Trends in U.S. outpatient antibiotic prescriptions during the COVID-19 pandemic

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Summary: From January to May 2020, the number of outpatients dispensed antibiotic prescriptions decreased substantially more than seasonally expected, likely related to the COVID-19 pandemic. Decreases were greatest among children and agents frequently prescribed for respiratory infections, dentistry, and surgical prophylaxis.

Abstract

Background: The objective of our study was to describe trends in U.S. outpatient antibiotic prescriptions from January through May 2020 and compare with trends in previous years (2017-2019).

Methods: We used data from the IQVIA Total Patient Tracker to estimate the monthly number of patients dispensed antibiotic prescriptions from retail pharmacies in January 2017-May 2020. We averaged estimates from 2017-2019 and defined expected seasonal change as the average percent change from January to May 2017-2019. We calculated percentage point and volume changes in the number of patients dispensed antibiotics from January to May 2020 exceeding expected seasonal changes. We also calculated average percent change in number of patients dispensed antibiotics per month in 2017- 2019 versus 2020. Data were analyzed overall and by agent, class, patient age, state, and prescriber specialty.

Results: From January to May 2020, the number of patients dispensed antibiotic prescriptions decreased from 20.3 to 9.9 million, exceeding seasonally expected decreases by 33 percentage points and 6.6 million patients. The largest changes in 2017-2019 versus 2020 were observed in April (-39%) and May (-42%). The number of patients dispensed azithromycin increased from February to March 2020 then decreased. Overall, beyond-expected decreases were greatest among children (≤19 years) and agents used for respiratory infections, dentistry, and surgical prophylaxis.

Conclusions: From January 2020 to May 2020, the number of outpatients with antibiotic prescriptions decreased substantially more than would be expected due to seasonal trends alone, possibly related to the COVID-19 pandemic and associated mitigation measures.

Keywords: Antibiotic, antibiotic stewardship, outpatient, COVID-19

Introduction

The coronavirus disease 2019 (COVID-19) pandemic and related mitigation measures, such as school closures and stay-at-home orders, substantially impacted healthcare- and medication-seeking patterns throughout the United States.¹⁻⁴ These measures also potentially affected transmission of infections commonly managed with outpatient antibiotics. Antibiotics are among the most commonly prescribed medications in U.S. outpatient healthcare and antibiotic stewardship is a focus of national-and state-level efforts, underscoring the importance of evaluating impacts of the COVID-19 pandemic on outpatient antibiotic prescribing. Prescribing of azithromycin, which was under exploration for treatment of COVID-19, initially increased during the pandemic;²⁻³ however, examination of prescribing for other antibiotics during the COVID-19 pandemic has been limited. Outpatient antibiotic use varies by season and is typically highest in winter, likely related to the incidence of respiratory diseases,⁵ with decreases during the spring. However, impacts of the COVID-19 pandemic, including associated mitigation measures and changes in healthcare delivery, on outpatient antibiotic use during spring 2020 is unknown. The objective of our analysis was to describe and compare trends in U.S. outpatient antibiotic prescriptions between January 2020 and May 2020 (the first several months of the COVID-19 pandemic.) with historic trends to assess how antibiotic prescribing changed during the pandemic.

Methods

Data Source and Study Population

We used 2017-2020 data from IQVIA Total Patient Tracker (TPT), a proprietary IQVIA dataset, to estimate the number of unique patients dispensed antibiotic prescriptions from retail pharmacies in the United States. IQVIA collects data from approximately 48,900 U.S. retail pharmacies, representing over 3.5 billion transactions annually and covering 92% of all retail prescriptions, and generates national projections of numbers of unique, individual patients receiving dispensed prescriptions. IQVIA TPT data are updated monthly and are available approximately one month after collection, with data available through May 2020 at the time of this analysis. IQVIA TPT contains data on drug active ingredient, drug class, patient age, patient sex, prescriber specialty, and state. These data have previously been used for regulatory oversight,⁶ public health surveillance^{7,8} and studies of medication dispensing trends.³ We included only systemic (oral or parenteral) antibiotics and excluded antibiotics prescribed by veterinarians. IQVIA TPT data were accessed through an online portal.

We categorized antibiotic prescriptions by active ingredient and therapeutic class. We categorized patient age as: \leq 19 years, 20-64 years, and \geq 65 years. We further categorized the \leq 19 years group into \leq 4 years and 5-19 years to examine differences in trends in younger and older children.

Data analysis

We estimated the number of patients dispensed antibiotic prescriptions each month by agent, therapeutic class, and patient age group. Although estimates for all antibiotics were not available at the state and specialty level, select antibiotic information was available, thus we estimated the number of patients dispensed prescriptions for commonly-used antibiotics by prescriber specialty (for amoxicillin, amoxicillin-clavulanate, azithromycin, cefdinir, and cephalexin) and by state (for amoxicillin and azithromycin). We chose one month from each season, January (winter) and May (spring), to evaluate seasonal changes. We averaged the number of patients dispensed antibiotic prescriptions in 2017-2019 to create a historic baseline prior to the pandemic for comparison with estimates from 2020. We calculated the following endpoints for each strata (See Supplemental Table 1): (1) average percent change in the number of patients dispensed antibiotic prescriptions in 2017-2019 versus 2020 for each month; (2) change in the number of patients dispensed antibiotic prescriptions from January to May for

each time period (2017-2019 average and 2020); (3) percent change in the number of patients dispensed antibiotic prescriptions from January 2020 to May 2020 for each time period.

