American Journal of Infection Control 51 (2023) 520–526

Contents lists available at ScienceDirect

American Journal of Infection Control

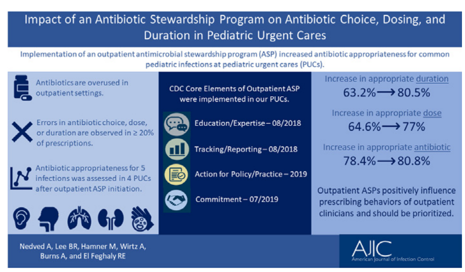
journal homepage: www.ajicjournal.org

Major Article

Impact of an antibiotic stewardship program on antibiotic choice, dosing, and duration in pediatric urgent cares

Amanda Nedved MD [a,b], Brian R. Lee PhD, MPH [b,c], Megan Hamner MD [d], Ann Wirtz PharmD, BCPPS [b,e], Alaina Burns PharmD, BCPPS [b,e], Rana E. El Feghaly MD, MSCI [b,d,*]

[a] Department of Pediatrics, Division of Urgent Care, Children's Mercy Kansas City, Kansas City, MO
[b] University of Missouri-Kansas City, Kansas City, MO
[c] Department of Pediatrics, Division of Health Services and Outcomes Research, Children's Mercy Kansas City, Kansas City, MO
[d] Department of Pediatrics, Division of Infectious Diseases, Children's Mercy Kansas City, Kansas City, MO
[e] Department of Pediatrics, Division of Pharmacy, Children's Mercy Kansas City, Kansas City, MO



Key words:
Pediatric
Antibiotic stewardship
Outpatient

A B S T R A C T

Background: Many antimicrobial stewardship programs (ASPs) focus on decreasing unnecessary antibiotics. We describe the impact of an outpatient ASP on choice, dose, and duration of antibiotics when used for common infections in pediatric urgent care (PUC) centers.
Methods: We reviewed encounters at 4 PUC centers within our organization for patients 6 months to 18 years old with acute otitis media, group A streptococcal pharyngitis, community-acquired pneumonia, urinary tract infection, and skin and soft tissue infections who received systemic antibiotics. We determined appropriate antibiotic choice, dose, and duration for each diagnosis. Pearson's χ^2 test compared appropriate prescribing before ASP implementation (July 2017-July 2018) and postimplementation (August 2018-December 2020). Control charts trended improvement over time.
Results: Our study included 35,917 encounters. The percentage of prescriptions with the recommend agent at the appropriate dose and duration increased from a mean of 32.7% to 52.4%. The center lines for appropriate agent, dose, and duration all underwent upward shifts. The most substantial changes were seen in antibiotic duration (63.2%-80.5%), and appropriate dose (64.6%-77%).
Conclusions: Implementation of an outpatient ASP improved prescribing patterns for choosing the appropriate agent, duration, and dose for many common infections in our PUCs.

Antibiotic overuse puts patients at risk for adverse events and contributes to global antibiotic resistance. More than 2.8 million antibiotic-resistant infections occur in the United States each year, and more than 35,000 people die as a result.[1] Much of this antibiotic use occurs in ambulatory settings.[2] Over 65 million antibiotics are prescribed to children in ambulatory settings in the United States every year.[3] Antimicrobial stewardship programs (ASPs) have been shown to reduce antibiotic overuse with improved patient outcomes, particularly in inpatient settings.[4,5]

Abbreviations: AAP, American Academy of Pediatrics; AOM, acute otitis media; ASP, antimicrobial stewardship program; CAP, community-acquired pneumonia; CDC, Centers for Disease Control and Prevention; GAS, group A streptococcal; ICD-10, International Classification of Diseases 10th iteration; IDSA, Infectious Diseases Society of America; PUC, pediatric urgent care; SSTI, skin and soft tissue infection; UTI, urinary tract infection

* Address correspondence to: Rana E. El Feghaly, MD, MSCI, Division of Infectious Diseases, Children's Mercy Kansas City, 2401 Gillham Rd, Kansas City, MO 64108.
E-mail address: relfeghaly@cmh.edu (R.E. El Feghaly).

Conflicts of interest: The authors have indicated they have no potential conflicts of interest to disclose.

https://doi.org/10.1016/j.ajic.2022.07.027
0196-6553/

Acknowledging outpatient antibiotic overuse and the impact of ASPs, the Centers for Disease Control and Prevention (CDC), the American Academy of Pediatrics (AAP), and the Pediatric Infectious Diseases Society identified high-quality antibiotic prescribing practices as an important target for outpatient ASPs.[6,7] Approximately 20% of necessary antibiotics prescribed in the outpatient setting include at least 1 prescribing error (wrong agent, dose, and/or duration).[8] Choosing broad-spectrum antibiotics instead of recommended first-line narrow-spectrum options increases the patient's risk for adverse events and contributes to antibiotic resistance.[9] Underdosing antibiotics is a common prescribing error[10] that puts patients at risk for complications due to delays in reaching therapeutic efficacy and higher risk of treatment failures. On the other hand, clinicians who prescribe antibiotics at doses higher than recommended or for prolonged durations increase the patient's risk for adverse drug events.[11,12]

Many studies have focused on decreasing the frequency of unnecessary antibiotic prescriptions when antibiotics are not indicated for a specific diagnosis, such as viral upper respiratory tract infections.[13-15] However, the impact an ASP has on the quality of antibiotic prescriptions for diagnoses where antibiotics may be indicated is less studied, particularly in the PUC setting. In this study, we evaluate the impact of implementing an outpatient ASP on the antibiotic choice, dose, and duration for common pediatric infections in a PUC setting.

