Geographic Variability in Antibiotic Prescribing Rates in Medicaid

Alexia G. Aguilar[1†], Priscilla C. Canals[1†], Kimberly A. Miller[1], and Brian J. Piper[1,2]
[1]Geisinger Commonwealth School of Medicine, Scranton, PA 18509
[2]Center for Pharmacy Innovation and Outcomes, Forty Fort, PA 18704
[†]Doctor of Medicine Program
Correspondence: aaguilar@som.geisinger.edu

Abstract

Background: Antibiotic resistance is a persistent and growing concern. There is a lack of data identifying the current state of antibiotic prescription patterns in the Medicaid program. We analyzed temporal and regional trends in antibiotic prescribing data across the United States (U.S.) to identify regional disparities.

Methods: We analyzed prescribing rates over the past 2 years in Medicaid Part D for 8 antibiotics. Four were broad spectrum: azithromycin, ciprofloxacin, levofloxacin, and moxifloxacin; and 4 were narrow spectrum: amoxicillin, cephalexin, doxycycline, and trimethoprim/sulfamethoxazole. We identified the geographical distribution of these antibiotics across the U.S. Furthermore, we evaluated total antibiotic prescriptions per state per quarter during 2018 and 2019 collected from the Medicaid State Drug Utilization database. Prescription rates were reported per 1,000 Medicaid enrollees. The states were divided into specific geographic regions according to the U.S. Census to determine which regions have the highest and lowest prescription rates. We analyzed the data and constructed figures using International Business Machine Corporation's Statistical Package for the Social Sciences (IBM SPSS), Statistical Analysis System's John's Macintosh Project (SAS JMP), and GraphPad Prism.

Results: Antibiotic prescriptions decreased 9.6% from 2018 to 2019. Amoxicillin was the predominant antibiotic, followed by azithromycin, cephalexin, trimethoprim/sulfamethoxazole, doxycycline, ciprofloxacin, levofloxacin, and moxifloxacin. Substantial geographic and quarterly variation in antibiotic prescribing existed. The South prescribed 52.2% more antibiotics (580/1,000) in 2019 than the West (381/1,000). We identified a significant correlation between the 2018 and 2019 prescription rates ($r = 0.95$, $p < 0.001$).

Conclusions: This study identified the geographical prescribing rates of 8 antibiotics during 2018 and 2019. The south had the highest prescribing rates among all the regions. Areas of high antibiotic prescribing rates may benefit from programs to reduce unnecessary prescribing. Further analysis on state level Medicaid or prescribing policies may be done to identify reasons for such high prescribing rates.

Introduction

Due to the increasing use of antibiotics over the past century, antibiotic resistance has become one of the most pressing threats to public health today. According to the World Health Organization, increasing antibiotic resistance is one of the biggest threats to global health, food security, and development of human defenses today (1). Studies have discovered overuse and inappropriate prescribing of antibiotics in a variety of health care settings (2–5). According to a 2019 report released by the Centers for Disease Control and Prevention, more than 2.8 million antibiotic-resistant infections occur in the United States (U.S.) each year, and more than 35,000 people die as a result. (6). Most of these antibiotic prescriptions are for respiratory infections commonly caused by viruses, which do not respond to antibiotics. (7). Antibiotics are often prescribed unnecessarily (8, 9), and 30–50% of prescriptions for them are not associated with an indication (10–12). Sulfonamides and urinary anti-infective agents are the classes most likely to be prescribed without documentation (11). Up to 25% of antibiotics prescribed in the outpatient setting to Medicaid beneficiaries were not associated with a provider visit and therefore are not screened by existing antimicrobial stewardship systems (13). Further, among 298 million prescriptions filled by 53 million Medicaid patients between 2004 and 2013, 45% of prescriptions for antibiotics were made without any clear rationale. Twenty-eight percent of antibiotics were prescribed without evidence of seeing the provider, and 17% were given without documentation for infection-related diagnosis. Inappropriate antibiotic prescribing leads to antibiotic resistance on individual as well as community levels, particularly against public health threats such as carbapenem-resistant Enterobacteriaceae and methicillin-resistant *Staphylococcus aureus* (14). Furthermore, overuse of antibiotics increases the risk of adverse effects such as rash, GI upset, and renal dysfunction (6). The risk of infection with *Clostridium difficile* increases with duration of exposure to antibiotics (15, 16). Recent data supports the relationship between early antibiotic exposure before age 2 and subsequent negative outcomes such as obesity, autoimmune disorders, and asthma (17).

