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MAJOR ARTICLE

Regional Variation in Outpatient Antibiotic Prescribing for Acute Respiratory Tract Infections in a Commercially Insured Population, United States, 2017

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Background. Studies have shown that the Southern United States has higher rates of outpatient antibiotic prescribing rates compared with other regions in the country, but the reasons for this variation are unclear. We aimed to determine whether the regional variability in outpatient antibiotic prescribing for respiratory diagnoses can be explained by differences in prescriber clinical factors found in a commercially insured population.

Methods. We analyzed the 2017 IBM MarketScan Commercial Database of commercially insured individuals aged <65 years. We included visits with acute respiratory tract infection (ARTI) diagnoses from retail clinics, urgent care centers, emergency departments, and physician offices. ARTI diagnoses were categorized based on antibiotic indication. We calculated risk ratios and 95% CIs stratified by ARTI tier and region using log-binomial models controlling for patient age, comorbidities, care setting, prescriber type, and diagnosis.

Results. Of the 14.9 million ARTI visits, 40% received an antibiotic. The South had the highest proportion of visits with an antibiotic prescription (43%), and the West the lowest (34%). ARTI visits in the South are 34% more likely receive an antibiotic for rarely antibiotic-appropriate ARTI visits when compared with the West in multivariable modeling (relative risk, 1.34; 95% CI, 1.33–1.34).

Conclusions. It is likely that higher antibiotic prescribing in the South is in part due to nonclinical factors such as regional differences in clinicians' prescribing habits and patient expectations. There is a need for future studies to define and characterize these factors to better inform regional and local stewardship interventions and achieve greater health equity in antibiotic prescribing.

Keywords. antibiotic; antibiotic stewardship; outpatient; regional variation; respiratory tract infection.

Antibiotics are frequently prescribed in outpatient settings in the United States but are often prescribed unnecessarily. Antibiotic use contributes to antibiotic resistance, excess health care costs, and adverse health events, such as allergic reactions and *Clostridioides difficile* infection [1, 2]. Although the national volume of outpatient antibiotic prescriptions has declined in recent years, differences in prescribing rates across United States Census regions have remained [1, 3–5]. The West Census region consistently has the lowest outpatient antibiotic prescribing rates, while the South Census region has the highest [4–6].

Several studies have either described regional differences in antibiotic prescribing or examined clinical factors related to antibiotic prescribing patterns [5, 7]. However, few studies have analyzed how clinical factors contribute to regional variation in outpatient prescribing for acute respiratory tract infections (ARTIs), which are a frequent reason for outpatient visits and contribute to the majority of unnecessary antibiotic prescriptions [4, 8]. The objective of this study was to describe regional variability in outpatient antibiotic prescribing for ARTIs and explore whether these differences could be explained by clinical factors, such as patient age, setting of care, medical comorbidities, prescriber type, and diagnosis in a commercially insured population.

METHODS

Data Source

This analysis used the 2017 IBM MarketScan Commercial Database (IBM Watson Health, Ann Arbor, MI, USA), which is comprised of medical and prescription drug data from over 300 employers and 25 health plans in the United States [9]. The Database is based on a large convenience sample and

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contains reconciled claims data for individuals ≤65 years of age who are covered by employer-sponsored private health insurance. Medical claims were linked to outpatient prescription drug claims and person-level enrollment information through unique enrollee identifiers.

Study Population

Visits for ARTIs were identified by service date and unique enrollee identification number. Visits to retail health clinics (RHs), urgent care centers (URGs), emergency departments (EDs), and physician offices in 2017 were captured. Region was defined as the US Census region (Northeast, Midwest, South, West) where the visit occurred. Visits were included if the beneficiary was enrolled in medical coverage all 12 months before the visit, the month of the visit, and the month after the visit; additionally, we limited the sample to beneficiaries enrolled in prescription drug coverage the day of and 3 days after the visit. Visits were excluded if there were no International Classification of Diseases, Tenth Revision (ICD-10), codes listed, if a patient had a visit to >1 setting on the same day, or if the visit region, patient age, or prescriber type was unknown. We further excluded visits with a same-day hospitalization. Prescriber type was categorized according to clinical specialty and included adult primary care physicians, pediatric primary care physicians, specialists, ED prescribers, URG prescribers, dentists, nurse practitioners, physician assistants, other, and multiple.