Using these values, we calculated additional endpoints to evaluate changes in 2020 compared with what would be seasonally expected. We considered the percent change in average numbers of patients dispensed antibiotic prescriptions from January to May in 2017-2019 to be the expected seasonal change. To estimate changes in the number of patients dispensed antibiotic prescriptions beyond expected seasonal changes, we calculated the difference between the 2017-2019 average percent change and the 2020 observed percent change and reported this difference as the additional percentage change. For example, a 15% average decrease from January 2017-2019 to May 2017-2019 and a 50% decrease from January 2020 to May 2020, would result in an additional percentage change of -35 percentage points. We estimated seasonally expected changes in numbers of patients dispensed antibiotic prescriptions by multiplying the observed January 2020 numbers of patients dispensed prescriptions by the seasonally expected (2017-2019 average) January to May percent change. We estimated the number of patients dispensed antibiotic prescriptions above or below seasonal expectation by subtracting the seasonally expected change from the observed change in the number of patients dispensed antibiotic prescriptions above or below seasonal expectation by subtracting the seasonally expected change from the observed change in the number of patients dispensed antibiotic prescriptions above or below seasonal expectation by subtracting the seasonally expected change from the observed change in the number of patients dispensed antibiotic prescriptions from January to May 2020.

For comparisons among age groups and states, we used U.S. Census population projections⁹ for 2017-2020 to calculate rates of antibiotic dispensing per 1000 persons.

The IQVIA TPT online portal was used to generate reports that were further analyzed using SAS 9.4 (SAS Institute, Cary, NC). Analyses were conducted by the Centers for Disease Control and Prevention as part of public health surveillance activities. This activity was reviewed by CDC and was conducted consistent with applicable federal law and CDC policy.¹

Results

From January 2020 to May 2020, the number of patients dispensed antibiotic prescriptions decreased from 20.3 million to 9.9 million, 6.6 million fewer than seasonally expected, representing an additional decrease of 33 percentage points beyond the expected seasonal decline (Table 1). Monthly numbers of patients with antibiotic prescriptions in 2020 were only slightly lower than 2017-2019 averages in January through March, with decreases of 4% in January and February and 9% in March (Figure 1). Much larger differences were seen in April and May; the number of patients with prescriptions was 39% and 42% lower, respectively, than 2017-2019 averages for these months.

Larger than seasonally expected decreases from January 2020 to May 2020 in the number of patients dispensed antibiotic prescriptions occurred across antibiotic classes and agents (Table 1). The largest beyond-expected decreases were observed among the penicillin (2.3 million fewer patients), macrolide (1.5 million fewer patients), and cephalosporin (1.1 million fewer patients) classes. By agent, amoxicillin accounted for 2.2 million fewer patients than expected and 34% of the total beyond seasonally expected decrease in patients dispensed antibiotic prescriptions, while azithromycin accounted for 1.4 million fewer patients and 21% of the total beyond expected decrease. The largest additional percentage changes in patients dispensed antibiotic prescriptions (January to May 2020 compared with January to May 2017-2019 average) were observed for cefdinir (-46 percentage points) and amoxicillin (-43 percentage points). While, overall, the number of patients dispensed azithromycin prescriptions decreased from January 2020 to May 2020, the number of patients dispensed azithromycin prescriptions increased by 5% from February 2020 to March 2020, followed by a 71%

¹ See e.g., 45 C.F.R. part 46.102(I)(2), 21 C.F.R. part 56; 42 U.S.C. §241(d); 5 U.S.C. §552a; 44 U.S.C. §3501 et seq.

decrease from March 2020 to May 2020 (Figure 2). In March 2020, the number of patients dispensed azithromycin prescriptions was similar to that in 2017-2019; however, in May 2020 it was 62% lower than the historic average.

The observed 2020 January to May decrease in the number of patients dispensed amoxicillin and azithromycin prescriptions exceeded the expected seasonal decline across states. However, in March 2020, the number of patients dispensed azithromycin prescriptions exceeded the historical average in 11 states (Supplemental Table 2): New York (37% higher in 2020 than 2017-2019 average), New Jersey (32%), Florida (16%), Oklahoma (7%), Louisiana (6%), Georgia (5%), Alabama (5%), Texas (3%), Mississippi (3%), Arkansas (2%), Idaho (1%). In April 2020, the number of patients dispensed azithromycin prescriptions was lower than the historical average in all states except New York and New Jersey, where 2020 numbers exceeded historical averages by 10%. In May 2020, the number of patients dispensed azithromycin prescriptions was lower than the historical average in all states. For amoxicillin, the number of patients dispensed prescriptions was lower in 2020 than the historical average in all states in March through May.

Decreases in the number of patients dispensed antibiotic prescriptions from January to May 2020 exceeded expected values across age groups (Figure 3). Standardized per 1000 persons, the beyond seasonally expected decrease among children was double the decrease in adults 20-64 years: - 31.4 versus -14.4 patients with antibiotic prescriptions per 1000 persons. Decreases beyond expected were greater among children ≤4 years (41.3 patients with prescriptions per 1000 persons) compared with children 5-19 years (28.3 per 1000 persons). The decrease in the number of patients dispensed antibiotic prescriptions beyond expected was also higher among older adults ≥65 years (-21.7 patients with antibiotic prescriptions per 1000 persons) compared with antibiotic prescriptions per 1000 persons) compared with antibiotic prescriptions per 1000 persons).

