ORIGINAL ARTICLE

Patient, Provider, and Practice Characteristics Associated with Inappropriate Antimicrobial Prescribing in Ambulatory Practices

Monica L. Schmidt, MPH, PhD;[1] Melanie D. Spencer, PhD, MBA;[1] Lisa E. Davidson, MD[2]

OBJECTIVE. To reduce inappropriate antimicrobial prescribing across ambulatory care, understanding the patient-, provider-, and practice-level characteristics associated with antibiotic prescribing is essential. In this study, we aimed to elucidate factors associated with inappropriate antimicrobial prescribing across urgent care, family medicine, and pediatric and internal medicine ambulatory practices.

DESIGN, SETTING, AND PARTICIPANTS. Data for this retrospective cohort study were collected from outpatient visits for common upper respiratory conditions that should not require antibiotics. The cohort included 448,990 visits between January 2014 and May 2016. Carolinas HealthCare System urgent care, family medicine, internal medicine and pediatric practices were included across 898 providers and 246 practices.

METHODS. Prescribing rates were reported per 1,000 visits. Indications were defined using the *International Classification of Disease, Ninth and Tenth Revisions, Clinical Modification* (ICD-9/10-CM) criteria. In multivariable models, the risk of receiving an antibiotic prescription was reported with adjustment for practice, provider, and patient characteristics.

RESULTS. The overall prescribing rate in the study cohort was 407 per 1,000 visits (95% confidence interval [CI], 405–408). After adjustment, adult patients seen by an advanced practice practitioner were 15% more likely to receive an antimicrobial than those seen by a physician provider (incident risk ratio [IRR], 1.15; 95% CI, 1.03–1.29). In the pediatric sample, older providers were 4 times more likely to prescribe an antimicrobial than providers aged ≤30 years (IRR, 4.21; 95% CI, 2.96–5.97).

CONCLUSIONS. Our results suggest that patient, practice, and provider characteristics are associated with inappropriate antimicrobial prescribing. Future research should target antibiotic stewardship programs to specific patient and provider populations to reduce inappropriate prescribing compared to a "one size fits all" approach.

Infect Control Hosp Epidemiol 2018;1–9

Nearly 47 million unnecessary antibiotic prescriptions are written each year in the outpatient setting.[1] Indications such as viral upper respiratory infections, acute bronchitis, and bronchiolitis have clear guidelines that do not support the use of antibiotics.[2,3] Overuse of antibiotics has been the primary driver for increasing prevalence of multidrug-resistant bacterial infections that affect vulnerable populations and contribute to increased mortality.[4–7]

To combat increasing resistance to available antibiotics, the White House released a National Action Plan in 2015 that set a goal of reducing inappropriate outpatient antibiotic use by 50% by 2020.[8] Since that time, several studies have been published that describe baseline prescribing rates in outpatient practices.[9–14] Many of these reports focused on a single outpatient setting, such as primary care, or used national data such as the National Ambulatory Health Care Data or the National Ambulatory Medical Care Survey for their analysis.[12] Few studies have included practice types, provider, and patient characteristics to determine their impact on antimicrobial prescribing for common indications in the ambulatory care space.

Understanding characteristics that influence prescribing rates across different environments, providers, and patients will inform strategies for effective antimicrobial stewardship and improve patient care in the outpatient setting. The goal of this study was to identify patient, provider and practice characteristics that may contribute to inappropriate antibiotic prescribing. We targeted 4 clinical conditions where antimicrobials are not indicated: acute upper respiratory infection (URI), acute bronchitis, bronchiolitis, and nonsuppurative otitis media.[2,15–17] Several patient factors were included: indication for the visit, age, race, gender, Charlson comorbidity index (CCI), and average number of visits per patient during the analysis period. At the practice level, characteristics

Affiliations: 1. Center for Outcomes Research and Evaluation, Carolinas HealthCare System, Charlotte, North Carolina; 2. Division of Infectious Disease, Carolinas Medical Center, Carolinas HealthCare System, Charlotte, North Carolina.

Received May 25, 2017; accepted November 2, 2017

 DOI: 10.1017/ice.2017.263

included practice type, rural versus urban setting, and year of visit. Finally, provider level factors included age of provider and provider type.

METHODS

Data Description

Carolinas HealthCare System (CHS) is a large, integrated network of acute-care hospitals, ambulatory care, urgent care, free-standing emergency departments and skilled nursing facilities. Between 2014 and 2016, the average annual number of outpatient visits for common upper respiratory infections was 377,617 (95% confidence interval [CI], 376,970–378,264). As an integrated system, sites across the care continuum share the same electronic medical record (EMR) system where prescriptions and primary, secondary, and tertiary diagnoses for each outpatient visit are documented. These EMR data are captured and updated daily in our data warehouse, which is used for research and quality monitoring purposes.

Using this validated data source, ambulatory visits between January 1, 2014, and May 31, 2016, were extracted for this study. These data included any outpatient visit where the patient had any of the following diagnoses (*International Classification of Disease, Ninth and Tenth Revisions, Clinical Modification* [ICD-9/10-CM] diagnostic categories[9,12]): acute bronchitis, bronchiolitis, nonsuppurative otitis media, or viral URI (Supplementary Table 1).[2,3,12,18–20] These diagnoses were selected to reflect guidelines indicating that antibiotic prescribing is not appropriate.[2,15–17] There was no overlap between acute bronchitis, bronchiolitis, and URI. For our study, URI included pharyngitis, nasopharyngitis, acute supraglottis, acute epiglottitis, cough, and acute tracheitis. Bronchitis and bronchiolitis were specified by acute codes for these indications.

