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Let's Talk About Antibiotics: A randomized trial of two interventions to reduce antibiotic misuse

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Data Sharing Statement: Deidentified data limited to visit-based inappropriate prescribing rates, patient characteristics, and dummy variables for clinic site will be shared. No protected health information will be shared. Data will be provided as a comma-separated values file with a data dictionary defining all variables included in the file and will be transferred via a secure file transfer protocol after establishing a data use agreement. No additional data or codes will be made available. The data will be made available after publication of the primary studies to researchers who provide a detailed methodologically sound proposal. Proposals should be submitted to Dr. Goggin (kgoggin@cmh.edu).

Abstract

Background: Children with acute respiratory tract infections (ARTIs) receive ≈11.4 million unnecessary antibiotic prescriptions annually. A chief contributor is inadequate parent–clinician communication, however efforts to reduce overprescribing have only indirectly targeted communication or been impractical.

Objectives: Compare two feasible (Higher vs Lower Intensity) interventions for enhancing parent-clinician communication on the rate of inappropriate antibiotic prescribing.

Design: Multisite, parallel group, cluster randomized comparative effectiveness trial. Data collected between March 2017 and March 2019.

Setting: Academic and private practice outpatient clinics.

Participants: MD/DO or CPNP/APRN clinicians (n=41, 85% of eligible approached) and 1,599 parent-child dyads (ages 1-5 years with ARTI symptoms, 71% of eligible approached).

Interventions: All clinicians received 20-minutes ARTI diagnosis and treatment education. Higher Intensity clinicians received an additional 50-minute communication skills training. All parents viewed a 90-second antibiotic education video.

Main Outcome(s) and Measure(s): Appropriateness of antibiotic prescribing assessed via blinded medical record review.

Results: Most clinicians completed the study (93%), were MD/DO (66%), female (78%) and averaged 8 years in practice. All parent-child dyad provided data for the main outcome (54% male, 53% ≤2 years). Inappropriate antibiotic prescribing was similar among patients who consulted with a Higher Intensity (7.8%) versus a Lower Intensity (9.4%) clinician. A generalized linear mixed effect regression model (adjusted for the 2-stage nested design, clinician type, clinic setting, and clinician experience) revealed that the odds of receiving

inappropriate antibiotic treatment did not significantly vary by group (AOR=0.99, p=0.98). Parent and clinician satisfaction with the interventions was high.

Conclusions and Relevance: Rate of inappropriate prescribing was low in both arms. The absence of a significant difference between groups indicates that communication principles previously thought to drive inappropriate prescribing may need to be re-examined or may not have as much of an impact in practices where prescribing has improved in recent years.

Trial Registration: NCT03037112.

Strengths and limitations of this study:

- Large number of clinicians and parent-child dyads engaged.
- Feasible interventions modeled on prior successful interventions.
- Rigorous methods conducted in real world clinical settings.
- Lack of a control group or baseline antibiotic prescribing information.

In the United States (US), most antibiotic prescribing occurs in the outpatient setting[1] where children with acute respiratory tract infections (ARTIs) receive 34 million antibiotic prescriptions annually.[2] Estimates indicate that at least 29% of these prescriptions are unnecessary.[3]

Antibiotic prescribing behavior is a complex and multifaceted process, but the interaction between parents or legal guardians (hereafter referred to as parents) and clinicians is central. Clinicians cite strong parent demand as a major cause of inappropriate prescribing.[4–7] Clinicians often capitulate to this perceived pressure because they don't want parents/patients to leave "empty handed",[8–10] fear receiving poor encounter satisfaction scores from parents,[11] and/or view explaining why antibiotics are not necessary as time consuming and unrewarding.[8,9]

Efforts to reduce inappropriate antibiotic prescribing in the pediatric setting have typically taken the form of educational interventions to increase antibiotic knowledge among clinicians and/or parents, electronic decision support systems, and/or behavioral interventions informed by behavioral economics and psychological science.[12–15] Many have been successful, with those that target parent-clinician communication and simultaneously intervene on parents and clinicians evidencing the strongest results.[13] Of the communication interventions tested, only one has directly targeted clinicians' perceptions of parental expectations for antibiotics alongside antibiotic education and shared decision-making.[16] This United Kingdom based study provided intensive communication training for clinicians and a multipage patient–clinician interactive educational booklet to enhance shared decision making. Clinicians in the intervention arm demonstrated statistically and clinically significant reductions in antibiotic prescribing as compared to control clinicians. While impactful, the intervention was viewed impractical for most real-world settings.[17]

Effective interventions that are efficacious and feasible in routine outpatient pediatric care in the United States are lacking. Using the Francis et al.[16] intervention as our model, we sought to 1) develop a version of this efficacious intervention that would enhance parent-clinician communication while being feasible in ambulatory pediatric care, and 2) compare it to a feasible educational intervention on the rate of inappropriate antibiotic prescribing.

METHODS

STUDY OVERVIEW

This was a multisite, parallel group, cluster randomized comparative effectiveness trial conducted in two pediatric outpatient clinics, with clinicians randomized (1:1) to a Higher Intensity intervention (prescribing education and communication skills training) or a Lower Intensity intervention (prescribing education only). Parent-child dyads enrolled in the study were exposed to either intervention according to the clinician who conducting their clinic visit. We hypothesized that compared to parent-child dyads managed by clinicians trained in the Lower Intensity intervention, parent-child dyads managed by clinicians in the Higher Intensity intervention would evidence lower rates of inappropriate antibiotic prescriptions. (See protocol paper for additional details.[18]) Ethical approval was obtained from the Children's Mercy Hospital Pediatric Institutional Review Board (#16060466).

Patient and public involvement: In the early planning stages for this study, we conducted focus groups and individual interviews with clinical, parent, payer and community stakeholders to assess the viability and inform the design of the study. We then recruited a Parent Research Associate who became a core member of our research team, attended all study meetings, and co-led our Community Advisory Board (CAB). Our CAB was comprised of 15 parent, provider and community stakeholders and was diverse (i.e., three males, seven Latinx [three exclusively

Spanish speaking] and three African-American members). CAB meetings occurred regularly throughout the study. All aspect of the study design, settings, participant burden, materials, procedures, interpretation of data and dissemination of study findings were informed by the CAB and Community Research Associate. Study results were disseminated to all clinic providers. A parent summary of findings will be provided to study sites to share with parents after this paper is published.

STUDY SETTING

The study was conducted at an academic medical facility (Children's Mercy Primary Care Clinics; CMH PCC) and both locations of a private practice (Heartland Primary Care; HPC).

PARTICIPANTS

Clinicians

All clinicians at both clinics were screened for eligibility. Inclusion criteria were being a pediatrician (MD or DO) or nurse practitioner (CPNP or APRN) and actively and independently conducting consultations with our target population. Eligible clinicians were recruited during study orientation sessions where interested clinicians completed informed consent and were given a sealed envelope prepared by the study statistician that contained their group assignment. Clinicians were stratified by patient volume and clinic.

Parent-Child Dyads

Parent-child dyads were recruited from March 2017 to March 2019. Study staff pre-screened all potentially eligible parent-child dyads and provided a study flyer during check-in.

Interested dyads were given information about the study and offered eligibility screening. Dyads were eligible if the patient was between ages 1 and 5 years, had ARTI symptoms and his/her parent was fluent in English or Spanish.[18] Children were not eligible if they had received an antibiotic in the last 30 days, had a concurrent probable bacterial non-respiratory infection, known immunocompromising conditions, complex chronic care condition,[19] required hospitalization during the visit or had previously participated in the study.

INTERVENTION COMPONENTS AND DESCRIPTION OF ARMS

Parent Video

The 90-second video used gain-framed messages[20,21] to explain when antibiotics are and are not indicated while emphasizing the risk of side effects and resistant organisms. Research has shown that people react to the same trade-off in different ways depending on whether the possible outcomes are presented as losses or gains.[20] We tailored all parent materials to highlight the gains of not using antibiotics (e.g., staying safe from side effects) that might increase parents' comfort with not getting an antibiotic prescription for their child. The video also highlighted information that clinicians should provide (e.g., estimate of illness duration, recommendations for system relief) during a visit. The video was successful in reducing parents' interest in obtaining an antibiotic for their child, especially among those with higher baseline interest.[22]

Parent Educational Trifold Brochure

The inside of the brochure provided "gain-framed" information about when antibiotics are and are not necessary and the risks involved in taking antibiotics. The outside of the brochure included a place to write the child's first name and parent tips for communicating with clinicians.

It also included check boxes for the clinician to indicate the diagnosis, if antibiotics were needed, recommended home care treatments, and expected recovery time.

Clinician General Antibiotic Education

Using didactic and interactive learning strategies, study physicians (AM, JN) provided a 20-minute, in-person general antibiotic education training on diagnosis and treatment of ARTI. The training covered pros and cons of antibiotics, impact of inappropriate use, Centers for Disease Control and Prevention antibiotic prescribing guidelines, common reasons for antibiotic misuse and viewing/discussing the 90-second parent video.

Clinician Communication Skills Training

The in-person, 50-minute communication skills training provided by the study's behavioral psychologist (KG) used didactic and interactive learning strategies including viewing/discussing motivational role model videos. The goal was to enhance clinicians' skills and confidence in the use of proven parent-centered communication strategies and the parent educational trifold brochure. Clinicians were also trained to consider parents' ratings of their interest in obtaining antibiotics after viewed the video.

Lower Intensity Intervention

This intervention was modeled on proven parent-focused and clinician-focused educational interventions.[e.g.,13,23] Clinicians completed the general antibiotic education described above.

In exam rooms prior to the consultation, parents who saw a clinician trained in the Lower Intensity intervention completed the baseline survey, saw the video and the inside of the parent brochure, and rated their desire for antibiotics all via a tablet computer. They did not receive a hard copy of the study brochure and their interest in an antibiotic rating was not shared with their clinician.

Higher Intensity Intervention

The higher intensity, *Let's Talk About Antib*iotics (LTAA), intervention was informed by a series of evidence-based interventions conducted in the UK and Europe,[16,24–29] Clinicians randomized to this arm completed the general antibiotic education and communication skills training described above. Before meeting with dyads, clinicians in this arm were provided with parents' ratings of their interest in obtaining antibiotics after watching the parent video via a sticky note on the exam room door. To assess fidelity to the communication skills, a subsample of visits (10%) were audio recorded and objectively coded by blinded raters using established methods.[30,31]

In exam rooms prior to the consultation, parents who saw a clinician trained in the Higher Intensity intervention completed the baseline survey, saw the video and the inside of the parent brochure, rated their desire for antibiotics via a tablet computer and received a personalized (child's name written in) hard copy of the study brochure.