Among patients dispensed amoxicillin prescriptions, the greatest decreases beyond seasonally expected declines occurred in patients treated by primary care prescribers (pediatrics, emergency medicine), gastroenterologists, nurse practitioners, and physician assistants (Table 2). A substantial decrease, -45 percentage points, was also observed in patients treated by orthopedic surgeons. Among patients dispensed cephalexin prescriptions, otolaryngologists and additional surgical specialties (plastic surgery: -31 percentage points and other surgery: -29 percentage points) were also among the specialties with the greatest declines beyond expected. Notably, percent changes in monthly numbers of patients with antibiotic prescriptions between 2017-2019 and 2020 decreased in March and April and then increased in May among patients treated by dentists, medical subspecialists, and surgeons while declines continued in May among primary care specialties (Supplemental table 3).

Discussion

From January to May 2020, over 6 million fewer outpatients were dispensed antibiotic prescriptions from retail pharmacies than would be expected based on the same timeframe in prior years. Decreases were seen across all antibiotic classes and agents, with the greatest beyond seasonally expected declines among agents commonly prescribed for respiratory diseases, dentistry, and surgical prophylaxis. Temporal and geographic azithromycin trends varied from trends in other antibiotic classes with increases in the number of patients dispensed azithromycin prescriptions. Declines beyond seasonal expectations were greatest in children, especially young children (≤4 years), followed by older adults. The greatest beyond-seasonally expected decreases during the COVID-19 pandemic period examined here were observed in prescribing by primary care, advanced practice providers, and select subspecialty and surgical providers, although monthly trends varied between these groups.

We observed marked beyond seasonally expected declines in outpatient antibiotic prescribing during the COVID-19 pandemic. These decreases may be driven by declines in non-COVID-19 disease transmission and by changes in healthcare access and care-seeking. Studies have found declines in U.S. outpatient visits during the pandemic. Several studies of emergency departments found visits for non-COVID-19 related conditions decreased >40% during the pandemic.^{4,10,11} Data published by the Commonwealth Fund from a convenience sample of U.S. outpatient visits showed a decline of almost 60% in March,¹² mirroring the decrease in outpatients dispensed antibiotic prescriptions from March to April. Similarly, a study of a sample of patients with commercial and Medicare Advantage insurance found that outpatient visit rates decreased by around 50% in March.¹³ However, these studies demonstrated rebounds in number of outpatient visits in April and May,^{12,13} differing from trends observed in antibiotic prescribing. Pandemic-related declines in routine vaccination ^{14,15} and chronic disease medication dispensing¹⁶ have also been observed. In addition, a study using a nationallyrepresentative survey found that an estimated 41% of adults in the United States have delayed medical care during the pandemic due to concerns about COVID-19.¹⁷ Decreases in antibiotic prescriptions from dentists, surgical, and subspecialty prescribers and in agents commonly used in dentistry and surgical prophylaxis suggest that decreases in elective and sub-specialty medical care may have contributed to declines in antibiotic prescriptions. Greater decreases observed in antibiotic prescriptions for children compared with adults may be indicative of declines in respiratory disease transmission caused by daycare and school closures and other COVID-19 mitigation efforts. Overall decreases across all antibiotic classes may also be due to fewer healthcare encounters for non-COVID-19 related conditions.

Further decreases in outpatient antibiotic prescribing are uncertain. Although many states began re-opening efforts in May, we observed that the number of patients prescribed antibiotics continued to decrease in May 2020 relative to previous years. This ongoing decrease appeared to be driven by primary care prescriber specialties. Among many medical subspecialty and surgical specialties there was an increase in May compared with previous months in the number of patients with antibiotic prescriptions, likely correlating with resumption of elective and non-urgent subspecialty care and surgeries. Ongoing surveillance will be important as the pandemic continues and to evaluate long-term trends in outpatient antibiotic use.

Trends for azithromycin differed temporally and geographically from trends for other antibiotics, with implications for patient safety and antimicrobial resistance. Similar to trends reported for hydroxychloroquine,^{2,3} nationally, azithromycin prescribing increased slightly from February to March 2020 and then decreased. Azithromycin, particularly in combination with hydroxychloroquine, was suggested as a potential therapy for COVID-19 among hospitalized patients based on extrapolations from in vitro studies of other respiratory infections,^{18,19} medical reports,²⁰ and widely-reported press conferences.²¹ Compared with historic levels, increases in patients dispensed azithromycin prescriptions in March and April were highest in New York and New Jersey, which experienced high COVID-19 case counts during these months.

Increases in outpatient azithromycin prescriptions are concerning for several reasons. First, limited clinical data are available on the effectiveness of azithromycin for the management of COVID-19. Second, azithromycin is associated with QTc prolongation, a potentially life-threatening cardiac adverse event, particularly in older adults.^{22,23} Due to the risk of adverse events, if azithromycin is combined with hydroxychloroquine, close monitoring by healthcare professionals is recommended.²⁴ Third, azithromycin use for COVID-19 may result in antibiotic resistance and diminished effectiveness for recommended indications (e.g., sexually transmitted infections,²⁵ community-acquired pneumonia²⁶).

