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Taste Perceptions of Common Pediatric Antibiotic Suspensions and Associated Prescribing Patterns in Medical Residents

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OBJECTIVE Palatability of medication is an important factor for adherence, especially in pediatric populations that tend to use oral suspensions for antibiotic therapy. Our study is the first to evaluate the impact of taste on prescribing patterns of antibiotic suspensions. The objective was to determine if taste testing common antibiotic suspensions altered prescribing patterns of medical residents, through data extracted from the electronic health record.

METHODS After assessing 5 “primer” tastes (sweet, salty, bitter, sour, umami [savory]), residents were randomized to sample 6 antibiotic suspensions to rate their taste perception. A 12-month retrospective and prospective analysis of outpatient prescribing practices of the residents followed, and the results were compared to the resident cohort randomized to no taste test.

RESULTS The 43 residents prescribed 207 liquid antibiotic prescriptions for 176 patients, with no difference in patient characteristics between residents in the taste test versus non–taste test group. Although amoxicillin was most preferable and amoxicillin-clavulanate least, the only significant finding was a greater prescribing rate of cefdinir among those who had tasted it and an inverse relationship between cephalexin taste preference and percentage prescribing amoxicillin in the taste group. Residents who tasted were poor in identifying primer tastes, but this did not impact prescribing patterns.

CONCLUSIONS Among 6 commonly prescribed antibiotic suspensions, amoxicillin remains a highly preferred taste among prescribers. Interestingly, after the taste test there was a significantly greater prescribing rate of cefdinir among those who had tasted it and somewhat lower prescribing rate for amoxicillin-clavulanate.

ABBREVIATIONS EHR, electronic health record

KEYWORDS antibiotics; child; drug prescriptions; electronic health records; taste

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Introduction

Medication adherence is important in all patients because poor adherence can negatively impact patient outcomes,[1] and in the case of antibiotics, it can contribute to antibiotic resistance.[2] Several factors impact a child’s adherence to a medication regimen, including the child’s age, medication volume (i.e., depending on concentration of the suspension or solution), frequency and duration of administration,[3,4] formulary and insurance coverage,[5] and past experiences, such as side effects, or anticipated drug interactions. When determining which medication to prescribe to their pediatric patients, health care providers need to consider clinical guideline recommendations, their own preference or experience with the drug, cost of the medication, and parent preference.[6] Palatability of the medication is another important factor that impacts adherence.[7,8]

Pediatric anti-infective therapy is more complicated than that of adults because of pediatric populations’ tolerance of different formulations (i.e., challenges to swallowing pills, preferences for flavors and textures).[9] Liquid preparations can allow for flexible calculated dosing to better account for pediatric age and weight.[9] Typically, there is more than one antibiotic option for common pediatric infections. Some antibiotics, such as amoxicillin and cephalosporins, have been found to be more pleasant tasting than others, such as penicillin and clindamycin (which can have an unpleasant aftertaste).[7,8] A study with adult health care volunteers analyzed the appearance, smell, texture, taste, and aftertaste of 22 antibiotic suspensions and found higher ratings for cephalosporins.[10] Another study with parents of young children rated palatability differences between brand and generic antibiotic suspension formulations.[11] A study with children aged 6 to 12 years found no significant differences between preferred antibiotic tastes except consistently least preference for cloxacillin.[12] Another study with 3- to 14-year-olds tested compared brand versus generic suspension formulations for 3 antibiotics and found no difference for 2 of the 3 formulations, although compliance was identical for all 3.[13]

Familiarity with the palatability of common antibiotic suspensions could influence the medication prescribers' choice for their pediatric patients. Bradshaw et al[14] explored prescribers' opinions before and after a taste test of medications commonly used in pediatric patients, but it did not track the actual prescribing trends of the prescribers. A study from Canada assessed the perceived palatability of antiretroviral medications and adherence in children and the prescribing trends of their physicians.[15] To our knowledge, there is no previously published study exploring the impact on prescribing patterns of commonly prescribed antibiotics for pediatrics before and after a taste test of the antibiotics.

The objective of this study was to determine if taste testing common antibiotic suspensions altered prescribing patterns of medical residents, as determined by electronic health record (EHR) chart review. The primary end-point evaluated for a difference in residents' prescribing of 6 commonly used antibiotic suspensions, comparing a group that had pretasted them to a group that had not. The secondary end-point included evaluating whether antibiotic tasting preference was predictive of prescribing in the treatment group (tasters) with consideration of pre-tasting prescribing. Association between antibiotic taste preference and prescribing was also evaluated as a secondary end-point. The investigators hypothesized that medical residents would reduce their prescribing for less palatable antibiotic suspensions for pediatric infections.