It has been found that geographic areas with high antibiotic consumption are associated with increased antibiotic resistance, and that broad-spectrum antibiotics are more likely to be associated with antibiotic resistance (18). The South census region of the United States has the highest prescribing rate among the rest of the country (19, 20).

Examination of antibiotic prescription variation in the U.S. in 2011 found that the most common antibiotic categories were penicillins followed by macrolides. Among individual antibiotics, the most prescribed antibiotic agents were azithromycin followed by amoxicillin. When examining geographic trends in prescriptions, prescribing rates were highest in the South. Specifically, Kentucky had the highest prescriptions rates (1,281 prescriptions per 1,000 persons) which was about four-fold higher than Alaska with the lowest (348 per 1,000 persons) (19). A report of California Medicaid beneficiaries also found penicillins to be the most prescribed antibiotic class, followed

by macrolides, cephalosporins, sulfonamides, quinolones, and tetracyclines (18). Amoxicillin, azithromycin, cephalexin, doxycycline, and sulfamethoxazole/trimethoprim were the most frequently used agents in their respective class (18).

Due to the public health risks that arise from antibiotic resistance, it is imperative to be continuously vigilant to identify and avoid unnecessary prescriptions. This study examined the temporal and geographical patterns of antibiotic prescribing rates among U.S. Medicaid program beneficiaries.

Methods

Participants

Medicaid is a joint federal and state program that provides coverage for 75 million people or 21% of the U.S. population (21). It is one of the largest payers for health care in the U.S. All states provide coverage for outpatient prescription drugs (21).

Procedures

State antibiotic prescription totals and population data during 2018–2019 were collected from the Medicaid State Drug Utilization database. Total number of prescriptions and Medicaid enrollee data were used to calculate individual antibiotic prescribing rates per state.

Antibiotics were identified using the generic and trade names (22). Antibiotics were further categorized as broad or narrow spectrum based on their potential for influencing antibacterial resistance as well as their spectrum of activity according to the National Committee For Quality Assurance's "antibiotics of concern." Azithromycin, levofloxacin, moxifloxacin, and ciprofloxacin are broad-spectrum antibiotics, while amoxicillin, cephalexin, doxycycline, and trimethoprim sulfamethoxazole are narrow-spectrum antibiotics (23, 24).

The states were divided into geographic regions according to the U.S. Census. These regions were defined as: the South (Alabama, Arkansas, Delaware, District of Columbia, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, and West Virginia), the West (Alaska, Arizona, California, Colorado, Hawaii, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming), the Midwest (Illinois, Indiana, Iowa, Kansas, Michigan, Minnesota, Missouri, Nebraska, North Dakota, Ohio, South Dakota, and Wisconsin), and the Northeast (Connecticut, Maine, Massachusetts, New Hampshire, New Jersey, New York, Pennsylvania, Rhode Island, and Vermont).

Data analysis

After the total number of prescriptions was collected and prescription rate per 1,000 enrollees was calculated, we input the data into IMB SPSS. We conducted t-tests and linear regressions to find associations between variables. Pearson correlations were completed between antibiotics for each year. We created figures and heatmaps through Statistical Analysis System's John's Macintosh Project (SAS JMP) and GraphPad Prism to show variation across regions in the United States. Variability was reported as the standard error of the mean (SEM). A p-value of < 0.05 was considered statistically significant.

Results

In 2019, a total of 33,011,946 of the antibiotics included for analysis were prescribed with an average prescribing rate of 464 prescriptions/1,000 enrollees. The total amount prescribed was 9.61% lower than that observed in 2018 (36,519,951 total antibiotics, 494 prescriptions/1,000 enrollees).

There was considerable variation in antibiotic prescribing rates among different regions (Figure 1). The South census region had the highest prescribing rate (580 prescriptions/1,000 enrollees in 2019, 601 prescriptions/1,000 enrollees in 2018) compared to the West census region, which had the lowest (381 prescriptions/1,000 enrollees in 2019, 420 prescriptions/1,000 enrollees in 2018).