PRIMARY OUTCOME

The primary outcome was rate of inappropriate antibiotic prescribing (i.e., number of patients receiving an inappropriate prescription / number of patients in arm). Inappropriate

prescribing was assessed by blinded study physicians (AM, JN) who reviewed the medical record documentation for each patient. Prescriptions were considered inappropriate if they were, prescribed: (1) for a viral ARTI, (2) for a presumed bacterial ARTI that does not meet Table 1 criteria, (3) broad-spectrum antibiotic for a bacterial ARTI in a child without a penicillin allergy, or (4) non-recommended alternative antibiotic for a bacterial ARTI (see Table 1) in a child with a penicillin allergy.

To guard against the potential for clinicians to use diagnostic codes to support their antibiotic prescribing,[7] study physicians reviewed detailed symptoms, physical examination findings and diagnostic tests to assess the appropriateness of the patient's diagnosis. Ten percent of all chart reviews were verified by the other study physician blinded to the initial coding, inconsistencies were reconciled.

SECONDARY OUTCOMES

Data on revisits and adverse drug reactions were collected via follow-up phone calls with parents two weeks after the visit. Parents were asked if any additional treatment occurred. Side effects and adverse drug reactions were assessed if antibiotics were prescribed.

Shared-decision-making was assessed using an adapted version of the three-item CollaboRATE questionnaire.[32] Parents rated "How much effort was made to: (1) help you understand your child's health issue?"; (2) listen to the things that matter most to you about your child's health issues?"; and (3) include what matters most to you in choosing what to do next?" on a 10-point response scale ranging from "no effort was made" to "every effort was made." The scale's psychometric properties have been established.[33]

Quality of parent-clinician communication was assessed with the question, "How satisfied were you with the communication between you and your child's healthcare clinician?"

Overall visit satisfaction was assessed with the question, "Overall, how satisfied were you with the visit?" Both items were scored on a five-point scale ranging from "very dissatisfied" to "very satisfied."

ANALYSES

All analyses were conducted using an intent-to-treat strategy. We constructed a 2-stage nested design, with parents nested within clinicians (Level-1 units) and study site (Level-2 units) generalized linear mixed-effect regression models (GLMM) to assess the impact of intervention type on our primary outcome of inappropriate antibiotic prescribing using Stata.[34] Alternative covariance structures were investigated, but as hypothesized, the exchangeable structure was sufficient. We employed robust standard errors to help minimize misspecification and examine time as a potential random effect. We examined the effects of the potential covariates on the outcomes with the goal of identifying the most parsimonious final models and we explored the heterogeneity of treatment effect. Variables considered included: clinic, clinician type, years of experience, patient age and sex, parent education level, race/ethnicity, preferred language, relationship to patient and insurance type. We created a binary indicator for each variable and included each as an interaction term in separate regression model. We examined these interaction terms across intervention arms and explored within-arm differential trends in our primary and secondary outcomes over time.

SAMPLE SIZE CALCULATION AND POWER

Prior research examining our primary outcome showed 30% of the antibiotics prescribed in the outpatient ARTI visits were inappropriate.[3,35] Prior intervention studies produced 20%–

81% reductions in inappropriate prescribing.[36,37] Based on the intraclass correlation coefficient (ICC) observed in the Meeker et al. study,[37] we assume an ICC of .04. With 40 clinicians, α of .05 and 80% power, we estimated that a sample size of 760 per arm would be needed to detect a 9% difference between arms. Allowing for an attrition rate of 5%, we aimed to recruit 1600 participants to ensure adequate power.

RESULTS

Clinicians

All clinicians (N = 51) were screened for eligibility; five were ineligible, four failed to respond after multiple contacts and one declined to enroll in the study. All 41 clinicians enrolled conducted clinic visits with enrolled participants. Three clinicians (all in the Higher Intensity arm) left their practices during the study leaving 38 clinicians who all completed the follow-up survey and interview. Most clinicians were female (78%) and MD/DO physicians (66%) with 8 median years in practice (IQR 4,14; range 1-40). Clinician demographics were similar across arms and between those who did and did not participate in the study.

Parent-Child Dyads

Figure 1 illustrates the flow of parent-child dyads from pre-screening through the two-week follow-up visit. Table 2 displays demographics for the 1599 dyads included in the primary analysis. Demographic characteristics of parents and children were similar among those exposed to the Higher or Lower Intensity intervention. Spanish speaking parents and those who had more education were more likely to complete the two-week assessment, no other differences were observed. Missing survey responses were rare overall (<1% for all variables) and did not exhibit any systematic patterns so we did not impute values.

Fidelity Assessment

Analysis confirmed a similar mean duration of visits (Higher = 11.7 vs. Lower = 10.2 minutes) with Higher Intensity providers consistently delivering more of the recommended communication content than Lower Intensity providers.

Primary Outcome: Inappropriate Antibiotic Prescribing

A total of 429 (26.8%) patients received an antibiotic prescription with 139 (32.4%) of meeting criteria for being inappropriate (Table 3). The most common reasons for an antibiotic to be considered inappropriate were being prescribed for a presumed bacterial ARTI that did not meet diagnostic criteria (n=109; 78.4%) and prescribing a broad-spectrum antibiotic for a child without a penicillin allergy (n=24; 17.3%). Overall, antibiotic prescribing rate was low and did not vary significantly based on intervention arm, study site, or clinician type. In the unadjusted GLMM, we found that the odds of receiving inappropriate antibiotic treatment for the Higher Intensity arm did not vary significantly when compared to the Lower Intensity arm (odds ratio [OR] = 1.09; 95% confidence interval [CI]: 0.56, 2.10; Table 4).

Heterogeneity of Treatment Effect

After adjusting for clinician type, clinic setting, and clinician experience there was still no significant intervention effect (AOR = 0.99; 95% CI: 0.52, 1.89). The interaction of the treatment arm and clinician type was significant in the adjusted GLMM model (AOR = 0.12; 95%: 0.04, 0.37). Specifically, the MD/DO clinicians in the Higher Intensity intervention were less likely to prescribe an inappropriate antibiotic than MD/DO clinicians in the Lower Intensity intervention arm. The reverse was true for the CPNP/APRN clinicians. No interaction between intervention and sex or location was observed. After adjusting for clinic setting and clinician experience, male Higher Intensity clinicians still evidenced significantly lower odds of prescribing an inappropriate antibiotic compared to their Lower Intensity male clinician

counterparts (AOR: 0.14; CI: 0.05, 0.37; p <.0001). Findings for female clinicians were not significant. No interaction between treatment and any of the parent-patient dyad variables (i.e., patient age or sex, parent education level, race/ethnicity, preferred language, relationship to patient or insurance type) was observed.

Secondary Outcomes

Revisits and Adverse Drug Reactions: Approximately 12% of patients had a return visit within two weeks of their index visit. The rate of revisits did not vary between patients seen by Higher or Lower Intensity clinicians (12.2% vs. 11.9%, p = 0.879). Adverse reactions to the prescribed antibiotic were similar across arms (16.5% vs. 12.8%, p = 0.27).

Shared Decision-Making: Parents' CollaboRATE ratings were extremely high overall (likely evidencing a ceiling effect) and similar across Higher and Lower Intensity arms (median 9.0 [IQR: 8.7, 9.0] vs. 9.0 [IQR: 8.3, 9.0], p = 0.85).

Quality of Parent–Clinician Communication and Visit Satisfaction: Parent rated satisfaction with their clinician's communication during the visit (median 5 [IQR: 5, 5] vs. 5 [IQR: 5, 5], p = 0.20) and their overall visit satisfaction (median 5 [IQR: 5, 5] vs. 5 [IQR: 5, 5], p = 0.38) were also very high overall and similar between arms.

Clinician Satisfaction and Feasibility

Most clinicians (84%) reported being "very satisfied" with the program, thought it would be "very" (71%) effective in reducing inappropriate prescribing and all would recommend it to other clinicians.

Parent Satisfaction

The majority of parents who completed the two-week follow-up survey (N=1337) reported being "very" (92%) satisfied with the program and 93% reported that they would recommend it to others.

DISCUSSION

This randomized comparative effectiveness trial comparing two feasible interventions for enhancing parent-clinician communication found no evidence of a difference in inappropriate antibiotic prescriptions. Inappropriate antibiotic prescribing was lower than recently published estimates of inappropriate prescribing in the Midwest (14.3%),[38] which have been on the decline especially among pediatricians.[39] Nevertheless, it was still higher than findings from other successful intervention studies (rates from 1.5% - 3.9%).[15,40] In the main outcome analysis, the odds of receiving an inappropriate antibiotic did not vary significantly between the Higher and Lower Intensity arms, even after adjusting for clinician type, clinic setting, and clinician experience.

Secondary outcomes of revisits and adverse reactions did not vary between patients seen by Higher or Lower Intensity clinicians. These findings indicate that there is no evidence that one of the interventions presented a greater risk to patients than the other. Parent ratings of shared decision making, satisfaction with quality of parent-clinician communication and visit satisfaction were all very high and similar between arms. Ceiling effects on the measures were apparent and likely reduced our ability to observe any true differences between arms. Nevertheless, these findings indicate that both interventions were highly satisfactory to parents.

In this study there was evidence that Higher Intensity male MD/DO clinicians were significantly less likely to prescribe inappropriate antibiotics than their MD/DO counterparts in the Lower Intensity arm. Why we observed this difference in this study is unclear and we likely have too few CPNP/APRN clinicians to draw any definitive conclusions about this subgroup, but

there is data to support the notion that CPNP/APRN are simply more likely to adhere to guidelines[41] so the educational training provided in both arms was likely sufficient to ensure similar low rates of inappropriate prescribing among CPNP/APRNs. Future studies should continue to explore difference in response to intervention between different types of clinicians.

The lack of a statistically significant or clinically meaningful main effect may indicate that shared decision-making and the other communication factors targeted by the Higher Intensity intervention were not as strongly related to inappropriate prescribing as had been expected. This may indicate a cultural shift in parental expectations and/or clinician comfort in withholding unnecessary antibiotics, challenging the relevance of early literature to the social and communication dynamics at play today. It may be that the antibiotic education training for clinicians in both arms and study video that significantly reduced parents' desires for an antibiotic[22] might have been enough to make a meaningful impact on prescribing. Other recent studies have found success focusing on clinician education about appropriate antibiotic prescribing and the effects of peer comparison.[37,40] Clinician education interventions may be sufficient to yield long-term benefits, as parental expectations for antibiotics continue to decrease from an overall cultural shift or from exposure to a high-quality parent education video like the one used in this study.

LIMITATIONS

The overall low rate of inappropriate antibiotic prescribing across interventions and sites is encouraging, but our design did not allow us to draw conclusions about the role of either intervention in these lower rates compared to usual care. Future studies should target settings with high rates of inappropriate prescribing. Higher Intensity intervention clinicians may not

have been given a sufficient "dose" of the training. Lack of a control group or baseline antibiotic prescribing information limits our ability to understand how the rates of inappropriate prescribing we observed in the two intervention arms differs from usual practice at the study sites.

