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Public Health Surveillance of Outpatient Antibiotic Prescription Trends, United States, 2011–2019

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Introduction

Optimizing antibiotic use is critical for reducing adverse drug events and slowing the development of antimicrobial resistance. The U.S. Centers for Disease Control and Prevention (CDC) has led efforts to track and report national antibiotic prescribing practices.^{1,2} A previously published analysis using IQVIA[®] Xponent data showed a decrease in overall prescribing rates during 2011–2016, largely driven by decreases among pediatric patient populations.² Using a patented projection methodology, IQVIA[®] data captures about 93% of outpatient prescriptions dispensed in U.S. retail pharmacies and projects 100% of retail prescriptions sold.³ These data are used for national surveillance of antibiotic use, as well as other drugs, and publicly shared on CDC's Antimicrobial Resistance & Patient Safety Portal (<https://arpsp.cdc.gov/>).^{4,5} In 2017, IQVIA[®] revised its methodology to only include filled and dispensed prescriptions, decreasing the number of prescriptions captured in the database.³ The objective of this analysis was to assess the antibiotic prescribing trends from 2011–2019 for public health surveillance accounting for methodological changes by using the Joinpoint-jump regression program.

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Disclaimer: This activity was considered exempt from human subjects review by the Centers for Disease Control and Prevention (CDC) and was conducted consistent with applicable federal law and CDC policy (see the following: 45 C.F.R. part 46; 21 C.F.R. part 56; 42 U.S.C. §241(d), 5 U.S.C. §552a, 44 U.S.C. §3501 et seq.). The findings and conclusions in this article are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

Methods

We used IQVIA® Xponent data and U.S. Census Bureau population estimates to determine annual rates of antibiotic prescribing (per 1,000 population) stratified by patient age group, sex, prescriber's U.S. Census region, and antibiotic class during 2011–2019 as previously described.² From 2011–2019, the database captured 74%–92% of all U.S. retail outpatient prescriptions and projected to 100% of prescriptions nationally. Data were abstracted and descriptive analyses completed using SAS, version 9.4 (SAS Institute Inc).

We used the Joinpoint-jump regression program (version 4.9.1.0; National Cancer Institute) to assess statistically significant increases or decreases in antibiotic prescribing trends during 2011–2019; overall rate and stratified by age, sex, region, and antibiotic class.⁶ Joinpoint regression models are used to assess trends over time, similar to interrupted time series and segmented regression techniques. Joinpoint regressions have been used to estimate changes in rates of cancer incidence,⁶ mortality,⁷ and prescribing of opioids.⁸ The model identifies the best-fitting points (years) with a statistically significant increase or decrease in antibiotic prescribing trends. To account for changes in the data methodology and avoid bias associated with a standard Joinpoint model, mid-2016 was a parameter added to the model as a jump trend, since 2016 was the last year of data using the previous methodology.^{6,9,10} Joinpoint-jump models have been applied to address discontinuous increases/decreases, or “jumps,” in a data series, even though it may not affect the underlying trend, such as in changes in International Classification of Diseases from ICD-9 to ICD-10 codes.⁹ The jump model requires knowing the time of when the discontinuous data change occurred, with the benefit of accounting for the size of the jump if known. Data must be sorted in aggregate by the time-point variable as the last level of sorting. We fitted a log-linear model to the prescription rates using year as the independent variable. The absence of a Joinpoint segment was used to identify a linear trend during 2011–2019, and where nonlinear trends were identified, we assessed a single Joinpoint with trend segments from 2011–2016 and 2016–2019. The methodology change is placed at the halfway point of 2016 (i.e., 2016.5) to represent that 2016 is using the prior methodology, and 2017 is using the revised methodology. We reported the annual percent change (APC) with 95% confidence intervals (CIs) for each trend segment, and the average annual percent change (AAPC) with 95% CIs for the entire period. We estimated prevalence ratios and 95% CIs using Poisson regression models with a log link comparing prescribing rates in 2019 to 2011. We followed the National Center for Health Statistics guideline on assessing trends where prevalence ratios are reported for linear trends and APCs are reported for nonlinear trend segments.¹⁰ All statistical tests were 2-sided and *P*-value <0.05 was considered statistically significant.