Kentucky and Louisiana were the top two states with the highest prescribing rates in 2018 and 2019 (Figure 2 and 3). Alaska and Oregon had the lowest prescribing rates in 2018, while Oregon and Washington state had the lowest in 2019.

Figure 4 shows that from 2018 to 2020, amoxicillin was the most prescribed antibiotic (48.1%), followed by azithromycin (18.3%). Additionally, we found a similar trend in antibiotic prescriptions during different quarters (quarter 1: January to March, quarter 2: April to June, quarter 3: July to September, quarter 4: October to December). Prescriptions fell from April to the end of September, suggesting that there is a higher rate of prescription during cooler months.

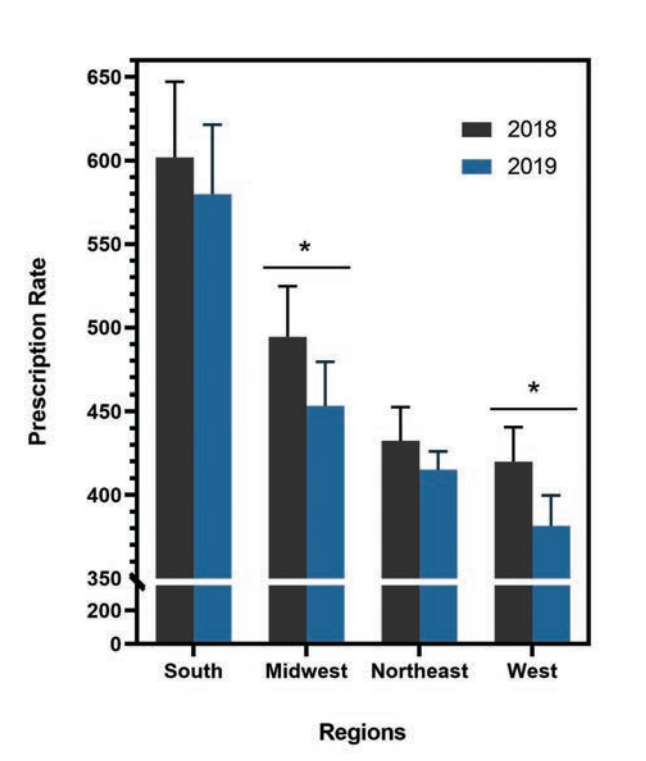

Figure 1. Antibiotic prescription rates in Medicaid Part D by Census regions. There was considerable variation in antibiotic prescribing rates among different regions. The South census region had the highest prescribing rate (580 prescriptions/1,000 enrollees in 2019, 601 prescriptions/1,000 enrollees in 2018) compared to the West census region which had the lowest (381 prescriptions/1,000 enrollees in 2019, 420 prescriptions/1,000 enrollees in 2018).

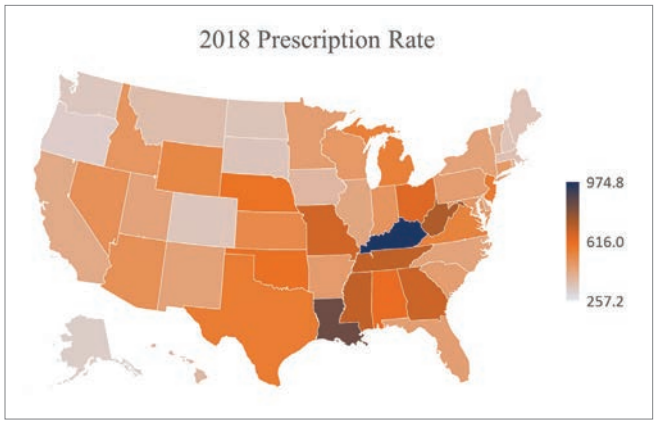

Figure 2. Total prescribing rate per state in 2018.