Materials and Methods

This study had 2 distinct phases: 1) a taste test for medical resident participants and 2) a retrospective and prospective analysis of the prescribing practices of the participants before and after the taste test. Pre-taste prescribing data were collected to enhance identifying homogeneity between the 2 groups, and to determine if taste preferences were predictive of antibiotic prescribing with consideration of pre-tasting use patterns.

A total of 27 pediatric and 16 medicine-pediatric residents enrolled in the author's institution's residency programs were eligible to participate in the study. Study inclusion for the taste test included all residents who were present on the day of the taste test and who agreed to participate. Additionally, we excluded those who reported allergies to any of the antibiotics. Initial determination of selected antibiotics was made by a pilot data pull from the Epic EHR (Epic Corp, Verona, WI) of the most frequently prescribed outpatient pediatric antibiotic oral suspensions from the 12 months prior to May 1, 2020 in the healthcare system regardless of indication or antimicrobial coverage. (Supplemental Table). Nonliquid formulations were excluded.

In the taste test, we randomly assigned participants to 1 of 3 groups with a different order of antibiotic suspension presentation. Before taste testing the antibiotics, we assessed the participants' taste perception by blind tasting 5 tastes to assess for perception of discrete tastes: sweet, salty, bitter, sour, and umami (savory), the primary tastes in humans.[16] The Supplemental Table contains details on the 5 "primer" solutions. The participants were offered 3 mL of each solution and asked to identify the taste in an electronic Research Electronic Data Capture (REDCap, Vanderbilt, Nashville, TN)[17] survey administered during the test. We asked the participants not to swallow the solutions, but swish-and-spit and rinse out their mouth with water prior to the subsequent sample. Next, the participants blindly tasted 3 mL of each of the 6 oral suspension antibiotics (freshly compounded, unrefrigerated) and reported taste perception on a 9-point hedonic scale ranging from "dislike extremely" to "like extremely."[18] At the end of the taste test, a debriefing session with the residents revealed each tasted antibiotic and the order of tasting.

In the second phase of the study, we conducted a retrospective and prospective analysis of the prescribing practices of the resident participants before and after the taste test using the EHR data. Inclusion was all pediatric patients, younger than 18 years at time of visit, with an outpatient encounter between May 1, 2020 and April 30, 2021, who received an included oral antibiotic suspension prescription from residents in the program, regardless of the resident's participation in the taste test. This yearlong period was bifurcated by the date of the taste test, with 6 months prior to the taste test serving as baseline data retrospectively, and 6 months following the taste test, as prospective data. The encounter-level report included patient demographics (age, sex, insurance type), encounter information (encounter type, location, and diagnoses), and medication order (antibiotic, dose, route of administration, prescriber, and known allergies). The encounter diagnoses referred to the patient's chief complaint(s) during the encounter. Data were reviewed, and duplicates were identified and removed if they included the same patient, encounter date, diagnosis, and prescribed antibiotic and dose. Prior to data sharing and analysis, the honest data broker cleaned and deidentified the data.

We analyzed group differences on demographic characteristics using χ^2, *t*-test, or Wilcoxon rank-sum test where appropriate. We analyzed tasting preference scores using analysis of variance with post hoc analysis (Bonferroni). The primary outcome of difference in the percent of each antibiotic prescribed between groups in the post-tasting period was analyzed using *t*-test (Wilcoxon rank-sum if failure of normality assumption). We analyzed associations between relevant variables with Kendall τ. For each antibiotic, we conducted ordinal logistic regression (due to non-normality) on