Outpatient antibiotic stewardship efforts will continue to be important for ensuring patient safety during the COVID-19 pandemic and beyond. Prior to the COVID-19 pandemic, at least one-third of outpatient antibiotic prescriptions were considered unnecessary.^{27,28} It is unclear how much of the

decline observed in our study may be decreases in unnecessary antibiotic prescribing due to reduced healthcare visits and how much may be due to reduced disease transmission. It is also unknown how much of this decrease may represent needed care that was not received. Ongoing surveillance of complications of common bacterial infections (e.g., mastoiditis as a complication of acute otitis media) and antibiotic-associated adverse events may be needed to evaluate the impact of reductions on both necessary and unnecessary antibiotic prescribing. Additionally, ongoing surveillance of vaccination rates and vaccine-preventable disease incidence may inform antibiotic stewardship efforts. Encouraging routine vaccination uptake, especially influenza vaccination, may be especially important during the COVD-19 pandemic to prevent increases in non-COVID respiratory infections.²⁹

Large healthcare delivery changes due to COVID-19 may create new challenges and opportunities for antibiotic stewardship in outpatient settings. The Centers for Medicare & Medicaid Services has substantially expanded coverage of telehealth opportunities during the public health emergency.³⁰ A market research company estimated that telehealth visits increased by 50% during the pandemic and are expected to top 1 billion by the end of 2020, with primary care visits projected at 200 million.³¹ Continued coverage of telehealth services for low- and intermediate-acuity healthcare needs will be relevant to antibiotic stewardship because these types of encounters may include evaluation and management of common outpatient infections, such as sinusitis and acute otitis media. Telehealth has been used during the pandemic to triage patients to home monitoring or appropriate medical settings. Similar approaches may be beneficial for triaging common outpatient respiratory infections and identifying cases that may require additional diagnostic evaluation or in-office testing (e.g., acute otitis media, pharyngitis) versus those that may be more appropriate for home care without antibiotics (e.g., viral upper respiratory infections). Antibiotic use in telemedicine has not been widely studied, and it is not clear from previous studies how well guideline-concordant care is delivered in telemedicine as

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compared with in-person visits.³²⁻³⁴ Concerted stewardship efforts may be needed in this new and growing setting to ensure appropriate antibiotic use and patient safety.

Our study has limitations. First, as these data do not include visit information, we cannot determine the relative contributions of factors such as decreased infection incidence, decreased healthcare utilization, or shifts in healthcare settings (e.g., telemedicine versus in-person) to reductions in antibiotic dispensing. Second, we could not evaluate the impact of prescribing changes on disease complications or adverse health outcomes. Third, the IQVIA TPT dataset does not contain diagnosis information; therefore, we could not evaluate indications or appropriateness of antibiotic prescriptions included in this study. Fourth, for prescriber specialty and state, the IQVIA TPT dataset does not contain aggregated data for all antibiotic classes. Therefore, we selected commonly-used agents to examine major trends. Fifth, in this dataset, nurse practitioners, physician assistants, and osteopathic medicine physicians are categorized by provider type rather than specialty. Sixth, this analysis did not include antibiotics dispensed by mail-order; however, we expect few antibiotics to be dispensed via mail-order pharmacy, as most are one-time prescriptions for an acute illness. Finally, we were unable to separate whether changes observed in our study were due solely to the COVID-19 pandemic or influenced by other secular trends, such as general decreases in outpatient antibiotic prescribing.³⁵ However, a study of national outpatient antibiotic prescriptions showed only a 5% decrease in dispensed prescriptions from 2011 to 2016,³⁶ suggesting that changes observed in 2020 exceed previously-observed secular trends.

Conclusion

During the early period of the COVID-19 pandemic, the number of outpatients with antibiotic prescriptions dispensed from retail pharmacies decreased substantially more than would be expected due to seasonal trends alone. Decreases were greatest among children and agents frequently prescribed for respiratory infections, dentistry, and surgical prophylaxis. Trends in azithromycin prescriptions varied from other antibiotic classes, likely related to transient interest in azithromycin in COVID-19 management. Ongoing surveillance of antibiotic prescribing, antibiotic-associated adverse events, antibiotic-resistant infections, and complications of common infections is needed to evaluate the longterm impacts of these changes in outpatient antibiotic trends. Shifts in healthcare delivery, particularly the use of telehealth, are likely to be sustained, and should prompt assessment of effective antibiotic stewardship interventions^{37,38} to optimize antibiotic prescribing practices and ensure patient safety. , rtin