Only oral antibiotic prescriptions were included for this study. The classes of antibiotics were categorized as follows in order of frequency: macrolides, penicillins, cephalosporins, quinolones, and other less frequently prescribed antibiotics (ie, tetracyclines or lincomycin derivatives). We captured the route of delivery for the drug prescribed in our data and included only oral prescriptions written during the outpatient visit.

A total of 448,990 visits were extracted for study inclusion, which involved 281,315 unique patients seen across 246 practices and 898 providers. We included urgent care, family medicine, internal medicine, and pediatrics practices, and we extracted only visits in which there was any diagnosis of URI, acute bronchitis, bronchiolitis or nonsuppurative otitis media (Figure 1). The primary outcome of interest was visit-level antibiotic prescribing. Prescribing an antibiotic was defined as a visit where ≥1 antibiotic prescription was written. Prescribing rates were standardized per 1,000 visits by indication.

Data extracted to support the analyses included several patient-level characteristics: age, race, gender, Charlson comorbidity index at the time of the visit, and primary insurance type. Providers were divided into 2 categories: (1) advanced practice providers (APP) that included nurse providers and physician assistants or (2) physicians holding a medical doctor or doctor of osteopath degree. The age of the provider at the time of the visit was also captured. Practice-level factors included the year the visit occurred and type of practice (internal medicine, family medicine, urgent care, or pediatrics). The year of the visit was included in the analyses to control for practice-level changes that were not directly captured in our model but occurred over time. For example, new policies may have been implemented or diagnosis shifting may have occurred that could impact prescribing trends. By including the calendar year in the model, we adjusted for these changes in prescribing rates due to policy changes.

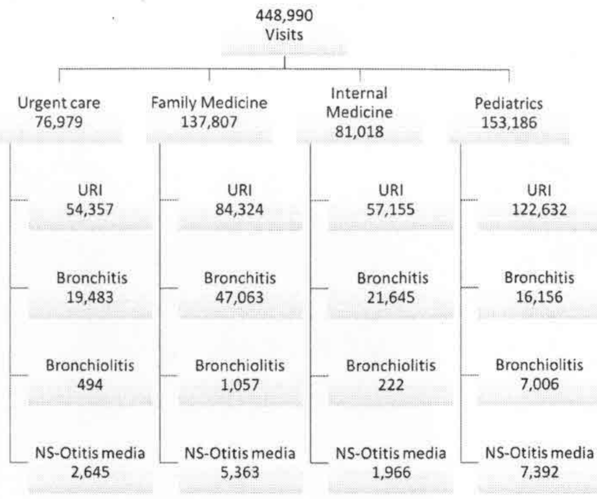

FIGURE 1. Number of patient visits by practice type and diagnosis.

Statistical Analyses

All analyses were performed using Stata software version 14.0 (StatCorp, College Station, TX). Standardized prescribing rates were calculated by obtaining the total number of visits during which an antimicrobial was prescribed, divided by the total number of visits for each of the 5 indications, then multiplied by 1,000. Rates were reported across indications by patient demographics, provider characteristics and practice type (Table 1).

To adjust for factors that could confound prescribing rates between visits within a single provider, we constructed 2 multivariable models using Poisson regression with robust errors clustered on providers with incident risk ratios reported.[21–23] The measured outcome was whether an antibiotic was prescribed at the visit (yes/no). Two models were built to separate pediatric patients (ages 0–19 years) from adult patients (20–65 years and older) given the systematic differences in the care of these 2 populations. Incident risk ratios (IRRs) were reported to facilitate ease of interpreting the risk of receiving an antibiotic. Patient, provider, and practice factors chosen for the models were selected from literature review and guidelines.[3,24–26] Once the factors were selected, they were not dropped from our models and the estimates reported. Clustered errors, using providers as the unit of clustering, adjusted for similarities in prescribing practices within individual providers.[24]

RESULTS

The overall prescribing rate for the 4 indications evaluated (adults and pediatrics) was 407 prescriptions per 1,000 visits (95% CI, 405–408) (Table 1). In the unadjusted analysis, the highest rate of inappropriate prescribing was for acute bronchitis at 703 prescriptions per 1,000 visits (95% CI, 700–706) (Table 1). Family medicine practices had more visits for acute bronchitis than other practice types, while pediatric practices had the most visits for URI (supplementary table 3). For visits with a bronchitis diagnosis for which an antibiotic prescription was written, the most frequently prescribed antibiotic classes were macrolides (59.9%) followed by penicillins (17.2%),

TABLE 1. Antimicrobial Prescribing Rates per 1,000 Visits by Indication[a]