Antibiotic claims were linked to the enrollee's most recent outpatient visit to any included setting on the same day as or within 3 days before the antibiotic fill date. Antibiotics linked to excluded settings were excluded from analysis. Only oral antibiotics and prescriptions not marked as refills were included. Comorbidity data were collected from all ICD-10 codes recorded on both outpatient and inpatient service claims in the previous 365 days from the earliest date of enrollment. The number of comorbidities for each enrollee was calculated using the Elixhauser Index for adults (ages 18–64) and the Pediatric Complex Chronic Conditions Classification System for children (ages 0–17) [10, 11]. Both indices have been used to identify preexisting conditions among large administrative data sources [12–17].

Diagnosis Assignment

Visits were assigned a single diagnosis based on a previously described 3-tiered system that categorizes conditions based on whether antibiotics are always (Tier 1), sometimes (Tier 2), or rarely indicated (Tier 3) [1], adapted for ICD-10 codes [18]. We limited our analysis to visits with common ARTI diagnoses (pneumonia, pharyngitis, sinusitis, acute otitis media, acute exacerbation of bronchitis, asthma/allergy, bronchitis/bronchiolitis, influenza, nonsuppurative otitis media, and viral upper respiratory infection) (Supplementary Table 1).

Analysis

We summarized ARTI visits by region, patient age, setting of care, rural or nonrural location (Metropolitan Statistical Area [MSA]), number of comorbidities, diagnosis, and whether an antibiotic was prescribed. We calculated antibiotic prescribing rates (number of visits with antibiotics divided by the total number of visits) for ARTI diagnoses, stratified by region. We determined that the minimum sufficient model would need to control for patient age, comorbidities, setting of care, and prescriber type, in addition to region. We calculated risk ratios and 95% CIs using 2 multivariate, log-binomial models. For 1 model, we stratified by diagnostic tier, with the West, the lowest prescribing region, as the reference for each stratum to explore regional differences *within* diagnostic tiers. We hypothesized that diagnostic patterns may also differ by region. Therefore, we created an additional model with an interaction term between region and diagnostic tier, in addition to stratifying by diagnostic tier and visit region, to account for this potential effect modification. Tier 3 ARTIs in the West were used as the reference for all strata, as prescribing rates for this region and tier were consistently lower than other regions and diagnostic tiers. In all multivariate modeling, we controlled for setting of care, prescriber type, patient age, and number of comorbidities. Analyses were conducted using SAS 9.4 (Cary, NC, USA). This analysis was reviewed by a Human Subjects Advisor in the National Center for Emerging and Zoonotic Infectious Diseases at the CDC and was determined not to involve human subjects and thus to not be subject to review by the Institutional Review Board.

RESULTS

Characteristics of ARTI Visits

Of the 100 468 255 eligible outpatient visits in 2017 (Supplementary Table 2), 14 942 525 (15%) were for ARTIs and were included in the analysis (Table 1). Most ARTI visits occurred in the South (53%), followed by the Northeast (18%), Midwest (17%), and West (12%). Over half (56.1%) of ARTI visits were for patients age 0–19 years, which was consistent across regions. Most ARTI visits involved patients with no comorbidities (61.8%), with little regional variation. Over 90% (91.9%) of visits occurred in physician offices, followed by URG (7.3%), ED (0.7%), and RH (0.2%). Nearly half (49.8%) of all ARTI visits were seen by adult and pediatric primary care prescribers. Although 12% of ARTI visits occurred in a rural area, this differed across the regions such that 5% of ARTI visits in the Northeast and 15% of the visits in the South were in rural areas.

Antibiotic Prescribing for ARTIs

Antibiotics were prescribed in 6 018 070 (40.3%) ARTI visits, with rates being highest in the South (42.5%) and lowest in

Table 1. Characteristics of Acute Respiratory Tract Infection Visits and Visits With an Antibiotic by United States Census Region, MarketScanCommercial Database, 2017