Table 1. Group Comparisons

Variable	No Tasting	Tasting	p value
Resident level, n (%)			
PGY-1	8 (30.8)	6 (37.5)	0.516
PGY-2	6 (23.1)	5 (31.2)	
PGY-3	8 (30.8)	5 (31.2)	
PGY-4	4 (15.4)	0 (0)	
Female, n (%)	16 (61.5)	10 (62.5)	0.950
Program, n (%)			
Medicine–pediatrics	14 (53.8)	2 (12.5)	0.010*
Pediatrics	12 (46.15)	14 (87.5)	
Patient level			
Age, mean ± SD, yr	3.84 (3.24)	4.11 (3.76)	0.586
Female, n (%)	63 (55.3)	53 (57.0)	0.803
Prescription insurance			
Total	114 (100)	93 (100)	0.299
Medicaid	67 (58.8)	62 (66.7)	
Private pay	28 (24.6)	22 (23.7)	
Self-pay	19 (16.7)	9 (9.7)	
Antibiotic allergies	11 (9.6)	11 (11.8)	0.613
Prescription level			
Antibiotics	114 (100)	93 (100)	0.0496*
Amoxicillin	38 (33.3)	32 (34.4)	
Amoxicillin-clavulanate	18 (15.8)	11 (11.8)	
Azithromycin	6 (5.3)	0 (0.0)	
Cefdinir	3 (2.6)	10 (10.8)	
Cephalexin	20 (17.5)	20 (21.5)	
Sulfamethoxazole-trimethoprim	17 (14.9)	9 (9.7)	
Other	12 (10.5)	11 (11.8)	
Prescription diagnosis groups	114 (100)	93 (100)	0.409
Gastrointestinal	0 (0.0)	3 (3.2)	
Genitourinary	18 (15.8)	19 (20.4)	
Head, eyes, ears, neck, throat	51 (44.7)	44 (47.3)	
Skin	32 (28.1)	19 (20.4)	
Respiratory	3 (2.6)	1 (1.1)	
Prophylaxis	8 (7.0)	5 (5.4)	
Other	2 (1.8)	2 (2.2)	

PGY, postgraduate year

* Significant from applicable Exact test

post-tasting percent using taste preference as the predictor variable. This was repeated, adjusting for pre-tasting period antibiotic percentage and primer tasting. On the primary outcome, the estimated sample size using $\alpha = 0.05$, power = 80%, SD of 20% to detect a 20% difference in percent antibiotic prescribing was 17 per group. These same parameters would support an unbalance grouping of 15 and 23 (assuming unequal variance). Analysis was done using Stata 16.1 (Statacorp LLC, College Station, TX).

Results

Table 1 displays the characteristics of the residents participating in the study, and the prescriptions at the encounter level. There were no differences between those who participated in the taste testing and those who did not, except more medicine-pediatrics residents were non-tasters. During the study period, 303 antibiotic prescriptions were written by the residents for 249 patients with various infections. The overall mean age of participants was 6.8 ± 5.5 years, and 59% were female. Of those, 207 prescriptions were written for an oral suspension or liquid antibiotic to 176 patients. The age of the oral suspension population was 4.1 ± 3.6 years, and 57% were female. Table 1 also displays the encounter-level characteristics for the prescriptions, with no difference in patient age, sex, insurance coverage, patient allergies, or diagnostic groups for prescriptions or in total antibiotics prescribed.

In the "primer" tasting administered to the group prior to the antibiotic tasting only around 50% of the

Table 2. Antibiotic Percent Usage (of Total Antibiotics) by Tasting Group (Post-tasting Period)

Antibiotic	Non-tasting Group, % of Total (n = 26)	Tasting Group, % of Total (n = 16)	Difference (95% CI)	p value
Amoxicillin	12.50	18.75	−6.25 (−23.03 to 10.53)	0.444
Azithromycin	4.49	0	4.49 (−3.65 to 12.62)	0.754
Amoxicillin + clavulanate	20.77	6.25	14.52 (−3.60 to 32.64)	0.113
Cephalexin	19.49	16.67	2.82 (−15.69 to 21.34)	0.993
Sulfamethoxazole + trimethoprim	12.50	11.46	1.04 (−15.26 to 17.34)	0.776
Cefdinir	1.35	15.62	−14.28 (−24.06 to −4.50)	0.021*
Other	5.83	18.75	−12.92 (−27.65 to 1.81)	0.087

* Significant from Wilcoxon rank-sum test with exact probability given

prescribers identified all the primer tastes correctly. The sweet and salty tastes were correctly identified most commonly (87.5%), followed by bitter (75%). Sour and umami were identified at the lowest rate (68.8%). Of note, all tasting residents were nonsmokers.