	Mean Antimicrobial Prescriptions per 1,000 Visits (95% CI)				
	Viral URI	Bronchitis	Bronchiolitis	Nonsuppurative Otitis Media	Overall Indications
Practice Type					
Urgent care	381 (377–385)	739 (733–745)	358 (315–400)	384 (366–403)	471 (468–475)
Family medicine	376 (373–379)	678 (674–682)	364 (335–393)	274 (262–286)	475 (472–478)
Internal medicine	407 (403–411)	651 (645–657)	540 (474–606)	248 (230–267)	469 (465–472)
Pediatrics	201 (199–203)	801 (795–807)	259 (249–270)	463 (452–474)	279 (277–282)
Provider Level					
Physician	556 (554–559)	866 (863–869)	706 (689–723)	620 (610–631)	657 (655–659)
Advanced care provider	843 (838–847)	936 (932–940)	953 (935–971)	840 (821–859)	876 (873–879)
Age (pediatric)					
0–2 y	190 (187–193)	548 (535–562)	236 (226–245)	474 (460–489)	227 (225–230)
3–9 y	227 (224–230)	857 (850–864)	447 (407–487)	483 (466–500)	319 (316–323)
10–19 y	260 (255–265)	835 (827–843)	726 (657–795)	362 (359–385)	373 (368–377)
Age (adult)					
20–39 y	426 (422–431)	732 (725–739)	546 (466–626)	289 (271–306)	508 (504–512)
40–64 y	440 (436–444)	692 (688–697)	580 (527–632)	255 (241–269)	523 (520–526)
≥65 y	401 (396–405)	635 (629–641)	502 (436–567)	230 (209–251)	483 (480–487)
Race					
White	347 (344–350)	706 (702–711)	296 (279–314)	361 (349–373)	440 (438–443)
African American	267 (261–272)	686 (675–697)	241 (213–270)	376 (345–408)	353 (348–358)
Asian	179 (164–194)	764 (720–807)	220 (132–309)	397 (288–506)	257 (241–272)
Other	214 (207–221)	702 (698–705)	287 (275–299)	346 (306–385)	394 (393–396)
Year of Visit					
2014	321 (318–323)	704 (700–709)	247 (231–263)	291 (280–303)	411 (408–413)
2015	315 (312–317)	706 (701–710)	302 (288–316)	389 (378–400)	406 (404–408)
2016	299 (295–304)	690 (683–697)	303 (282–324)	454 (438–470)	396 (392–400)
Patient's Insurance Provider at Time of Visit					
Managed care	325 (322–327)	733 (730–737)	277 (264–290)	350 (341–359)	418 (416–420)
Medicaid	240 (237–243)	711 (703–719)	275 (261–289)	487 (470–504)	310 (307–313)
Medicare	394 (389–399)	626 (620–632)	519 (454–584)	223 (202–245)	477 (473–480)
Commercial	343 (334–352)	758 (745–770)	324 (264–384)	368 (332–403)	456 (449–464)
Self-pay	344 (333–356)	678 (662–695)	314 (242–386)	450 (398–503)	448 (438–457)
Other	281 (245–318)	488 (439–537)	280 (100–459)	363 (157–569)	292 (269–314)
Age of Provider					
≤30 y	99 (87–111)	324 (281–367)	21 (0–51)	295 (179–410)	141 (128–154)
31–40 y	283 (280–286)	635 (628–642)	198 (180–217)	380 (364–395)	356 (353–359)
41–50 y	317 (314–320)	684 (680–689)	297 (283–311)	327 (315–339)	401 (398–403)
51–60 y	370 (366–373)	693 (688–698)	374 (352–396)	405 (391–420)	471 (468–474)
>60	289 (285–293)	650 (643–656)	255 (228–282)	387 (369–405)	404 (401–408)
Overall visits	N/A	N/A	N/A	N/A	407 (405–408)
Overall indications	315 (313–317)	703 (700–706)	284 (275–294)	368 (361–375)	N/A

NOTE. NA, not available.
[a]Standardization of prescribing rates = (total visits where antimicrobial was prescribed/total visits) × 1,000.

quinolones (14.5%), cephalosporins (8.0%), and other (0.4%) (supplementary Table 1). Across all antibiotic classes, the 3 most frequently prescribed antibiotics were azithromycin (46.6%) followed by amoxicillin (18.1%), and amoxicillin-clavulanate (11.8%). Penicillins were the most frequently prescribed antibiotic for nonsuppurative otitis media (62.5%) and bronchiolitis (51.0%). Azithromycin was most frequently prescribed for URI in adults and for acute bronchitis in pediatric patients (Supplementary Table 4).

Across all practice types the rates of prescribing were greater for APPs compared to physician providers (Table 1). At the practice level, family medicine practices had the highest rate of prescribing, while pediatric practices had the lowest rate. There was a 133.4% increase in the antibiotic prescribing rate across all indications for patients aged 0 to 64 years (227–523 per 1,000 visits) (Table 1 pediatric and adult overall rates). Prescribing rates began to decline for patients aged > 64 years.

In the adjusted analyses for the pediatric sample, the risk of receiving an antimicrobial at a visit increased as patient age increased (Table 2). For example, patients 3–9 years of age had a 25% greater risk of receiving an antimicrobial than those aged 0–2 years (IRR, 1.25; 95% CI, 1.19–1.32), and this rate increased further for those aged 10–19 years (Table 2). African-American and Asian pediatric patients were less likely than white patients to receive an antibiotic at a visit (Table 2). Pediatric patients with commercial insurance plans were 10% more likely to receive an antibiotic prescription than those with managed care plans (IRR, 1.10; 95% CI, 1.00–1.22).

