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Original Article

Outpatient antimicrobial stewardship targets for treatment of skin and soft-tissue infections

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Abstract

Objective: We sought to identify factors associated with long duration and/or non–first-line choice of treatment for pediatric skin and soft-tissue infections (SSTIs).

Design: Retrospective cohort study.

Setting: Ambulatory encounter claims of Medicaid-insured children lacking chronic medical conditions treated for SSTI and/or animal bite injury in Ohio in 2014.

Methods: For all diagnoses, long treatment duration was defined as treatment >7 days. Non–first-line choice of treatment for SSTI included treatment with 2 antimicrobials dispensed on the same calendar day or any treatment not listed in the Infectious Diseases Society of America guidelines. The adjusted odds of (1) long treatment duration and (2) non–first-line choice of treatment were calculated for patient age, prescriber type, and patient county of residence characteristics (ie, rural vs metropolitan area and poverty rate).

Results: Of 10,310 encounters with complete data available, long treatment duration was prescribed in 7,968 (77.3%). The most common duration of treatment prescribed was 10 days. A non–first-line choice was prescribed in 1,030 encounters (10%). Dispensation of 2 antimicrobials on the same calendar day was the most common reason for the non–first-line choice, and of these, trimethoprim-sulfamethoxazole plus a first-generation cephalosporin was the most common regimen. Compared to pediatricians, the adjusted odds ratio of long treatment duration was significantly lower for all other primary care specialties. Conversely, nonpediatricians were more likely to prescribe a non–first-line treatment choice. Patient residence in a high-poverty county increased the odds of both long duration and non–first-line choice of treatment.

Conclusions: Healthcare claims may be utilized to measure opportunities for first-line choice and/or shorter duration of treatment for SSTI.

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In 2015, the National Action Plan for Combating Antibiotic-Resistant Bacteria set the goal of reducing inappropriate antibiotic use in outpatient settings by 50% by 2020.[1] Stewardship efforts with feedback on prescribing patterns have focused primarily on respiratory conditions[2] and have been shown to successfully decrease inappropriate prescribing. After respiratory infections,[3] skin and soft-tissue infections (SSTIs) are the next most common diagnoses associated with antimicrobial prescribing among pediatric outpatients, accounting for 11.9% of antibiotic prescriptions.[4,5] The burden of inappropriate prescribing and/or excessive days of therapy for these infections is still not completely clear. Recent quality improvement strategies have shown that shorter courses of therapy (≤7 days) for inpatients with SSTIs did not result in readmissions or poor outcomes.[6] This finding highlights an important stewardship opportunity that may be extrapolated to the outpatient setting. The objective of this study was to utilize healthcare claims data to examine factors associated with long duration and/or non–first-line choice of antibiotic treatment for pediatric outpatient SSTI. We also examined animal bites as another skin and soft-tissue–related indication for antibiotic therapy.

Methods

As previously described,[7] we analyzed healthcare claims of children aged 0–18 years in 2014 from Partners for Kids, an accountable care organization serving ~330,000 Medicaid managed-care children in central and southeastern Ohio. The treatment provided to these children included multiple institutions as well as community providers in both academic and nonacademic settings. From medical claims, we identified an outpatient encounter for SSTI or presumed animal bite (Figure 1

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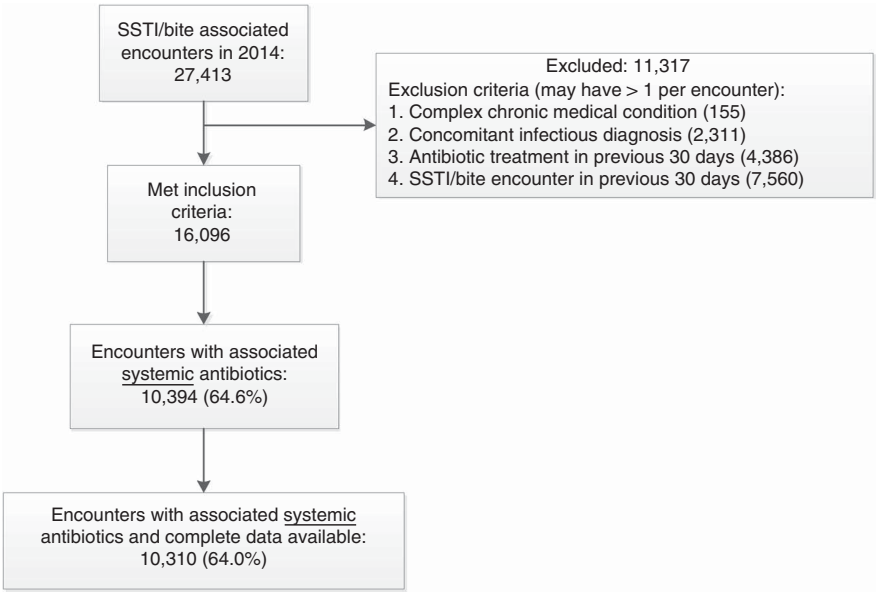