	Northeast No. Thousands (%)[a]		Midwest No. Thousands (%)[a]		South No. Thousands (%)[a]		West No. Thousands (%)[a]		Total No. Thousands (%)[a]	
Characteristic	All Visits	Antibiotic Prescribed	All Visits	Antibiotic Prescribed	All Visits	Antibiotic Prescribed	All Visits	Antibiotic Prescribed	All Visits	Antibiotic Prescribed
Total	2682	998 (37.2)	2549	1032 (40.5)	7996	3400 (42.5)	1715	588 (34.3)	14 943	6018 (40.3)
Gender										
Female	1428	547 (38.3)	1372	569 (41.5)	4440	1935 (43.6)	909	322 (35.5)	8149	3374 (41.4)
Male	1253	450 (35.9)	1177	464 (39.4)	3556	1465 (41.2)	806	266 (33.0)	6794	2644 (39.9)
Age group[b]										
0–2 y	241	95 (39.7)	220	100 (45.3)	693	331 (47.8)	145	57 (39.4)	1299	583 (9.7)
3–9 y	695	280 (40.3)	595	269 (45.4)	1791	796 (44.5)	377	146 (38.8)	3459	1492 (24.8)
10–19 y	662	218 (32.9)	645	233 (36.0)	1893	730 (38.6)	409	126 (30.9)	3610	1307 (21.7)
20–39 y	360	135 (37.5)	380	150 (39.4)	1202	527 (43.8)	265	91 (34.4)	2207	903 (15.0)
40–64 y	724	269 (37.2)	708	280 (39.6)	2418	1016 (42.0)	518	167 (32.2)	4367	1732 (28.8)
Setting[c]										
Emergency department	10	3 (36.0)	24	12 (49.2)	59	24 (41.5)	11	4 (36.4)	103	44 (42.2)
Retail clinic	2	1 (49.5)	7	4 (57.6)	14	7 (50.7)	3	2 (51.6)	25	13 (52.5)
Urgent care	223	125 (56.0)	119	73 (61.5)	619	396 (63.9)	125	71 (56.3)	109	664 (61.1)
Office	2447	868 (35.5)	2400	943 (39.3)	7304	2973 (40.7)	1576	512 (32.5)	13 727	5297 (38.6)
Prescriber type[c]										
Adult primary care physician[d]	535	275 (51.4)	662	353 (53.3)	2137	1233 (57.7)	518	242 (41.1)	3852	2103 (54.6)
Pediatric primary care physician	810	343 (42.4)	556	263 (47.3)	1847	868 (47.0)	375	153 (40.9)	3588	1627 (45.3)
Specialist[e]	596	55 (9.2)	600	53 (8.8)	1891	186 (9.8)	444	43 (9.7)	3531	337 (9.5)
Emergency department[e]	86	52 (60.7)	17	10 (59.0)	106	68 (63.9)	24	12 (51.1)	234	143 (61.0)
Urgent care[f]	170	104 (60.8)	147	93 (63.6)	474	301 (63.5)	64	36 (56.1)	855	534 (62.4)
Dentist[g]	1	0 (29.8)	2	1 (44.3)	6	2 (33.7)	0	0 (40.8)	10	3 (35.5)
Nurse practitioner[h]	54	28 (52.1)	140	78 (55.4)	391	238 (61.0)	36	18 (48.5)	622	362 (58.2)
Physician assistant[h]	29	16 (53.6)	60	33 (55.5)	92	53 (57.7)	30	14 (46.6)	210	116 (54.9)
Other[i]	65	23 (34.9)	167	86 (51.4)	436	223 (51.2)	61	21 (33.5)	729	352 (48.3)
Multiple[j]	334	102 (30.4)	199	63 (31.7)	616	228 (37.0)	162	50 (30.6)	1312	442 (33.7)
Geographic location[k]										
Nonrural	1862	679 (36.5)	2038	809 (39.7)	5433	2198 (40.5)	1488	501 (33.7)	10 821	4188 (38.7)
Rural	132	55 (42.1)	346	161 (46.7)	1200	610 (50.8)	94	39 (41.0)	1772	866 (48.9)
Unknown	689	264 (38.3)	166	61 (37.0)	1363	591 (43.4)	133	48 (36.4)	2350	964 (41.0)
No. of medical comorbidities[l]										
0	1670	636 (38.1)	1612	668 (41.5)	4875	2097 (43.0)	1071	380 (35.5)	9227	3781 (62.8)
1–2	927	331 (35.7)	859	333 (38.7)	2826	1175 (41.6)	602	193 (32.1)	5215	2031 (33.7)
≥3	85	31 (36.4)	78	32 (40.6)	295	128 (43.6)	43	15 (35.2)	501	206 (3.4)

