First-line antibiotic selection in outpatient settings

Danielle L. Palms, MPH[a]; Lauri A. Hicks, DO[a]; Monina Bartoces, PhD[a]; Adam L. Hersh, MD, PhD[b]; Rachel Zetts, MPH[c]; David Y. Hyun, MD[c]; Katherine E. Fleming-Dutra, MD[a#]

[a] Centers for Disease Control and Prevention, Atlanta, GA

[b] Pediatric Infectious Diseases, University of Utah, Salt Lake City

[c] The Pew Charitable Trusts, Washington, DC

Word Count: 825 words

Corresponding Author

Katherine E. Fleming-Dutra, MD

Division of Healthcare Quality Promotion

Centers for Disease Control and Prevention

Office: 404-639-4243

1600 Clifton Road MS H16-3

Atlanta, GA 30329

ftu2@cdc.gov

Abstract:

Using the 2014 IBM MarketScan Commercial Database, we compared antibiotic selection for pharyngitis, sinusitis, and acute otitis media in retail clinics, emergency departments, urgent cares, and offices. Only 50% of visits for these conditions received recommended first-line antibiotics. Improving antibiotic selection for common outpatient conditions is an important stewardship target.

Improving antibiotic selection is important to optimize treatment, to minimize risks of antibiotic resistance and adverse events, and is a key stewardship target according to the Centers for Disease Control and Prevention (CDC) *Core Elements of Outpatient Antibiotic Stewardship*.(1) The most common diagnoses for which antibiotics are prescribed in outpatient settings are sinusitis, acute otitis media (AOM), and pharyngitis, diagnoses for which antibiotics are sometimes indicated. In a previous study of antibiotic prescribing for these conditions in emergency department (ED) and office visits, first-line antibiotics (according to treatment guidelines) were prescribed in only half of visits when antibiotics were prescribed.(2) Additionally, a previous study has shown that antibiotic prescribing for conditions for which antibiotics are never appropriate (e.g., colds) varies among outpatient settings in the United States, with the highest prescribing for these conditions in urgent care settings.(3) However, evidence is lacking regarding antibiotic selection patterns for common conditions in retail health and urgent care settings, growing sites of U.S. outpatient care. Here, we compare antibiotic selection for pharyngitis, sinusitis, and AOM in retail clinics, EDs, urgent cares, and offices in order to target outpatient antibiotic stewardship efforts.

We used the 2014 IBM® MarketScan® Commercial Database (IBM® Watson Health™). Exclusion criteria and methods for linking dispensed outpatient antibiotics to visits were previously described.(3) Diagnoses were determined using a previously-described system.(4) We included pediatric (<18 years) and adult (18-64 years) visits for pharyngitis and sinusitis and pediatric AOM visits (specifically suppurative otitis media), as there are evidence-based guidelines recommending first-line antibiotics for these conditions.(4) Antibiotics were categorized using the 2016 Red Book supplement national drug codes and therapeutic classes.

Antimicrobial Agents and Chemotherapy

Among antibiotic visits, we calculated, by healthcare setting, the percent of visits with first-line therapy, defined as amoxicillin or penicillin for pharyngitis and amoxicillin or amoxicillin-clavulanate for sinusitis and pediatric AOM.(2) To focus on uncomplicated visits, visits with parenteral antibiotics for sinusitis or AOM or antibiotics from multiple subcategories listed in the Table were excluded. However, pharyngitis visits with parenteral antibiotics were included, as intramuscular penicillin is a recommended first-line treatment option. The study did not require institutional review board review, as the data were de-identified and deemed non-humans subjects by the National Center for Emerging and Zoonotic Infectious Diseases' advisor on human subjects research. Analyses were conducted using DataProbe 5.0 (IBM® Watson Health™) and SAS version 9.4 (SAS Institute, Cary, NC).