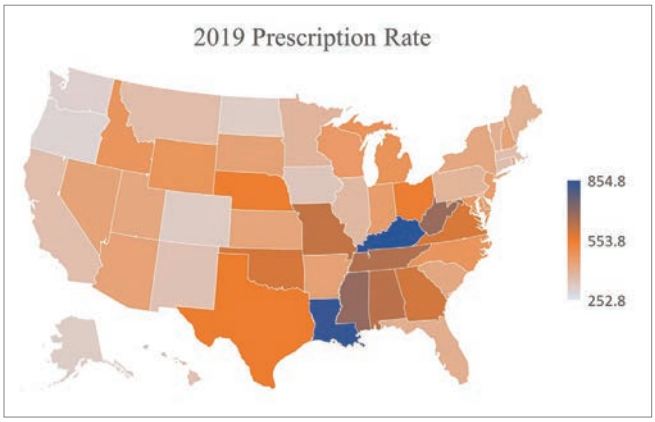

Figure 3. Total prescribing rate per state in 2019.

The correlation between population-corrected antibiotic prescriptions in 2018 is shown in Table 1. The correlation between the grand total was generally significantly associated with individual agents except for moxifloxacin. This pattern was replicated in 2019 (Table 2).

Discussion

Antibiotic misuse, overuse, and subsequent resistance are major public health issues (1, 6). Patients prescribed antibiotics have been shown to develop resistance that is most impactful during the month after therapy but continues for up to a year (25). In one study at a single center, investigators found that 12.3% of antibiotics prescribed in the outpatient setting were not consistent with current guideline recommendations (26). The most common antibiotic prescribed in this study was azithromycin, followed by amoxicillin-clavulanate and amoxicillin. In a study that evaluated prescribing of antibiotics in children, azithromycin and amoxicillin were found to be the most frequently prescribed (27). This is consistent with our data, which showed amoxicillin to be the most prescribed antibiotic, followed by azithromycin.

Infections of the upper respiratory and urinary tracts are the most common indications for antibiotic use in adults and children in the outpatient setting. Beta lactam and macrolide antibiotics are used for the treatment of upper respiratory tract infections in both adults and children. Doxycycline is used for upper respiratory tract infections in adults, while trimethoprim/sulfamethoxazole (TMP/SMX) is prescribed for urinary tract infections and skin and skin structure infections. TMP/SMX is also often used in the treatment of upper respiratory tract infections despite recommendations against its use for this indication due to its spectrum of action (28).

Our results showed a total of 36,519,951 antibiotics prescribed in 2018 and 33,011,946 prescribed in 2019. The prescribing rate was found to be 464 prescriptions/1,000 enrollees. Our findings show a higher rate of antibiotic prescribing compared to other studies (24). Further, we determined that the South census region had the highest prescribing rate, while the West census region had the lowest. This is consistent with findings from other studies (19, 29). Trends in antibiotic prescribing varied based on the quarter in the year. The highest antibiotic prescribing rates occurred found during October to March,

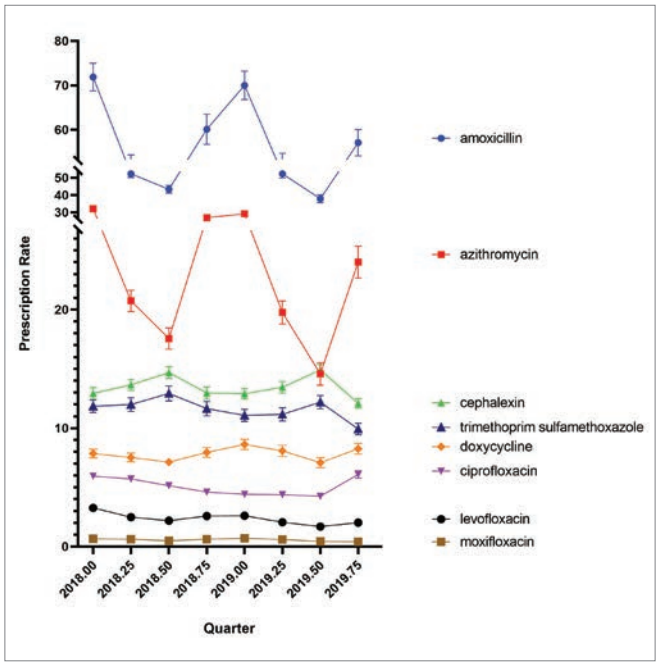

Figure 4. Quarterly antibiotic prescribing rates.

while prescribing rates fell from April to the end of September. This is consistent with trends in upper respiratory tract infections. These are often more prevalent during fall or winter months and decrease during warmer months.