Table 1. Continued

Characteristic	Northeast No. Thousands (%)[a]		Midwest No. Thousands (%)[a]		South No. Thousands (%)[a]		West No. Thousands (%)[a]		Total No. Thousands (%)[a]	
	All Visits	Antibiotic Prescribed	All Visits	Antibiotic Prescribed	All Visits	Antibiotic Prescribed	All Visits	Antibiotic Prescribed	All Visits	Antibiotic Prescribed
Diagnostic tier[m]										
Antibiotics always indicated (Tier 1)	60	35 (58.3)	41	26 (62.5)	110	69 (62.4)	37	24 (63.1)	249	153 (61.5)
Antibiotic sometimes indicated (Tier 2)	1262	748 (59.2)	1218	81 (66.2)	3738	2591 (69.3)	700	434 (62.0)	6917	4578 (66.2)
Antibiotics rarely indicated (Tier 3)	1360	15 (15.8)	1290	201 (15.6)	4149	741 (17.9)	978	131 (13.4)	7777	1287 (16.6)

Abbreviations: ARTI, acute respiratory tract infection; ED, emergency department; UC, urgent care.

[a]No. Thousands—number of visits in thousands; all percentages calculated as the *n* visits with an antibiotic/*n* total visits in that category (row percentage).

[b]MarketScan Commercial data sets contain data on individuals aged <65 years. Calculated based on median age during MarketScan enrollment in each year.

[c]Urgent care and emergency department are included as options for both setting of care and prescriber type and are categorized according to IBM Watson Health standards.

[d]Adult primary care prescriber category includes prescribers categorized as "adult nonspecific" and "family physicians."

[e]Specialist includes prescribers categorized under the following specialties: dermatologist, ambulatory surgery centers, surgery, surgery specialists, pediatric specialists, pediatric surgeons.

[f]Emergency department and urgent care prescriber categories could encompass many specialties but denote a prescriber working primarily in an ED or UC setting, respectively.

[g]MarketScan commercial data sets do not capture dental claims.

[h]Specialized experience or training for physician assistants and nurse practitioners is not captured by MarketScan commercial data sets.

[i]Other includes prescribers categorized under the follow specialties: radiology, physical medicine and rehab, psychiatry, psychologist, optician, pharmacist, dietitian, nursing services, psychiatric nurse, therapist, renal dialysis therapy, acupuncturist, spiritual healers, health educator/agency, transportation, health resort, home health organization/agency, public health agency, unknown clinic, and case manager.

[j]Prescriber was categorized as multiple if >1 prescriber type was recorded during 2017 for the same prescriber.

[k]Geographic location was categorized according to IBM Watson Health standards. Nonrural refers to a Metropolitan Statistical Area, and Rural refers to a non–Metropolitan Statistical Area.

[l]Number of medical comorbidities calculated using the Elixhauser Comorbidity index for patients ≥18 years of age, and Pediatric Complex Chronic Conditions Classification System for patients ≤17 years of age.

[m]ARTI Tier 1: pneumonia. ARTI Tier 2: acute exacerbation of chronic obstructive pulmonary disease, acute otitis media, pharyngitis, sinusitis. ARTI Tier 3: asthma/allergy, bronchitis/bronchiolitis, influenza, nonsuppurative otitis media, viral upper respiratory tract infection.

the West (34.3%) (Table 1). Over half of antibiotic visits (56%) were for pediatric patients (ages 0–19), and most patients had no comorbidities (62.8%). Although office visits accounted for the greatest volume of visits, they had the lowest antibiotic prescribing rate for ARTIs (38.6%) compared with URG (61.1%), RH (52.5%), and ED (42.2%). Regarding prescriber type, URG and ED clinicians had the highest rate of ARTI visits with an antibiotic prescription (62.4% and 61.0%, respectively), and pediatricians had the lowest (45.3%). Nonpediatric physicians, NPs, and PAs all prescribed antibiotics in over half of ARTI visits (range, 54.6%–58.2%). When stratified by specialty, prescribers in the South prescribed more antibiotics than prescribers in other regions. Antibiotic prescribing for Tier 1 ARTI visits (pneumonia) was similar across all regions (range, 58.1%–63.1%). For Tier 2 ARTI visits, the South had the highest antibiotic prescribing rate (69.3%) and the Northeast the lowest (59.2%). Antibiotic prescribing for Tier 3 ARTIs was highest in the South (17.9%) and lowest in the West (13.4%). The South also had the highest proportion of rural visits (18.0%) with antibiotics.

