrolides, penicillins, quinolones, trimethoprim-sulfamethoxazole, β-lactams with increased activity, urinary anti-infectives, and others.

Provider specialties were based on American Medical Association self-designated practice specialties and aggregated into 17 specialty groups: family practice, pediatrics, internal medicine, dentistry, nurse practitioner, physician assistants, emergency medicine, dermatology, medical subspecialty, surgery, obstetrics and gynecology, urology, otolaryngology, internal medicine/pediatrics, infectious diseases, pediatric subspecialty, and other. To estimate provider denominators and providers per capita, the IMS Health Xponent prescription database was used to extract the total number of prescribers in each provider specialty.

Population data were obtained from the US Census bridging files by age group, sex, and race for each county. We obtained other county-level data from the American Community Survey (per capita income), the Area Resource File (proportion with a 4-year postsecondary education), and the Centers for Disease Control and Prevention's Behavioral Risk Factor Surveillance System (obesity data). Prescription and provider data were aggregated for each of the approximately 3000 counties in the United States.

The total number of prescriptions, corresponding to the county of the prescribing provider, and county-level census denominators were used to calculate per-capita (per 1000) prescribing rates by county, state, and US census region (https://www.census.gov/geo/reference/gtc/gtc_census_divreg.html). For the age group analyses, persons <20 years of age and those ≥20 years of age were defined as children and adults, respectively. The total number of prescriptions was calculated for each provider specialty.

We conducted an exploratory analysis using logistic regression modeling to examine the relationship between socioeconomic and population health factors (independent variables) and antibiotic prescribing (dependent variable) at the county level. Specifically, for the dependent variable, counties were dichotomized as high or low prescribing based on the top quartile and the remaining complement (bottom 3 quartiles), respectively. County-level independent variables were categorized as follows: Prescribers per capita and the proportions of person obese, ≤2 years of age, or black were dichotomized at the median, with counties below the median as the referent. Per capita

