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BRIEF REPORT

Impact of the Coronavirus Disease 2019 Pandemic on Outpatient Antibiotic Prescriptions in the United States

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In April 2020, there were significant reductions in prescription fills of each of the 10 most prescribed outpatient antibiotics in the United States. Monthly azithromycin, amoxicillin-clavulanate, and levofloxacin fills did not rebound significantly from April through July 2020. Coronavirus disease 2019 had an immediate and sustained impact on US outpatient antibiotic prescribing.

Keywords. coronavirus disease 2019; COVID-19; antibiotics; prescriptions; outpatient; United States.

There are limited nationwide data on the impact of the coronavirus disease 2019 (COVID-19) pandemic on antibiotic prescribing. In the United States (US), most antibiotic prescriptions are filled in outpatient settings [1]. A recent study estimated that US outpatient amoxicillin and azithromycin prescription fills were 64% and 63% lower, respectively, for April 19–26, 2020, than in the same week in 2019 [2]. However, this study did not account for long-term prepandemic trends or prescriptions after April 2020. Our objectives were to measure the impact of COVID-19 on outpatient prescribing of the 10 most commonly filled antibiotic agents in the US through July 2020 and to compare trends with those from before the pandemic.

METHODS

Monthly prescription fill data were obtained for August 2014 through July 2020 from the IQVIA National Prescription Audit (NPA) databases (Durham, NC, USA). The IQVIA NPA databases provide projected total retail prescription drug sales using information from over 93% of retail pharmacies in the US (chain stores, food stores, independent pharmacies, mass merchandisers). Data are presented in this paper as monthly prescription fills per 1000 persons, based on US Census monthly population estimates [3]. An interrupted time-series regression model (segmented regression, Newey-West standard errors) was used to estimate changes in prescription fills from August 2014 through March 2020 and April 2020 through July 2020, controlling for previous trends and autocorrelation (seasonal effects). P values <.05 were considered significant. Data were analyzed using STATA 16.1 (StataCorp LLC, College Station, TX, USA).

RESULTS

During the prepandemic period (August 2014–March 2020), there were significant decreases in monthly prescription fills per 1000 persons of ciprofloxacin ($P < .001$), levofloxacin ($P < .001$), sulfamethoxazole-trimethoprim ($P < .001$), and clindamycin ($P = .006$), as well as significant increases in monthly fills per 1000 persons of doxycycline and nitrofurantoin ($P < .001$) (Table 1; Supplementary Figure 1). Monthly prescription fills per 1000 persons of amoxicillin, azithromycin, amoxicillin-clavulanate, and cephalexin were not significantly changed during this time period. In April 2020, there were significant reductions in monthly prescription fills per 1000 persons of all 10 antibiotics (range, 13%–56%; $P < .001$).

From April through July 2020, there were no significant changes in monthly prescription fills of azithromycin, amoxicillin-clavulanate, or levofloxacin per 1000 persons. Monthly fills of other antibiotics per 1000 persons significantly increased during these months ($P < .001$), and trends in fills exceeded those observed during the prepandemic period ($P < .001$). Through July 2020, monthly fills of azithromycin, amoxicillin-clavulanate, levofloxacin, and amoxicillin per 1000 persons did not return to prepandemic levels. Monthly fills of ciprofloxacin, sulfamethoxazole-trimethoprim, clindamycin, doxycycline, nitrofurantoin, and cephalexin rebounded to prepandemic levels.

DISCUSSION

To our knowledge, this is the first study to report outpatient antibiotic prescription patterns in the US during the COVID-19 pandemic and to put these data in the context of long-term prepandemic trends. We demonstrated that prescription fills of the 10 most commonly prescribed outpatient antibiotics decreased significantly in April 2020, after most routine health care services were suspended. Thereafter, monthly prescription fills of 7 agents rebounded over the next 3 months, and trends through July 2020 exceeded prepandemic trends. In

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Table 1. Outpatient Antibiotic Prescription Fills in the United States, August 2014 Through July 2020