TABLE 2. Pediatrics Poisson Regression Model with Provider Clustered Errors

			95% CI		
Variable	IRR	Robust SE	Low	High	*P* Value
Patient Factors					
Indication for Antimicrobial (ref. upper respiratory infection)					
Bronchitis	3.32	0.21	2.94	3.76	<.001[a]
Bronchiolitis	1.38	0.12	1.16	1.63	<.001[a]
Nonsuppurative otitis media	2.13	0.19	1.79	2.54	<.001[a]
Age category (ref. 0–2 y)					
3–9 y	1.25	0.03	1.19	1.32	<.001[a]
10–19 y	1.31	0.05	1.22	1.41	<.001[a]
Male (ref. female)	0.99	0.01	0.97	1.01	.218
Race (ref. white)					
African American	0.86	0.03	0.80	0.92	<.001[a]
Asian	0.69	0.04	0.61	0.78	<.001[a]
Other	0.99	0.01	0.96	1.02	.515
Charlson comorbidity score at time of visit	1.02	0.02	0.99	1.05	.247
Payer (ref. managed care)					
Medicaid	1.04	0.05	0.95	1.15	.385
Commercial	1.10	0.05	1.00	1.22	.049[a]
Self-pay	1.03	0.03	0.97	1.10	.313
Other	0.64	0.09	0.48	0.84	.002[a]
Average number of visits per patient	1.03	0.01	1.02	1.04	<.001[a]
Practice Factors					
Practice type (ref. urgent care, pediatrics)					
Family medicine, pediatrics	0.92	0.08	0.78	1.08	.283
Pediatrics	0.84	0.07	0.70	1.00	.045[a]
Year of visit (ref. 2014)					
2015	0.98	0.02	0.93	1.02	.301
2016	0.97	0.04	0.90	1.05	.495
Practice in metropolitan service area	1.19	0.10	1.00	1.40	.046[a]
Provider Factors					
Provider level (ref. physician)					
Advanced practice practitioner	1.18	0.16	0.91	1.55	.216
Age of provider (ref. ≤30 y)					
31–40 y	2.97	0.52	2.11	4.19	<.001[a]
41–50 y	3.61	0.66	2.52	5.18	<.001[a]
51–60 y	4.21	0.75	2.96	5.97	<.001[a]
>60 y	2.96	0.50	2.12	4.13	<.001[a]

NOTE. IRR, incident risk ratio.
[a]Significance level, $P<.05$.

However, patients with other methods of payments that included worker's compensation plans, homeless without insurance, and community grant coverage were 36% less likely to receive an antibiotic prescription (IRR, 0.64; 95% CI, 0.48–0.84).

At the practice level, pediatric practices were 16% less likely to prescribe an antimicrobial than urgent care practices (IRR, 0.84; 95% CI, 0.70–1.00). Practices seeing pediatric patients and residing in an urban setting prescribed more antibiotics than those in rural settings (Table 2).

Among providers, the risk of a patient receiving an antibiotic increased as the provider's age increased up to age 61 across all indications (Table 1). When adjusted in the pediatric sample, providers aged 51–60 years at the time of the visit were 4 times more likely to prescribe an antimicrobial compared to providers aged ≤30 years (IRR, 4.21; 95% CI, 2.96–5.97), but the risk began to decrease for providers aged ≥60 years (IRR, 2.96; 95% CI, 2.12–4.13) (Table 2).

In the adult adjusted model, patient age and race were associated with prescribing (Table 3). Patients aged 40–64 years were 4% more likely to receive an antibiotic than patients aged 20–39 years (IRR, 1.04; 95% CI, 1.02–1.05). All other races were less likely to receive an antibiotic than white patients (Table 3). Patients with Medicaid, Medicare or other payment methods were also less likely to receive an antimicrobial compared to

TABLE 3. Adults Poisson Regression Model with Provider Clustered Errors

			95% CI		
Variable	IRR	Robust SE	Low	High	*P* Value
Patient Factors					
Indication for antimicrobial (ref. upper respiratory infection)					
Bronchitis	1.60	0.04	1.53	1.68	<.001[a]
Bronchiolitis	1.30	0.10	1.12	1.52	.001[a]
Nonsuppurative otitis media	0.60	0.03	0.55	0.66	<.001[a]
Age (ref. 20–39 y)					
40–64 y	1.04	0.01	1.02	1.05	<.001[a]
≥ 65 y	1.03	0.02	1.00	1.06	.037[a]
Male (ref. female)	1.00	0.01	0.99	1.02	.507
Race (ref. white)					
African American	0.85	0.02	0.82	0.89	<.001[a]
Asian	0.85	0.03	0.79	0.92	<.001[a]
Other	0.95	0.01	0.93	0.97	<.001[a]
Charlson comorbidity score at time of visit	0.99	0.00	0.98	0.99	<.001[a]
Payer (ref. managed care)					
Medicaid	0.91	0.02	0.87	0.96	<.001[a]
Medicare	0.95	0.01	0.92	0.97	<.001[a]
Commercial	1.05	0.02	1.00	1.09	.043[a]
Self-Pay	0.96	0.04	0.88	1.06	.435
Other	0.65	0.05	0.57	0.75	<.001[a]
Average number of visits per patient	0.96	0.01	0.95	0.97	<.001[a]
Practice Factors					
Practice type (ref. urgent care, adults)					
Family medicine, adults	0.96	0.05	0.86	1.07	.458
Internal medicine adults	0.90	0.05	0.80	1.00	.060
Year of visit (ref. 2014)					
2015	1.02	0.02	0.99	1.05	.273
2016	1.00	0.02	0.96	1.05	.988
Practice in metropolitan service area	1.36	0.12	1.15	1.61	<.001[a]
Provider Factors					
Provider level (ref. physician)					
Advanced practice practitioner	1.15	0.07	1.03	1.29	.014[a]
Age of provider (ref. ≤30 y)					
31–40 y	1.83	0.45	1.13	2.96	.014[a]
41–50 y	1.88	0.46	1.16	3.03	.010[a]
51–60 y	1.92	0.47	1.19	3.11	.008[a]
>60 y	1.80	0.45	1.11	2.93	.018[a]

NOTE. IRR, incident risk ratio.
[a]Significance level, $P < .05$.

those with managed care plans (Table 3). For adults seen in a metropolitan area, the risk of receiving an antibiotic was 36% greater than in rural practices (IRR, 1.36; 95% CI, 1.15–1.61). However, the type of practice was not associated with antimicrobial prescribing for adult visits.