**Table 1. Antibiotic Prescribing According to Antibiotic Category, Antibiotic Agent, Sex, and Region in 2011**

| Characteristic | Prescriptions, No. in Millions (%)[a] | Prescriptions per 1000 Persons, Rate |
|---|---|---|
| Overall | | |
| Antibiotic category | | |
| Penicillins | 60.3 (23) | 193 |
| Macrolides | 59.1 (23) | 190 |
| Cephalosporins | 35.6 (14) | 114 |
| Quinolones | 27.6 (11) | 89 |
| β-lactams, increased activity | 21.6 (8) | 69 |
| Tetracyclines | 21.1 (8) | 68 |
| Trimethoprim-sulfamethoxazole | 20.3 (8) | 65 |
| Urinary anti-infectives | 8.5 (3) | 27 |
| Lincosamides | 7.8 (3) | 25 |
| Other | 0.5 (0.2) | 2 |
| Total | 262.5 | 842 |
| Antibiotic agent (top 5) | | |
| Azithromycin | 54.1 | 174 |
| Amoxicillin | 52.9 | 170 |
| Amoxicillin-clavulanate | 21.2 | 68 |
| Ciprofloxacin | 20.9 | 67 |
| Cephalexin | 20.0 | 64 |
| Sex | | |
| Female | 156.8 (60) | 990 |
| Male | 103.1 (40) | 672 |
| US census region | | |
| South | 108.0 (41) | 931 |
| Midwest | 60.2 (23) | 897 |
| Northeast | 47.1 (18) | 848 |
| West | 47.2 (18) | 647 |
| Children (aged <20 y) | | |
| Antibiotic category | | |
| Penicillins | 26.2 (36) | 317 |
| Macrolides | 15.9 (22) | 192 |
| Cephalosporins | 13.1 (18) | 158 |
| β-lactams, increased activity | 7.6 (10) | 91 |
| Trimethoprim-sulfamethoxazole | 4.7 (6) | 57 |
| Tetracyclines | 4.2 (6) | 51 |
| Lincosamides | 0.7 (1) | 8 |
| Quinolones | 0.7 (1) | 8 |
| Urinary anti-infectives | 0.6 (1) | 7 |
| Other | 0.1 (0.1) | 0 |
| Total | 73.7 | 889 |
| Antibiotic agent (top 5) | | |
| Amoxicillin | 24.9 | 300 |
| Azithromycin | 15.2 | 183 |
| Amoxicillin-clavulanate | 7.2 | 87 |
| Cefdinir | 6.1 | 74 |
| Cephalexin | 4.6 | 56 |
| Age group, y | | |
| 0–2 | 15.4 (21) | 1287 |
| 3–9 | 29.1 (40) | 1018 |
| 10–19 | 29.3 (40) | 691 |
| Sex | | |
| Female | 38.1 (52) | 941 |
| Male | 35.6 (48) | 841 |
| US census region | | |
| South | 32.0 (43) | 1028 |
| Midwest | 17.5 (24) | 976 |
| Northeast | 11.8 (16) | 858 |
| West | 12.4 (17) | 618 |
| Adults (aged ≥20 y) | | |
| Antibiotic category | | |
| Macrolides | 41.8 (23) | 183 |
| Penicillins | 32.7 (18) | 143 |
| Quinolones | 26.3 (14) | 115 |
| Cephalosporins | 21.8 (12) | 95 |
| Tetracyclines | 16.3 (9) | 71 |
| Trimethoprim-sulfamethoxazole | 15.1 (8) | 66 |
| β-lactams, increased activity | 13.6 (7) | 59 |
| Urinary anti-infectives | 7.8 (4) | 34 |
| Lincosamides | 6.9 (4) | 30 |
| Other | 0.5 (0.3) | 2 |
| Total | 182.7 | 789 |
| Antibiotic agent (top 5) | | |
| Azithromycin | 37.7 | 165 |
| Amoxicillin | 26.8 | 117 |
| Ciprofloxacin | 19.9 | 87 |
| Cephalexin | 14.9 | 65 |
| Trimethoprim-sulfamethoxazole | 14.8 | 65 |
| Age group, y | | |
| 20–39 | 57.3 (31) | 685 |
| 40–64 | 82.1 (45) | 790 |
| ≥65 | 43.4 (24) | 1048 |
| Sex | | |
| Female | 116.6 (64) | 990 |
| Male | 66.1 (36) | 596 |
| US census region | | |
| South | 74.2 (41) | 873 |
| Midwest | 42.1 (23) | 855 |
| Northeast | 34.4 (19) | 825 |
| West | 32.0 (18) | 606 |

[a] Totals may not add to number of prescriptions for all ages owing to missing data, and percentages may not equal 100% owing to rounding and missing data.

income and the proportion with a 4-year college education were evaluated using thirds with the bottom third as the referent. The proportion female was categorized using quartiles with the bottom quartile as the referent. We decided how to categorize variables (eg, quartiles) based on the distribution of data for each variable.

We performed separate multivariable modeling for each independent variable (exposure) and the dichotomized dependent variable, treating the other independent variables as potential confounders. First, we performed univariate regression analysis to determine unadjusted odds ratio between the exposure and antibiotic prescribing. For the multivariable analysis, we considered a variable a confounder if there was a change of ≥10% in the odds ratio of the exposure variable [20]. Unadjusted and adjusted odds ratios and 95% confidence intervals were computed using SAS software (version 9.3; SAS Institute).

## RESULTS

Healthcare providers prescribed 262.5 million courses of outpatient antibiotics in 2011, for a prescribing rate of 842 prescriptions per 1000 persons (Table 1). Penicillins were the most common antibiotic category prescribed, followed closely by macrolides. The most commonly prescribed antibiotic agent was azithromycin at a rate just slightly higher than amoxicillin.