METHODS

Setting

We performed a mixed-methods analysis of antibiotics prescribed by clinicians at 3 free-standing PUC centers located throughout a large midwestern metro area=. These PUCs are part of a large academic-affiliated pediatric healthcare institution. The PUCs are staffed by general pediatricians and advanced practice registered nurses who primarily work in the PUC setting and complete over 90,000 encounters every year.

Outpatient ASP design and initiatives

Our outpatient ASP is led by pediatric infectious diseases physicians, pediatric infectious diseases pharmacists, and a biostatistician, with strong collaborations with frontline clinicians from the PUCs. Our team followed the CDC's 4 core elements of outpatient ASPs to develop our program starting in August 2018.

1) Tracking and reporting: In March 2018, we created a report identifying antibiotics used in 16 common pediatric infectious diagnoses using International Classification of Diseases (ICD)-10 codes from PUC encounters.[16] The report helped us identify diagnoses where guideline recommendations are commonly followed, as well as areas with the greatest opportunities for improvement. We began sharing location-specific rates of appropriate antibiotic selection with PUC frontline clinicians semi-annually during division meetings in August 2018.
2) Education and Expertise: In addition to the semi-annual educational sessions, we developed an outpatient ASP handbook as a tool to help clinicians diagnose and treat common outpatient infections such as acute otitis media (AOM), acute bacterial rhinosinusitis, Group A streptococcal (GAS) pharyngitis, community-acquired pneumonia (CAP), urinary tract infections (UTI), skin and soft tissue infections (SSTIs). The handbook includes guidance on first-line antibiotic agents, and recommended doses and duration for each diagnosis. The handbook also includes alternatives for patients with penicillin allergy, and for treatment failure. We first shared our outpatient ASP handbook with PUC clinicians in August 2018 and continue to update it and share it yearly, both in printed pocket-size copies and online.[17]
3) Action for policy and practice: We worked with our institution's medical informatics team to create prescription folders for common diagnoses (such as AOM, and SSTIs) within the electronic health record (EHR). The prescription folders are labeled by diagnosis and contain precompleted order sentences with the recommended agent, dose, and duration for clinicians to easily access when placing orders. Most of these interventions took place after 2019.
4) Commitment: In July 2019, we displayed antibiotic stewardship commitment letters based on the CDC's MITIGATE tool kit.[18] Our institution's leadership signed the letters and we placed them in exam rooms. Our clinicians signed similar letters and placed them in clinical workspaces. This commitment reaffirmed our clinicians' dedication to providing guideline-concordant care.

Study design and outcome measures

We developed an EHR report to identify all PUC encounters of patients between 6 months and 19 years of age with the following discharge diagnoses: AOM, CAP, GAS pharyngitis, UTI, and certain SSTIs (nonfacial cellulitis, abscess, and animal bites) (Supplement 1) who received systemic antibiotics between July 2017 and December 2020. We chose our diagnoses based on the availability of established national guidelines.[19-25] We excluded patients who were transferred, admitted, or had a concomitant diagnosis that may have required systemic antibiotics.[16] We did not include patients < 6 months or > 19 years because these patients were typically outside the scope of the national guidelines. For each patient, we collected demographics (age, gender, race, ethnicity, language, insurance) and clinical information (all primary and secondary diagnoses, weight, oral antibiotic prescribed, dose, duration). We used established national guidelines[19-25] and our local antibiogram[17] to determine appropriateness of antibiotic choice, dose, and duration for each diagnosis (Table 1).

Our primary outcome measure evaluated the comprehensive adherence of the prescription to the recommended diagnosis-specific antibiotic agent, dose, and duration (all 3 adherent to be considered appropriate). Secondary outcomes evaluated the rates of the individual variables of antibiotic choice, dose, and duration for appropriateness.