Among antibiotic visits to retail clinics (N=13,889), EDs (N=107,820), urgent cares (N=474,378), and offices (N=4,268,329) for these three conditions, 50% received first-line antibiotics. The percent of visits for all three conditions with first-line therapy was 70% in retail clinics, 57% in EDs, 49% in urgent cares, and 50% in offices. In all settings, first-line therapy was higher for children (62%) than adults (41%). First-line therapy for adults was highest in retail clinics at 68% of visits versus 45% in EDs, 44% in urgent cares, and 40% in offices. (Figure) For pediatric AOM, first-line therapy ranged from 78% in retail clinics and EDs to 69% of urgent care visits. For pharyngitis and sinusitis, retail clinics had the highest percent of first-line therapy (72% and 68%) versus 45-51% of visits in the other settings. (Table) Macrolides were the most common non-first-line therapy.

Only 50% of visits for common respiratory conditions received first-line antibiotics. Among outpatient settings, retail clinics had the highest percent of visits (70%) with first-line antibiotics prescribed for respiratory conditions. Across all settings, children received first-line antibiotics more often than adults. However, all settings can improve antibiotic selection, as first-line therapy should be used in at least 80% of visits for these conditions. This target of 80% accounts for visits for treatment

failures, in which the patient has already received a first-line antibiotic, and for visits by patients with reported allergies to first-line agents (i.e., penicillin-class antibiotics).(2, 5, 6)

Clinicians in retail clinics may be selecting more appropriate antibiotics for these conditions than in other outpatient settings due to the use of protocols encouraging guideline-concordant prescribing.(7) Protocols may also contribute to the similarities between first-line prescribing for children and adults in retail clinics. Furthermore, better antibiotic selection among children compared to adults in all settings coincides with decreasing U.S. outpatient antibiotic prescribing rates among children but not adults.(8) These trends may be due in part to public health efforts to improve antibiotic use among children.(8)

This study has limitations. We cannot clinically validate diagnosis codes or facility codes in these de-identified claims data. Assumptions were required to link dispensed antibiotics to visits. Results from this convenience sample may not be generalizable. Additionally, these data are from 2014, and may not reflect the most current trends in antibiotic selection, especially as more recent data indicate that overall use of broad-spectrum antibiotics may be slightly decreasing in the United States.(9)

Antibiotic stewardship based on the *Core Elements of Outpatient Antibiotic Stewardship* can be used to improve antibiotic selection.(10) Lessons learned from retail clinics and pediatric visits may help improve healthcare quality for adults and in all outpatient settings.

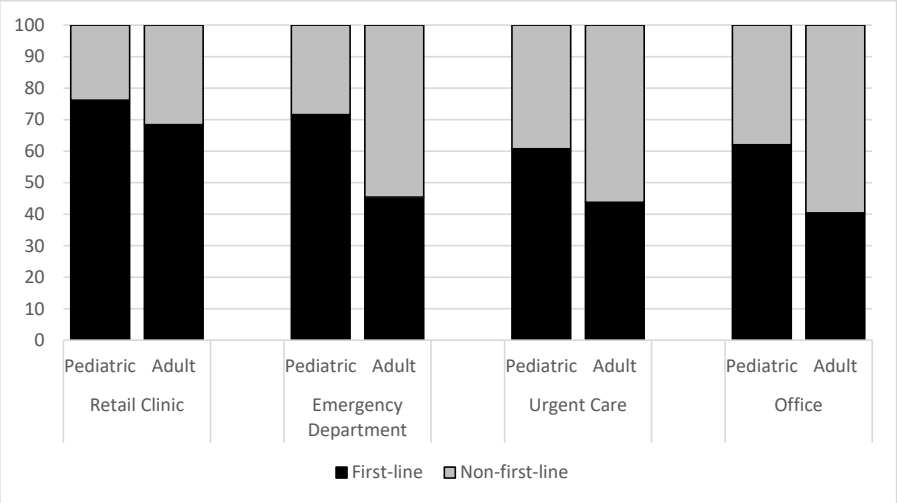
Funding Source: This work was funded by the Centers for Disease Control and Prevention. The Centers for Disease Control and Prevention was involved in the design of the study; analysis, and interpretation of the data; review of the manuscript; and decision to submit the manuscript for publication.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