CONCLUSION

Implementing evidence-based clinician and parent interventions to improve antibiotic prescribing can be feasible in both academic and private pediatric outpatient settings. Clinician education coupled with high-quality parent education delivered via video may be sufficient to yield low inappropriate antibiotic prescribing rates. Some clinicians may differentially benefit from more intensive intervention.

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Author Contributions

Dr. Goggin conceptualized, designed and oversaw the study, designed and implemented the parent education and clinician communication training, designed and directed all study procedures and materials, directed the data analysis and interpretation of results, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr. Hurley contributed to the design of the study, facilitated recruitment, intervention delivery and data collection, contributed to data analysis and interpretation of results, led qualitative data analysis and interpretation of results, drafted sections of the initial manuscript, and critically reviewed the manuscript for important intellectual content.

Dr. Lee contributed to the design of the study, conducted the data analysis, contributed to the interpretation of results, drafted sections of the initial manuscript, and critically reviewed the manuscript for important intellectual content.

Ms. Bradley-Ewing and Ms. Bickford contributed to the design of all aspects of the study, co-led the engagement with the Community Advisory Board and critically reviewed the manuscript for important intellectual content.

Ms. Pina, and Ms. Donis De Miranda contributed to the design study procedures, conducted recruitment and data collection, conducted the analysis and interpretation of qualitative results, drafted sections of the initial manuscript, and critically reviewed the manuscript for important intellectual content.

Drs. Yu, Weltmer, Linnemayr, and Butler contributed to the design of the study and critically reviewed the manuscript for important intellectual content.

Drs. Newland and Myers designed the study, designed and implemented the ARTI diagnosis and treatment training, conducted the blind review of the EMR, and critically reviewed the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

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Table 1: Diagnostic Criteria for Bacterial Acute Respiratory Tract Infections (ARTIs) and Appropriate Antibiotic Selection

Bacterial ARTI	Diagnostic Criteria	Primary Antibiotic	Secondary Antibiotics for Penicillin Allergy
Acute Otitis Media (either criteria)	1. Fever ≥38.3°C (101°F) with either a or b: a. Moderate to severe bulging of tympanic membrane on exam, or b. Mild bulging of TM and recent (<48hrs) onset of ear pain 2. New onset of otorrhea not due to acute otitis externa	amoxicillin	cefdinir, cefpodoxime, ceftriaxone, cefuroxime, clindamycin
Sinusitis (any of the 3 criteria)	1. Daytime cough or nasal discharge for greater than 10 days 2. High fever (>39°C) with purulent nasal discharge or facial pain lasting 3 consecutive days at the beginning of the illness 3. Worsening signs or symptoms characterized by the new onset of fever, headache, or increase in nasal discharge following a typical viral URI	amoxicillin	cefdinir, cefpodoxime, cefuroxime, clindamycin
Community acquired Pneumonia (either criteria)	1. Fever, tachypnea, and focal findings on pulmonary exam 2. a) Fever, b) Tachypnea, cough, or retractions AND c) Chest radiograph consistent with a focal consolidation	amoxicillin	cefpodoxime, cefprozil, cefuroxime, clindamycin
Streptococcal pharyngitis (both criteria)	1. Fever, pharyngitis, & positive rapid streptococcal antigen test or culture 2. Lack of viral signs and symptoms	amoxicillin	cephalexin (preferred unless previous type I hypersensitivity reaction to penicillin) clindamycin, azithromycin

Table 2: Parent and Patient Demographics (N = 1599)

		Higher Intensity	Lower Intensity
Sex of Parent			
	Female	584 (83.9%)	764 (84.6%)
Ethnicity of Parent			
	Hispanic	129 (18.5%)	171 (18.9%)
Race of Parent			
	Asian	13 (1.9%)	10 (1.1%)
	Black	90 (12.9%)	104 (11.5%)
	White	537 (77.2%)	721 (79.8%)
	Multi-Racial	15 (2.2%)	24 (2.7%)
	Other	10 (1.4%)	13 (1.4%)
	Chose not to answer	31 (4.5%)	31 (3.4%)
Preferred Language			
	Spanish	41 (5.9%)	60 (6.6%)
Education			
	Less than High School	38 (5.5%)	49 (5.4%)
	High School degree or GED	151 (21.7%)	183 (20.3%)
	Some College	228 (32.8%)	335 (37.1%)
	Secondary Degree	196 (28.2%)	240 (26.6%)
	Post Secondary Degree	79 (11.4%)	94 (10.4%)
	Other/Unknown	4 (0.6%)	2 (0.2%)
Patient Age			
	1	249 (35.8%)	307 (34.0%)
	2	126 (18.1%)	172 (19.0%)
	3	104 (14.9%)	145 (16.1%)
	4	96 (13.8%)	136 (15.1%)
	5	121 (17.4%)	143 (15.8%)
Patient Sex			
	Female	327 (47.1%)	414 (45.9%)
	Male	367 (52.9%)	488 (54.1%)
Patient Sex			
	Viral URI / Pharyngitis / OME	352 (50.6%)	440 (48.7%)
	Strep Throat	20 (2.9%)	16 (1.8%)
	AOM	126 (18.1%)	162 (17.9%)
	Sinusitis	2 (0.3%)	4 (0.4%)
	Pneumonia	6 (0.9%)	13 (1.4%)
	Multiple or Other Diagnosis	190 (27.3%)	268 (29.7%)

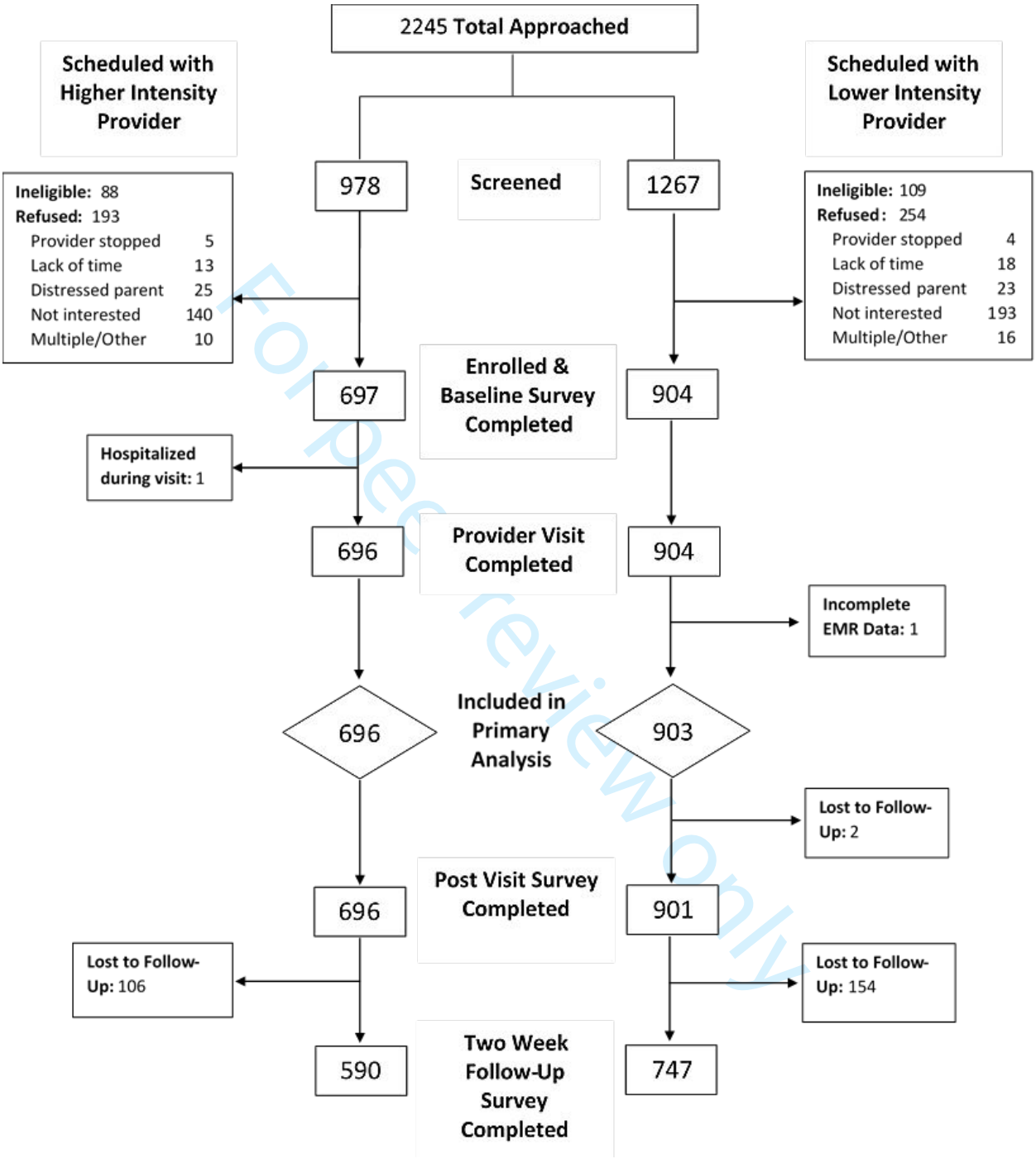
Table 3: Chi-Square Comparison of Overall and Inappropriate Antibiotic Prescribing (N = 1599)

	Any Antibiotic prescribed			Inappropriate antibiotic prescribed		
	n	Freq (%)	P value	n	Freq (%)	P value
Study Arm			0.291			0.244
Higher	696	196 (28.2%)		696	54 (7.8%)	
Lower	903	233 (25.8%)		903	85 (9.4%)	
Site			0.630			0.455
Private Practice	1292	350 (27.1%)		1292	109 (8.4%)	
Academic	307	79 (25.7%)		307	30 (9.8%)	
Clinician Type			0.129			0.572
MD/DO	907	230 (25.4%)		907	82 (9.0%)	
CPNP/APRN	692	199 (28.8%)		692	57 (8.2%)	

Table 4: Odd Ratios of Receiving Inappropriate Antibiotic (N = 1599).