Data analysis

We assigned encounters into either preimplementation of our outpatient ASP (July 2017-July 2018) or postimplementation periods (August 2018-December 2020). We categorized patient age in years (<2, 2-12, and 13+). We modeled diagnosis-specific appropriateness as binary indicators (ie, appropriate vs inappropriate) for each variable: antibiotic agent, dose, and duration as well as a composite metric requiring all 3 variables to be appropriate. We evaluated appropriate dosing and duration only if the appropriate agent was prescribed. Encounters with a diagnosis-specific inappropriate antibiotic agent or encounters with missing dose/duration documentation were excluded when examining appropriate dose and duration. We used Pearson's χ^2test to compare the proportion of appropriate antibiotic prescribing (choice, dose, and duration) between the pre- and postimplementation periods. We also evaluated changes in dosing (under, appropriate, and overdosing) and duration in days (<5, 5-7, 8-10, >10) for each diagnosis before and after the implementation of our outpatient ASP. All analyses were completed using R software (version 4.0.3; Vienna, Austria; https://www.R-project.org). We used

Table 1
Criteria for appropriate agent, duration, and dose by diagnosis and the guidelines used to establish the appropriateness

Discharge diagnosis	Antimicrobial agent	Dose*	Duration	National guideline
Acute otitis media	Amoxicillin	40-50 mg/kg/dose twice daily (max. 2,000 mg/dose)	<24 mo: 10 d ≥24 mo: 5-7 d	AAP guidelines for AOM [19]
Community acquired pneumonia	Amoxicillin	40-50 mg/kg/dose twice daily (max. 2,000 mg/dose)	5-7 d	AAP guidelines for CAP [18], AAP Red Book [24]
Group A streptococcal pharyngitis	Amoxicillin	50 mg/kg/dose once daily (max. 1,000 mg)	10 days	IDSA guidelines for GAS [20]
	Penicillin VK	<27 kg: 250 mg BID or TID ≥27kg: 500 mg BID or TID		
	Penicillin G Benzathine	≤27 kg: 600,000 units <27 kg: 1.2 million units	1 time only	
Urinary tract infection‡	Cephalexin	17-25 mg/kg/dose TID (max. 500 mg)	<24 mo: 7-14 d Cystitis: 24 mo - 12 y: 5-7 d Cystitis: ≥12 y: 3 d Pyelonephritis: 7-14 d	AAP guidelines for UTI [22, 23], AAP Red Book [24]
Cellulitis (Nonfacial)‡	Cephalexin	17 mg/kg/dose TID (max. 500 mg)	5-7 d	IDSA guidelines for skin and soft tissue infections [21], AAP Red Book [24]
Abscess‡	Clindamycin	10 mg/kg/dose TID (max. 600 mg)	5-7 d	
	Trimethoprim-sulfamethoxazole	§4-6 mg/kg/dose BID (max. 160 mg)		
Animal bite (Prophylaxis)	Amoxicillin/clavulanate	†22.5 mg/kg/dose BID (max. 875 mg)	3 d	

AAP, American Academy of Pediatrics; BID, twice a day; IDSA, Infectious Diseases Society of America; max., maximum per dose; TID, 3 times a day.
*Allowed 10% above or below recommended dose to account for convenience dosing when no range was given.
†Dose based on amoxicillin component.
‡First line options chosen based on local antibiogram.
§Dose based on trimethoprim component

QI Macros 2018 (Denver, CO; https://www.qimacros.com/) to create Shewhart p-charts to trend improvement over time and evaluated for special-cause variation per Shewhart rules 1) shift – 8 or more points in a row above or below the center line, and 2) trend – 6 consecutive points increasing or decreasing.[26]

This study was granted exempt status by our institutional review board.

RESULTS

During the study period, 35,917 encounters met inclusion criteria (13,208 preimplementation and 22,709 postimplementation). Supplement 2 describes the demographics of the included encounters. The most common diagnoses included AOM (53.5%), GAS (24.6%), and nonfacial cellulitis (6.4%) (Supplement 2).

Starting in September 2018, the percentage of prescriptions written for the recommended agent at the appropriate dose and duration (adherence to all 3 variables) underwent 3 special cause variations with upward shifts of the center line. The mean increased from 32.7% to 52.4%. Using the rules of special cause variation, we saw a similar upward shift in the center line for encounters with recommended first-line antibiotic agent in December 2018 from 78.4% at baseline to 80.8%. The center line for first-line antibiotics prescribed at the recommended dose underwent 2 upward shifts related to special cause variation starting in September 2018 and increased from 64.6% at baseline to 77%. Finally, the center line for first-line antibiotics prescribed for the recommended duration underwent 3 upward shifts due to special cause variation starting in January 2019 and increased from a baseline of 63.2%-80.5% (Fig 1). When using Pearson's χ^2, we also noted that the percentage of encounters with recommended first-line antibiotic agent increased slightly from 78.5% at baseline to 79.5% postimplementation (P = .025). However, the percentage of encounters with antibiotics prescribed for the recommended duration increased from 63.6% preimplementation to 69.7% postimplementation (P < .001); and those with antibiotics prescribed with the recommended dose increased from 63.6% preimplementation to 69.7% postimplementation (P < .001) (Table 2). Supplement 3 summarizes the proportion of antibiotic prescriptions that had each type of inappropriate prescribing behavior by diagnosis prior to and after implementation of our ASP.