References

1. Sanchez G, Fleming-Dutra K, Roberts R, Hicks L. 2016. Core Elements of Outpatient Antibiotic Stewardship. Morbidity and mortality weekly report Recommendations and reports 65:1-12.
2. Hersh AL, Fleming-Dutra KE, Shapiro DJ, Hyun DY, Hicks LA. 2016. Frequency of First-line Antibiotic Selection Among US Ambulatory Care Visits for Otitis Media, Sinusitis, and Pharyngitis. JAMA Intern Med 176:1870-1872.
3. Palms DL, Hicks LA, Bartoces M, Hersh AL, Zetts R, Hyun DY, Fleming-Dutra KE. 2018. Comparison of Antibiotic Prescribing in Retail Clinics, Urgent Care Centers, Emergency Departments, and Traditional Ambulatory Care Settings in the United States. JAMA Intern Med 178:1267-1269.
4. Fleming-Dutra KE, Hersh AL, Shapiro DJ, Bartoces M, Enns EA, File TM, Jr., Finkelstein JA, Gerber JS, Hyun DY, Linder JA, Lynfield R, Margolis DJ, May LS, Merenstein D, Metlay JP, Newland JG, Piccirillo JF, Roberts RM, Sanchez GV, Suda KJ, Thomas A, Woo TM, Zetts RM, Hicks LA. 2016. Prevalence of Inappropriate Antibiotic Prescriptions Among US Ambulatory Care Visits, 2010-2011. Jama 315:1864-73.
5. Piccirillo JF, Mager DE, Frisse ME, Brophy RH, Goggin A. 2001. Impact of first-line vs second-line antibiotics for the treatment of acute uncomplicated sinusitis. JAMA: the Journal of the American Medical Association 286:1849-56.
6. Capra AM, Lieu TA, Black SB, Shinefield HR, Martin KE, Klein JO. 2000. Costs of otitis media in a managed care population. Pediatr Infect Dis J 19:354-5.
7. Hansen-Turton T, Ryan S, Miller K, Counts M, Nash DB. 2007. Convenient care clinics: the future of accessible health care. Dis Manag 10:61-73.
8. Centers for Disease C, Prevention. 2008. Progress in introduction of pneumococcal conjugate vaccine--worldwide, 2000-2008. MMWR Morb Mortal Wkly Rep 57:1148-51.
9. King LM, Bartoces M, Fleming-Dutra KE, Roberts RM, Hicks LA. 2019. Changes in US Outpatient Antibiotic Prescriptions From 2011–2016. Clin Infect Dis doi:10.1093/cid/ciz225.
10. Sanchez GV, Fleming-Dutra KE, Roberts RM, Hicks LA. 2016. Core Elements of Outpatient Antibiotic Stewardship. MMWR Recomm Rep 65:1-12.

Figure. First-line antibiotic selection for pharyngitis, sinusitis, and pediatric acute otitis media by age across settings, 2014.[a,b]



[a] Pediatric visits include pediatric pharyngitis, sinusitis, and acute otitis media visits that received an antibiotic. Adult visits include adult pharyngitis and sinusitis visits that received an antibiotic.

[b] First-line therapy includes amoxicillin or penicillin for pharyngitis; amoxicillin or amoxicillin-clavulanate for sinusitis and acute otitis media. Non-first-line therapy includes all other antibiotics.

127 **Table. Antibiotic selection for pharyngitis, sinusitis, and pediatric acute otitis media visits by setting,**