	UNADJUSTED				ADJUSTED			
			95% CI				95% CI	
	OR	P Value	Lower	Upper	OR	P Value	Lower	Upper
Intervention Arm								
Higher Intensity (versus Lower)	1.09	0.81	0.56	2.10	0.99	0.98	0.52	1.89
Clinician type								
CPNP/APRN (versus MD/DO)	1.24	0.53	0.63	2.44	1.29	0.45	0.67	2.46
Practice Type								
Academic (versus private)	1.21	0.56	0.63	2.30	1.13	0.70	0.60	2.16
Clinician years of experience								
10+ years (versus <10 years)	1.40	0.31	0.73	2.66	1.42	0.30	0.73	2.77

Figure 1: Parent-child Dyads Enrollment



CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	4-5
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	5
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6-9
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	9-10
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	11
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	6
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	6
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	6
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	6
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	9

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	8-9
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	9-11
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	10-11
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	11-12
	13b	For each group, losses and exclusions after randomisation, together with reasons	11-12
Recruitment	14a	Dates defining the periods of recruitment and follow-up	2,6
	14b	Why the trial ended or was stopped	11
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	11-12,Table 2
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Fig 1, Table 3
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	12-14
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	12-14
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	12-14
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	16
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	14-16
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	14-16
Other information			
Registration	23	Registration number and name of trial registry	1,3
Protocol	24	Where the full trial protocol can be accessed, if available	Ref 18
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	1, 18

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

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Let's Talk About Antibiotics: A randomized trial of two interventions to reduce antibiotic misuse

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Let's Talk About Antibiotics: A randomized trial of two interventions to reduce antibiotic misuse

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Trial Registration: NCT03037112

Data Sharing Statement: Deidentified data limited to visit-based inappropriate prescribing rates, patient characteristics, and dummy variables for clinic site will be shared. No protected health information will be shared. Data will be provided as a comma-separated values file with a data dictionary defining all variables included in the file and will be transferred via a secure file transfer protocol after establishing a data use agreement. No additional data or codes will be made available. The data will be made available after publication of the primary studies to researchers who provide a detailed methodologically sound proposal. Proposals should be submitted to Dr. Goggin (kgoggin@cmh.edu).

Abstract

Background: Children with acute respiratory tract infections (ARTIs) receive ≈11.4 million unnecessary antibiotic prescriptions annually. A noted contributor is inadequate parent–clinician communication, however efforts to reduce overprescribing have only indirectly targeted communication or been impractical.

Objectives: Compare two feasible (Higher vs Lower Intensity) interventions for enhancing parent-clinician communication on the rate of inappropriate antibiotic prescribing.

Design: Multisite, parallel group, cluster randomized comparative effectiveness trial. Data collected between March 2017 and March 2019.

Setting: Academic and private practice outpatient clinics.

Participants: Clinicians (n=41, 85% of eligible approached) and 1,599 parent-child dyads (ages 1-5 years with ARTI symptoms, 71% of eligible approached).

Interventions: All clinicians received 20-minutes ARTI diagnosis and treatment education. Higher Intensity clinicians received an additional 50-minute communication skills training. All parents viewed a 90-second antibiotic education video.

Main Outcome(s) and Measure(s): Inappropriate antibiotic treatment was assessed via blinded medical record review by study clinicians and a priori defined as prescriptions for the wrong diagnosis or use of the wrong agent. Secondary outcomes were re-visits, adverse drug reactions (both assessed two weeks after the visit) and parent ratings of provider communication, shared decision-making and visit satisfaction (assessed at end of the visit on Likert-type scales).

Results: Most clinicians completed the study (n=38, 93%), were doctors (n=25, 66%), female (n=30, 78%) and averaged 8 years in practice. All parent-child dyad provided data for the main outcome (n=855 [54%] male, n=1043 [53%] ≤2 years). Inappropriate antibiotic prescribing was

similar among patients who consulted with a Higher Intensity (54/696, 7.8%) versus a Lower Intensity (85/904, 9.4%) clinician. A generalized linear mixed effect regression model (adjusted for the 2-stage nested design, clinician type, clinic setting, and clinician experience) revealed that the odds of receiving inappropriate antibiotic treatment did not significantly vary by group (AOR=0.99, 95% CI: 0.52, 1.89, p=0.98). Secondary outcomes of revisits and adverse reactions did not vary between arms, and parent ratings of satisfaction with quality of parent-provider communication (5/5), shared decision making (9/10) and visit satisfaction (5/5) were similarly high in both arms.

Conclusions and Relevance: Rate of inappropriate prescribing was low in both arms. Clinician education coupled with parent education may be sufficient to yield low inappropriate antibiotic prescribing rates. The absence of a significant difference between groups indicates that communication principles previously thought to drive inappropriate prescribing may need to be re-examined or may not have as much of an impact in practices where prescribing has improved in recent years.

Trial Registration: NCT03037112.

Strengths and limitations of this study:

- Large number of clinicians and parent-child dyads engaged.
- Feasible interventions modeled on prior successful interventions.
- Rigorous methods conducted in real world clinical settings.
- Lack of a control group or baseline antibiotic prescribing information.

In the United States (US), most antibiotic prescribing occurs in the outpatient setting[1] where children with acute respiratory tract infections (ARTIs) receive 34 million antibiotic prescriptions annually.[2] Estimates indicate that at least 29% of these prescriptions are unnecessary.[3]

Antibiotic prescribing behavior is a complex and multifaceted process, but the communication between parents or legal guardians (hereafter referred to as parents) and clinicians is central. Clinicians cite strong parent demand as a major cause of inappropriate prescribing.[4–7] Clinicians often capitulate to this perceived pressure because they don't want parents/patients to leave "empty handed",[8–10] fear receiving poor encounter satisfaction scores from parents,[11] and/or view explaining why antibiotics are not necessary as time consuming and unrewarding.[8,9]

Efforts to reduce inappropriate antibiotic prescribing in the pediatric setting have typically taken the form of educational interventions to increase antibiotic knowledge among clinicians and/or parents, electronic decision support systems, and/or behavioral interventions informed by behavioral economics and psychological science.[12–15] Many have been successful, with those that target parent-clinician communication and simultaneously intervene on parents and clinicians evidencing the strongest results.[13] Of the communication interventions tested, only one has directly targeted clinicians' perceptions of parental expectations for antibiotics alongside antibiotic education and shared decision-making.[16] This United Kingdom based study provided intensive communication training for clinicians and a multipage patient–clinician interactive educational booklet to enhance shared decision making. Clinicians in the intervention arm demonstrated statistically and clinically significant reductions in antibiotic prescribing as

compared to control clinicians. While impactful, the intervention was viewed impractical for most real-world settings.[17]

Effective interventions that are efficacious and feasible in routine outpatient pediatric care in the United States are lacking. Using the Francis et al.[16] intervention as our model, we sought to: 1) develop a version of this efficacious intervention that would enhance parent-clinician communication while being feasible in ambulatory pediatric care, and 2) compare it to a feasible educational intervention on the rate of inappropriate antibiotic prescribing.

METHODS

STUDY OVERVIEW

This was a multisite, parallel group, cluster randomized comparative effectiveness trial conducted in two pediatric outpatient clinics, with clinicians randomized (1:1) to a Higher Intensity intervention (prescribing education and communication skills training) or a Lower Intensity intervention (prescribing education only). Parent-child dyads enrolled in the study were exposed to either intervention according to the clinician who conducting their clinic visit. We hypothesized that compared to parent-child dyads managed by clinicians randomized to the Lower Intensity intervention, parent-child dyads managed by clinicians randomized to the Higher Intensity intervention would evidence lower rates of inappropriate antibiotic prescriptions. (See protocol paper for additional details.[18]) Ethical approval was obtained from the Children's Mercy Hospital Pediatric Institutional Review Board (#16060466).

PATIENT AND PUBLIC INVOLVEMENT

In the early planning stages for this study, we conducted focus groups and individual interviews with clinical, parent, payer and community stakeholders to assess the viability and

inform the design of the study. We then recruited a Parent Research Associate who became a core member of our research team, attended all study meetings, and co-led our Community Advisory Board (CAB). Our CAB was comprised of 15 parent, provider and community stakeholders and was diverse (i.e., three males, seven Latinx [three exclusively Spanish speaking] and three African American members). CAB meetings occurred regularly throughout the study. All aspect of the study design, settings, participant burden, materials, procedures, interpretation of data and dissemination of study findings were informed by the CAB and Community Research Associate. Study results were disseminated to all clinic providers. A parent summary of findings will be provided to study sites to share with parents after this paper is published.

STUDY SETTING

The study was conducted at an academic medical facility (Children's Mercy Primary Care Clinics; CMH PCC) in Kansas City, Missouri, USA and both locations of a private practice (Heartland Primary Care; HPC) in Kansas City and Lenexa, Kansas, USA.

PARTICIPANTS

Clinicians

All clinicians at both clinics were screened for eligibility. Inclusion criteria were being a pediatrician (Medical Doctor [MD] or Doctor of Osteopathic Medicine [DO]) or nurse practitioner (Certified Pediatric Nurse Practitioner [CPNP] or Advanced Practice Registered Nurse [APRN]) and actively and independently conducting consultations with our target population. Eligible clinicians were recruited during study orientation sessions where interested

clinicians completed informed consent and were given a sealed envelope prepared by the study statistician that contained their group assignment. Clinicians were stratified by patient volume and clinic.

Parent-Child Dyads

Parent-child dyads were recruited from March 2017 to March 2019. Study staff pre-screened all potentially eligible parent-child dyads and provided a study flyer during check-in. Interested dyads were given information about the study and offered eligibility screening. If more than one caregiver was present, they were asked to designate one person who would independently complete the written informed consent and all assessments. Clinicians had no role in identifying potentially eligible dyads, screening, consenting or data collection. Clinic staff who scheduled patients' appointments were blinded to clinician randomization. Dyads were eligible if the patient was between ages 1 and 5 years, had ARTI symptoms and his/her parent was fluent in English or Spanish.[18] Children were not eligible if they had received an antibiotic in the last 30 days, had a concurrent probable bacterial non-respiratory infection, known immunocompromising conditions, complex chronic care condition,[19] required hospitalization during the visit or had previously participated in the study.

INTERVENTION COMPONENTS AND DESCRIPTION OF ARMS

Parent Video

The 90-second video used gain-framed messages[20,21] to explain when antibiotics are and are not indicated while emphasizing the risk of side effects and resistant organisms. Research has shown that people react to the same trade-off in different ways depending on whether the possible outcomes are presented as losses or gains.[20] We tailored all parent materials to highlight

the gains of not using antibiotics (e.g., staying safe from side effects) that might increase parents' comfort with not getting an antibiotic prescription for their child. The video also highlighted information that clinicians should provide (e.g., estimate of illness duration, recommendations for system relief) during a visit. The video was successful in reducing parents' interest in obtaining an antibiotic for their child, especially among those with higher baseline interest.[22]

Parent Educational Trifold Brochure

The inside of the brochure provided "gain-framed" information about when antibiotics are and are not necessary and the risks involved in taking antibiotics. The outside of the brochure included a place to write the child's first name and parent tips for communicating with clinicians. It also included check boxes for the clinician to indicate the diagnosis, if antibiotics were needed, recommended home care treatments, and expected recovery time.

Clinician General Antibiotic Education

Using didactic and interactive learning strategies, study physicians (AM, JN) provided a 20-minute, in-person general antibiotic education training on diagnosis and treatment of ARTI. The training covered pros and cons of antibiotics, impact of inappropriate use, Centers for Disease Control and Prevention antibiotic prescribing guidelines, common reasons for antibiotic misuse and viewing/discussing the 90-second parent video. Refresher trainings for all study clinicians were provided twice during the study.