When evaluated by diagnoses, appropriate antibiotic agent improved in AOM from 75.8% to 77.2% (P = .03), and UTI from 74.9% to 89.5% (P < .001) following implementation of our ASP (Table 2). During the study period, clinicians decreased the rate of prescribing cefdinir for these diagnoses (11% down to 7.8% for AOM, and 13.1% down to 0.9% for UTI). The rate of cephalexin prescriptions for cellulitis increased from 70.5% to 75.1% (P = .02), while use of clindamycin to cover for possible methicillin-resistant *Staphylococcus aureus* for abscesses increased from 53.6% to 67.7% following implementation of our ASP. Clinicians prescribed macrolides for <5% of all diagnoses at baseline except for CAP (11.4%). The rate of macrolide prescriptions for CAP increased to 14.1% during the postimplementation period (P < .001) (Supplement 4).

GAS pharyngitis had a high proportion of appropriate duration at baseline (99.4%) and remained unchanged, given that it is usually treated with a 10-day course of amoxicillin or a 1-time dose of intramuscular penicillin. All other diagnoses had improvements in appropriate duration (all P < .001) after implementation of our ASP (Table 2). Prior to implementation, clinicians tended to prescribe antibiotics for longer durations than recommended, as compared to postimplementation (Fig 2).

Prior to implementation of our ASP, clinicians tended to underdose prescriptions based on the recommended weight-based guidelines for all diagnoses except animal bites, which tended to have higher than recommended doses prescribed (Fig 3). The percentage of appropriate dosing improved for AOM (75.7%- 82.3%; P < .001), CAP (67.7%-75.4%; P < .001), UTI (53.7%-71.6%; P < .001), non-facial cellulitis (46.9%-72.1%; P < .001), and animal bites (49.0%-57.6.6%; P = .050) after implementation of our ASP (Table 2).

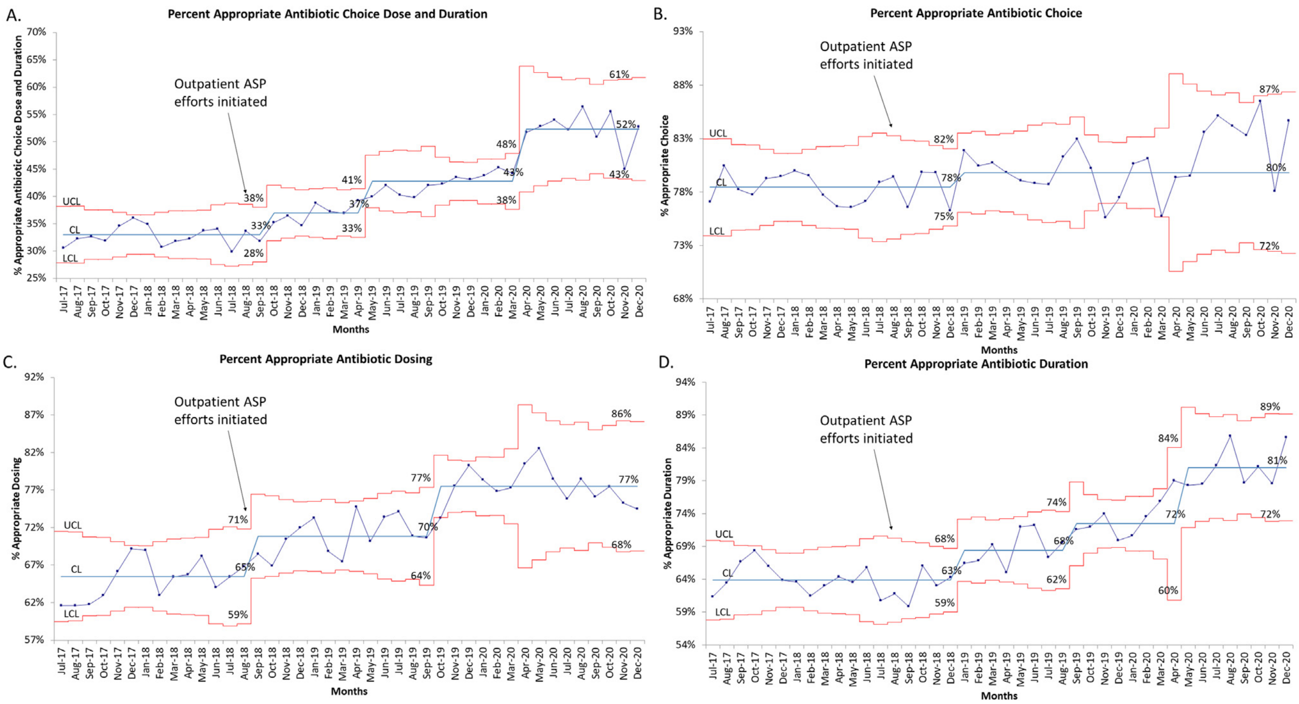


Fig 1. Control chart (Shewhart p-chart) of (A) the percentage of prescriptions with recommended first-line antibiotic written for the recommended dose and duration (all 3 guideline-adherent), (B) the percentage of prescriptions written for the first-line recommend agent, (C) the percentage of first-line recommended antibiotic prescriptions written for the appropriate dose, and (D) the percentage of first-line recommended antibiotic prescriptions written for the appropriate duration over time for all included diagnoses.