The correlations in population corrected antibiotic use per state showed that regional patterns were generally homogenous for all agents in both 2018 and 2019 except moxifloxacin. This suggests that the use pattern for this broad-spectrum fluoroquinolone was distinct from other agents.

While we were fortunate to be using a database that collects data from across the entire United States, Medicaid only accounts for 20% of the population. Other limitations include limited data reporting from some states for certain antibiotics, for example amoxicillin/clavulanic acid was removed from the study due to limited data reported on the antibiotic.

Experimental Parameters	A	B	C	D	E	F	G	H	Grand Total
amoxicillin (A)	1.00								
azithromycin (B)	0.81*	1.00							
cephalexin (C)	0.43*	0.50*	1.00						
ciprofloxacin (D)	0.42*	0.60*	0.53*	1.00					
doxycycline (E)	0.14	0.36*	0.48*	0.64*	1.00				
levofloxacin (F)	0.57*	0.70*	0.53*	0.81*	0.68*	1.00			
moxifloxacin (G)	0.29*	0.16	0.03	0.18	0.21	0.07	1.00		
trimethoprim/sulfamethoxazole (H)	0.69*	0.85*	0.59*	0.70*	0.56*	0.76*	0.03	1.00	
Grand Total	0.93*	0.93*	0.59*	0.59*	0.37*	0.74*	0.23	0.87*	1.00

* $p < 0.001$

Table 1. Correlation matrix showing associations between antibiotics in 2018. Correlation coefficients were derived from pooled data from the Medicaid State Drug and Utilization database. * $p < 0.001$

Experimental Parameters	A	B	C	D	E	F	G	H	Grand Total
amoxicillin (A)	1.00								
azithromycin (B)	0.81*	1.00							
cephalexin (C)	0.40*	0.43*	1.00						
ciprofloxacin (D)	0.61*	0.76*	0.47*	1.00					
doxycycline (E)	0.15	0.30*	0.41*	0.59*	1.00				
levofloxacin (F)	0.57*	0.67*	0.52*	0.85*	0.64*	1.00			
moxifloxacin (G)	0.35*	0.22	0.13	0.03	0.26	0.07	1.00		
trimethoprim/sulfamethoxazole (H)	0.72*	0.86*	0.55*	0.84*	0.54*	0.76*	0.04	1.00	
Grand Total	0.90*	0.94*	0.55*	0.77*	0.37*	0.74*	0.27	0.89*	1.00

* $p < 0.001$

Table 2. Correlation matrix showing associations between antibiotics in 2019. Correlation coefficients were derived from pooled data from the Medicaid State Drug and Utilization database. * $p < 0.001$

Conclusion

This study provides an overview of antibacterial prescribing practices in the Medicaid system. Findings include discrepancies in antibacterial prescribing rates among different regions across the U.S. as well as during different times of the year. Future research plans include identifying state-level antibiotic prescribing policies as well as how COVID-19 has impacted antibiotic prescription rates.

Acknowledgments

We thank Geisinger Commonwealth School of Medicine's Center of Excellence for their work in organizing and coordinating this project.

Disclosures

This work was supported by Health Resources and Services Association (HRSA) Center of Excellence (grant number D34HP310250).

References

1. World Health Organization. Antibiotic Resistance 2020 [Available from: https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance.
2. Fridkin S, Baggs J, Fagan R, Magill S, Pollack LA, Malpiedi P, et al. Vital signs: improving antibiotic use among hospitalized patients. *MMWR Morb Mortal Wkly Rep*. 2014;63(9):194-200.