Clinician Communication Skills Training

The in-person, 50-minute communication skills training provided by the study's behavioral psychologist (KG) used didactic and interactive learning strategies including viewing/discussing motivational role model videos. The goal was to enhance clinicians' skills and confidence in the use of proven parent-centered communication strategies and the parent educational trifold brochure (See protocol paper for additional details.[18]). Clinicians were also trained to consider parents' ratings of their interest in obtaining antibiotics after viewed the video.

Lower Intensity Intervention

This intervention was modeled on proven parent-focused and clinician-focused educational interventions.[e.g.,13,23] Clinicians completed the general antibiotic education described above.

In exam rooms prior to the consultation, parents who saw a clinician trained in the Lower Intensity intervention completed the baseline survey, saw the video and the inside of the parent brochure, and rated their desire for antibiotics all via a tablet computer. They did not receive a hard copy of the study brochure and their interest in an antibiotic rating was not shared with their clinician.

Higher Intensity Intervention

The higher intensity, *Let's Talk About Antib*iotics (LTAA), intervention was informed by a series of evidence-based interventions conducted in the UK and Europe,[16,24–29] Clinicians

randomized to this arm completed the general antibiotic education and communication skills training described above. Before meeting with dyads, clinicians in this arm were provided with parents' ratings of their interest in obtaining antibiotics after watching the parent video via a sticky note on the exam room door. To assess fidelity to the communication skills and check for contamination between arms, a subsample of all visits (10%) were audio recorded and objectively coded by blinded raters using established methods.[30,31]

In exam rooms prior to the consultation, parents who saw a clinician trained in the Higher Intensity intervention completed the baseline survey, saw the video and the inside of the parent brochure, rated their desire for antibiotics via a tablet computer and received a personalized (child's name written in) hard copy of the study brochure.

Strategies to Reduce the Risk Of Contamination

We employed several strategies to reduce the likelihood of contamination between study arms. Specifically, we (1) designed intervention components to not be easily transferred between clinicians (e.g., the brochure was distributed by study staff to ensure that only parents who were consulted by clinicians in the Higher Intensity arm receive them), (2) ensured that all communication (written or in person) with clinicians in the Lower Intensity arm did not reveal any of the strategies from the Higher Intensity arm, (3) reviewed the importance of keeping intervention arms distinct during clinician training and asked Higher Intensity clinicians to pledge not to share any details or materials with their colleagues randomized to the Lower Intensity arm, and (4) trained Higher Intensity arm clinicians in communication strategies for dealing with Lower Intensity arm colleagues who ask for more information.

PRIMARY OUTCOME

The primary outcome was rate of inappropriate antibiotic prescribing (i.e., number of patients receiving an inappropriate prescription / number of patients in arm). Inappropriate prescribing was assessed by blinded study physicians (AM, JN) who reviewed the medical record documentation for each patient. Prescriptions were considered inappropriate if they were, prescribed: (1) for a viral ARTI, (2) for a presumed bacterial ARTI that does not meet Table 1 criteria, (3) broad-spectrum antibiotic for a bacterial ARTI in a child without a penicillin allergy, or (4) non-recommended alternative antibiotic for a bacterial ARTI (see Table 1) in a child with a penicillin allergy.

To guard against the potential for clinicians to use diagnostic codes to support their antibiotic prescribing,[7] study physicians reviewed detailed symptoms, physical examination findings and diagnostic tests to assess the appropriateness of the patient's diagnosis. Ten percent of all chart reviews were verified by the other study physician blinded to the initial coding, inconsistencies were reconciled.

SECONDARY OUTCOMES

Data on revisits and adverse drug reactions were collected via follow-up phone calls with parents two weeks after the visit. Revisits were assessed by asking parents if they sought any additional treatment for their child for the same symptoms or complications from any treatment provided in the initial visit. Side effects and adverse drug reactions were assessed if antibiotics were prescribed.

Shared-decision-making was assessed immediately following the visit using an adapted version of the three-item CollaboRATE questionnaire.[32] Parents rated "How much effort was made to: (1) help you understand your child's health issue?"; (2) listen to the things that matter

most to you about your child's health issues?"; and (3) include what matters most to you in choosing what to do next?" on a 10-point response scale ranging from "no effort was made" to "every effort was made." The scale's psychometric properties have been established.[33]

Quality of parent-clinician communication was assessed immediately following the visit with the question, "How satisfied were you with the communication between you and your child's healthcare clinician?" Overall visit satisfaction was assessed with the question, "Overall, how satisfied were you with the visit?" Both items were scored on a five-point scale ranging from "very dissatisfied" to "very satisfied."

ANALYSES

All analyses were conducted using an intent-to-treat strategy. We constructed a 2-stage nested design, with parents nested within clinicians (Level-1 units) and study site (Level-2 units) generalized linear mixed-effect regression models (GLMM) to assess the impact of intervention type on our primary outcome of inappropriate antibiotic prescribing using Stata.[34] Alternative covariance structures were investigated, but as hypothesized, the exchangeable structure was sufficient. We employed robust standard errors to help minimize misspecification and examine time as a potential random effect. We examined the effects of the potential prespecified covariates on the outcomes with the goal of identifying the most parsimonious final models and we explored the heterogeneity of treatment effect. Variables considered included: clinic, clinician type, years of experience, patient age and sex, parent education level, race/ethnicity, preferred language, relationship to patient and insurance type. We created a binary indicator for each variable and included each as an interaction term in separate regression model. We

examined these interaction terms across intervention arms and explored within-arm differential trends in our primary and secondary outcomes over time.

SAMPLE SIZE CALCULATION AND POWER

Prior research examining our primary outcome showed 30% of the antibiotics prescribed in the outpatient ARTI visits were inappropriate.[3,35] Prior intervention studies produced 20%–81% reductions in inappropriate prescribing.[36,37] Based on the intraclass correlation coefficient (ICC) observed in the Meeker et al. study,[37] we assume an ICC of .04. With 40 clinicians, α of .05 and 80% power, we estimated that a sample size of 760 per arm would be needed to detect a 9% difference between arms. Allowing for an attrition rate of 5%, we aimed to recruit 1600 participants to ensure adequate power.

RESULTS

Clinicians

All clinicians at both sites (N = 51) were voluntarily screened for eligibility; five were ineligible, four failed to respond after multiple contacts and one declined to enroll in the study. All 41 clinicians enrolled [22 (54%) randomized to the Higher Intensity arm; 19 (46%) randomized to Lower Intensity arm] conducted clinic visits with enrolled participants. Three clinicians (all in the Higher Intensity arm) left their practices during the study leaving 38 clinicians who all completed the follow-up survey and interview. Most clinicians were female (n=30, 78%) and MD/DO physicians (n=25, 66%) with 8 median years in practice (IQR 4,14; range 1-40). Clinician demographics were similar across arms and between those who did and did not participate in the study.

Parent-Child Dyads

Figure 1 illustrates the flow of parent-child dyads from pre-screening through the two-week follow-up visit. Table 2 displays demographics for the 1599 dyads included in the primary analysis. Demographic characteristics of parents and children were similar among those exposed to the Higher or Lower Intensity intervention. Spanish speaking parents and those who had more education were more likely to complete the two-week assessment, no other differences were observed. Missing survey responses were rare overall (<1% for all variables) and did not exhibit any systematic patterns so we did not impute values.

Fidelity Assessment

Analysis of 141 visit audio recordings confirmed a similar mean duration of visits (Higher = 11.7 vs. Lower = 10.2 minutes) and no evidence of contamination between arms. Compared to Lower Intensity clinicians, Higher Intensity clinicians consistently delivered more of the communication content they were taught in training and no Higher Intensity materials were used in sessions conducted by Lower Intensity clinicians.

Primary Outcome: Inappropriate Antibiotic Prescribing

A total of 429 (26.8%) patients received an antibiotic prescription with 139 (32.4%) meeting criteria for being inappropriate (Table 3). The most common reasons for an antibiotic to be considered inappropriate were being prescribed for a presumed bacterial ARTI that did not meet diagnostic criteria (n=109; 78.4%) and prescribing a broad-spectrum antibiotic for a child without a penicillin allergy (n=24; 17.3%). The rate of inappropriate prescriptions among all enrolled patients in each arm was similar among Higher Intensity (54 of 696; 7.8%) and Lower Intensity (85 of 903; 9.4%) clinicians. Inappropriate antibiotic prescribing also did not vary significantly based on study site or clinician type. In the unadjusted GLMM, we found that the odds of receiving inappropriate antibiotic treatment for the Higher Intensity arm did not vary

significantly when compared to the Lower Intensity arm (odds ratio [OR] = 1.09; 95% confidence interval [CI]: 0.56, 2.10; ICC = 0.11; Table 4).

Heterogeneity of Treatment Effect

After adjusting for clinician type, clinic setting, and clinician experience there was still no significant intervention effect (AOR = 0.99; 95% CI: 0.52, 1.89). However, the interaction of the treatment arm and clinician type was significant in the adjusted GLMM model (AOR = 0.12; 95%: 0.04, 0.37). Specifically, the MD/DO clinicians in the Higher Intensity intervention were less likely to prescribe an inappropriate antibiotic than MD/DO clinicians in the Lower Intensity intervention arm. The reverse was true for the CPNP/APRN clinicians. No interaction between intervention and gender or location was observed. No interaction between treatment and any of the parent-patient dyad variables (i.e., patient age or sex, parent education level, race/ethnicity, preferred language, relationship to patient or insurance type) was observed.

Secondary Outcomes

Revisits and Adverse Drug Reactions: Approximately 12% of patients had a return visit within two weeks of their index visit. The rate of revisits did not vary between patients seen by Higher or Lower Intensity clinicians (12.2% vs. 11.9%, p = 0.879). Adverse reactions to the prescribed antibiotic were similar across arms (16.5% vs. 12.8%, p = 0.27).

Shared Decision-Making: Parents' CollaboRATE ratings were extremely high overall (likely evidencing a ceiling effect) and similar across Higher and Lower Intensity arms (median 9.0 [IQR: 8.7, 9.0] vs. 9.0 [IQR: 8.3, 9.0], p = 0.85).

Quality of Parent–Clinician Communication and Visit Satisfaction: Parent rated satisfaction with their clinician's communication during the visit (median 5 [IQR: 5, 5] vs. 5

[IQR: 5, 5], p = 0.20) and their overall visit satisfaction (median 5 [IQR: 5, 5] vs. 5 [IQR: 5, 5], p = 0.38) were also very high overall and similar between arms.

Clinician Satisfaction and Feasibility

Most clinicians (84%) reported being "very satisfied" with the program, thought it would be "very" (71%) effective in reducing inappropriate prescribing and all would recommend it to other clinicians.

Parent Satisfaction

The majority of parents who completed the two-week follow-up survey (N=1337) reported being "very" (92%) satisfied with the program and 93% reported that they would recommend it to others.