The Figure illustrates the antibiotic taste preferences for the prescribers in the corresponding group. Taste preferences were ranked on a 9-point scale (from 9, *like extremely*, to 1, *dislike extremely*). There were statistically significant differences that existed between antibiotic taste scores (overall analysis of variance $p < 0.0001$). The amoxicillin suspension had the most preferred taste and amoxicillin-clavulanate had the least preferred taste. Statistically significant differences that exist between antibiotic tastes are illustrated by the brackets in the Figure. The amoxicillin-clavulanate distinguished itself as significantly more distasteful compared with amoxicillin ($p < 0.0001$), cefdinir ($p = 0.001$), azithromycin ($p = 0.004$), and cephalexin ($p = 0.021$).

On the primary study end-point, a summary of percent antibiotic usage (of total) in the post-tasting period is shown in Table 2, comparing the taste group to the non-taste group. There was no statistically significant difference in percentage use of antibiotics comparing the taste group to the non-taste group with the exception of cefdinir, where there was significantly greater use of this antibiotic in the taste group compared with the non-taste group ($p = 0.0213$).

With respect to secondary study end-points, in the taste group there was no statistically significant association between the percent of the antibiotic prescribed and the taste preference score for that specific antibiotic (Kendall τ p value range, 0.0710–0.2204). There was an inverse relationship between the taste preference for cephalexin and the percentage prescribing amoxicillin in the taste group (Kendal $\tau = -0.4987$; $p = 0.0493$).

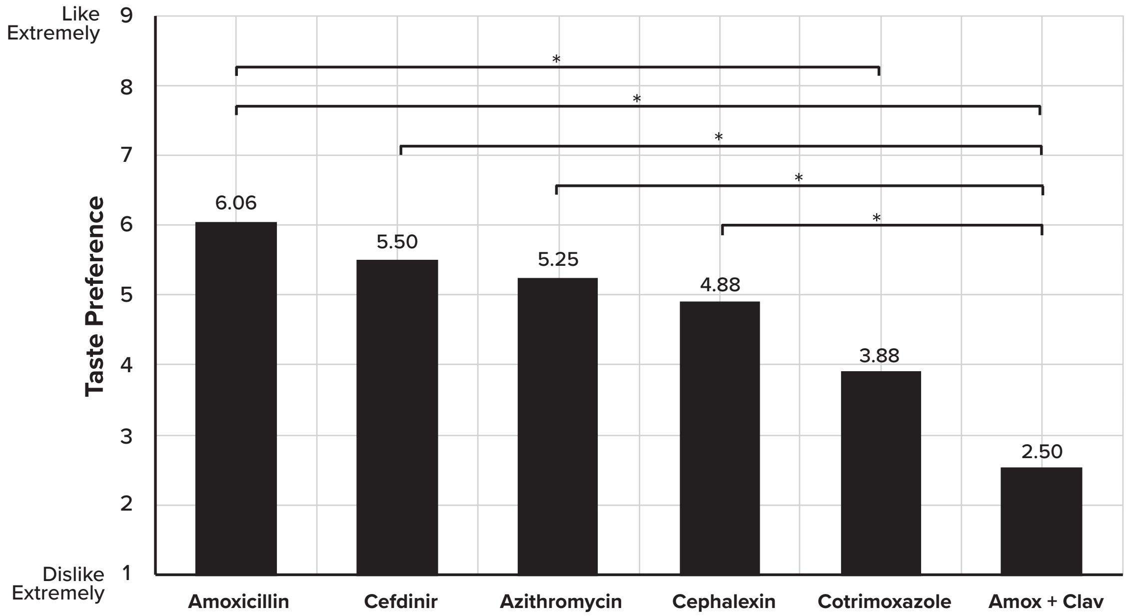
Within the tasting group, the influence of tasting preference on prescribing percentage was evaluated using ordinal logistic regression with and without pre-tasting prescribing percentage; this was done for each antibiotic. Treating the post-tasting percent of each antibiotic prescribed as an ordinal outcome (due to non-normality of distribution), there was no statistically significant relationship that emerged using the taste preference scores for that antibiotic as the predictor variable (β coefficient p values range, 0.094–0.998). Azithromycin was not analyzed because of a lack of prescriptions.

Pre-tasting and post-tasting prescribing were compared to ordinal logistic regression as well. Post-tasting prescribing percentage for each antibiotic was regressed using pre-tasting prescribing percentage, taste preferences, and primer tasting as predictor variables. Neither pre-tasting prescribing (β coefficient p values range, 0.181–0.884) nor taste preference (β coefficient p values range, 0.087–0.248) nor primer tasting accuracy (β coefficient p values range, 0.250–0.751) emerged as statistically significant predictors of post-tasting prescribing in the tasting group. Azithromycin was not analyzed because of a lack of prescriptions and amoxicillin-clavulanate did not reach convergence in the model.