NOTES

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References

- Jeffery MM, D'Onofrio G, Paek H, et al. Trends in Emergency Department Visits and Hospital Admissions in Health Care Systems in 5 States in the First Months of the COVID-19 Pandemic in the U.S. JAMA Intern Med. 2020;180(10):1328-1333.
- Vaduganathan M, Van Meijgaard J, Mehra MR, Joseph J, O'Donnell CJ, Warraich HJ. Prescription Fill Patterns for Commonly Used Drugs During the COVID-19 Pandemic in the United States. JAMA. 2020;323(24):2524-2526.
- Shehab N, Lovegrove M, Budnitz DS. U.S. Hydroxychloroquine, Chloroquine, and Azithromycin Outpatient Prescription Trends, October 2019 Through March 2020. JAMA Intern Med. 2020. doi: 10.1001/jamainternmed.2020.2594. Online ahead of print.
- Hartnett KP K-PA, DeVies J, et al. Impact of the COVID-19 Pandemic on Emergency Department Visits — United States, January 1, 2019–May 30, 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69(23):699-704.
- 5. Durkin MJ, Jafarzadeh SR, Hsueh K, et al. Outpatient Antibiotic Prescription Trends in the United States: A National Cohort Study. *Infect Control Hosp Epidemiol.* 2018;39(5):584-589.
- Ibrahim IT. Pediatric Utilization Patterns of Opioid Analgesics (OAs). U.S. Food and Drug
 Administration. Presented at the Meeting of the Pediatric Advistory Committee, Sep 26, 2019.
 Available at: <u>https://www.fda.gov/media/131133/download</u>. Accessed Oct 19, 2020.
- Centers for Disease Control and Prevention. 2019 Annual Surveillance Report of Drug-Related Risks and Outcomes — United States Surveillance Special Report. Centers for Disease Control and Prevention, U.S. Department of Health and Human Services. Published Nov 1, 2019.

Available at: https://www.cdc.gov/drugoverdose/pdf/ pubs/2019-cdc-drugsurveillancereport.pdf. Accessed Oct 19, 2020.

- Schieber LZ, Guy GP, Jr., Seth P, Losby JL. Variation in Adult Outpatient Opioid Prescription Dispensing by Age and Sex - United States, 2008-2018. *MMWR Morb Mortal Wkly Rep*. 2020;69(11):298-302.
- Centers for Disease Control and Prevention. Census Population Projections. Available at: <u>https://wonder.cdc.gov/population.html</u>. Accessed Oct 19, 2020.
- 10. Jeffery MM, D'Onofrio G, Paek H, et al. Trends in Emergency Department Visits and Hospital Admissions in Health Care Systems in 5 States in the First Months of the COVID-19 Pandemic in the U.S. JAMA Intern Med. 2020 ;180(10):1328-1333.
- Kim JW, Friedman J, Clark S, et al. Implementation of a Pediatric Emergency Telemedicine Program. *Pediatr Emerg Care.* 2020;36(2):e104-e107.
- Mehrotra A, Chernew ME, Linetsky D, Hatch H, Cutler DM. The Impact of the COVID-19
 Pandemic on Outpatient Care: Visits Return to Prepandemic Levels, but Not for All Providers and
 Patients. Published Oct 15 2020; Available at:

https://www.commonwealthfund.org/publications/2020/oct/impact-covid-19-pandemicoutpatient-care-visits-return-prepandemic-levels. Accessed Nov 30, 2020.

- Patel SY, Mehrotra A, Huskamp HA, Uscher-Pines L, Ganguli I, Barnett ML. Trends in Outpatient
 Care Delivery and Telemedicine During the COVID-19 Pandemic in the US. JAMA Intern Med.
 2020. doi:10.1001/jamainternmed.2020.5928. Online ahead of print.
- Bramer CA, Kimmins LM, Swanson R, et al. Decline in Child Vaccination Coverage During the
 COVID-19 Pandemic Michigan Care Improvement Registry, May 2016-May 2020. MMWR Morb
 Mortal Wkly Rep. 2020;69(20):630-631.

- Santoli JM, Lindley MC, DeSilva MB, et al. Effects of the COVID-19 Pandemic on Routine Pediatric Vaccine Ordering and Administration - United States, 2020. MMWR Morb Mortal Wkly Rep. 2020;69(19):591-593.
- Vaduganathan M, van Meijgaard J, Mehra MR, Joseph J, O'Donnell CJ, Warraich HJ. Prescription
 Fill Patterns for Commonly Used Drugs During the COVID-19 Pandemic in the United States.
 JAMA. 2020;323(24):2524-2526.
- Czeisler MÉ, Marynak K, Clarke KEN, et al. Delay or Avoidance of Medical Care Because of COVID-19–Related Concerns — United States, June 2020. *MMWR Morb Mortal Wkly Rep.* 2020;69(36):1250–1257.
- 18. Bermejo-Martin JF, Kelvin DJ, Eiros JM, Castrodeza J, Ortiz de Lejarazu R. Macrolides for the treatment of severe respiratory illness caused by novel H1N1 swine influenza viral strains. *J Infect Dev Ctries.* 2009;3(3):159-161.
- Li C, Zu S, Deng YQ, et al. Azithromycin Protects against Zika virus Infection by Upregulating virus-induced Type I and III Interferon Responses. *Antimicrob Agents Chemother*. 2019;63(12):e00394-19.
- Gautret P, Lagier J-C, Parola P, et al. Hydroxychloroquine and azithromycin as a treatment of COVID-19: results of an open-label non-randomized clinical trial. *Int J Antimicrob Agents*. 2020;56(1):105949.
- 21. Grady DG, Kannapell A. Trump Urges Coronavirus Patients to Take Unproven Drug. *The New York Times.* April 4, 2020.
- 22. U.S. Food and Drug Administration. FDA Drug Safety Communication: Azithromycin (Zithromax or Zmax) and the risk of potentially fatal heart rhythms. Published Mar 12, 2013. Available at: https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-azithromycin-zithromax-or-zmax-and-risk-potentially-fatal-heart. Accessed Oct 19, 2020.