Results

From 2011 to 2019, a total of 2.4 billion oral antibiotic prescriptions were dispensed in the U.S. (Table S1). The highest prescription rate was reported in 2011 (877 prescriptions per 1,000 persons) and the lowest prescription rate was in 2018 and 2019 (765 prescriptions per 1,000 persons). Adults aged ≥65 years, females, and the South region consistently accounted for the highest prescription rates during the study period. Penicillins, macrolides,

and cephalosporins accounted for the antibiotic classes with the highest prescription rates overall.

The Joinpoint-jump model showed an overall linear trend (Table 1), with the 2011–2019 AAPCs in similar directions to the prevalence ratios comparing 2019 to 2011. The overall prescribing rate was 13% lower in 2019 than 2011. There were significant decreases in antibiotic prescribing rates by age group, sex, and region between 2019 and 2011. The greatest overall decreases in prescribing rates between 2019 and 2011 were among children aged <20 years (908 to 684, –25%), followed by adults aged 20–64 years (778 to 703, –10%), then older adults aged ≥65 years (1,113 to 1,099, –1%) (Figure S1).

The largest annual decrease during the study period across all age groups was for macrolides (AAPC: aged <20 years, –8%; aged 20–64 years, –3.8%; aged ≥65 years, –5.1%).

Among adults aged 20–64 years, penicillins showed a significant increasing prescribing trend pre-jump and a significant decreasing trend post-jump, with similar increasing but non-significant pre- and post-jump trends for adults aged ≥65 years, while there was an overall significant decrease among children aged <20 years. From 2016 to 2019, the largest annual decrease occurred in fluoroquinolones across all age groups (AAPC: aged <20 years, –14.8%; aged 20–64 years, –12.7%; aged ≥65 years, –11.2%). Among adults, during the study period, prescribing rates increased for beta-lactams (AAPC: aged 20–64 years, 6.4%; aged ≥65 years, 5.6%). While no changes were seen for prescribing trends of cephalosporins during the study period among adults aged 20–64 years, an increase was observed among adults aged ≥65 years (AAPC: 2.4%) and a decrease was observed among children aged <20 years (AAPC: –2.8%).

Discussion

The rate of oral antibiotic prescriptions dispensed in U.S. outpatient pharmacies decreased by 13% from 2019 compared to 2011, largely driven by reductions in prescribing among children aged <20 years. This overall decline was on track to meet the 2020 goal of a 15% reduction in antibiotic prescribing nationally.¹¹ While a decrease was observed across all age groups, it was smallest among older adults, highlighting the need to further evaluate prescribing practices in this population and identify potential targets for improvement. Consistent with previous analyses, the South region had the highest rates of prescribing and one of the lowest rates of decline. Among all age groups the greatest decreases were seen for broad-spectrum antibiotics, specifically macrolides and fluoroquinolones.² Among adults, however, increases were seen for beta-lactams and cephalosporins. These trends may indicate a shift in prescribing from macrolides and fluoroquinolones to beta-lactams, cephalosporins and other antibiotic classes.¹²

Joinpoint-jump models are helpful for detecting underlying continuous trends despite sudden changes or “jumps” in data collected over time.⁹ Using this approach to account for data collection changes by IQVIA[®] starting in 2017, our results showed overall linear trends nationally and by patient characteristics, indicating that using such an approach to account for the data changes may be unnecessary. However, when assessing trends by antibiotic class, some classes do appear to have jumps; use of the Joinpoint-jump model or

analysis of the two periods separately may be warranted. Specifically, further investigation of prescribing trends for penicillins is needed to better understand whether the increase pre-jump and decrease post-jump among adults are real prescribing trends or reflect improved data quality due to IQVIA's methodological changes.

Limitations of the data have been previously reported and include the lack of diagnosis associated with the prescription thus not allowing the assessment of appropriateness. Also, prescriptions included are limited to antibiotics dispensed in outpatient, retail pharmacies.² The Joinpoint-jump model package cannot conduct multivariate analyses and is hence only useful for descriptive analyses. Additionally, our analysis focuses on pre-COVID-19 pandemic data as we assume in the Joinpoint-jump model, similar to another study, that the location of the jump is known, and only one such jump is allowed.⁹ However, changes in prescribing due to the COVID-19 pandemic may require identifying another data jump due to declines in antibiotic prescribing associated with decreased outpatient visits, which may result in confounding between the APC of segments and the size of the jumps. Strengths of this analysis include the application of the Joinpoint-jump model to evaluate secular trends in prescribing while accounting for the data jump due to changes in the data collection methodology,^{9,13} as well as the estimation of changes between 2011 and 2019 to monitor progress in antibiotic prescribing practices.