Among children, healthcare providers prescribed 73.7 million courses of antibiotics for a prescribing rate of 889 prescriptions per 1000 persons. Penicillins were the most commonly prescribed antibiotic category, and amoxicillin was the most commonly prescribed agent (Table 1). Infants and children ≤2 years of age were prescribed antibiotics at a higher rate than other age groups (1287 prescriptions per 1000 persons aged ≤2 years vs 1018 and 691 prescriptions per 1000 persons aged 3–9 or 10–19 years, respectively; both $P < .001$).

Among adults (patients aged ≥20 years), healthcare providers prescribed 182.7 million courses of antibiotics, for a prescribing rate of 789 prescriptions per 1000 persons. Macrolides were the most commonly prescribed antibiotic category, and azithromycin was the most commonly prescribed agent. Persons ≥65 years of age were prescribed antibiotics at the highest rate among adults (1048 prescriptions per 1000 persons aged ≥65 years vs 685 and 790 prescriptions per 1000 persons aged 20–39 or 40–64 years; both $P < .001$). Prescribing was markedly higher for female than for male patients (Table 1), particularly among the ≥20 year old age group (female patients, 990 prescriptions per 1000 persons; male patients, 596 prescriptions per 1000 persons; $P < .001$).

Numbers of prescriptions varied considerably by provider specialty (Table 2). As anticipated, primary care providers prescribed the most courses. Among primary care providers, family practitioners prescribed the highest overall number of antibiotic courses, followed by pediatricians and internists. Of the remaining specialties, dentists prescribed the most courses, representing 10% of all prescriptions. When the number of prescriptions written per provider was assessed within each specialty, dermatologists had the highest prescribing rate per provider (724 prescriptions per provider in 2011; Table 2).

**Table 2. Antibiotic Courses Prescribed and Prescriptions Per Provider in 2011, by Provider Specialty**

| Provider Specialty | Prescriptions, No. in Millions (%) | Providers, No. | Prescriptions per Provider, Rate |
|---|---|---|---|
| All Providers | 262.5 | 911 814 | 289 |
| Persons <20 y | 73.8 (29) | . . . | . . . |
| Persons ≥20 y | 182.8 (71) | . . . | . . . |
| Family practice | 64.1 (24) | 96 073 | 667 |
| Persons <20 y | 12.9 (21) | . . . | . . . |
| Persons ≥20 y | 49.7 (79) | . . . | . . . |
| Dermatology | 8.2 (3) | 11 329 | 724 |
| Pediatrics | 32.4 (12) | 54 228 | 598 |
| Otolaryngology | 4.1 (2) | 9536 | 430 |
| Emergency medicine | 13.8 (5) | 32 346 | 427 |
| Internal medicine/pediatrics | 1.4 (1) | 3329 | 421 |
| Internal medicine | 32.1 (12) | 83 841 | 383 |
| Physician assistants | 17.5 (7) | 63 467 | 276 |
| Infectious diseases | 1.3 (1) | 6166 | 211 |
| Dentistry | 25.6 (10) | 122 706 | 208 |
| Obstetrics/gynecology | 6.7 (3) | 37 590 | 178 |
| Nurse practitioners | 19.5 (7) | 109 741 | 178 |
| Surgery (general) | 6.9 (3) | 69 536 | 99 |
| Pediatric subspecialty | 0.8 (<1) | 8273 | 97 |
| Medical subspecialty | 6.9 (3) | 74 424 | 93 |
| Other | 8.2 (3) | 113 783 | 72 |
| Urology | 6.0 (2) | 10 131 | 59 |

When we considered geographic variation in prescribing, overall prescribing rates were consistently highest in the South census region, compared with other regions of the country (Table 1). Among US states, Kentucky had the highest overall prescribing rate (1281 prescriptions per 1000 persons) and Alaska had the lowest (348 prescriptions per 1000 persons; $P < .001$) (Figures 1*A*–*D*).