Fig. 1. Online. Encounters for children with skin/soft tissue infection and/or animal bites included in the analysis.

online). Visits included were office visits, emergency department visits, and other outpatient facility claims. No inpatient claims were included. To minimize potential confounding variables, we included encounters only if the patient had not received antibiotics in the previous 30 days, did not have another SSTI encounter in the previous 30 days, and did not have a complex chronic condition[8] or a concomitant presumed infectious diagnosis listed on the medical claim (Table 1 online). From pharmacy claims, we identified antibiotics (excluding topical and inhaled formulations) dispensed within 3 days following the medical encounter. If antibiotics were dispensed on multiple days within the 3-day period, only those on the earliest dispense date were included in the analysis. The reason for antibiotic treatment was inferred from the primary and secondary *International Classification of Disease Ninth Revision* (ICD-9) codes listed on the medical claim. The national provider identification number listed on the pharmacy prescription claim indicated the specialty of the prescriber. Specialties were grouped as follows: pediatric medicine (primary care or subspecialty), family medicine, nurse practitioner, physician assistant, emergency medicine, or other. The pharmacy claims also included the duration of treatment as described by the retail pharmacists. Encounter diagnoses were grouped into 1 of 2 subcategories: SSTI (cellulitis/abscess or impetigo/folliculitis) or presumed animal bite (Table 1 online).

Long Duration and Non–First-Line Treatment Definition

We defined a long treatment duration for SSTIs and presumed animal bites as >7 days. In accordance with national guidelines, non–first-line therapy for SSTIs was defined as dispensation of 2 unique antibiotics on the same calendar day or any treatment other than amoxicillin, amoxicillin-clavulanate, clindamycin, a penicillinase resistant penicillin, tetracyclines, trimethoprim-sulfamethoxazole, or a first-generation cephalosporin.[9,10] Among encounters for presumed animal bites, any treatment other than amoxicillin-clavulanate or the combination of clindamycin plus trimethoprim-sulfamethoxazole was considered non–first-line treatment.

Statistical Analyses

To identify the factors associated with the outcomes of long treatment duration or non–first-line choice of treatment, we assessed univariate logistic regression models, followed by multivariable logistic regression models, with the multivariable model including relevant demographic, clinical, and/or statistically significant factors in univariate analyses. The 2 models were performed for (1) long treatment duration, and (2) non–first-line antimicrobial choice. Patient age (0–2, 3–5, and ≥6 years), prescriber type, category of diagnosis, and patient county of residence characteristics were included as covariates. County characteristics included the metropolitan versus rural area designation of the US Department of Health and Human Services Office of Rural Health Policy (https://www.hrsa.gov/sites/default/files/ruralhealth/resources/forhpeligibleareas.pdf) and poverty rate (percent of children aged <18 years living in poverty in 2014) from the US Census Bureau Small Area Income and Poverty Estimates (SAIPE).[11] Counties with poverty rates greater than the median in the cohort (>25%) were defined as high poverty. Age categories were chosen a priori in accordance with a prior analysis of overall antimicrobial prescribing in the same cohort in 2014.[12] Results were considered statistically significant for 2-sided $P < .05$ for univariate and multivariable analyses. All analyses were conducted using SAS version 9.4 software (SAS Institute, Cary, NC). Model assumptions were verified using Hosmer-Lemeshow tests and residual plots.

Results

In total, 10,394 encounters were associated with 10,450 unique antimicrobial prescriptions dispensed within 3 days that met inclusion criteria for SSTI and/or animal bite in 2014. Analysis was limited to 10,310 encounters due to incomplete data (eg, missing provider type and/or county of residence). Among these included encounters, 7,344 (71.2%) had codes indicating cellulitis/abscess; 2,445 (23.7%) had codes indicating impetigo/folliculitis

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Table 1. Factors Associated with Long Treatment Duration and Non–First-Line Choice of Treatment for Skin and Soft-Tissue Infections and Presumed Animal Bites