- Zaroff JG, Cheetham TC, Palmetto N, et al. Association of Azithromycin Use With Cardiovascular Mortality. *JAMA Netw Open.* 2020;3(6):e208199.
- 24. Roden DM, Harrington RA, Poppas A, Russo AM. Considerations for Drug Interactions on QTc Interval in Exploratory COVID-19 Treatment. *J Am Coll Cardiol.* 2020;75(20):2623-2624.
- 25. 25. Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015.
 MMWR Morb Mortal Wkly Rep. 2015;64(Rr-03):1-137.
- 26. Metlay JP, Waterer GW, Long AC, et al. Diagnosis and Treatment of Adults with Communityacquired Pneumonia. An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America. *Am J Respir Crit Care Med.* 2019;200(7):e45-e67.
- Fleming-Dutra KE, Hersh AL, Shapiro DJ, et al. Prevalence of Inappropriate Antibiotic
 Prescriptions Among U.S. Ambulatory Care Visits, 2010-2011. JAMA. 2016;315(17):1864-1873.
- Hersh AL, King LM, Shapiro DJ, Hicks LA, Fleming-Dutra KE. Unnecessary antibiotic prescribing in U.S. ambulatory care settings, 2010-2015. *Clin Infect Dis*. 2020;ciaa667. doi: 10.1093/cid/ciaa667. Online ahead of print.
- 29. Centers for Disease Control and Prevention. Interim Guidance for Immunization Services During the COVID-19 Pandemic. Updated Jun 9, 2020. Available at:

https://www.cdc.gov/vaccines/pandemic-guidance/index.html. Accessed Oct 19, 2020.

30. Centers for Medicare & Medicaid Services. Non-Emergent, Elective Medical Services, and Treatment Recommendations. Published Apr 7, 2020. Available at: <u>https://www.cms.gov/files/document/cms-non-emergent-elective-medical-</u>

recommendations.pdf. Accessed Oct 19, 2020.

31. Coombs B. Telehealth visits are booming as doctors and patients embrace distancing amid the coronavirus crisis. *CNBC*. Published Apr 4, 2020. Available at:

https://www.cnbc.com/2020/04/03/telehealth-visits-could-top-1-billion-in-2020-amid-thecoronavirus-crisis.html. Accessed Oct 19, 2020.

- 32. Halpren-Ruder D, Chang AM, Hollander JE, Shah A. Quality Assurance in Telehealth: Adherence to Evidence-Based Indicators. *Telemed J E Health*. 2019; Jul;25(7):599-603.
- Johnson KM, Dumkow LE, Burns KW, Yee MA, Egwuatu NE. Comparison of Diagnosis and Prescribing Practices Between Virtual Visits and Office Visits for Adults Diagnosed With Sinusitis Within a Primary Care Network. *Open Forum Infect Dis.* 2019;6(9):ofz393-ofz393.
- Ray KN, Shi Z, Gidengil CA, Poon SJ, Uscher-Pines L, Mehrotra A. Antibiotic Prescribing During
 Pediatric Direct-to-Consumer Telemedicine Visits. *Pediatrics*. 2019;143(5):e20182491.
- 35. Centers for Disease Control and Prevention. Outpatient antibiotic prescriptions United States,
 2018. Available at: https://www.cdc.gov/antibiotic-use/community/programs-
 measurement/state-local-activities/outpatient-antibiotic-prescriptions-US-2018.html
 Accessed
 Oct 19, 2020.
- 36. King LM, Bartoces M, Fleming-Dutra KE, Roberts RM, Hicks LA. Changes in US Outpatient Antibiotic Prescriptions from 2011-2016. *Clin Infect Dis*. 2020;70(3):370-377.
- 37. Sanchez GV, Fleming-Dutra KE, Roberts RM, Hicks LA. Core Elements of Outpatient Antibiotic Stewardship. *MMWR Morb Mortal Wkly Rep.* 2016;65(6):1-12.
- 38. King LM, Fleming-Dutra KE, Hicks LA. Advances in optimizing the prescription of antibiotics in outpatient settings. *BMJ*. 2018;363:k3047.

rscriptions Dispen-Table 1. Estimated Number of Patients with Antibiotic Prescriptions Dispensed from Retail Pharmacies and Beyond Seasonally Expected

Changes by Antibiotic Class and Agent, United States, January 2017 through May 2020^a

	2017-2019 average					2020 o	2020 January to May 2020 change beyond seasonally expected			
Antibiotic Class and Selected Agents ^b	No. patients dispensed antibiotic prescriptions, in millions		January to May change		No. patients dispensed antibiotic prescriptions, in millions		January to May change		Additional percentage ^d	No., in millions ^e
K	January	Мау	No., in millions	% ^c	January	Мау	No., in millions	% ^c		
Total	21.1	17.2	-3.9	-19	20.3	9.9	-10.4	-51	-33	-6.6
Penicillins	5.7	4.7	-1.0	-17	5.6	2.3	-3.3	-59	-42	-2.3
Amoxicillin	5.3	4.3	-0.9	-18	5.2	2.0	-3.2	-61	-43	-2.2
Penicillin V	0.4	0.4	0.0 ^f	-6	0.3	0.2	-0.1	-33	-27	-0.1