DISCUSSION

This randomized comparative effectiveness trial comparing two feasible interventions for enhancing parent-clinician communication found no evidence of a difference in inappropriate antibiotic prescriptions. Inappropriate antibiotic prescribing was lower than recently published estimates of inappropriate prescribing in the US Midwest (14.3%),[38] which have been on the decline especially among pediatricians.[39] Nevertheless, it was still higher than findings from other successful intervention studies (rates from 1.5% - 3.9%).[15,40] In the main outcome analysis, the odds of receiving an inappropriate antibiotic did not vary significantly between the Higher and Lower Intensity arms, even after adjusting for clinician type, clinic setting, and clinician experience.

Secondary outcomes of revisits and adverse reactions did not vary between patients seen by Higher or Lower Intensity clinicians. These findings indicate that there is no evidence that one of the interventions presented a greater risk to patients than the other. Parent ratings of

shared decision making, satisfaction with quality of parent-clinician communication and visit satisfaction were all very high and similar between arms. Ceiling effects on the measures were apparent and likely reduced our ability to observe any true differences between arms. Nevertheless, these findings indicate that both interventions were highly satisfactory to parents.

In this study, Higher Intensity MD/DO clinicians were significantly less likely to prescribe inappropriate antibiotics than their MD/DO counterparts in the Lower Intensity arm. The reverse was true for the CPNP/APRN clinicians. The reasons for this difference among MD/DO clinicians are unclear and we likely have too few CPNP/APRN clinicians to draw any definitive conclusions about this subgroup, but there is data to support the notion that CPNP/APRN are simply more likely to adhere to guidelines[41] so the educational training provided in both arms was likely sufficient to ensure similar low rates of inappropriate prescribing among CPNP/APRNs. Future studies should continue to explore difference in response to intervention between different types of clinicians.

The lack of a statistically significant or clinically meaningful main effect may indicate that shared decision-making and the other communication factors targeted by the Higher Intensity intervention were not as strongly related to inappropriate prescribing as had been expected. This may indicate a cultural shift in parental expectations and/or clinician comfort in withholding unnecessary antibiotics, challenging the relevance of early literature to the social and communication dynamics at play today. It may be that the antibiotic education training for clinicians in both arms and study video that significantly reduced parents' desires for an antibiotic[22] might have been enough to make a meaningful impact on prescribing. Other recent studies have found success focusing on clinician education about appropriate antibiotic prescribing and the effects of peer comparison.[37,40] Clinician education interventions may be

sufficient to yield long-term benefits, as parental expectations for antibiotics continue to decrease from an overall cultural shift or from exposure to a high-quality parent education video like the one used in this study.

LIMITATIONS

The overall low rate of inappropriate antibiotic prescribing across interventions and sites is encouraging, but our design did not allow us to draw conclusions about the role of either intervention in these lower rates compared to usual care. Future studies should target settings with high rates of inappropriate prescribing. Higher Intensity intervention clinicians may not have been given a sufficient "dose" of the training. Lack of a control group or baseline antibiotic prescribing information limits our ability to understand how the rates of inappropriate prescribing we observed in the two intervention arms differs from usual practice at the study sites.

CONCLUSION

Implementing evidence-based clinician and parent interventions to improve antibiotic prescribing can be acceptable to clinicians and parents and feasible in both academic and private pediatric outpatient settings. Clinician education coupled with high-quality parent education delivered via video may be sufficient to yield low inappropriate antibiotic prescribing rates.

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Author Contributions

Dr. Goggin conceptualized, designed and oversaw the study, designed and implemented the parent education and clinician communication training, designed and directed all study procedures and materials, directed the data analysis and interpretation of results, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr. Hurley contributed to the design of the study, facilitated recruitment, intervention delivery and data collection, contributed to data analysis and interpretation of results, led qualitative data analysis and interpretation of results, drafted sections of the initial manuscript, and critically reviewed the manuscript for important intellectual content.

Dr. Lee contributed to the design of the study, conducted the data analysis, contributed to the interpretation of results, drafted sections of the initial manuscript, and critically reviewed the manuscript for important intellectual content.

Ms. Bradley-Ewing and Ms. Bickford contributed to the design of all aspects of the study, co-led the engagement with the Community Advisory Board and critically reviewed the manuscript for important intellectual content.

Ms. Pina, and Ms. Donis De Miranda contributed to the design study procedures, conducted recruitment and data collection, conducted the analysis and interpretation of qualitative results, drafted sections of the initial manuscript, and critically reviewed the manuscript for important intellectual content.

Drs. Yu, Weltmer, Linnemayr, and Butler contributed to the design of the study and critically reviewed the manuscript for important intellectual content.

Drs. Newland and Myers designed the study, designed and implemented the ARTI diagnosis and treatment training, conducted the blind review of the EMR, and critically reviewed the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Figure 1: Parent-child Dyads Enrollment

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Table 1: Diagnostic Criteria for Bacterial Acute Respiratory Tract Infections (ARTIs) and Appropriate Antibiotic Selection

Bacterial ARTI	Diagnostic Criteria	Primary Antibiotic	Secondary Antibiotics for Penicillin Allergy
Acute Otitis Media (either criteria)	1. Fever ≥38.3°C (101°F) with either a or b: a. Moderate to severe bulging of tympanic membrane on exam, or b. Mild bulging of TM and recent (<48hrs) onset of ear pain 2. New onset of otorrhea not due to acute otitis externa	amoxicillin	cefdinir, cefpodoxime, ceftriaxone, cefuroxime, clindamycin
Sinusitis (any of the 3 criteria)	1. Daytime cough or nasal discharge for greater than 10 days 2. High fever (>39°C) with purulent nasal discharge or facial pain lasting 3 consecutive days at the beginning of the illness 3. Worsening signs or symptoms characterized by the new onset of fever, headache, or increase in nasal discharge following a typical viral URI	amoxicillin	cefdinir, cefpodoxime, cefuroxime, clindamycin
Community acquired Pneumonia (either criteria)	1. Fever, tachypnea, and focal findings on pulmonary exam 2. a) Fever, b) Tachypnea, cough, or retractions AND c) Chest radiograph consistent with a focal consolidation	amoxicillin	cefpodoxime, cefprozil, cefuroxime, clindamycin
Streptococcal pharyngitis (both criteria)	1. Fever, pharyngitis, & positive rapid streptococcal antigen test or culture 2. Lack of viral signs and symptoms	amoxicillin	cephalexin (preferred unless previous type I hypersensitivity reaction to penicillin) clindamycin, azithromycin

Table 2: Parent and Patient Demographics (N = 1599)

		Higher Intensity	Lower Intensity
Gender of Parent			
	Female	584 (83.9%)	764 (84.6%)
Ethnicity of Parent			
	Hispanic	129 (18.5%)	171 (18.9%)
Race of Parent			
	Asian	13 (1.9%)	10 (1.1%)
	Black	90 (12.9%)	104 (11.5%)
	White	537 (77.2%)	721 (79.8%)
	Multi-Racial	15 (2.2%)	24 (2.7%)
	Other	10 (1.4%)	13 (1.4%)
	Chose not to answer	31 (4.5%)	31 (3.4%)
Preferred Language			
	Spanish	41 (5.9%)	60 (6.6%)
Education			
	Less than High School	38 (5.5%)	49 (5.4%)
	High School degree or GED	151 (21.7%)	183 (20.3%)
	Some College	228 (32.8%)	335 (37.1%)
	Secondary Degree	196 (28.2%)	240 (26.6%)
	Post Secondary Degree	79 (11.4%)	94 (10.4%)
	Other/Unknown	4 (0.6%)	2 (0.2%)
Patient Age			
	1	249 (35.8%)	307 (34.0%)
	2	126 (18.1%)	172 (19.0%)
	3	104 (14.9%)	145 (16.1%)
	4	96 (13.8%)	136 (15.1%)
	5	121 (17.4%)	143 (15.8%)
Patient Sex			
	Female	327 (47.1%)	414 (45.9%)
	Male	367 (52.9%)	488 (54.1%)
Patient Diagnosis			
	Viral URI / Pharyngitis / OME	352 (50.6%)	440 (48.7%)
	Strep Throat	20 (2.9%)	16 (1.8%)
	AOM	126 (18.1%)	162 (17.9%)
	Sinusitis	2 (0.3%)	4 (0.4%)
	Pneumonia	6 (0.9%)	13 (1.4%)
	Multiple or Other Diagnosis	190 (27.3%)	268 (29.7%)

Table 3: Chi-Square Comparison of Overall and Inappropriate Antibiotic Prescribing (N = 1599)

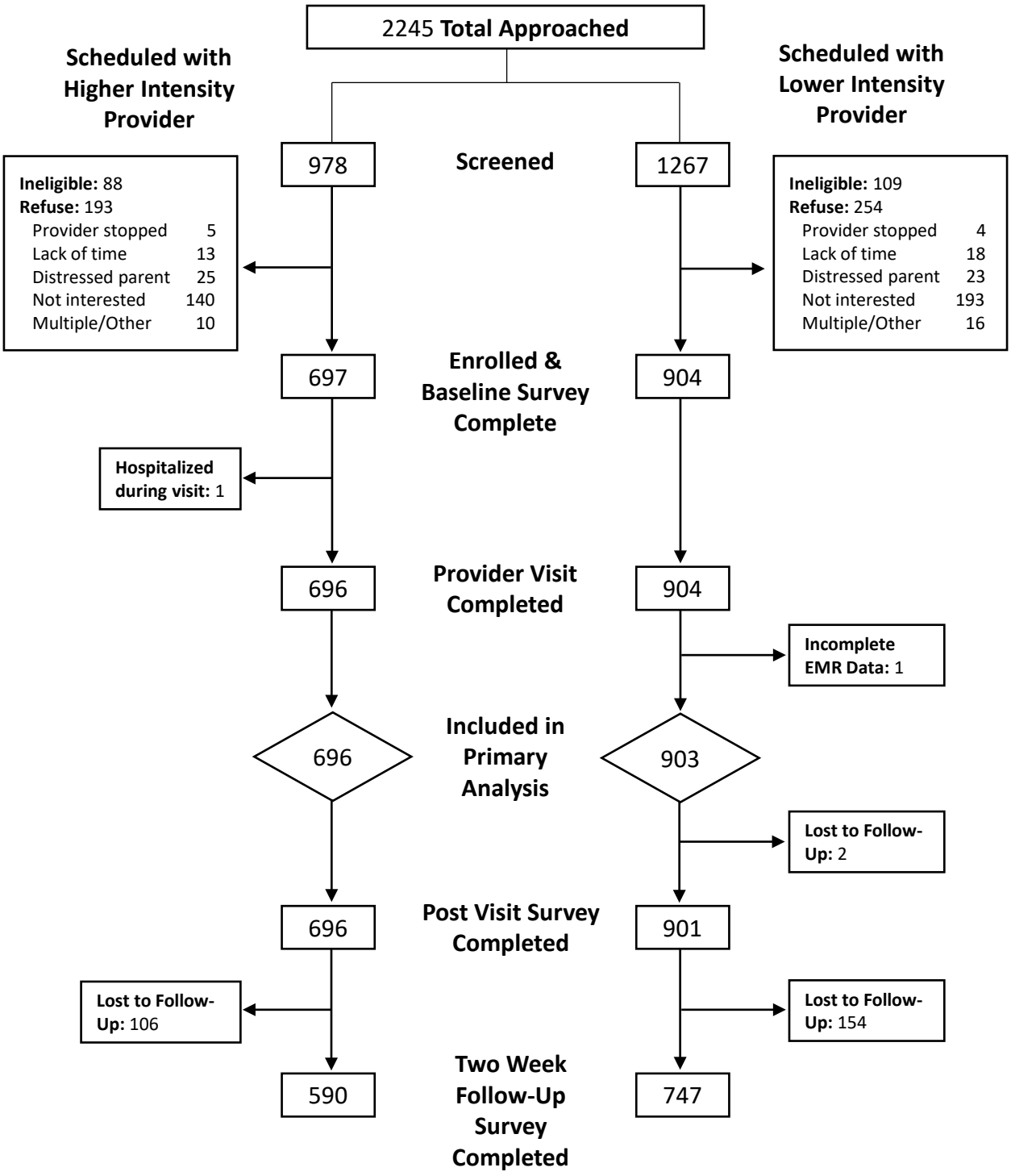
	Any Antibiotic prescribed			Inappropriate antibiotic prescribed		
	n	Freq (%)	P value	n	Freq (%)	P value
Study Arm			0.291			0.244
Higher	696	196 (28.2%)		696	54 (7.8%)	
Lower	903	233 (25.8%)		903	85 (9.4%)	
Site			0.630			0.455
Private Practice	1292	350 (27.1%)		1292	109 (8.4%)	
Academic	307	79 (25.7%)		307	30 (9.8%)	
Clinician Type			0.129			0.572
MD/DO	907	230 (25.4%)		907	82 (9.0%)	
CPNP/APRN	692	199 (28.8%)		692	57 (8.2%)	