	Long Duration		Non–First-Line Choice	
	aOR (95% CI)[a]	*P* Value	aOR (95% CI)[a]	*P* Value
County of residence				
Rural	0.71 (0.586–0.848)	.0002	1.73 (1.352–2.219)	<.0001
High Poverty	1.45 (1.207–1.747)	<.0001	1.23 (0.962–1.571)	.0987
Prescriber type				
Pediatric medicine	Referent		Referent	
Emergency medicine	0.37 (.317–0.423)	<.0001	3.14 (2.549–3.868)	<.0001
Family medicine	0.43 (0.368–0.507)	<.0001	2.77 (2.212–3.469)	<.0001
Nurse practitioner	0.64 (0.546–0.752)	<.0001	1.82 (1.452–2.291)	<.0001
Physician assistant	0.37 (0.313–0.448)	<.0001	2.81 (2.182–3.627)	<.0001
Other	0.33 (0.275–0.404)	<.0001	2.34 (1.766–3.098)	<.0001
Facility charge only[b]	0.36 (0.277–0.456)	<.0001	1.42 (0.887–2.282)	.1431
Age, y				
0–2	Referent		Referent	
3–5	0.91 (0.776–1.074)	.2717	1.21 (0.95–1.534)	.1231
≥6	0.67 (0.592–0.762)	<.0001	1.66 (1.378–1.994)	<.0001
Type of infection				
Presumed animal bite	0.41 (0.255–0.682)	.0005	2.05 (1.145–3.66)	.0157
Impetigo/ folliculitis	1.25 (0.798–1.973)	.3256	1.54 (0.931–2.547)	.0925
Cellulitis/ abscess	1.05 (0.663–1.673)	.8253	2.22 (1.314–3.747)	.0029

Note. aOR, adjusted odds ratio; CI, confidence interval.
[a]Adjusted odds ratios presented account for all factors listed in the model (all are listed in the table).
[b]A facility, rather than a specific prescriber, was listed on the pharmacy claim. Most facility charges only are in an emergency department setting.

(some encounters had codes for both); and 660 (6.4%) had codes indicating presumed animal bites. For 90% of the encounters, the prescriber type was pediatric medicine, family medicine, nurse practitioner, physician assistant, or emergency medicine. Median patient age was 7 years (IQR, 3–13 years); 4,175 (40.5%) resided in a high-poverty county; and 4,269 (41.4%) resided in a rural county. The most commonly prescribed antimicrobials were trimethoprim-sulfamethoxazole (n = 3,318, 32.2%), cephalexin (n = 3009, 29.2%), amoxicillin-clavulanate (n = 1,312, 12.7%), and clindamycin (n = 1,282, 12.4%).

Duration of Treatment

A long duration treatment was prescribed in association with 7,968 encounters (77.3%). The most common duration of therapy was 10 days (7,240 encounters, 70.2% of the cohort), and ≤7 days of treatment was prescribed in 2,356 encounters (22.7%). The results from our multivariable analysis are presented in Table 1. Factors that decreased the odds of long treatment duration included (1) residence in a rural county (aOR, 0.71 [95% CI, 0.59–0.85] compared to metropolitan county), (2) nonpediatrician prescribers (aORs all significantly lower than for pediatric medicine), (3) age ≥6 years (aOR, 0.67 [95% CI, 0.59–0.76] compared to age 0–2 years), and (4) diagnosis of presumed animal bite (aOR, 0.41; 95% CI, 0.26–0.68).

Choice of Treatment

Non–first-line treatment choices were prescribed in 1,030 encounters (10.0%). Among these, dispensation of 2 antibiotics on the same calendar day was the most common reason (n = 612, 59.4%), and the most common combination therapy dispensed was trimethoprim-sulfamethoxazole and a first-generation cephalosporin (n = 480). Patients aged 6 years and older and patients seen by nonpediatricians were more likely to receive a non–first-line antibiotic choice. According to Table 1, cellulitis/abscess was associated with greater odds of non-first-line antibiotic, not impetigo/folliculitis.

Discussion

We utilized healthcare claims to define possible outpatient antimicrobial stewardship targets for children with SSTI or animal bites. These data indicate that monitoring for duration of treatment for such infections and for antibiotic choice, specifically the combination of trimethoprim-sulfamethoxazole and a first-generation cephalosporin, could be considered.