DISCUSSION

The percentage of high-quality antibiotic prescriptions that adhered to guideline recommendations for the first-line antibiotic agent at the recommended dose for the recommended duration increased after implementing an outpatient ASP. Individual diagnoses such as AOM, UTI, abscess, and nonfacial cellulitis showed significant improvements in the individual rates of prescribing the recommended agent, dose, and duration. The percentage of prescriptions that adhered to the recommended dose and duration for animal bites also increased. Of the diagnoses included, GAS pharyngitis was the only diagnosis that did not show improvement in at least 1 measure; however, dosing for this condition is quite standard.

Our evaluation of improvement over time did show some fluctuations with intermittent periods of worsening. This is consistent with previous studies that report a seasonality to antibiotic prescribing

Table 2
Percentage of encounters with recommended agent, duration, and dose by diagnosis before and after implementation of an ASP in our PUC centers.

		Pre	Post	*P value*
Recommended agent		10,369 (78.5%)	18,056 (79.5%)	.025
	AOM	5,113 (75.8%)	9,611 (77.2%)	.033
	CAP	554 (74.1%)	1,424 (71.2%)	.139
	GAS pharyngitis	3,383 (85.8%)	4,250 (87.1%)	.079
	UTI	393 (74.9%)	933 (89.5%)	<.001
	Cellulitis (non-facial)	562 (70.5%)	1126 (75.1%)	.020
	Abscess	151 (68.6%)	294 (77.8%)	.015
	Bites	213 (92.2%)	418 (92.1%)	.999
Recommended duration		6,594 (63.6%)	12,590 (69.7%)	<.001
	AOM	2,435 (47.6%)	5,719 (59.5%)	<.001
	CAP	341 (61.6%)	1,014 (71.2%)	<.001
	GAS pharyngitis	3,362 (99.4%)	4,224 (99.4%)	.999
	UTI	206 (52.4%)	661 (70.8%)	<.001
	Cellulitis (non-facial)	178 (31.7%)	715 (63.5%)	<.001
	Abscess	40 (26.5%)	131 (44.6%)	<.001
	Bites	32 (15.0%)	126 (30.1%)	<.001
Recommended dose		6,720 (64.9%)	13,212 (73.3%)	<.001
	AOM	3,865 (75.7%)	7,901 (82.3%)	<.001
	CAP	375 (67.7%)	1,070 (75.4%)	<.001
	GAS pharyngitis	1,805 (53.4%)	2,337 (55.0%)	.152
	UTI	211 (53.7%)	668 (71.6%)	<.001
	Cellulitis (nonfacial)	263 (46.9%)	811 (72.1%)	<.001
	Abscess	98 (68.5%)	191 (65.2%)	.519
	Bites	103 (49.0%)	234 (57.6%)	.050

AOM, acute otitis media; ASP, antimicrobial stewardship program; CAP, community-acquired pneumonia, GAS, Group A streptococcal; PUC, pediatric urgent care; UTI, urinary tract infection.

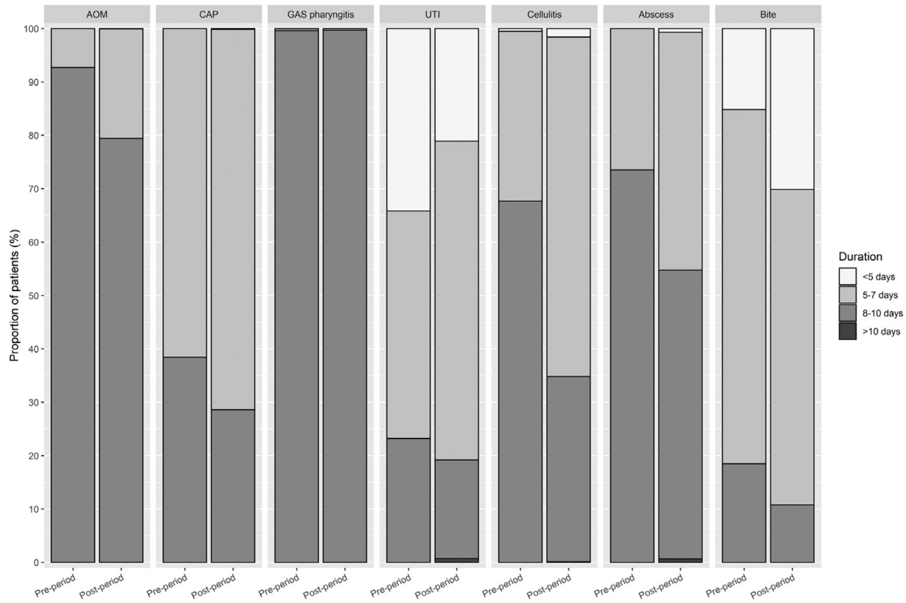


Fig 2. Stacked bar chart of trends in duration before and after implementation of the antibiotic stewardship program in our pediatric urgent care clinics.

rates and antimicrobial resistance which are higher in winter months.[27] Additionally, the coronavirus-disease of 2019 (COVID-19) pandemic may have contributed to the fluctuations in the last few months of our analysis. For example, in CAP, the percentage of prescriptions that adhered to the recommended duration increased. However, macrolide prescriptions for CAP increased after implementation. Further evaluation is needed to identify what contributed to this increase in macrolide prescribing.