	Estimated Monthly Prescription Fills,[a] Base Level[b]		Monthly Trend in Prescription Fills,[a] August 2014–March 2020			Change in Prescription Fills,[a] April 2020[c]				Monthly Trend in Prescriptions Fills,[a] April 2020–July 2020			Relative Change in Trend of Monthly Prescription Fills,[a] April 2020—July 2020[d]		
Antibiotic	No. of Prescriptions	95% CI	Monthly Trend	95% CI	*P* Value	Change, %	Change, No.[a]	95% CI	*P* Value	Monthly Trend	95% CI	*P* Value	Monthly Trend	95% CI	*P* Value
Amoxicillin	16.12	14.46 to 17.77	–0.007	–0.040 to 0.259	.68	**–56**	**–8.69**	**–10.02 to –7.37**	**<.001**	**1.248**	**1.033 to 1.463**	**<.001**	**1.255**	**1.034 to 1.476**	**<.001**
Azithromycin	14.07	11.66 to 16.47	–0.438	–0.092 to 0.004	.07	**–49**	**–5.01**	**–7.26 to –2.77**	**<.001**	–0.121	–0.884 to 0.642	.75	–0.077	–0.845 to 0.690	.84
Amoxicillin-clavulanate	7.35	6.36 to 8.33	0.018	–0.003 to 0.038	.09	**–49**	**–3.97**	**–4.90 to –3.05**	**<.001**	0.182	–0.044 to 0.408	.11	0.164	–0.065 to 0.393	.16
Ciprofloxacin	6.72	6.46 to 6.98	**–0.049**	**–0.053 to –0.045**	**<.001**	**–16**	**–0.54**	**–0.70 to –0.38**	**<.001**	**0.229**	**0.184 to 0.273**	**<.001**	**0.278**	**0.233 to 0.323**	**<.001**
Cephalexin	5.78	5.54 to 6.02	0.0001	–0.005 to 0.005	.94	**–27**	**–1.70**	**–1.92 to –1.47**	**<.001**	**0.655**	**0.574 to 0.736**	**<.001**	**0.655**	**0.573 to 0.736**	**<.001**
Sulfamethoxazole-trimethoprim	5.71	5.51 to 5.90	**–0.192**	**–0.023 to –0.016**	**<.001**	**–20**	**–0.84**	**–1.00 to –0.69**	**<.001**	**0.258**	**0.214 to 0.302**	**<.001**	**0.277**	**0.232 to 0.322**	**<.001**
Levofloxacin	4.09	3.64 to 4.51	**–0.03**	**–0.037 to –0.022**	**<.001**	**–38**	**–0.64**	**–0.91 to –0.38**	**<.001**	0.033	–0.03 to 0.097	.30	0.063	–0.001 to 0.127	.06
Doxycycline	3.87	3.66 to 4.08	**0.036**	**0.030 to 0.042**	**<.001**	**–25**	**–1.62**	**–1.93 to –1.30**	**<.001**	**0.157**	**0.089 to 0.225**	**<.001**	**0.121**	**0.052 to 0.189**	**.001**
Clindamycin	2.61	2.51 to 2.71	**–0.003**	**–0.004 to –0.001**	**.005**	**–29**	**–0.67**	**–0.74 to –0.59**	**<.001**	**0.242**	**0.205 to 0.298**	**<.001**	**0.244**	**0.208 to 0.281**	**<.001**
Nitrofurantoin	2.28	2.18 to 2.38	**0.013**	**0.012 to 0.015**	**<.001**	**–13**	**–0.48**	**–0.59 to –0.36**	**<.001**	**0.183**	**0.145 to 0.222**	**<.001**	**0.17**	**0.131 to 0.209**	**<.001**

Data were analyzed using a interrupted time-series regression model with Newey-West standard errors (STATA 16.1). Significant results appear as bolded text.

[a]Presented as prescription fills per 1000 persons, using US Census monthly estimates of the national population.

[b]Estimated number of prescription fills per 1000 persons at start of prepandemic period.

[c]Change in prescription fills from March 2020 to April 2020, based on values from predicted trends for each drug (Supplementary Figure 1).