	2017-2019 average 2020 observed									to May 2020 d seasonally
Antibiotic Class and Selected Agents ^b	No. patients dispensed antibiotic prescriptions, in millions		January to May change		No. patients dispensed antibiotic prescriptions, in millions		January to May change		expec Additional percentage ^d	ted No., in millions ^e
	January	May	No., in millions	% ^c	January	May	No., in millions	% ^c		
Macrolides	4.9	3.0	-1.9	-39	4.3	1.2	-3.1	-73	-34	-1.5
Azithromycin	4.7	2.9	-1.9	-39	4.1	1.1	-3.0	-74	-34	-1.4
Cephalosporins	3.2	2.9	-0.3	-9	3.3	1.9	-1.4	-42	-33	-1.1
Cephalexin	1.6	1.8	0.1	8	1.7	1.4	-0.3	-18	-26	-0.4
Cefdinir	1.1	0.8	-0.3	-26	1.1	0.3	-0.8	-72	-46	-0.5
Extended spectrum beta-lactams	2.9	2.1	-0.8	-27	3.0	1.1	-1.9	-62	-35	-1.1
Amoxicillin- clavulanate	2.9	2.1	-0.8	-27	3.0	1.1	-1.9	-62	-35	-1.1
Fluoroquinolones	2.1	1.7	-0.4	-17	1.6	1.0	-0.5	-35	-18	-0.3
Ciprofloxacin	1.2	1.1	0.0 ^f	-3	0.9	0.8	-0.2	-20	-17	-0.2
Levofloxacin	0.9	0.6	-0.3	-35	0.6	0.3	-0.4	-56	-21	-0.1

		2017-2019	average		Si	2020 of	2020 January to May 2020 change beyond seasonally expected			
Antibiotic Class and Selected Agents ^b	No. patients dispensed antibiotic prescriptions, in millions		January to May change		No. patients dispensed antibiotic prescriptions, in millions		January to May change		Additional percentage ^d	No., in millions ^e
	January	Мау	No., in millions	% ^c	January	May	No., in millions	% ^c		
Tetracyclines	2.0	1.9	-0.1	-5	2.4	1.5	-0.8	-35	-30	-0.7
Doxycycline	1.7	1.6	-0.1	-6	2.1	1.3	-0.8	-38	-31	-0.6
Sulfonamides and combinations	1.5	1.5	0.01	1	1.3	1.1	-0.2	-17	-18	-0.2
Sulfamethoxazole- trimethoprim	1.4	1.5	0.0 ^f	1	1.3	1.1	-0.2	-18	-19	-0.2
Lincosamides	0.8	0.8	0.0 ^f	3	0.7	0.6	-0.1	-20	-23	-0.2
Clindamycin	0.8	0.8	0.0 ^f	3	0.7	0.6	-0.1	-20	-23	-0.2
Other	0.0 ^f	0.1	0.0 ^f	10	0.1	0.0 ^f	0.0 ^f	-23	-33	0.0 ^e

^a Data are from IQVIA Total Patient Tracker (January 2017-May 2020) and were accessed July 16, 2020.

^b Classes and agents do not sum to total as patients with ≥ 1 dispensed antibiotic prescription are only counted once in the total and not all agents shown.

^c Percent change from January to May calculated as: (No. patients with antibiotic prescriptions in May - No. patients with antibiotic prescriptions in January)/ No. patients with antibiotic prescriptions in January.

^d Additional percentage change calculated as: Observed percent change from January to May in 2020 – Average percent change from January to May between 2017-2019.

^e Change beyond seasonally expected in the number of patients with antibiotic prescriptions calculated as: observed change in the number of patients with dispensed antibiotics prescriptions from January to May 2020 – (2017-2019 average percent change in the number of patients with dispensed antibiotic prescriptions from January to May x Number of patients with dispensed antibiotic prescriptions in January 2020).

^fNumber has an absolute value of <50,000 and is rounded to 0.0 million.

Table 2. Estimated Number of Patients with Antibiotic Prescriptions Dispensed from Retail Pharmacies and Beyond Seasonally Expected

Changes by Select Antibiotic Agent and Prescriber Specialty, United States, January 2017 through May 2020 ^a

	2017-2019 average					2020 ob	oserved	2020 January to May change beyond seasonally expected		
c.e	No. patients dispensed antibiotic prescriptions		January to May iotic change s		No. patients dispensed antibiotic prescriptions		January to May change		Additional percentage ^d	No. ^e
Prescriber Specialty ^b	January	May	No.	% ^c	January	May	No.	% ^c		
Amoxicillin										
Pediatrics	886,936	657,138	-229,798	-26	804,580	106,388	-698,191	-87	-61	-489,731
Gastroenterology	17,587	18,573	986	6	17,442	7,900	-9,542	-55	-60	-10,520
Nurse Practitioner	871,027	666,221	-204,807	-24	1,008,406	220,770	-787,636	-78	-55	-550,527
Physician Assistants	506,634	389,337	-117,297	-23	532,135	117,931	-414,204	-78	-55	-291,003
Emergency Medicine	148,624	115,199	-33,425	-22	133,292	35,893	-97,399	-73	-51	-67,422