ASPs in inpatient settings have resulted in significant declines in antibiotic use, resistance, and cost over the years.[5,28-30] Reducing antimicrobial use in outpatient settings, where the highest burden of antibiotic use occurs,[2,3,31] is a public health priority emphasized by the CDC, Joint Commission, and AAP.[6,7,32] Our results add to the growing body of evidence that ASP interventions promote high-quality antibiotic prescribing behaviors for common pediatric conditions where antibiotics may be indicated. While the ASP interventions occurred sequentially, they likely had a compound effect. The multifaceted approach of providing intermittent provider education and feedback, an easily accessible antibiotic dosing guide, and EHR improvements likely contributed to the success of our outpatient ASP. This is consistent with previous studies that show multifaceted approaches to antibiotic stewardship to be the most successful in improving antimicrobial prescribing habits.[33]

Previous studies reported that urgent care centers had the highest rates of unnecessary antibiotic prescribing among outpatient settings.[34] Many ASP initiatives focus on decreasing antibiotics for diagnoses where antibiotics are not indicated.[15,35,36] However, our results suggest that opportunities exist to improve the quality of antibiotic prescriptions in choosing the recommended agent, dose, and duration. In pediatric institutions where clinician prescribing behavior

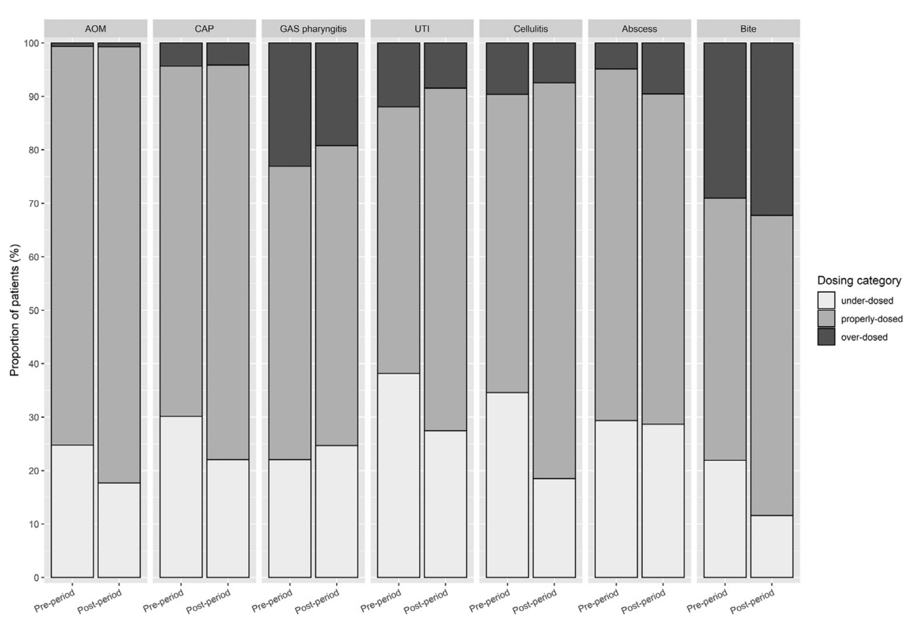


Fig 3. Stacked bar chart of trends in dosing before and after implementation of an antibiotic stewardship program in our pediatric urgent care setting.

already reflects a high rate of guideline-concordance for indication and first-line agent choice, we recommend focusing initiatives on improving the quality of antibiotic prescriptions for diagnoses where antibiotics may be indicated. Because these initiatives focus on optimizing prescribing behavior rather than restricting use of prescriptions, clinicians may be more willing to adopt the change.

Prior to implementation of our ASP, our PUC clinicians often prescribed antibiotics for longer durations than recommended. For each excess day of antibiotics, the rates of adverse effects and antibiotic-resistant bacteria for an individual increase significantly.[11,12] With >65 million antibiotics prescribed in pediatrics each year, ASP initiatives that focus on decreasing duration of antibiotics can reduce millions of days of antibiotics. After implementation, we saw a significant increase in the percentage of encounters with shorter durations of antibiotic prescriptions in concordance with guideline recommendations. Similarly, Sun et al. demonstrated that it is relatively easy to change clinician's duration prescribing habits with a simple change in the EHR.[37]

Choosing the appropriate antibiotic at the appropriate dose is important to treat specific infections effectively while minimizing adverse effects. In our study, PUC clinicians often prescribed antibiotics at a dose lower than recommended. Underdosing can result in subtherapeutic levels of antibiotics, treatment failures, and partially treated infections. Optimizing antibiotic dosing to the recommended guidelines may decrease rates of broad-spectrum antibiotics that clinicians prescribe for children who present due to treatment failure from inappropriate dosing of a narrow-spectrum antibiotic.