We chose to define >7 days as a long duration of treatment for SSTI based on national guidelines, prospective studies, and studies that have utilized quality improvement methodology. The Infectious Diseases Society of America guidelines[9,10] recommend 7 days of treatment for impetigo, 5 days of treatment for uncomplicated cellulitis based on a prospective study,[13] and 7–10 days for purulent cellulitis. Treatment for SSTI in 2 large prospective trials showed higher rates of clinical cure when adding an antimicrobial agent after drainage for those with purulent cellulitis,[14,15] and in one of these trials, 7 days of treatment with trimethoprim-sulfamethoxazole after skin drainage resulted in a high rate of clinical cure.[15] Some pediatric data suggest that even shorter courses of 3 days of treatment may be sufficient for drained purulent cellulitis in children with documented methicillin-susceptible *Staphylococcus aureus*.[16] In addition, Schuler et al[6] used quality improvement methodology in hospitalized pediatric patients with SSTIs and demonstrated that increasing the percentage of children treated with shorter total durations of antimicrobials (≤7 days) for uncomplicated SSTIs was not associated with readmissions or documented recurrences. Although the American Academy of Pediatrics Red Book recommends only 3–5 days of antibiotics treatment to prevent infection after certain animal bite wounds,[17,18] we defined long treatment duration as >7 days, even for presumed animal bites, because it is difficult to distinguish prophylaxis from treatment of bite-related infection using claims data.

Several findings in this study highlight challenges for targeted stewardship efforts. Children residing in rural counties were more likely to receive a shorter duration of treatment than children residing in metropolitan counties, but they were also more likely

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to receive a non–first-line choice of antibiotic. Pediatricians were more likely than all other prescriber types to treat with a long duration (>7 days), but they were less likely to choose a non–first-line antimicrobial agent. Differences in rates of prescribing for upper respiratory infection have been described between physicians and other providers,[19] but we are unaware of such differences between providers with regard to SSTI. Our findings emphasize the need for comprehensive education and feedback to providers of all types and in all practice settings, including rural areas.

We focused this study on what we assume to be relatively uncomplicated clinical scenarios in that patients had not been seen for the same condition in the last month and had not had recent antimicrobial exposure. We also included any possible agents that are listed in national guidelines as first-line antibiotic choices for non–bite-associated SSTIs. However, without additional clinical data, we could not assess whether the antibiotic prescribed was appropriate for a given patient encounter. For example, amoxicillin is considered a first-line option for erysipelas, and though this would not be appropriate for staphylococcal infections, diagnostic codes provided on medical claims may not reliably distinguish erysipelas from cellulitis or abscess. This permissive definition may have led to an underestimate of the opportunity for improved stewardship. In contrast, our analysis of claims data reliably identified combination antibiotic treatment as a common non–first-line choice for SSTI. The most common combination treatment dispensed on the same calendar day was trimethoprim-sulfamethoxazole plus a first-generation cephalosporin. In 2 prospective trials of adults and children with uncomplicated cellulitis, the addition of trimethoprim-sulfamethoxazole to a first-generation cephalosporin did not confer any additional clinical benefit.[20,21]

There are inherent limitations of claims data (eg, lack of precise granular clinical data and reliance on codes to gather data). Specific to this study, claims data do not distinguish between abscess and cellulitis, though we chose 7 days or less as short duration, which should apply to both conditions. Treatment for non–bite-associated cellulitis or abscess likely does not require 2 classes of antimicrobials, so the non–first-line choice definition we used should apply to both conditions. The duration of 7 days may have been long for some conditions, such as mammalian bite prophylaxis, though the code for bites was only applied in 6.4% of the total cohort. We did not have clinical follow-up data for these patients, and we did not have data for those who may have failed treatment. Also, Franklin County has the most members in Partners for Kids, and Nationwide Children's Hospital is an academic medical center in this county with a large urgent care and ambulatory network in the area. Findings among pediatricians in this study may have disproportionately reflected the prescribing habits of pediatricians with an academic affiliation. Furthermore, we lacked allergy data, which may have affected choice of treatment. However, first-line treatment options for both SSTIs and presumed animal bites included a variety of antibiotic classes. Therefore, allergy likely did not affect the results significantly. In addition, we were unable to confirm the accuracy of coding by practitioners and coding for drainage procedures, which may have affected our results. The duration of antibiotic therapy was provided on the healthcare claim by retail pharmacists without standardized methodology, and we were unable to determine how long patients were instructed to take the medication. Finally, we recognize that several studies supporting shorter course therapy were published after 2014, so dissemination of this understanding was not available to clinicians in 2014.[6,15,16] This represents an opportunity to examine changing prescribing patterns over time.

In conclusion, while most outpatient stewardship efforts to date have appropriately focused on acute respiratory infections, the management of SSTIs is another essential opportunity to monitor trends in antibiotic use. Even with its inherent limitations, healthcare claims data has the potential to identify opportunities for improved antimicrobial stewardship for relatively uncomplicated SSTIs. The duration of >7 days for SSTI was identified in 77.3% of such encounters in this cohort in 2014. Future interventions could utilize claims data to provide audit and feedback to providers regarding treatment of SSTI.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2018.124

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