Among infants and children ≤2 years of age, the prescribing rate in the South census region (1605 per 1000 persons) was much higher than the rates in the Northeast (1093 per 1000 persons) and West (855 per 1000 persons) (both $P < .001$; Figure 1*B*). Among US states, Louisiana had the highest prescribing rate in this age group (2197 prescriptions per 1000

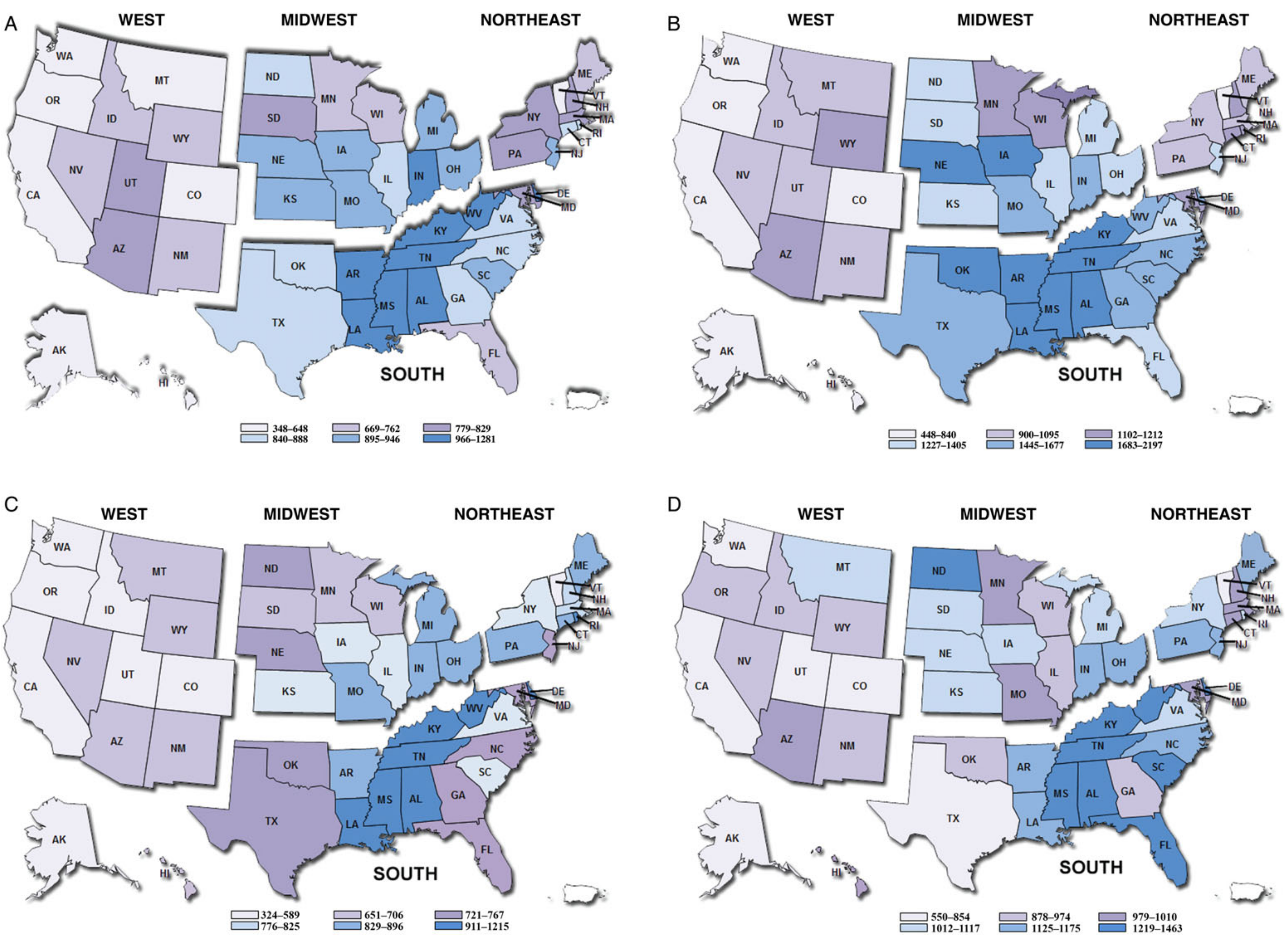


**Figure 1.** Antibiotic prescribing per 1000 persons by state (sextiles) in 2011 for all ages (*A*) and persons aged ≤2 (*B*), 3–64 (*C*), or ≥65 (*D*) years.