Multivariate Models

The first model was stratified by diagnostic tier and used the West as the reference within each stratum to examine regional differences within similar diagnoses (Table 2). There was little regional variation in antibiotic prescribing for Tier 1 ARTIs, with visits in the Midwest receiving slightly fewer antibiotics for these visits than the West (relative risk [RR], 0.97; 95% CI, 0.96–0.97). Visits in the Northeast and South were 5% (RR, 1.05; 95% CI, 1.04–1.05) and 9% (RR, 1.09; 95% CI, 1.08–1.09) more likely to receive an antibiotic for Tier 2 ARTIs than the West, respectively. All regions were more likely to receive an antibiotic for Tier 3 ARTIs than the West, with the South having the highest likelihood of antibiotic prescribing: Tier 3 ARTI visits in the South were 34% more likely than the West to result in an antibiotic (RR, 1.34; 95% CI, 1.33–1.34), the Northeast 21% more likely (RR, 1.21; 95% CI, 1.20–1.21), and the Midwest 18% more likely (RR, 1.18; 95% CI, 1.17–1.18).

For the second model, we used Tier 3 ARTIs in the West as the reference for all strata (Table 3; Supplementary Figure 1). As expected, all regions were >3 times more likely to prescribe antibiotics for Tier 1 ARTIs compared with Tier 3 ARTIs in the West. For Tier 2 ARTIs, visits in the South were the most likely to receive an antibiotic when compared with the reference (RR, 3.99; 95% CI, 3.97–4.01), followed by the Midwest (RR, 3.87; 95% CI, 3.85–3.89). Visits in the South for Tier 3 ARTIs were 35% more likely to receive an antibiotic as those in the West for the same diagnoses (RR, 1.35; 95% CI, 1.34–1.35). The Midwest and Northeast regions were 18% and 17%, respectively, more likely to receive an antibiotic for Tier 3 ARTIs than the West.

DISCUSSION

In this analysis of nearly 15 million visits for ARTIs in a commercially insured population in 2017, regional variability in outpatient antibiotic prescribing persisted for ARTI diagnoses for which antibiotics are rarely recommended after controlling for patient age, comorbidities, prescriber type, and setting of care. This suggests that nonclinical factors such as regional differences in clinicians' prescribing habits may be affecting a clinician's decision to prescribe an antibiotic. In particular, the South accounted for a disproportionately high rate of antibiotic prescribing for ARTIs, a trend that remained in the adjusted multivariate models.

Unmeasured factors may be contributing at 1 or multiple levels: patient, prescriber, health care system, health care payer, or local/state policies. For example, differences in patient expectations or prescribers' perceptions of patient expectations may differ regionally and be based on past experiences. A recent study evaluated antibiotic prescribing rates for ARTIs in URG and found that receiving an antibiotic for an ARTI increases the likelihood of future antibiotic prescriptions for

Table 2. Adjusted Multivariate Model[a] Comparing Antibiotic Prescribing for Acute Respiratory Tract Infections by United States Census Region, Stratified by Diagnostic Tier,[b] MarketScan Commercial Database, 2017

	Northeast Risk Ratio (95% CI)	Midwest Risk Ratio (95% CI)	South Risk Ratio (95% CI)	West Risk Ratio (95% CI)
Antibiotics always indicated (Tier 1)[b]	1.00 (0.99–1.00)	0.97 (0.96–0.97)	1.00 (0.99–1.00)	Reference
Antibiotic sometimes indicated (Tier 2)[b]	1.05 (1.04–1.05)	1.00 (0.99–1.00)	1.09 (1.08–1.09)	Reference
Antibiotics rarely indicated (Tier 3)[b]	1.21 (1.20–1.21)	1.18 (1.17–1.18)	1.34 (1.33–1.34)	Reference

Abbreviation: ARTI, acute respiratory tract infection.

[a]Risk ratios calculated using multivariable log binomial model, adjusted for setting, prescriber type, patient age, and number of comorbidities.

[b]ARTI Tier 1: pneumonia. ARTI Tier 2: acute exacerbation of chronic obstructive pulmonary disease, acute otitis media, pharyngitis, sinusitis. ARTI Tier 3: asthma/allergy, bronchitis/bronchiolitis, influenza, nonsuppurative otitis media, viral upper respiratory tract infection.