Discussion

Our study explored residents' prescribing patterns of liquid antibiotics in relation to tasting of said antibiotics. Overall, amoxicillin emerged as the most preferable tasting antibiotic and amoxicillin-clavulanate least preferred from the 6 most commonly prescribed antibiotic suspensions in the sample population. We also found that, when looking during a 1-year period, there was a significantly greater prescribing rate of cefdinir among those who had tasted it,and amoxicillin-clavulanate prescribing was less in the taste group, although this did not reach significance. Our findings mirrored those of Gee and Hagemann[8] mostly, except for the amoxicillin-clavulanate finding, and the Bradshaw et al[14] study with amoxicillin as most palatable and a post-taste shift towards cefdinir. In the taste group, pretasting antibiotic prescribing and taste preferences were not predictive of post-tasting an-

Figure. Antibiotic taste preferences.



Amox, amoxicillin; Clav, clavulanate; Cotrimoxazole, sulfamethoxazole-trimethoprim

* Indicates statistical significance at $p < 0.05$
† Taste preference scale 1= dislike extremely; 9 = like extremely

tibiotic prescribing. Additionally, there was no significant association between prescribing patterns and the taste preference score for a specific antibiotic. Of note, only half of residents correctly identified “primer” tastes, with sweet and salty being most accurate, but those did not predict antibiotic prescribing.

Previous studies on antibiotic taste impact on prescribing have relied on self-report by the prescribers,[19] we tracked actual prescribing patterns from the EHR, which is increasingly used for analysis and research.[20] Obtaining actual antibiotic prescribing data from the EHR has been done in other studies[21,22] and is preferable to relying on perception or recall from clinicians. Our study differs from those by Gee and Hagemann[8] and Bradshaw et al[14] in that we first tested the primer tastes in our patients to assess for perception of discrete tastes. Although we did not use any particular sweetener or flavoring for our antibiotic preparations, the Gee and Hagemann[8] study found that participants did not appear to favor a particular sweetener or flavor among liquid antibiotics anyway. Although Gee and Hagemann[8] compared 24 antibiotics and Bradshaw et al[14] 2 medications (not only antibiotics) for specific conditions, our study compared 6 antibiotics based on the most commonly prescribed options from a previous year data analysis and we felt these would be most reflective of prescribing practice. Importantly, we monitored patterns of prescribing the antibiotics tasted before and after the taste test and compared these to those for non-tasters.

Compared with adults, children have a stronger preference for sweet and salty tastes[23] with a dislike for bitter tastes, and this preference sustains throughout childhood until late adolescence.[24] Some children also may have greater sensitivity to bitter taste based on presence or absence of a “taster allele.”[25] In addition to taste, the presence of irritant or volatile compounds in the formulation can be a deterrent to medication palatability.[26] Additionally, in children, textures (grittiness or chalkiness), appearance (colors of pink versus off-white), liquids using alcohol, water, or a simple syrup, and aftertaste may also play a role in the assessment of taste of a medication.[12] Coupled with their own taste perceptions, clinicians’ awareness of these factors can help inform their engagement with families and child patients when prescribing liquid antibiotics. Taste perception is driven by genetics, experiences, and even affective states, and so clinicians should recognize factors that drive palatability are individualized and make clinical decisions at a patient level. They should also be aware of strategies to engage children and families in ways to mitigate poor palatability, if unavoidable, by other strategies; and, where avoidable, to consider suitable alternatives to ensure pediatric adherence to liquid medications. Parents are experts in their own child’s taste preferences, and can identify successful strategies to overcome barriers, especially because parents’ perception about diagnostics, medication effectiveness, and side effects can impact adherence.[27] Taste is just one of the factors impacting pediatric medication adherence; others, including age and cultural and socioeconomic factors, are vitally important, and it is recommended that prescribing clinicians take a holistic view of the child and family unit and engage in shared decision-making when considering prescribing and adherence.