After adjusting for patient and practice factors, APPs were 15% more likely to prescribe an antibiotic than physician providers (IRR, 1.15; 95% CI, 1.03–1.29) in adult patients (Table 3), but this did not hold true for pediatric visits (Table 2). The age of the prescribing provider was associated with an increased risk of prescribing an antibiotic and was similar in the pediatric sample (Table 3).

DISCUSSION

Antimicrobial stewardship in the acute inpatient care setting has demonstrated effectiveness in decreasing inappropriate antibiotic utilization over the last 20 years and has been associated with decreasing antimicrobial resistance.[26–29] Studies have identified multiple interventions that have been part of successful inpatient stewardship, such as front-end restriction or post-prescription review and feedback.[29,30] In contrast to the outpatient setting, inpatient stewardship focuses on a somewhat static patient population; patients are admitted for several days and can be followed over time to evaluate clinical progress, to review culture data, and to conduct interventions.[31]

Antimicrobial stewardship in the outpatient setting seeks to address a population that differs in acuity, microbiologic etiology, and patient characteristics. While outpatients are typically less acutely ill than inpatients, national data demonstrate that the volume of antibiotics used in the outpatient setting is much greater, with up to 30% of all outpatient antibiotic prescriptions deemed unnecessary and up to 50% inappropriate for the indication.[20,32] Traditional interventions used in the inpatient setting cannot be practically applied to outpatient stewardship.[33] Because of these differences, the large (and diverse) population of patients that need to be reached, and limited resources available for outpatient antimicrobial stewardship programs, clear evidence is needed to determine which patient populations should be targeted for interventions that can be easily implemented and will yield the greatest reduction in inappropriate prescribing.

A good starting point for identifying how to reduce inappropriate outpatient prescribing is to evaluate diagnoses for which antibiotics are rarely, if ever, indicated. We chose 4 common conditions that do not routinely require antibiotics: acute bronchitis, bronchiolitis, nonsuppurative otitis media, and URI. While these conditions are commonly seen across all outpatient practices, our findings demonstrate that variation in prescribing patterns exists and is associated with several patient, practice, and provider characteristics. The breadth of this study, which included evaluation of prescribing rates for more than 448,990 patient visits, is a key strength that supported the detailed analysis to detect these differences.

Some of our findings were consistent across practice settings. For example, acute bronchitis was the most common indication for which an antibiotic was prescribed. The most common drug prescribed for bronchitis was azithromycin in both adult and pediatric populations. Previous studies and our results suggest that patient and provider education on appropriate prescribing for bronchitis, including guidance on correct use of azithromycin, may be an effective way to reduce prescribing rates.[26,34–37]

Our analysis found that patient age was strongly associated with the rates of antimicrobial prescribing even after adjusting for other factors, such as comorbidities, gender, race, and indication. The study results demonstrated that, as patient age increased, the risk of receiving an antimicrobial for any of the 4 indications also rose to age 64, with IRRs increasing by age category in both adult and pediatric models (Tables 2 and 3). After age 64, the rates declined (Table 3). The underlying reason for this association could not be not identified in this study. Based on previous studies and on qualitative work in progress, we hypothesize that working-age patients may pressure providers to prescribe antibiotics based on their misunderstanding of which illnesses will improve with antibiotic treatment and on their need to return quickly to work and family responsibilities.[38,39] These patient dynamics and the pressure they place on provider decisions need to be better understood. In-depth qualitative research could assess this hypothesis and help elucidate the interactions between providers and patients of varying ages that lead to unnecessary prescribing. This information is essential to informing effective antibiotic stewardship interventions.

Many publications have evaluated patient characteristics and attitudes surrounding antimicrobial prescribing.[36,38,39] However, we found that provider characteristics may also impact prescribing rates. A study conducted in urgent care, emergency, and primary care outpatient clinics of the Veterans Affairs Health System found significant variation by provider in prescribing for acute respiratory illnesses, but it did not evaluate provider-specific factors, such as age and level of training.[40] Our results showed significant variation based on provider age, with younger providers prescribing fewer inappropriate antibiotics than older providers.

In the present study, we also found higher levels of inappropriate prescribing by APPs compared to other providers for the adult patient population. For pediatric patients, higher prescribing rates were not associated with APPs. Our findings are similar to other previously published literature which have also found increased associations with prescribing by APPs, especially for acute respiratory tract infections.[9] Future national stewardship efforts should target education and antimicrobial stewardship interventions for APPs as their role in patient care continues to grow.[9] Unlike other recent studies, we found that prescribing rates were also higher in urban versus rural practice settings, after adjusting for other variables.[41] Our patient population is limited to the southeastern region of the United States, which has been well documented to have the highest prescribing rates.[20,41] Further evaluation is needed to better identify socioeconomic factors contributing to prescribing in outpatient population.