persons), and Alaska had the lowest (448 prescriptions per 1000 persons; $P < .001$).

Among persons ≥65 years of age, the prescribing rate in the South census region was 1160 prescriptions per 1000 persons, compared with 882 prescriptions per 1000 persons in the West, the region with the lowest rate ($P < .001$; Figure 1*D*). Kentucky had the highest prescribing rate in this age group (1463 prescriptions per 1000 persons), and Alaska had the lowest (550 prescriptions per 1000 persons; $P < .001$).

Table 3 shows unadjusted and adjusted odds ratios with corresponding 95% confidence intervals assessing the association between the county-level independent variables and county-level antibiotic prescribing rates. County-level parameters that were significantly associated with county-level prescribing by univariate regression analysis included prescribers per capita, proportion with a 4-year college education, per capita income, proportion obese, proportion ≤2 years of age, proportion female, and proportion black (Table 3). The proportions of the population who were obese or black were highest in the South, the census region with the highest prescribing rate. In the multivariable models, county-level variables in their highest categories that were independently associated with increased odds of high county-level prescribing included prescribers per capita, proportion obese, proportion ≤2 years of age, and proportion female. However, 4-year college education and per capita income in their highest categories were associated with a decreased odds of high county-level prescribing (Table 3).

## DISCUSSION

We present a comprehensive description of outpatient antibiotic prescribing in the United States, a critical step in identifying where appropriate use interventions can have the most impact. The South census region consistently had the highest prescribing rates across all age groups. Even among infants and children ≤2 years of age, a group not expected to vary importantly by region regarding the need for antibiotics, some state prescribing rates in the South census region were >3 times higher those in the Northeast and West regions. Studies of antibiotic prescribing in Europe have also shown great variation in prescribing rates across different European countries, and US rates were among the highest when compared with European countries [21, 22]. The marked variability in US state prescribing rates is perhaps more challenging to explain, given national antibiotic prescribing policies and treatment guidelines.

Data from other studies suggest that inappropriate prescribing is more common in the South. In a study of prescribing for adults in ambulatory care, antibiotics were prescribed for respiratory conditions for which they are rarely indicated during 38% of visits in the West compared with 60% of visits in the South [23]. We hypothesized that variation in health status and access

**Table 3. Results of Univariate and Multivariable Regression Models Testing the Association Between County-Level Characteristics (Independent Variables) and High Antibiotic Prescribing (Dependent Variable)[a]**