It is challenging to change the prescribing behavior of physicians, although some strategies can be helpful, such as opinion leaders endorsing change, interactive educational programming, and performance feedback as well as pharmacist engagement in interactive discussion and shared educational material.[28] When there is no option but to prescribe a less palatable medication, clinicians should be aware of some "tips and tricks" to guide families to improve adherence, such as using cold (ice cubes or popsicles) to numb taste buds prior to medication, acidic juices to dissipate taste, counter-flavors to mask,[4] or custom flavoring by pharmacists.[29] However, caution must be taken about advising mixing an unpleasant tasting medication with food because it may lead to food aversion.[4] Liquid medication palatability is addressed by adding sweeteners, but this can impact dental health,[30] and sweeteners themselves may have a bitter or metallic aftertaste.[31] Another strategy is by blocking bitter taste using sodium salts,[32] although there are concerns about the intake of excess sodium. In some cases simple taste-masking is insufficient and use of excipients to improve palatability may be unsafe in children because of the impact on developing organ systems.[33] In this area, the content expertise of pharmacists is invaluable and prescribing clinicians can benefit from,[34] and should seek collaboration with, pharmacists to improve adherence.[35]

Our study had several limitations. This study was conducted at a single, academic-affiliated institution, and it only involved outpatient pediatric antibiotic prescribing. It reflects local prescribing practices and may not be generalizable to all populations or practice settings, especially because prescribing practices might vary depending on type of practice, local hospital antibiograms, and specific infections seen in the population served.[36] Because the study involved pediatric residents, it is unclear if their prescribing choices were influenced by the practice of their attending physicians, who were not included in this study. There is a known phenomenon of "prescriber etiquette" in which prescribers might be reluctant to alter or challenge prescriptions of their peers or senior clinicians.[37] Additionally, the perception of "flavor" includes not just taste perception but also odor qualities, through olfactory receptor stimulation and visual appearance, through visual receptor stimulation.[38] In our study, we did not have residents plug their nose while tasting to eliminate the interference from odor, nor did the residents close their eyes to eliminate visual interference.

Although we included the most frequently prescribed outpatient pediatric antibiotic oral suspensions in our health care system from the 12 months prior to our study start date, these antibiotics are not therapeutically interchangeable. These antibiotics have different mechanisms of action, different antimicrobial coverage, and different infection treatment indications. The prescription diagnosis groups greatly varied and were too broad to draw any specific conclusions. Also, these most frequently prescribed outpatient pediatric oral suspensions may not reflect whether our residents used our local hospital antibiograms but may reflect prescription insurance coverage.

The use of a blinded antibiotic tasting followed by an unblinded debriefing may also pose a limitation. Although a thorough debriefing was given, allowing prescribers to assign each antibiotic to the appropriate sample tasted, it is possible participants might not properly recall taste preference across all antibiotics. Also, recall of taste for up to 6 months after the taste test may not be ideal to reflect an influence on the prescribing choices. Because clinical indication is an important consideration, it is possible that no equivalent alternatives were available for less preferred tasting medications. Another limitation is that this only reflects taste and prescribing patterns for liquid antibiotics, and it is hard to ascertain what (if any) impact taste testing has on perception and prescribing of tablet or capsule formulations. In our study, overall number of prescriptions for liquid antibiotics was small, and larger numbers of prescriptions might have led to more significant prescribing changes. Finally, the COVID-19 pandemic could have resulted in altered antibiotic prescribing patterns, because of factors such as different access to clinicians during the pandemic, altered comfort of clinicians in prescribing based on remote (phone or video) encounters, or different symptom profile during this period. Although our study did occur during this time frame, we did not have adequate longitudinal data before the pandemic to draw any conclusions, although a study from the Netherlands found a reduction in infections and antibiotic prescriptions during the COVID-19 pandemic.[39]

Future directions will include surveying the resident physicians after the taste tests to probe for changes in practice as a result of their participation in the taste test and if they engaged in shared decision-making with parents or caregivers.[40] We will also explore a wider range of antibiotics for taste testing offering a wider range of tastes and include the academic attending physicians and community physicians in future studies. Finally, our study benefited from a collaboration between physicians and pharmacists, and future directions may include the interprofessional education of pediatric prescribers[41] around pediatric medication characteristics, including taste.

Conclusion

Among 6 commonly prescribed antibiotics, amoxicillin remains a highly preferred taste for antibiotic suspension among prescribers. Interestingly, there was a significantly greater prescribing rate of cefdinir among those who underwent the taste test compared with those who did not. Although prescribing for amoxicillin-clavulanate was lower, the difference was not significant.

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