We detected variation in prescribing rates by patient race. In both pediatric and adult samples, white patients received significantly more antibiotics than other races. These study results are consistent with those in many other studies, for both pediatric and adult populations.[42–44] Several studies have demonstrated that antibiotics are underprescribed for black adults, but the reasons for this are not fully understood.[45,46]

This study had several limitations. First, while data were analyzed at the visit level, administrative billing data were used to identify visits where any of the 4 indications were present as a diagnosis for a single visit. This strategy assumed that the antibiotic was given for the indication identified, which may

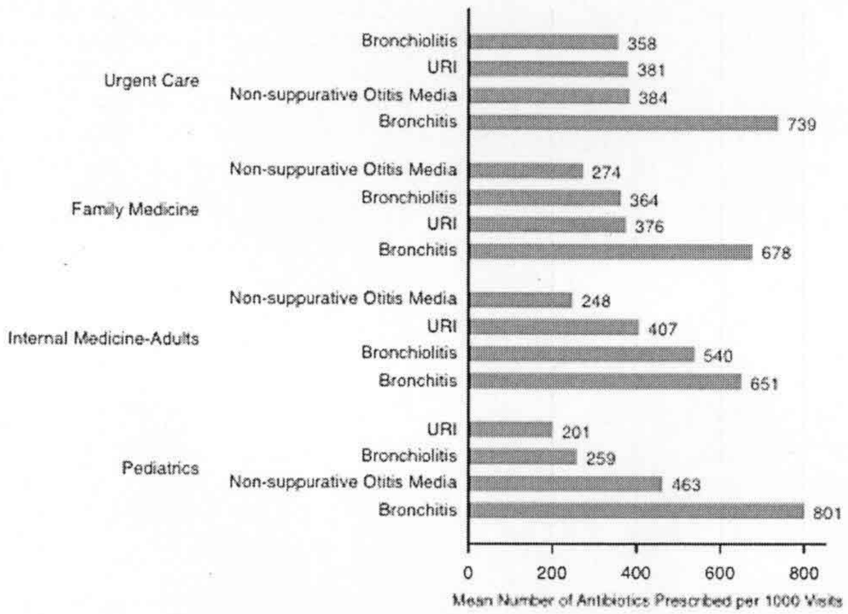

FIGURE 2. Prescribing rates per 1000 patient visits by practice type and diagnosis.

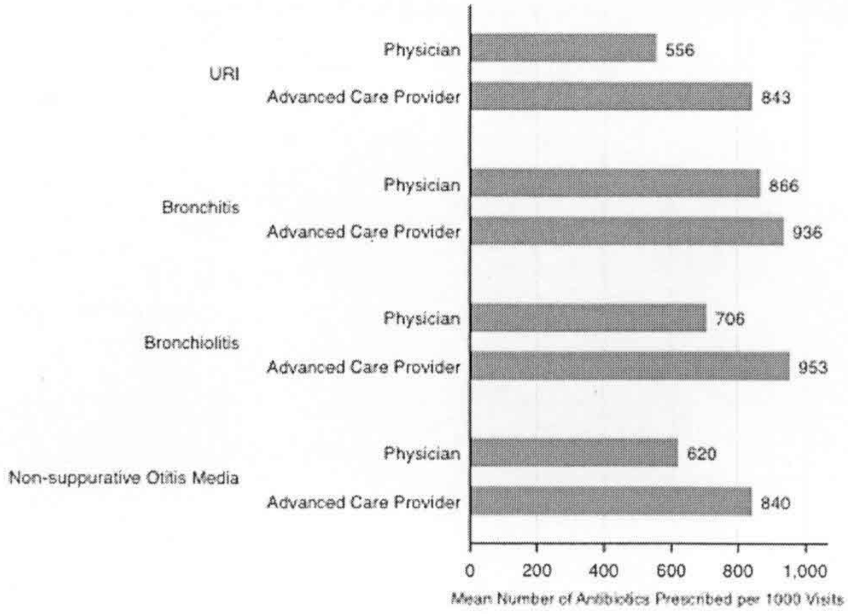

FIGURE 3. Prescribing rates per 1000 patient visits by diagnosis and provider type.

have affected the accuracy of prescribing rates. Although we also recognize limitations when using billing codes to define the study cohort, we followed prior strategies used by multiple publications to identify our visits to include in the analysis.[20,47] Despite these limitations, our study results are consistent with previously published work reporting that acute bronchitis is a frequent indication for antibiotic misuse.[10,48] Additionally, our findings support prior results that identified higher antibiotic prescribing rates for APPs than for physician providers.[9]

Our study identified variation in patient-, provider-, and practice-level factors associated with inappropriate antibiotic prescribing. Antibiotics are not recommended for any of the indications selected for inclusion in this study.[2,15,16,49] Understanding the factors that impact prescribing is critical to determining how to reduce the misuse of antibiotics. A "one size fits all" approach to antibiotic stewardship interventions may not be the best strategy to meet aggressive goals for reducing inappropriate prescribing. This study suggests that opportunities exist to tailor interventions to specific settings of care, provider types, and patient characteristics that could be more effective and efficient in improving appropriate prescribing and, ultimately, in reducing antibiotic resistance.

ACKNOWLEDGMENTS

Financial support: Support for this study was received from a grant awarded by The Duke Endowment to extend an existing acute-care antimicrobial stewardship program to the outpatient setting. The Duke Endowment provided Carolinas HealthCare with funding to collect baseline data, to perform qualitative research, and to provide education to patients, providers, and practices regarding antimicrobial stewardship. This paper reflects information collected prior to the roll out of an antimicrobial stewardship program to inform and tailor interventions to our ambulatory care setting. The Duke Endowment did not participate in analysis, preparation, review, or any aspect of the research performed at Carolinas HealthCare.

Potential conflicts of interest: All authors report no conflicts of interest relevant to this article.