128 **2014.**

	Retail clinic N=13,889	Emergency department N=107,820	Urgent care N=474,378	Medical office N=4,268,329	Total for all four settings N=4,864,416
	n (%)	n (%)	n (%)	n (%)	n (%)
Pharyngitis (pediatric & adult)					
First-line total[a]	3,420 (72.2)	24,709 (51.0)	83,994 (46.1)	604,395 (46.3)	716,518 (46.5)
Amoxicillin	2,410 (50.9)	20,173 (41.6)	74,725 (41.0)	543,659 (41.6)	640,967 (41.6)
Penicillin	1,010 (21.3)	4,536 (9.4)	9,269 (5.1)	60,736 (4.6)	75,551 (4.9)
Non-First-line total[a]	1,314 (27.8)	23,760 (49.0)	98,203 (53.9)	702,066 (53.7)	825,343 (53.5)
Amoxicillin-clavulanate	273 (5.8)	4,614 (9.5)	19,571 (10.7)	133,361 (10.2)	157,819 (10.2)
Macrolide	739 (15.6)	13,095 (27.0)	50,553 (27.7)	329,236 (25.2)	393,623 (25.5)
Cephalosporin	225 (4.8)	3,362 (6.9)	22,822 (12.5)	195,562 (15.0)	221,971 (14.4)
Quinolone	12 (0.3)	464 (1.0)	1,804 (1.0)	19,493 (1.5)	21,773 (1.4)
Other	65 (1.4)	2,225 (4.6)	3,453 (1.9)	24,414 (1.9)	30,157 (2.0)
Pharyngitis Total	4,734	48,469	182,197	1,306,461	1,541,861
Sinusitis (pediatric & adult)					

First-line total[a]	5,448 (68.3)	16,543 (48.9)	114,047 (46.8)	1,018,773 (45.4)	1,154,811 (45.6)
Amoxicillin	991 (12.4)	6,205 (18.4)	40,601 (16.7)	401,935 (17.9)	449,732 (17.8)
Amoxicillin-clavulanate	4,457 (55.9)	10,338 (30.6)	73,446 (30.2)	616,838 (27.5)	705,079 (27.9)
Non-first-line total[a]	2,530 (31.7)	17,262 (51.1)	129,480 (53.2)	1,226,137 (54.6)	1,375,409 (54.4)
Macrolide	1,023 (12.8)	10,541 (31.2)	71,563 (29.4)	613,835 (27.3)	696,962 (27.5)
Cephalosporin	405 (5.1)	2,152 (6.4)	32,175 (13.2)	321,306 (14.3)	356,038 (14.1)
Quinolone	206 (2.6)	2,119 (6.3)	12,359 (5.1)	163,586 (7.3)	178,270 (7.0)
Other	896 (11.2)	2,450 (7.2)	13,383 (5.5)	127,410 (5.7)	144,139 (5.7)
Sinusitis Total	7,978	33,805	243,527	2,244,910	2,530,220
Acute otitis media (pediatric only)					
First-line total[a]	922 (78.3)	20,003 (78.3)	33,806 (69.5)	504,098 (70.3)	558,829 (70.5)
Amoxicillin	771 (65.5)	17,404 (68.1)	28,302 (58.2)	408,561 (57.0)	455,038 (57.4)
Amoxicillin-clavulanate	151 (12.8)	2,599 (10.2)	5,504 (11.3)	95,537 (13.3)	103,791 (13.1)

Non-first-line total[a]	255 (21.7)	5,543 (21.7)	14,848 (30.5)	212,860 (29.7)	233,506 (29.5)
Macrolide	139 (11.8)	3,012 (11.8)	6,257 (12.9)	67,747 (9.4)	77,155 (9.7)
Cephalosporin	108 (9.2)	2,278 (8.9)	8,239 (16.9)	139,014 (19.4)	149,639 (18.9)
Quinolone	0 (0.0)	14 (0.1)	22 (0.0)	248 (0.0)	284 (0.0)
Other	8 (0.7)	239 (0.9)	330 (0.7)	5,851 (0.8)	6,428 (0.8)
AOM Total	1,177	25,546	48,654	716,958	792,335

[a] First-line therapy includes amoxicillin or penicillin for pharyngitis; amoxicillin or amoxicillin-clavulanate for sinusitis and acute otitis media. Non-first-line therapy includes all other antibiotics not considered first-line therapy for the diagnosis of interest. To focus on uncomplicated visits, visits with multiple antibiotics were excluded if the antibiotics were from more than one of the antibiotic subcategories listed in the Table (subcategories for sinusitis and AOM include amoxicillin, amoxicillin-clavulanate, macrolide, cephalosporin, quinolone, and other; pharyngitis had additional penicillin subcategory). For example, a visit with both a macrolide and cephalosporin prescribed (2 different categories of non-first-line agents) would be excluded.