| County-Level Characteristic | Prescriptions per 1000 Persons, Mean Rate | Unadjusted OR (95% CI) | Adjusted OR (95% CI) |
|---|---|---|---|
| Prescribers per 1000 persons, rate[b] | | | |
| Below median (0.1–1.8) | 816.6 | Referent | . . . |
| Above median (1.8–35.2) | 1033.8 | 1.6 (1.4–1.8) | 1.9 (1.6–2.2) |
| 4-year college, %[c] | | | |
| Lowest third (0.0–12.3) | 925.4 | Referent | . . . |
| Middle third (12.4–17.4) | 918.8 | 0.9 (.8–1.1) | 0.9 (.8–1.0) |
| Highest third (17.5–63.7) | 931.4 | 0.8 (.6–.9) | 0.6 (.5–.8) |
| Per capita income, $[d] | | | |
| Lowest third (10 180–20 112) | 964.9 | Referent | . . . |
| Middle third (20 116–23 772) | 935.8 | 0.9 (.7–1.0) | 0.8 (.7–.9) |
| Highest third (23 773–64 381) | 875.1 | 0.5 (.4–.6) | 0.5 (.4–.6) |
| Obese adults, %[e] | | | |
| Below median (11.7–29.1) | 867.9 | Referent | . . . |
| Above median (29.2–42.7) | 983.4 | 2.1 (1.8–2.4) | 1.7 (1.5–2.0) |
| Age ≤2 y, %[f] | | | |
| Below median (1.2–3.6) | 868.6 | Referent | . . . |
| Above median (3.6–7.1) | 981.8 | 1.5 (1.3–1.7) | 1.4 (1.2–1.6) |
| Females, %[g] | | | |
| Lowest quartile (33.0–49.8) | 783.5 | Referent | . . . |
| Second quartile (49.8–50.5) | 849.7 | 1.1 (.8–1.4) | 1.1 (.8–1.3) |
| Third quartile (50.5–51.1) | 965.5 | 1.8 (1.5–2.3) | 1.7 (1.4–2.2) |
| Highest quartile (51.1–56.6) | 1102.2 | 2.6 (2.1–3.2) | 2.4 (1.9–2.9) |
| Black race, %[h] | | | |
| Below median (0.1–3.0) | 850.9 | Referent | . . . |
| Above median (3.0–85.4) | 999.5 | 1.5 (1.3–1.7) | 1.2 (1.0–1.4) |

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

[a] High antibiotic prescribing was defined as counties with prescribing rates in the highest quartile for all counties.

[b] Adjusted for proportion with 4-year college education and proportion female.

[c] Adjusted for proportion obese, prescribers per 1000 persons, and proportion female.

[d] Adjusted for proportion obese and prescriber per 1000 persons.

[e] Adjusted for prescriber per 1000 persons, per capita income, and proportion female.

[f] Adjusted for proportion obese.

[g] Adjusted for prescribers per 1000 persons.

[h] Adjusted for proportion sex.

to healthcare may also partially explain the observed geographic variation. Counties with a high proportion of obese persons and more providers per population were more likely to have high prescribing rates. Female sex was also associated with high prescribing; differences in healthcare seeking behavior and the frequency of healthcare encounters and infections may contribute to this observed sex difference [24]. Previous studies in Canada and Europe identified low education and income as factors associated with high prescribing [16, 17], and we found the same pattern in our study. Further studies should thoroughly examine patient social determinants and provider characteristics influencing antibiotic prescribing.

Antibiotic courses prescribed by family practitioners accounted for 25% of all prescriptions, more than for any other specialty. Family practitioners represented the second most common provider in our study, so this finding was not unexpected. Given the high volume of prescribing among family practitioners, efforts to further characterize their prescribing practices may identify where the greatest gains could be made to improve antibiotic prescribing. An unanticipated finding was the contribution of prescribing by dentists (10% of antibiotic courses). A recent study reported poor adherence to treatment guidelines and a high frequency of inappropriate prescribing among dentists, a prescriber group for which appropriate antibiotic use education has not been targeted in the United States [25].

Although treatment guidelines for the most common bacterial infections (eg, bacterial rhinosinusitis, streptococcal pharyngitis, and otitis media) recommend β-lactams as first-line therapy [26, 27], azithromycin was the most frequently prescribed antibiotic overall. Studies have shown that broad-spectrum antibiotics, especially macrolides, are frequently prescribed for conditions for which an antibiotic is not indicated (eg, bronchitis) or when a β-lactam is the drug of choice (eg, pediatric pneumonia) [12, 28–30]. Guidelines for treatment of mild or moderate pediatric pneumonia in otherwise healthy children recommend amoxicillin as the first-line agent for school-aged children; macrolides are recommended only for school-aged children and adolescents with findings compatible with atypical pneumonia [31]. For treatment of common infections in adults, community-acquired pneumonia is one of the few syndromes for which macrolides are recommended as first-line therapy [32]. High prescribing of macrolides is probably explained by effective marketing strategies, patient demand [33], and convenient packaging and dosing (due to the drugs' long half-life and broad-spectrum activity) [34]. Unfortunately the characteristics that make macrolides desirable from a treatment perspective also promote resistance.