Address correspondence to Melanie D. Spencer, PhD, MBA, Center for Outcomes Research and Evaluation, 1540 Garden Terrace Suite 406, Carolinas HealthCare System, Charlotte, North Carolina 28203 (melanie.spencer@carolinashealthcare.org).

SUPPLEMENTARY MATERIAL

To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2017.263

REFERENCES

1. Talkington K, Hyun D, Zetts R, Kothari P. Antibiotic use in outpatient settings. The Pew Charitable Trusts website. http://www.pewtrusts.org/ ~ /media/assets/2016/05/antibioticuseinoutpatientsettings.pdf; Published May 2016. Accessed November 5, 2017.
2. Snow V, Mottur-Pilson C, Gonzales R, et al. Principles of appropriate antibiotic use for treatment of nonspecific upper respiratory tract infections in adults. *Ann Intern Med* 2001;134:487–489.
3. Harris AM, Hicks LA, Qaseem A, High Value Care Task Force of the American College of P, for the Centers for Disease C, Prevention. Appropriate antibiotic use for acute respiratory tract infection in adults: advice for high-value care from the American College of Physicians and the Centers for Disease Control and Prevention. *Ann Intern Med* 2016;164:425–434.
4. Napolitano LM. Emerging issues in the diagnosis and management of infections caused by multi-drug-resistant, gram-positive cocci. *Surg Infect (Larchmt)* 2005;6(Suppl 2):S5–S22.
5. Branski LK, Al-Mousawi A, Rivero H, Jeschke MG, Sanford AP, Herndon DN. Emerging infections in burns. *Surg Infect (Larchmt)* 2009;10:389–397.
6. Davoudi A, Najafi N, Alian S, et al. Resistance pattern of antibiotics in patient underwent open heart surgery with nosocomial infection in north of Iran. *Glob J Health Sci* 2015;8:288–297.
7. Bassetti M, Carnelutti A, Peghin M. Patient specific risk stratification for antimicrobial resistance and possible treatment strategies in gram-negative bacterial infections. *Expert Rev Anti Infect Ther* 2017;15:55–65.
8. National action plan for combating antibiotic-resistant bacteria. The White House website. https://www.whitehouse.gov/sites/default/files/docs/national_action_plan_for_combating_antibiotic-resistant_bacteria.pdf. Published 2015. Accessed October 20, 2016.
9. Sanchez GV, Hersh AL, Shapiro DJ, Cawley JF, Hicks LA. Outpatient antibiotic prescribing among United States nurse practitioners and physician assistants. *Open Forum Infect Dis* 2016;3:ofw168.
10. Roberts RM, Hicks LA, Bartoces M. Variation in US outpatient antibiotic prescribing quality measures according to health plan and geography. *Am J Manage Care* 2016;22:519–523.
11. Shamsuddin S, Akkawi ME, Zaidi ST, Ming LC, Manan MM. Antimicrobial drug use in primary healthcare clinics: a retrospective evaluation. *Int J Infect Dis* 2016;52:16–22.
12. Fleming-Dutra KE, Hersh AL, Shapiro DJ, et al. Prevalence of inappropriate antibiotic prescriptions among US ambulatory care visits, 2010–2011. *JAMA* 2016;315:1864–1873.
13. Dyar OJ, Beovic B, Vlahovic-Palcevski V, Verheij T, Pulcini C. How can we improve antibiotic prescribing in primary care? *Expert Rev Anti-infect Ther* 2016;14:403–413.
14. Tamma PD, Cosgrove SE. Addressing the appropriateness of outpatient antibiotic prescribing in the United States: an important first step. *JAMA* 2016;315:1839–1841.
15. American Academy of Family Physicians; American Academy of Otolaryngology-Head and Neck Surgery; American Academy of Pediatrics Subcommittee on Otitis Media With Effusion. Otitis media with effusion. *Pediatrics* 2004;113:1412–1429.
16. Ralston SL, Lieberthal AS, Meissner HC, et al. Clinical practice guideline: the diagnosis, management, and prevention of bronchiolitis. pediatrics. 2014;134:e1474–e1502. *Pediatrics* 2015; 136:782.
17. Hersh AL, Jackson MA, Hicks LA, American Academy of Pediatrics Committee on Infectious Diseases. Principles of judicious antibiotic prescribing for upper respiratory tract infections in pediatrics. *Pediatrics* 2013;132:1146–1154.
18. Snow V, Mottur-Pilson C, Gonzales R, et al. Principles of appropriate antibiotic use for treatment of acute bronchitis in adults. *Ann Intern Med* 2001;134:518–520.
19. Subcommittee on Urinary Tract Infection, Steering Committee on Quality Improvement and Management, Roberts KB. Urinary

tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. *Pediatrics* 2011;128:595–610.