[d]Change in trend for April 2020 through July 2020, relative to August 2014 to March 2020.

contrast, monthly azithromycin, amoxicillin-clavulanate, and levofloxacin prescription fills did not significantly rebound for April through July 2020. Moreover, monthly fills of these agents and amoxicillin did not return to prepandemic levels (Supplementary Figure 1). Azithromycin, amoxicillin-clavulanate, levofloxacin, and amoxicillin are recommended for the treatment of community-acquired pneumonia [4], and they are widely used against other respiratory tract infections. The 4 drugs are among the most common inappropriately prescribed antibiotics in the US, largely due to unnecessary treatment of acute respiratory conditions such as sinusitis, bronchitis, and nasopharyngitis [5, 6]. Taken together, the data demonstrate that the COVID-19 pandemic has had an immediate and sustained impact on US outpatient antibiotic prescribing.

The abrupt decreases in antibiotic prescription fills at the start of the pandemic were likely due to suspensions of nonemergent, non-COVID-19-related health care services in much of the country. Possible explanations for sustained reductions in azithromycin, amoxicillin-clavulanate, levofloxacin, and amoxicillin use are that patients were less likely to seek outpatient care for respiratory complaints that previously resulted in an antibiotic prescription, clinicians were less likely to prescribe an unnecessary antibiotic, and/or measures like physical distancing and school, daycare facility, and business closures lessened acquisition of certain bacterial infections. Increased prescribing of most agents after April 2020 might reflect reinstitution of at least some in-person health care services, as well as utilization of telemedicine. The relative impact of in-person and telemedicine encounters on antibiotic prescribing rates is unclear [7, 8].

The long-term impact of the COVID-19 pandemic on outpatient antibiotic prescribing and antimicrobial resistance (AMR) trends in the US is uncertain. Antibiotic usage will be influenced by diverse and interacting factors, including the resumption of deferred health care services, new developments in the management of COVID-19 such as validation of immunosuppressive treatments or protective vaccines, the epidemiology of severe acute respiratory syndrome coronavirus 2, influenza and other respiratory tract viral infections in 2020–2021, and indirect effects on public health delivery, health care resources, and economic systems [9]. Associations between community antibiotic use and AMR are complex, and attempts to evaluate them are complicated by unknown expected effect sizes, costs of surveillance, heterogeneity of clinical and stewardship practices, and other confounding factors [10]. As such, it is an oversimplification to assume that antibiotic prescription trends during the COVID-19 pandemic will correlate directly with AMR rates [9]. Data have not been published on US in-hospital antibiotic use during the pandemic. Monthly in-hospital antibiotic days of therapy (DOT) were significantly decreased for April 2020 through June 2020 at a health care system in Western Pennsylvania, outside of a COVID-19 epicenter, although DOT per bed day of care were significantly increased [11].

Outpatient antibiotic stewardship programs are less well established than in-hospital programs. The Centers for Disease Control and Prevention and the White House National Action Plan for Combating Antibiotic Resistant Bacteria have identified outpatient antimicrobial prescribing as a national stewardship priority [12]. The Core Elements of Outpatient Antibiotic Stewardship established antibiotic overprescribing for upper respiratory conditions as a high-priority area for intervention [13]. Along these lines, we noted encouraging trends before the COVID-19 pandemic, including significant reductions in monthly fills of fluoroquinolones (targets of US Food and Drug Administration safety warnings) [14], sulfamethoxazole-trimethoprim, and clindamycin. Monthly fills of doxycycline and nitrofurantoin (safe, niche-use agents with targeted spectra) were significantly increased. Taken together, the data suggest that there have been improvements in outpatient stewardship practices.

Limitations of this study include lack of information on local and regional trends, inability to differentiate azithromycin prescriptions against COVID-19 from those given for other indications, use of prescription fill data rather than written prescription data, interventions outside of the pandemic that may have affected prescribing, and an absence of specific prescription (ie, indication), patient, and provider-level information.

As the COVID-19 pandemic progresses, there is a pressing need for detailed studies of antibiotic use, AMR, and superimposed bacterial infections in the United States and globally [1]. It will be important to identify factors that have contributed to sustained reductions in the use of oral azithromycin, amoxicillin-clavulanate, levofloxacin, and amoxicillin below baseline levels in the first months of the pandemic. If inappropriate prescriptions were curtailed, insights might provide a foundation for developing successful outpatient stewardship strategies in the future.

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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