Ciprofloxacin, a fluoroquinolone approved only for treatment of adult infections, was the fourth most commonly prescribed antibiotic overall. Although ciprofloxacin is widely used to treat episodes of urinary tract infection [35], it is not recommended as the first-line agent, except when allergy is present or the prevalence of resistance to a first-line agent is known to be high [36]. Interventions targeting appropriate quinolone use hold promise for great impact; the prevalence of fluoroquinolone resistance among common community-associated pathogens (eg, *Streptococcus pneumoniae*) is low [37], representing an opportunity to minimize the spread of resistance. Fluoroquinolones are also important for treatment of gram-negative infections; fluoroquinolone resistance is increasingly common among gram-negative pathogens, and prior fluoroquinolone use has been shown to be a risk factor for colonization with fluoroquinolone-resistant *Escherichia coli* [38, 39].

Although our results represent a census of antibiotic prescribing in the outpatient setting, it is challenging to assess appropriateness because our data do not capture patient visits and diagnoses. There are no established benchmarks for the amount of US antibiotic prescribing that is assumed to be appropriate and to which we can make comparisons. Furthermore, we chose prescriptions per 1000 persons as our unit of measurement, so our results are not directly comparable to studies of European prescribing rates where defined daily doses have been used. Our data set did not contain information about dosing frequency and duration of therapy; therefore, several assumptions would have been required to calculate defined daily doses. When evaluating antibiotic use in children, prescriptions per 1000 persons is a more accurate measure, because the defined daily dose is calculated based on the average adult dosage [40].

Prescribing data may not accurately represent actual consumption of antibiotics, because we only captured prescriptions that were filled by pharmacies, and patient adherence to medication regimens varies. Although we believe that nonprescription use of antibiotics is low, we were unable to account for antibiotics that may have been obtained without a prescription (eg, the Internet). Moreover, our statistical analyses relied on county-level data to test associations between population characteristics and prescribing, so our results may not reflect the individual-level characteristics associated with prescribing.

In response to growing concern for antibiotic resistance, many organizations have launched initiatives to improve antibiotic use, including the Centers for Disease Control and Prevention (CDC). The CDC's Get Smart: Know When Antibiotics Work program (www.cdc.gov/getsmart) will be using the results of this study to identify opportunities for intervention and assess future progress toward improvement in antibiotic use. Improving antibiotic prescribing has the added benefit of reducing antibiotic-associated adverse events, such as *Clostridium difficile* colitis. These efforts will be concentrated in the regions and among the providers and populations where antibiotic prescribing is the highest. Accordingly, improving our understanding of the factors that contribute to lower antibiotic prescribing rates in the West may inform efforts to improve prescribing in the South. Primary care providers, who prescribe the most prescriptions, in particular family practitioners, should be targeted for appropriate antibiotic use education. Characterization of prescribing patterns in dentists may reveal previously unrecognized opportunities to curb prescribing. Interventions to improve antibiotic prescribing should address both overprescribing and inappropriate antibiotic choice. Public health, the healthcare community and the private sector must all work together to identify opportunities to safely and effectively reduce inappropriate antibiotic use in order to improve healthcare quality, lower costs, and reduce antibiotic selection pressure that leads to resistant infections.

## Notes

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***Disclaimer.*** The statements, findings, conclusions, and views contained and expressed herein are those of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention or of IMS Health or any of its affiliated or subsidiary entities.

***Potential conflicts of interest.*** R. J. H. is an employee of IMS Health. All other authors report no potential conflicts.

All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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