20. Fleming-Dutra KE, Hersh AL, Shapiro DJ, et al. Prevalence of inappropriate antibiotic prescriptions among US ambulatory care visits, 2010–2011. *JAMA* 2016;315:1864–1873.
21. Cameron AC, Pravin K. *Microeconomics Using Stata*. College Station, TX: Stata Press; 2010.
22. Zou GY, Donner A. Extension of the modified Poisson regression model to prospective studies with correlated binary data. *Statist Method Med Res* 2013;22:661–670.
23. Zou G. A modified poisson regression approach to prospective studies with binary data. *Am J Epidemiol* 2004;159:702–706.
24. McKay R, Mah A, Law MR, McGrail K, Patrick DM. Systematic review of factors associated with antibiotic prescribing for respiratory tract infections. *Antimicrob Agents Chemother* 2016;60:4106–4118.
25. Ivanovska V, Hek K, Mantel Teeuwisse AK, Leufkens HG, Nielen MM, van Dijk L. Antibiotic prescribing for children in primary care and adherence to treatment guidelines. *J Antimicrob Chemother* 2016;71:1707–1714.
26. Ubhi H, Patel M, Ludwig L. How well do outpatient prescriptions adhere to good antimicrobial stewardship? *Arch Dis Child* 2016; 101:e2.
27. Drekonja DM, Filice GA, Greer N, et al. Antimicrobial stewardship in outpatient settings: a systematic review. *Infect Control Hosp Epidemiol* 2015;36:142–152.
28. Sanchez GV, Fleming-Dutra KE, Roberts RM, Hicks LA. Core elements of outpatient antibiotic stewardship. *MMWR* 2016;65:1–12.
29. Dobson EL, Klepser ME, Pogue JM, et al. Outpatient antibiotic stewardship: Interventions and opportunities. *JAPhA* 2017;57: 464–473.
30. Drekonja D, Filice G, Greer N, et al. *Antimicrobial Stewardship Programs in Outpatient Settings: A Systematic Review*. Washington, DC: Department of Veterans Affairs; 2014.
31. Pollack LA, Srinivasan A. Core elements of hospital antibiotic stewardship programs from the Centers for Disease Control and Prevention. *Clin Infect Dis* 2014;59(Suppl 3):S97–S100.
32. Centers for Disease Control and Prevention. Office-related antibiotic prescribing for persons aged ≤14 years—United States, 1993–1994 to 2007–2008. *MMWR* 2011;60:1153–1156.
33. Gangat MA, Hsu JL. Antibiotic stewardship: a focus on ambulatory care. *S Dak Med* 2015;Spec No:44–48.
34. Fleming-Dutra KE, Demirjian A, Bartoces M, Roberts RM, Taylor TH Jr, Hicks LA. Variations in antibiotic and azithromycin prescribing for children by geography and specialty—United States, 2013. *Pediatr Infect Dis J* 2017. PMID: 28746259; doi: 10.1097/INF.0000000000001708.
35. Pinto LA, Pitrez PM, Luisi F, et al. Azithromycin therapy in hospitalized infants with acute bronchiolitis is not associated with better clinical outcomes: a randomized, double-blinded, and placebo-controlled clinical trial. *J Pediatr* 2012;161:1104–1108.
36. Kuzujanakis M, Kleinman K, Rifas-Shiman S, Finkelstein JA. Correlates of parental antibiotic knowledge, demand, and reported use. *Ambul Pediatr* 2003;3:203–210.
37. Altiner A, Brockmann S, Sielk M, Wilm S, Wegscheider K, Abholz HH. Reducing antibiotic prescriptions for acute cough by motivating GPs to change their attitudes to communication and empowering patients: a cluster-randomized intervention study. *J Antimicrob Chemother* 2007;60:638–644.
38. Holmes JH, Metlay J, Holmes WC, Mikanatha N. Developing a patient intervention to reduce antibiotic overuse. *AMIA Annu Symp Proc* 2003:864.
39. Pechere JC. Patients' interviews and misuse of antibiotics. *Clin Infect Dis* 2001;33(Suppl 3):S170–S173.
40. Jones BE, Sauer B, Jones MM, et al. Variation in outpatient antibiotic prescribing for acute respiratory infections in the veteran population: a cross-sectional study. *Ann Intern Med* 2015;163:73–80.
41. Antibiotic prescription fill rates declining in the United States. In: *The Health of America Report*. BlueCross BlueShield website. https://www.bcbs.com/the-health-of-america/reports/antibiotic-prescription-rates-declining-in-the-US. Published August 2017. Accessed November 5, 2017.
42. Gerber JS, Prasad PA, Localio AR, et al. Racial differences in antibiotic prescribing by primary care pediatricians. *Pediatrics* 2013;131:677–684.
43. Gahbauer AM, Gonzales ML, Guglielmo BJ. Patterns of antibacterial use and impact of age, race/ethnicity, and geographic region on antibacterial use in an outpatient medicaid cohort. *Pharmacotherapy* 2014;34:677–685.
44. Mangione-Smith R, Elliott MN, Stivers T, McDonald L, Heritage J, McGlynn EA. Racial/ethnic variation in parent expectations for antibiotics: implications for public health campaigns. *Pediatrics* 2004;113:e385–e394.
45. Kornblith AE, Fahimi J, Kanzaria HK, Wang RC. Predictors for under-prescribing antibiotics in children with respiratory infections requiring antibiotics. *Am J Emerg Med* 2017 Jul 28. pii: S0735-6757(17)30632-0. doi: 10.1016/j.ajem.2017.07.081.
46. Fleming-Dutra KE, Shapiro DJ, Hicks LA, Gerber JS, Hersh AL. Race, otitis media, and antibiotic selection. *Pediatrics* 2014;134:1059–1066.
47. Watson JR, Wang L, Klima J, et al. Healthcare claims data: an underutilized tool for pediatric outpatient antimicrobial stewardship. *Clin Infect Dis* 2017;64:1479–1485.
48. McCullough AR, Pollack AJ, Plejdrup Hansen M, et al. Antibiotics for acute respiratory infections in general practice: comparison of prescribing rates with guideline recommendations. *Med J Aust* 2017;207:65–69.
49. Chow AW, Benninger MS, Brook I, et al. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. *Clin Infect Dis* 2012;54:e72–e112.