Table 4: Odd Ratios of Receiving Inappropriate Antibiotic (N = 1599).

	UNADJUSTED				ADJUSTED [a]			
		95% CI				95% CI		
	OR	Lower	Upper	P Value	OR	Lower	Upper	P Value
Intervention Arm								
Higher Intensity (versus Lower)	1.09	0.56	2.10	0.81	0.99	0.52	1.89	0.98
Clinician type								
CPNP/APRN (versus MD/DO)	1.24	0.63	2.44	0.53	1.29	0.67	2.46	0.45
Practice Type								
Academic (versus private)	1.21	0.63	2.30	0.56	1.13	0.60	2.16	0.70
Clinician years of experience								
10+ years (versus <10 years)	1.40	0.73	2.66	0.31	1.42	0.73	2.77	0.30

[a] *Adjusting for intervention arm, clinician type, practice type, and clinician years of experience.*

Figure 1: Parent-Child Dyads Enrollment



CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	4-5
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	5
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6-9
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	9-10
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	11
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	6
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	6
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	6
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	6
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	9

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	8-9
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	9-11
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	10-11
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	11-12
	13b	For each group, losses and exclusions after randomisation, together with reasons	11-12
Recruitment	14a	Dates defining the periods of recruitment and follow-up	2,6
	14b	Why the trial ended or was stopped	11
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	11-12,Table 2
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Fig 1, Table 3
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	12-14
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	12-14
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	12-14
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	16
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	14-16
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	14-16
Other information			
Registration	23	Registration number and name of trial registry	1,3
Protocol	24	Where the full trial protocol can be accessed, if available	Ref 18
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	1, 18

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

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Let's Talk About Antibiotics: A randomized trial of two interventions to reduce antibiotic misuse

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Let's Talk About Antibiotics: A randomized trial of two interventions to reduce antibiotic misuse

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Trial Registration: NCT03037112

Abstract

Background: Children with acute respiratory tract infections (ARTIs) receive ≈11.4 million unnecessary antibiotic prescriptions annually. A noted contributor is inadequate parent–clinician communication, however efforts to reduce overprescribing have only indirectly targeted communication or been impractical.

Objectives: Compare two feasible (Higher vs Lower Intensity) interventions for enhancing parent-clinician communication on the rate of inappropriate antibiotic prescribing.

Design: Multisite, parallel group, cluster randomized comparative effectiveness trial. Data collected between March 2017 and March 2019.

Setting: Academic and private practice outpatient clinics.

Participants: Clinicians (n=41, 85% of eligible approached) and 1,599 parent-child dyads (ages 1-5 years with ARTI symptoms, 71% of eligible approached).

Interventions: All clinicians received 20-minutes ARTI diagnosis and treatment education. Higher Intensity clinicians received an additional 50-minute communication skills training. All parents viewed a 90-second antibiotic education video.

Main Outcome(s) and Measure(s): Inappropriate antibiotic treatment was assessed via blinded medical record review by study clinicians and a priori defined as prescriptions for the wrong diagnosis or use of the wrong agent. Secondary outcomes were re-visits, adverse drug reactions (both assessed two weeks after the visit) and parent ratings of provider communication, shared decision-making and visit satisfaction (assessed at end of the visit on Likert-type scales).

Results: Most clinicians completed the study (n=38, 93%), were doctors (n=25, 66%), female (n=30, 78%) and averaged 8 years in practice. All parent-child dyad provided data for the main outcome (n=855 [54%] male, n=1043 [53%] ≤2 years). Inappropriate antibiotic prescribing was

similar among patients who consulted with a Higher Intensity (54/696, 7.8%) versus a Lower Intensity (85/904, 9.4%) clinician. A generalized linear mixed effect regression model (adjusted for the 2-stage nested design, clinician type, clinic setting, and clinician experience) revealed that the odds of receiving inappropriate antibiotic treatment did not significantly vary by group (AOR=0.99, 95% CI: 0.52, 1.89, p=0.98). Secondary outcomes of revisits and adverse reactions did not vary between arms, and parent ratings of satisfaction with quality of parent-provider communication (5/5), shared decision making (9/10) and visit satisfaction (5/5) were similarly high in both arms.

Conclusions and Relevance: Rate of inappropriate prescribing was low in both arms. Clinician education coupled with parent education may be sufficient to yield low inappropriate antibiotic prescribing rates. The absence of a significant difference between groups indicates that communication principles previously thought to drive inappropriate prescribing may need to be re-examined or may not have as much of an impact in practices where prescribing has improved in recent years.

Trial Registration: NCT03037112.

Strengths and limitations of this study:

- Large number of clinicians and parent-child dyads engaged.
- Feasible interventions modeled on prior successful interventions.
- Rigorous methods conducted in real world clinical settings.
- Lack of a control group or baseline antibiotic prescribing information.

In the United States (US), most antibiotic prescribing occurs in the outpatient setting[1] where children with acute respiratory tract infections (ARTIs) receive 34 million antibiotic prescriptions annually.[2] Estimates indicate that at least 29% of these prescriptions are unnecessary.[3]

Antibiotic prescribing behavior is a complex and multifaceted process, but the communication between parents or legal guardians (hereafter referred to as parents) and clinicians is central. Clinicians cite strong parent demand as a major cause of inappropriate prescribing.[4–7] Clinicians often capitulate to this perceived pressure because they don't want parents/patients to leave "empty handed",[8–10] fear receiving poor encounter satisfaction scores from parents,[11] and/or view explaining why antibiotics are not necessary as time consuming and unrewarding.[8,9]

Efforts to reduce inappropriate antibiotic prescribing in the pediatric setting have typically taken the form of educational interventions to increase antibiotic knowledge among clinicians and/or parents, electronic decision support systems, and/or behavioral interventions informed by behavioral economics and psychological science.[12–15] Many have been successful, with those that target parent-clinician communication and simultaneously intervene on parents and clinicians evidencing the strongest results.[13] Of the communication interventions tested, only one has directly targeted clinicians' perceptions of parental expectations for antibiotics alongside antibiotic education and shared decision-making.[16] This United Kingdom based study provided intensive communication training for clinicians and a multipage patient–clinician interactive educational booklet to enhance shared decision making. Clinicians in the intervention arm demonstrated statistically and clinically significant reductions in antibiotic prescribing as

compared to control clinicians. While impactful, the intervention was viewed impractical for most real-world settings.[17]

Effective interventions that are efficacious and feasible in routine outpatient pediatric care in the United States are lacking. Using the Francis et al.[16] intervention as our model, we sought to: 1) develop a version of this efficacious intervention that would enhance parent-clinician communication while being feasible in ambulatory pediatric care, and 2) compare it to a feasible educational intervention on the rate of inappropriate antibiotic prescribing.

METHODS

STUDY OVERVIEW

This was a multisite, parallel group, cluster randomized comparative effectiveness trial conducted in two pediatric outpatient clinics, with clinicians randomized (1:1) to a Higher Intensity intervention (prescribing education and communication skills training) or a Lower Intensity intervention (prescribing education only). Parent-child dyads enrolled in the study were exposed to either intervention according to the clinician who conducting their clinic visit. We hypothesized that compared to parent-child dyads managed by clinicians randomized to the Lower Intensity intervention, parent-child dyads managed by clinicians randomized to the Higher Intensity intervention would evidence lower rates of inappropriate antibiotic prescriptions. (See protocol paper for additional details.[18]) Ethical approval was obtained from the Children's Mercy Hospital Pediatric Institutional Review Board (#16060466).

PATIENT AND PUBLIC INVOLVEMENT

In the early planning stages for this study, we conducted focus groups and individual

interviews with clinical, parent, payer and community stakeholders to assess the viability and inform the design of the study. We then recruited a Parent Research Associate who became a core member of our research team, attended all study meetings, and co-led our Community Advisory Board (CAB). Our CAB was comprised of 15 parent, provider and community stakeholders and was diverse (i.e., three males, seven Latinx [three exclusively Spanish speaking] and three African American members). CAB meetings occurred regularly throughout the study. All aspect of the study design, settings, participant burden, materials, procedures, interpretation of data and dissemination of study findings were informed by the CAB and Community Research Associate. Study results were disseminated to all clinic providers. A parent summary of findings will be provided to study sites to share with parents after this paper is published.

STUDY SETTING

The study was conducted at an academic medical facility (Children's Mercy Primary Care Clinics; CMH PCC) in Kansas City, Missouri, USA and both locations of a private practice (Heartland Primary Care; HPC) in Kansas City and Lenexa, Kansas, USA.