Monitoring antibiotic prescribing trends nationally and by patient characteristics and antibiotic class is important for tracking progress toward goals to reduce unnecessary prescribing, optimize the treatment of infections, and mitigate antimicrobial resistance. Understanding how to appropriately analyze trends using administrative data that have undergone methodological changes is important for public health practitioners to effectively use and correctly report the data over longer periods of time.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Data Availability Statement:

The data used in this study are not publicly available, but information on data access and use are available at: <https://www.iqvia.com/locations/united-states/library/fact-sheets/xponent>

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Table 1.

Trends in outpatient oral antibiotic prescriptions, United States, 2011–2019, IQVIA® Xponent data

Characteristics	Annual Percent Change (APC) ^b (95% CI)			Average Annual Percent Change (AAPC) ^b (95% CI)	Prevalence Ratio ^c (95% CI)
	No joinpoint segments ^a	1 joinpoint segment			
	2011–2019	2011–2016	2016–2019	2011–2019	2019 vs. 2011
Overall	−1.1 (−1.6, −0.6)	NA	NA	−1.1 (−1.6, −0.6)	0.87 (0.87, 0.87)
Age group (years)					
<20	−2.9 (−3.7, −2.1)	NA	NA	−2.9 (−3.7, −2.1)	0.75 (0.75, 0.75)
20–64	NA	0.0 (−0.8, 0.8)	−2.2 (−4.0, −0.4)	−0.8 (−1.4, −0.2)	-
≥65	−0.0 (−0.4, 0.4)	NA	NA	−0.0 (−0.4, 0.4)	0.99 (0.99, 0.99)
Sex					
Male	−1.1 (−1.7, −0.6)	NA	NA	−1.1 (−1.7, −0.6)	0.87 (0.87, 0.87)
Female	−0.8 (−1.4, −0.2)	NA	NA	−0.8 (−1.4, −0.2)	0.88 (0.88, 0.88)
Region					
Northeast	−0.7 (−1.1, −0.2)	NA	NA	−0.7 (−1.1, −0.2)	0.90 (0.90, 0.90)
Midwest	−1.2 (−1.9, −0.4)	NA	NA	−1.2 (−1.9, −0.4)	0.83 (0.83, 0.83)
South	−0.9 (−1.4, −0.4)	NA	NA	−0.9 (−1.4, −0.4)	0.90 (0.90, 0.90)
West	−1.7 (−2.3, −1.0)	NA	NA	−1.7 (−2.3, −1.0)	0.82 (0.82, 0.82)
Antibiotic classes					
Ages <20 years					
Tetracyclines	NA	−3.6 (−6.3, −0.8)	−0.7 (−3.8, 2.5)	−2.2 (−3.6, −0.7)	-
Cephalosporins	−2.8 (−3.6, −1.9)	NA	NA	−2.8 (−3.6, −1.9)	0.79 (0.79, 0.79)
Lincosamides	NA	3.0 (2.1, 4.0)	−3.2 (−8.5, 2.4)	1.4 (0.3, 2.6)	-
Macrolides	−8.0 (−9.1, −6.8)	NA	NA	−8.0 (−9.1, −6.8)	0.51 (0.51, 0.51)
Penicillins	−0.3 (−1.4, 0.7)	NA	NA	−0.3 (−1.4, 0.7)	0.90 (0.90, 0.91)
Fluoroquinolones	NA	0.5 (−1.8, 2.9)	−14.8 (−17.2, −12.2)	−7.4 (−8.7, −6.2)	-
Trimethoprim-sulfamethoxazole	−6.1 (−7.2, −4.9)	NA	NA	−6.1 (−7.2, −4.9)	0.53 (0.53, 0.53)
Beta-lactams, increased activity	−2.3 (−3.4, −1.3)	NA	NA	−2.3 (−3.4, −1.3)	0.80 (0.80, 0.80)
Other antibiotics	−10.2 (−16.7, −3.1)	NA	NA	−10.2 (−16.7, −3.1)	0.65 (0.64, 0.66)
Urinary anti-infectives	−0.5 (−1.1, 0.1)	NA	NA	−0.5 (−1.1, 0.1)	0.91 (0.9, 0.91)
Ages 20–64 years					
Tetracyclines	NA	−1.8 (−5.7, 2.3)	6.1 (2.1, 10.2)	2.1 (0.1, 4.1)	-
Cephalosporins	0.4 (0.0, 0.9)	NA	NA	0.4 (0.0, 0.9)	1.01 (1.01, 1.01)
Lincosamides	NA	4.1 (3.4, 4.8)	−2.8 (−6.6, 1.2)	2.3 (1.5, 3.2)	-
Macrolides	−3.8 (−4.8, −2.8)	NA	NA	−3.8 (−4.8, −2.8)	0.68 (0.68, 0.68)
Penicillins	NA	0.9 (0.5, 1.3)	−3.3 (−5.5, −1.1)	−0.2 (−0.6, 0.3)	-