3. Huttner B, Samore M. Outpatient antibiotic use in the United States: time to "get smarter." *Clin Infect Dis*. 2011;53(7):640-3.
4. Septimus EJ, Owens RC, Jr. Need and potential of antimicrobial stewardship in community hospitals. *Clin Infect Dis*. 2011;53 Suppl 1:S8-S14.
5. White AT, Clark CM, Sellick JA, Mergenhagen KA. Antibiotic stewardship targets in the outpatient setting. *Am J Infect Control*. 2019;47(8):858-63.
6. Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2019. 2019.
7. Centers for Disease Control and Prevention. Measuring Outpatient Antibiotic Prescribing 2020 [Available from: https://www.cdc.gov/antibiotic-use/data/outpatient-prescribing/index.html.
8. Barnett ML, Linder JA. Antibiotic Prescribing for Adults With Acute Bronchitis in the United States, 1996-2010. *JAMA*. 2014;311(19):2020-2.
9. Chua K-P, Fischer MA, Linder JA. Appropriateness of outpatient antibiotic prescribing among privately insured US patients: ICD-10-CM based cross sectional study. *BMJ*. 2019;364:k5092.
10. Fleming-Dutra KE, Hersh AL, Shapiro DJ, Bartoces M, Enns EA, File TM Jr., et al. Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011. *JAMA*. 2016;315(17):1864-73.
11. Ray MJ, Tallman GB, Bearden DT, Elman MR, McGregor JC. Antibiotic prescribing without documented indication in ambulatory care clinics: national cross sectional study. *BMJ*. 2019;367:l6461.
12. Havers FP, Hicks LA, Chung JR, Gaglani M, Murthy K, Zimmerman RK, et al. Outpatient Antibiotic Prescribing for Acute Respiratory Infections During Influenza Seasons. *JAMA* Netw Open. 2018;1(2):e180243.
13. Non-Infection-Related And Non-Visit-Based Antibiotic Prescribing Is Common Among Medicaid Patients. Health Affairs. 2020;39(2):280-8.
14. Ventola CL. The antibiotic resistance crisis: part 1: causes and threats. P t. 2015;40(4):277-83.
15. Brown KA, Fisman DN, Moineddin R, Daneman N. The magnitude and duration of Clostridium difficile infection risk associated with antibiotic therapy: a hospital cohort study. *PLoS One*. 2014;9(8):e105454.
16. Hensgens MP, Goorhuis A, Dekkers OM, Kuijper EJ. Time interval of increased risk for Clostridium difficile infection after exposure to antibiotics. *J Antimicrob Chemother*. 2012;67(3):742-8.
17. Ni J, Friedman H, Boyd BC, McGurn A, Babinski P, Markossian T, et al. Early antibiotic exposure and development of asthma and allergic rhinitis in childhood. *BMC Pediatrics*. 2019;19(1):225.
18. 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: *The Journal of Human Pharmacology and Drug Therapy*. 2014;34(7):677-85.
19. Hicks LA, Bartoces MG, Roberts RM, Suda KJ, Hunkler RJ, Taylor TH, Jr., et al. US outpatient antibiotic prescribing variation according to geography, patient population, and provider specialty in 2011. *Clin Infect Dis*. 2015;60(9):1308-16.
20. Kakpovbia E, Feng H, Feng PW, Cohen JM. Antibiotic prescribing trends among US dermatologists in Medicare from 2013 to 2016. *Journal of Dermatological Treatment*. 2021;32(1):70-2.
21. Medicaid. [Available from: https://www.medicaid.gov/medicaid/index.html.
22. Trade Names [Internet].
23. National Committee for Quality Assurance. HEIDIS 2017 Final NDC Lists 2017 [Available from: https://www.ncqa.org/hedis/measures/hedis-2017-national-drug-code-ndc-license/hedis-2017-final-ndc-lists/.
24. Lee GC, Reveles KR, Attridge RT, Lawson KA, Mansi IA, Lewis JS, et al. Outpatient antibiotic prescribing in the United States: 2000 to 2010. *BMC Medicine*. 2014;12(1):96.
25. Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *BMJ*. 2010;340:c2096.
26. Shively NR, Buehrle DJ, Clancy CJ, Decker BK. Prevalence of Inappropriate Antibiotic Prescribing in Primary Care Clinics within a Veterans Affairs Health Care System. *Antimicrob Agents Chemother*. 2018;62(8).
27. 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*. 2018;37(1):52-8.
28. Wong DM, Blumberg DA, Lowe LG. Guidelines for the use of antibiotics in acute upper respiratory tract infections. *Am Fam Physician*. 2006;74(6):956-66.
29. Kabbani S, Palms D, Bartoces M, Stone N, Hicks LA. Outpatient Antibiotic Prescribing for Older Adults in the United States: 2011 to 2014. *J Am Geriatr Soc*. 2018;66(10):1998-2002.