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		2017-2019) average	S	2020 ob	served		2020 January to May change beyond seasonally expected								
Prescriber Specialty ^b	No. patients dispensed antibiotic prescriptions		January to chang	January to May change		No. patients dispensed antibiotic prescriptions		o May je	Additional percentage ^d	No. ^e						
Amoxicillin Clavulanate	9															
Pediatrics	266,003	205,517	-60,485	-23	236,923	49,449	-187,474	-79	-56	-133,601						
Allergy	14,926	11,916	-3,009	-20	13,750	4,819	-8,932	-65	-45	-6,159						
Nurse Practitioner	669,411	470,824	-198,587	-30	828,517	236,059	-592,459	-72	-42	-346,671						
Physician Assistants	388,765	280,720	-108,045	-28	437,653	136,263	-301,391	-69	-41	-179,758						
Otolaryngology	67,109	56,001	-11,108	-17	62,521	27,805	-34,716	-56	-39	-24,367						
Azithromycin	<u> </u>															
Pediatrics	313,826	220,262	-93,564	-30	261,476	36,417	-225,060	-86	-56	-147,104						
Infectious Diseases	16,819	14,945	-1,874	-11	16,613	6,304	-10,308	-62	-51	-8,457						
Otolaryngology	29,703	22,319	-7,383	-25	25,340	9,143	-16,197	-64	-39	-9,898						
Nurse Practitioner	909,422	568,311	-341,111	-38	968,808	238,143	-730,665	-75	-38	-367,279						
Physician Assistants	598,614	353,974	-244,640	-41	556,381	117,035	-439,347	-79	-38	-211,966						
Cefdinir																
Pediatrics	259,819	202,681	-57,138	-22	236,715	42,021	-194,694	-82	-60	-142,637						
Nurse Practitioner	252,457	187,013	-65,444	-26	324,093	74,670	-249,423	-77	-51	-165,408						

		2017-2019	average	S	2020 ob:	2020 January to May change beyond seasonally expected					
Prescriber Specialty ^b	No. patients dispensed antibiotic prescriptions		January to May change		No. patients dispensed antibiotic prescriptions		January to May change		Additional percentage ^d	No. ^e	
Otolaryngology	29,238	25,146	-4,091	-14	29,110	10,824	-18,286	-63	-49	-14,213	
Allergy	5,919	5,013	-906	-15	5,298	1,910	-3,388	-64	-49	-2,577	
Physician Assistants	132,228	95,915	-36,313	-27	152,504	37,430	-115,074	-75	-48	-73,192	
Cephalexin	~ (7									
Physician Assistants	228,303	264,606	36,303	16	259,959	200,874	-59,086	-23	-39	-100,422	
Otolaryngology	18,731	19,111	380	2	16,958	10,671	-6,287	-37	-39	-6,631	
Nurse Practitioner	236,914	276,944	40,030	17	303,127	240,432	-62,695	-21	-38	-113,913	
Pediatrics	96,966	101,657	4,691	5	90,005	62,297	-27,707	-31	-36	-32,062	
Emergency Medicine	122,163	140,905	18,742	15	129,980	108,445	-21,535	-17	-32	-41,477	

^a Data are from IQVIA Total Patient Tracker (January 2017-May 2020) and were accessed July 16, 2020.

^b Specialties by agent do not sum to agent total as patients with ≥1 dispensed antibiotic prescription are only counted once in the total and only the top five specialties are shown for each antibiotic.

^c Percent change from January to May calculated as: (No. patients with antibiotic prescriptions in May - No. patients with antibiotic prescriptions in January)/ No. patients with antibiotic prescriptions in January. ^d Additional percentage change calculated as: Observed percent change from January to May in 2020 – Average percent change from January to May between 2017-2019.

^e Change beyond seasonally expected in the number of patients with antibiotic prescriptions calculated as: observed change in the number of patients with dispensed antibiotics prescriptions from January to May 2020 – (2017-2019 average percent change in the number of patients with dispensed antibiotic prescriptions from January to May x Number of patients with dispensed antibiotic prescriptions in January 2020).

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FIGURE LEGENDS:

Figure 1. Estimated Percent Change in the Number of Patients with Antibiotic Prescriptions Dispensed from Retail Pharmacies by Month, 2017-2019 Versus 2020, United States

Estimated percent change in numbers of unique patients dispensed antibiotic prescriptions, comparing January through May monthly averages during 2017-2019 to monthly values in 2020. Only systemic antibiotics were included. Data are from IQVIA Total Patient Tracker (January 2017-May 2020) and were accessed July 16, 2020.

Figure 2. Estimated Number of Patients with Prescriptions Dispensed from Retail Pharmacies, by Month for A) All Antibiotics and B) Azithromycin, 2017-2019 Versus 2020, United States

Estimated numbers of unique patients dispensed prescriptions from January 2017 to May 2020. Only systemic antibiotics were included. Data are from IQVIA Total Patient Tracker and were accessed July 16, 2020.

Figure 3. Observed versus Expected Number of Patients Dispensed Antibiotic Prescriptions from Retail Pharmacies per 1000 Persons by Age Group, January 2020 and May 2020, United States

Estimated numbers of unique patients dispensed antibiotic prescriptions from January 2020 and May 2020 standardized per 1000 persons. Population estimates are based on U.S. Census population projections.⁹ Only systemic antibiotics were included. Data are from IQVIA Total Patient Tracker and were accessed July 16, 2020