Characteristics	Annual Percent Change (APC) ^b (95% CI)			Average Annual Percent Change (AAPC) ^b (95% CI)	Prevalence Ratio ^c (95% CI)
	No joinpoint segments ^a	1 joinpoint segment			
	2011–2019	2011–2016	2016–2019	2011–2019	2019 vs. 2011
Fluoroquinolones	NA	−0.2 (−2.7, 2.4)	−12.7 (−15.3, −10.0)	−6.7 (−7.9, −5.3)	-
Trimethoprim-sulfamethoxazole	NA	3.5 (−5.2, 13.0)	−2.5 (−4.0, −1.0)	−1.1 (−2.8, 0.7)	-
Beta-lactams, increased activity	6.4 (5.3, 7.5)	NA	NA	6.4 (5.3, 7.5)	1.48 (1.48, 1.48)
Other antibiotics	NA	−4.1 (−10.4, 2.7)	18.5 (2.6, 36.9)	3.9 (−1.1,9.0)	-
Urinary anti-infectives	2.8 (2.4, 3.3)	NA	NA	2.8 (2.4, 3.3)	1.25 (1.25, 1.25)
Ages ≥65 years					
Tetracyclines	NA	1.8 (−1.8, 5.6)	9.5 (6.3, 12.7)	5.6 (3.9, 7.3)	-
Cephalosporins	2.4 (1.9, 2.9)	NA	NA	2.4 (1.9, 2.9)	1.24 (1.24, 1.24)
Lincosamides	NA	3.6 (2.6, 4.6)	−0.2 (−2.1,1.8)	2.2 (1.5, 2.9)	-
Macrolides	−5.1 (−2.9, −8.3)	NA	NA	−5.1 (−2.9,−8.3)	0.76 (0.76, 0.76)
Penicillins	NA	4.3 (−1.6,10.7)	0.5 (−0.4, 1.4)	1.4 (0.3, 2.6)	-
Fluoroquinolones	NA	−0.6 (−3.3, 2.2)	−11.2 (−13.8, −8.5)	−6.1 (−7.4,−4.7)	-
Trimethoprim-sulfamethoxazole	−0.4 (−1.3, 0.6)	NA	NA	−0.4 (−1.3,0.6)	0.94 (0.94, 0.95)
Beta-lactams, increased activity	5.6 (5.1, 6.2)	NA	NA	5.6 (5.1, 6.2)	1.55 (1.55, 1.55)
Other antibiotics	NA	−1.4 (−3.7, 0.8)	18.7 (13.8, 23.8)	5.7 (4.1, 7.3)	-
Urinary anti-infectives	NA	−2.6 (−4.7, −0.5)	5.4 (3.4, 7.5)	1.3 (0.3, 2.4)	-

Notes: not applicable.

^a Absence of a joinpoint was used to identify a linear trend and the APC was constant and equal to AAPC. Variables with NA indicates non-linear trends and the APC was estimated for both join-segments for 2011–2016 and 2016–2019.

^b If the confidence interval does not contain zero, then the APC or AAPC is different from zero at the significance level of $\alpha=0.05$.

^c If the confidence interval does not contain 1, then the prevalence ratio is different from 1 at the significance level of $\alpha=0.05$. With 2011 as the reference, prevalence ratio < 1 indicates a decrease, prevalence ratio = 1 indicates no change, and prevalence ratio > 1 indicates an increase in rates from 2011 to 2019.