This study has limitations. We evaluated prescribing practices in an academic PUC setting which may limit the generalizability of results. While most clinicians did not receive formal antimicrobial stewardship guidance prior to implementation of our ASP, the prescribing behavior may be influenced by the academic setting in which we practice. We did not evaluate if the correct diagnosis was made. We assumed antibiotics were indicated if a prescription was given and linked to an ICD-10 code listed. We also did not evaluate the use of delayed antibiotics, or no antibiotics prescribed for eligible encounters, such as for AOM. In addition, the recommended treatment options are derived from guidelines; there are instances where the guidelines may not be followed, such as in cases of severe illness, antibiotic allergy, or treatment failure. We did not include amoxicillin-clavulanate as a first-line antibiotic option for AOM, for example, although guidelines list it in cases of recurrent AOM or concomitant conjunctivitis. For UTI in particular, local antibiograms are more likely to influence first choice; in our institutions, 1st generation cephalosporin suspectibility of urine isolates exceeds 96%, cephalexin was therefore chosen as a first-line agent; this may not apply to institutions where cephalexin resistance is higher. Additionally, we acknowledge that many of the documented allergies to amoxicillin are likely an overestimate of true allergies. Fluctuations in the rate of amoxicillin allergy labels may have impacted the rates of appropriate first-line agent. Future interventions will focus on removing unnecessary amoxicillin allergy labels for eligible patients.

Developing initiatives that improve the quality of prescriptions when antibiotics are indicated can decrease the risk of adverse effects caused by prolonged antibiotic exposure and reduce unnecessary exposure to expensive, broad-spectrum antibiotics. ASPs positively influence the prescribing behaviors of outpatient clinicians and should be prioritized by institutions to improve healthcare delivery.

Acknowledgments

The authors would like to acknowledge the Children's Mercy Antimicrobial Stewardship Advisory Board for their support. Additionally, we would like to acknowledge the Medical Writing Center for editing this manuscript, and the Children's Mercy Division of Urgent Care for their willingness to participate in our antimicrobial stewardship efforts.

SUPPLEMENTARY MATERIALS

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.ajic.2022.07.027.

References

1. Centers for disease control and prevention. *Antibiotic Resistance Threats in the United States 2019*. U.S. Department of Health and Human Services; 2019.
2. Duffy E, Ritchie S, Metcalfe S, Van Bakel B, Thomas MG. Antibacterials dispensed in the community comprise 85%-95% of total human antibacterial consumption. *J Clin Pharm Ther*. 2018;43:59–64.
3. King LM, Bartoces M, Fleming-Dutra KE, Roberts RM, Hicks LA. Changes in US outpatient antibiotic prescriptions from 2011-2016. *Clin Infect Dis*. 2020;70:370–377.
4. Barlam TF, Cosgrove SE, Abbo LM, et al. Implementing an antibiotic stewardship program: guidelines by the infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis*. 2016;62:e51–e77.
5. Nathwani D, Varghese D, Stephens J, Ansari W, Martin S, Charbonneau C. Value of hospital antimicrobial stewardship programs [ASPs]: a systematic review. *Antimicrob Resist Infect Control*. 2019;8:35.
6. Gerber JS, Jackson MA, Tamma PD, Zaoutis TE, Diseases AAPCoI. Pediatric Infectious Diseases S. Policy statement: antibiotic stewardship in pediatrics. *J Pediatric Infect Dis Soc*. 2021;10:641–649.
7. Sanchez GV, Fleming-Dutra KE, Roberts RM, Hicks LA. Core elements of outpatient antibiotic stewardship. *MMWR Recomm Rep*. 2016;65:1–12.
8. Hersh AL, King LM, Shapiro DJ, Hicks LA, Fleming-Dutra KE. Unnecessary antibiotic prescribing in US ambulatory care settings, 2010-2015. *Clin Infect Dis*. 2021;72:133–137.
9. Gerber JS, Ross RK, Bryan M, et al. Association of broad- vs narrow-spectrum antibiotics with treatment failure, adverse events, and quality of life in children with acute respiratory tract infections. *JAMA*. 2017;318:2325–2336.
10. Doherty C, Mc Donnell C. Tenfold medication errors: 5 years' experience at a university-affiliated pediatric hospital. *Pediatrics*. 2012;129:916–924.
11. Rooney AM, Timberlake K, Brown KA, et al. Each additional day of antibiotics is associated with lower gut anaerobes in neonatal intensive care unit patients. *Clin Infect Dis*. 2020;70:2553–2560.
12. Vaughn VM, Flanders SA, Snyder A, et al. Excess antibiotic treatment duration and adverse events in patients hospitalized with pneumonia: a multihospital cohort study. *Ann Intern Med*. 2019;171:153–163.
13. Kronman MP, Gerber JS, Grundmeier RW, et al. Reducing antibiotic prescribing in primary care for respiratory illness. *Pediatrics*. 2020:146.
14. Meeker D, Linder JA, Fox CR, et al. Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices: a randomized clinical trial. *JAMA*. 2016;315:562–570.
15. Butler CC, Simpson SA, Dunstan F, et al. Effectiveness of multifaceted educational programme to reduce antibiotic dispensing in primary care: practice based randomised controlled trial. *BMJ*. 2012;344:d8173.
16. El Feghaly RE, Burns A, Goldman JL, Myers A, Purandare AV, Lee BR. Novel outpatient antibiotic prescribing report of respiratory infections in a pediatric health system's emergency departments and urgent care clinics. *Am J Infect Control*. 2020;49:398–400.
17. Children's Mercy Kansas City. Provider resources for antimicrobial stewardship. Accessed August 25 2022. https://www.childrensmercy.org/siteassets/media-documents-for-depts-section/documents-for-health-care-providers/evidence-based-practice/clinical-practice-guidelines–care-process-models/outpatient-antibiotic-handbook.pdf. 2021.
18. Centers for Medicare & Medicaid Services, Quality Improvement Organization Program, (U.S.) CfDCaP. MITIGATE antimicrobial stewardship toolkit : a guide for practical implementation in adult and pediatric emergency department and urgent care settings. 2018.
19. Bradley JS, Byington CL, Shah SS, et al. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. *Clin Infect Dis*. 2011;53:e25–e76.
20. Lieberthal AS, Carroll AE, Chonmaitree T, et al. The diagnosis and management of acute otitis media. *Pediatrics*. 2013;131:e964–e999.
21. Shulman ST, Bisno AL, Clegg HW, et al. Clinical practice guideline for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2012;55:1279–1282.
22. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis*. 2014;59:e10–e52.
23. Subcommittee On Urinary Tract I. Reaffirmation of AAP clinical practice guideline: the diagnosis and management of the initial urinary tract infection in febrile infants and young children 2-24 months of age. *Pediatrics*. 2016:138.
24. Subcommittee on Urinary Tract Infection SCoQI, Management, Roberts KB. Urinary tract infection: clinical practice guideline for the diagnosis and management of the initial UTI in febrile infants and children 2 to 24 months. *Pediatrics*. 2011;128:595–610.