Table 3. Adjusted Multivariate Model[a] Comparing Antibiotic Prescribing for Acute Respiratory Tract Infections by United States Census Region, Stratified by Diagnostic Tier[b] and Visit Region, MarketScan Commercial Database, 2017

	Northeast Risk Ratio (95% CI)	Midwest Risk Ratio (95% CI)	South Risk Ratio (95% CI)	West Risk Ratio (95% CI)
Antibiotics always indicated (Tier 1)[b]	3.32 (3.29–3.34)	3.44 (3.41–3.47)	3.47 (3.45–3.49)	3.55 (3.51–3.58)
Antibiotic sometimes indicated (Tier 2)[b]	3.69 (3.67–3.71)	3.87 (3.85–3.89)	3.99 (3.97–4.01)	3.69 (3.68–3.71)
Antibiotics rarely indicated (Tier 3)[b]	1.17 (1.16–1.18)	1.18 (1.17–1.19)	1.35 (1.34–1.35)	Reference

Abbreviation: ARTI, acute respiratory tract infection.

[a]Risk ratios calculated using multivariable log binomial model. Multivariable model, adjusted for setting, prescriber type, patient age, and number of comorbidities.

[b]ARTI Tier 1: pneumonia. ARTI Tier 2: acute exacerbation of chronic obstructive pulmonary disease, acute otitis media, pharyngitis, sinusitis. ARTI Tier 3: asthma/allergy, bronchitis/bronchiolitis, influenza, nonsuppurative otitis media, viral upper respiratory tract infection.

ARTIs [19]. With regard to prescriber or visit setting, there may be actual or perceived barriers to obtaining follow-up care and thus more readiness to prescribe. This may be true in a setting like URG or ED, where a patient is not established at the practice. Additionally, settings such as URG and ED have unique challenges when compared with traditional primary care settings, including a higher volume of acute care visits, rotating prescribers, decreased opportunities for patient–prescriber communication, and concerns about patient satisfaction, all of which have been shown to contribute to inappropriate antibiotic prescribing [20–22].

Most ARTI visits occurred in physician offices; however, this setting had the lowest proportion of ARTI visits that were prescribed antibiotics across all 4 regions. This finding may reflect nonclinical factors such as established patient–physician relationships, prescribing differences related to perceived or actual acuity of presentation, or the presence of follow-up visits for ARTIs for which an antibiotic is not prescribed but added to the denominator of visits in this setting. Higher rates of antibiotic prescribing for ARTIs were observed in URG, a finding that has previously been described [23]. A machine-learning project evaluating the impact of nonclinical drivers on inappropriate prescribing for ARTIs in a large claims data set found that the URG setting was the strongest predictor of inappropriate antibiotic prescribing [24]. This study also found that prescribers with a younger patient age mix were less likely to prescribe Inappropriately, mirroring our finding that pediatricians prescribed fewer antibiotics than other primary care specialties.

Efforts should also be made to explore more localized regional differences among patients receiving care for ARTIs, including markers of socioeconomic status. A qualitative study of general practitioners in the United Kingdom found that prescribers perceive certain patients as more vulnerable and less able to access treatments or medical care, and thus are more likely to prescribe these patients antibiotics [25]. Prescribers also cite a lack of patient education around antibiotic resistance and appropriate antibiotic use as a factor that can lead to inappropriate antibiotic prescribing [26]. Low health literacy is associated with poor adherence to treatment regimens and decreased communication with prescribers, and data suggest that health literacy varies greatly by region, with states in the South having the lowest median health literacy scores [27, 28].

To address the cultural factors that may be affecting regional differences in outpatient antibiotic prescribing, researchers could explore inter-regional differences between clinicians' antibiotic prescribing habits and patients' antibiotic use. While researchers have investigated how patient–prescriber characteristics and interactions can affect antibiotic prescribing, qualitative research could also provide more insight into the cultural context and regional differences behind clinical treatment decisions for ARTIs [29, 30]. Our analysis was done at the Census region level; however, future analyses could focus on smaller geographic or cultural areas to provide a more nuanced understanding of the factors contributing to regional variability in antibiotic prescribing.

To improve antibiotic use, antibiotic stewardship programs (ASPs) should utilize the CDC's *Core Elements of Outpatient Antibiotic Stewardship* [31]. The *Core Elements* provides a framework for antibiotic stewardship implementation in outpatient settings based on evidence-based interventions. Interventions and resources discussed in the *Core Elements* can be tailored to fit the unique cultural needs of the prescribers, patients, health care settings, or communities. Recent increases in federal funding to state and local health departments for antibiotic stewardship will expand local access to stewardship expertise across all US regions [32].

State and local ASPs can create educational campaigns focused on educating both prescribers and patients on appropriate antibiotic prescribing and use. Patient education campaigns focused on increasing health literacy as well as awareness of antibiotic resistance and appropriate antibiotic use may increase patient knowledge of when antibiotics may be effective, thus decreasing pressure on prescribers to prescribe inappropriately [26, 28]. These campaigns should be customized to meet the specific needs of the patient community. One study found that parental expectations for an antibiotic prescription for their children varied by racial and ethnic group; therefore, public health messaging on antibiotic stewardship should be designed differently to effectively reach all of these communities [33]. Clinicians can also utilize evidence-based communication strategies in patient encounters when explaining when antibiotics are and are not needed and educating about the potential harms of antibiotic treatment [29]. An example of leveraging local data to inform interventions was described in a retrospective review of 2017 Medicaid claims in Kentucky that found that antibiotic prescribing to children in rural counties was up to 3 times higher than in urban counties [34]. Based on these data, patient and prescriber interviews were conducted in the counties with the highest rates of pediatric antibiotic prescribing in order to ascertain common themes associated with inappropriate antibiotic prescribing and use. Researchers found that prescribers may alter prescribing habits due to their perception of a patient's socioeconomic status, lack of access to transportation, and whether patients have private or public health care insurance. This research culminated in the launch of the Kentucky Antibiotic Awareness (KAA) Campaign, a multifaceted educational campaign focusing on both prescribers and patients with the goal of reducing inappropriate antibiotic prescribing [35]. All materials created by KAA were customized according to the cultural needs of the local patient and prescriber communities.

Our study is subject to several limitations. The study population is a convenience sample of medical and pharmacy claims for individuals with employer-sponsored health insurance, and thus our findings may not be generalizable beyond this population. We explored regional differences based on the 4 Census regions, and thus may have missed regional patterns that occurred at the state or local level. MSA was not included in the models due to a high percentage of visits with missing data. We were unable to further explore or control for certain patient and prescriber factors that may affect prescribing for ARTIs. For example, patient race/ethnicity, prescriber age, and number of years practicing are not captured in this data set. Antibiotic selection and duration of therapy were also not included in this study but are important markers of appropriate prescribing for ARTIs and warrant further investigation. Our study relied on ICD-10 codes for diagnoses; thus, we were unable to verify the accuracy of the diagnoses or additional details related to diagnoses. Regional differences in coding practices could also account for some of these findings, as studies have shown that coding for ARIs may differ based on a clinician's status as a high or low prescriber [36]. Additionally, we used a lookback period of 12 months before the initial ARTI encounter to capture any documented comorbidities; however, it is possible that some comorbidities were undiagnosed, undocumented, or documented incorrectly and were therefore not counted in this study. Lastly, this study was conducted before the onset of the COVID-19 pandemic in 2020. Ongoing research is needed to assess how the pandemic has affected outpatient prescribing patterns, if these effects are sustained, and whether these changes differ regionally.

CONCLUSIONS

Outpatient antibiotic prescribing for antibiotic-inappropriate ARTIs varies regionally across the United States in this commercially insured population, even after controlling for patient age, comorbidities, setting of care, and prescriber type, suggesting the presence of additional clinical or nonclinical factors that influence antibiotic prescribing. Stewardship interventions based on the *Core Elements of Outpatient Antibiotic Stewardship* and tailored to the cultural needs of smaller geographic areas are needed. The CDC supports state, local, and territorial health departments to design and implement stewardship interventions in their jurisdictions, activities that recently received additional financial support from the federal government [32]. Identification of health equity and cultural drivers influencing regional antibiotic prescribing is needed to inform local stewardship efforts with the goal of improving antibiotic use.

Supplementary Data

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

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Patient consent. This study does not include factors necessitating patient consent. This analysis was reviewed by a Human Subjects Advisor in the National Center for Emerging and Zoonotic Infectious Diseases at the CDC and was determined not to involve human subjects and thus not subject to review by the Institutional Review Board.

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