25. Committee on Infectious Diseases. System-based treatment table. In: Kimberlin DW, Barnett ED, Lynfield R, Sawyer MH, eds. *Red Book 2021-2024 Rerport of the Committee on Infectious Diseases*. 32 ed. American Academy of Pediatrics; 2021:990–1003.
26. Provost LP MS. *The Health Care Data Guide: Learning from Data for Improvement*. 1st ed. Jossey-Bass; 2011.
27. Suda KJ, Hicks LA, Roberts RM, Hunkler RJ, Taylor TH. Trends and seasonal variation in outpatient antibiotic prescription rates in the United States, 2006 to 2010. *Antimicrob Agents Chemother*. 2014;58:2763–2766.
28. Garcia Reeves AB, Lewis JW, Trogdon JG, Stearns SC, Weber DJ, Weinberger M. Association between statewide adoption of the CDC's Core Elements of Hospital Antimicrobial Stewardship Programs and rates of methicillin-resistant Staphylococcus aureus bacteremia and Clostridioides difficile infection in the United States. *Infect Control Hosp Epidemiol*. 2020;41:430–437.
29. Huebner C, Flessa S, Huebner NO. The economic impact of antimicrobial stewardship programmes in hospitals: a systematic literature review. *J Hosp Infect*. 2019;102:369–376.
30. Lee CF, Cowling BJ, Feng S, et al. Impact of antibiotic stewardship programmes in Asia: a systematic review and meta-analysis. *J Antimicrob Chemother*. 2018;73:844–851.
31. Hersh AL, King LM, Shapiro DJ, Hicks LA, Fleming-Dutra KE. Unnecessary antibiotic prescribing in US ambulatory care settings, 2010-2015. *Clin Infect Dis*. 2021; 72:133–137.
32. Joint Commission on Hospital A. APPROVED: new antimicrobial stewardship standard. *Jt Comm Perspect*. 2016;36(1):3–4. 8.
33. Arnold SR, Straus SE. Interventions to improve antibiotic prescribing practices in ambulatory care. *Cochrane Database Syst Rev*. 2005 CD003539.
34. Palms DL, Hicks LA, Bartoces M, et al. Comparison of antibiotic prescribing in retail clinics, urgent care centers, emergency departments, and traditional ambulatory care settings in the United States. *JAMA Intern Med*. 2018;178: 1267–1269.
35. Al-Tawfiq JA, Alawami AH. A multifaceted approach to decrease inappropriate antibiotic use in a pediatric outpatient clinic. *Ann Thorac Med*. 2017;12:51–54.
36. Guzik J, Patel G, Kothari P, Sharp M, Ostrowsky B, Team UHFOAC. Antibiotic prescribing for acute respiratory infections in New York City: a model for collaboration. *Infect Control Hosp Epidemiol*. 2018;39:1360–1366.
37. Sun S, Jones RC, Fricchione MJ, et al. Short-duration electronic health record option buttons to reduce prolonged length of antibiotic therapy in outpatients. *Pediatrics*. 2021:147.