PARTICIPANTS

Clinicians

All clinicians at both clinics were screened for eligibility. Inclusion criteria were being a pediatrician (Medical Doctor [MD] or Doctor of Osteopathic Medicine [DO]) or nurse practitioner (Certified Pediatric Nurse Practitioner [CPNP] or Advanced Practice Registered Nurse [APRN]) and actively and independently conducting consultations with our target

population. Eligible clinicians were recruited during study orientation sessions where interested clinicians completed informed consent and were given a sealed envelope prepared by the study statistician that contained their group assignment. Clinicians were stratified by patient volume and clinic.

Parent-Child Dyads

Parent-child dyads were recruited from March 2017 to March 2019. Study staff pre-screened all potentially eligible parent-child dyads and provided a study flyer during check-in. Interested dyads were given information about the study and offered eligibility screening. If more than one caregiver was present, they were asked to designate one person who would independently complete the written informed consent and all assessments. Clinicians had no role in identifying potentially eligible dyads, screening, consenting or data collection. Clinic staff who scheduled patients' appointments were blinded to clinician randomization. Dyads were eligible if the patient was between ages 1 and 5 years, had ARTI symptoms and his/her parent was fluent in English or Spanish.[18] Children were not eligible if they had received an antibiotic in the last 30 days, had a concurrent probable bacterial non-respiratory infection, known immunocompromising conditions, complex chronic care condition,[19] required hospitalization during the visit or had previously participated in the study.

INTERVENTION COMPONENTS AND DESCRIPTION OF ARMS

Parent Video

The 90-second video used gain-framed messages[20,21] to explain when antibiotics are and are not indicated while emphasizing the risk of side effects and resistant organisms. Research has

shown that people react to the same trade-off in different ways depending on whether the possible outcomes are presented as losses or gains.[20] We tailored all parent materials to highlight the gains of not using antibiotics (e.g., staying safe from side effects) that might increase parents' comfort with not getting an antibiotic prescription for their child. The video also highlighted information that clinicians should provide (e.g., estimate of illness duration, recommendations for system relief) during a visit. The video was successful in reducing parents' interest in obtaining an antibiotic for their child, especially among those with higher baseline interest.[22]

Parent Educational Trifold Brochure

The inside of the brochure provided "gain-framed" information about when antibiotics are and are not necessary and the risks involved in taking antibiotics. The outside of the brochure included a place to write the child's first name and parent tips for communicating with clinicians. It also included check boxes for the clinician to indicate the diagnosis, if antibiotics were needed, recommended home care treatments, and expected recovery time.

Clinician General Antibiotic Education

Using didactic and interactive learning strategies, study physicians (AM, JN) provided a 20-minute, in-person general antibiotic education training on diagnosis and treatment of ARTI. The training covered pros and cons of antibiotics, impact of inappropriate use, Centers for Disease Control and Prevention antibiotic prescribing guidelines, common reasons for antibiotic misuse and viewing/discussing the 90-second parent video. Refresher trainings for all study clinicians were provided twice during the study.

Clinician Communication Skills Training

The in-person, 50-minute communication skills training provided by the study's behavioral psychologist (KG) used didactic and interactive learning strategies including viewing/discussing motivational role model videos. The goal was to enhance clinicians' skills and confidence in the use of proven parent-centered communication strategies and the parent educational trifold brochure (See protocol paper for additional details.[18]). Clinicians were also trained to consider parents' ratings of their interest in obtaining antibiotics after viewed the video.

Lower Intensity Intervention

This intervention was modeled on proven parent-focused and clinician-focused educational interventions.[e.g.,13,23] Clinicians completed the general antibiotic education described above.

In exam rooms prior to the consultation, parents who saw a clinician trained in the Lower Intensity intervention completed the baseline survey, saw the video and the inside of the parent brochure, and rated their desire for antibiotics all via a tablet computer. They did not receive a hard copy of the study brochure and their interest in an antibiotic rating was not shared with their clinician.

Higher Intensity Intervention

The higher intensity, *Let's Talk About Antib*iotics (LTAA), intervention was informed by a series of evidence-based interventions conducted in the UK and Europe,[16,24–29] Clinicians

randomized to this arm completed the general antibiotic education and communication skills training described above. Before meeting with dyads, clinicians in this arm were provided with parents' ratings of their interest in obtaining antibiotics after watching the parent video via a sticky note on the exam room door. To assess fidelity to the communication skills and check for contamination between arms, a subsample of all visits (10%) were audio recorded and objectively coded by blinded raters using established methods.[30,31]

In exam rooms prior to the consultation, parents who saw a clinician trained in the Higher Intensity intervention completed the baseline survey, saw the video and the inside of the parent brochure, rated their desire for antibiotics via a tablet computer and received a personalized (child's name written in) hard copy of the study brochure.

Strategies to Reduce the Risk Of Contamination

We employed several strategies to reduce the likelihood of contamination between study arms. Specifically, we (1) designed intervention components to not be easily transferred between clinicians (e.g., the brochure was distributed by study staff to ensure that only parents who were consulted by clinicians in the Higher Intensity arm receive them), (2) ensured that all communication (written or in person) with clinicians in the Lower Intensity arm did not reveal any of the strategies from the Higher Intensity arm, (3) reviewed the importance of keeping intervention arms distinct during clinician training and asked Higher Intensity clinicians to pledge not to share any details or materials with their colleagues randomized to the Lower Intensity arm, and (4) trained Higher Intensity arm clinicians in communication strategies for dealing with Lower Intensity arm colleagues who ask for more information.

PRIMARY OUTCOME

The primary outcome was rate of inappropriate antibiotic prescribing (i.e., number of patients receiving an inappropriate prescription / number of patients in arm). Inappropriate prescribing was assessed by blinded study physicians (AM, JN) who reviewed the medical record documentation for each patient. Prescriptions were considered inappropriate if they were, prescribed: (1) for a viral ARTI, (2) for a presumed bacterial ARTI that does not meet Table 1 criteria, (3) broad-spectrum antibiotic for a bacterial ARTI in a child without a penicillin allergy, or (4) non-recommended alternative antibiotic for a bacterial ARTI (see Table 1) in a child with a penicillin allergy.

Table 1: Diagnostic Criteria for Bacterial Acute Respiratory Tract Infections (ARTIs) and Appropriate Antibiotic Selection

Bacterial ARTI	Diagnostic Criteria	Primary Antibiotic	Secondary Antibiotics for Penicillin Allergy
Acute Otitis Media (either criteria)	1. Fever ≥38.3°C (101°F) with either a or b: a. Moderate to severe bulging of tympanic membrane on exam, or b. Mild bulging of TM and recent (<48hrs) onset of ear pain 2. New onset of otorrhea not due to acute otitis externa	amoxicillin	cefdinir, cefpodoxime, ceftriaxone, cefuroxime, clindamycin
Sinusitis (any of the 3 criteria)	1. Daytime cough or nasal discharge for greater than 10 days 2. High fever (>39°C) with purulent nasal discharge or facial pain lasting 3 consecutive days at the beginning of the illness 3. Worsening signs or symptoms characterized by the new onset of fever, headache, or increase in nasal discharge following a typical viral URI	amoxicillin	cefdinir, cefpodoxime, cefuroxime, clindamycin
Community acquired Pneumonia (either	1. Fever, tachypnea, and focal findings on pulmonary exam 2. a) Fever, b) Tachypnea, cough, or retractions AND c) Chest radiograph	amoxicillin	cefpodoxime, cefprozil, cefuroxime,

criteria)	consistent with a focal consolidation		clindamycin
Streptococcal pharyngitis (both criteria)	1. Fever, pharyngitis, & positive rapid streptococcal antigen test or culture 2. Lack of viral signs and symptoms	amoxicillin	cephalexin (preferred unless previous type I hypersensitivity reaction to penicillin) clindamycin, azithromycin

To guard against the potential for clinicians to use diagnostic codes to support their antibiotic prescribing,[7] study physicians reviewed detailed symptoms, physical examination findings and diagnostic tests to assess the appropriateness of the patient's diagnosis. Ten percent of all chart reviews were verified by the other study physician blinded to the initial coding, inconsistencies were reconciled.

SECONDARY OUTCOMES

Data on revisits and adverse drug reactions were collected via follow-up phone calls with parents two weeks after the visit. Revisits were assessed by asking parents if they sought any additional treatment for their child for the same symptoms or complications from any treatment provided in the initial visit. Side effects and adverse drug reactions were assessed if antibiotics were prescribed.

Shared-decision-making was assessed immediately following the visit using an adapted version of the three-item CollaboRATE questionnaire.[32] Parents rated "How much effort was made to: (1) help you understand your child's health issue?"; (2) listen to the things that matter most to you about your child's health issues?"; and (3) include what matters most to you in choosing what to do next?" on a 10-point response scale ranging from "no effort was made" to "every effort was made." The scale's psychometric properties have been established.[33]

Quality of parent-clinician communication was assessed immediately following the visit with the question, "How satisfied were you with the communication between you and your child's healthcare clinician?" Overall visit satisfaction was assessed with the question, "Overall, how satisfied were you with the visit?" Both items were scored on a five-point scale ranging from "very dissatisfied" to "very satisfied."

ANALYSES

All analyses were conducted using an intent-to-treat strategy. We constructed a 2-stage nested design, with parents nested within clinicians (Level-1 units) and study site (Level-2 units) generalized linear mixed-effect regression models (GLMM) to assess the impact of intervention type on our primary outcome of inappropriate antibiotic prescribing using Stata.[34] Alternative covariance structures were investigated, but as hypothesized, the exchangeable structure was sufficient. We employed robust standard errors to help minimize misspecification and examine time as a potential random effect. We examined the effects of the potential prespecified covariates on the outcomes with the goal of identifying the most parsimonious final models and we explored the heterogeneity of treatment effect. Variables considered included: clinic, clinician type, years of experience, patient age and sex, parent education level, race/ethnicity, preferred language, relationship to patient and insurance type. We created a binary indicator for each variable and included each as an interaction term in separate regression model. We examined these interaction terms across intervention arms and explored within-arm differential trends in our primary and secondary outcomes over time.

SAMPLE SIZE CALCULATION AND POWER

Prior research examining our primary outcome showed 30% of the antibiotics prescribed in the outpatient ARTI visits were inappropriate.[3,35] Prior intervention studies produced 20%–81% reductions in inappropriate prescribing.[36,37] Based on the intraclass correlation coefficient (ICC) observed in the Meeker et al. study,[37] we assume an ICC of .04. With 40 clinicians, α of .05 and 80% power, we estimated that a sample size of 760 per arm would be needed to detect a 9% difference between arms. Allowing for an attrition rate of 5%, we aimed to recruit 1600 participants to ensure adequate power.

RESULTS

Clinicians

All clinicians at both sites (N = 51) were voluntarily screened for eligibility; five were ineligible, four failed to respond after multiple contacts and one declined to enroll in the study. All 41 clinicians enrolled [22 (54%) randomized to the Higher Intensity arm; 19 (46%) randomized to Lower Intensity arm] conducted clinic visits with enrolled participants. Three clinicians (all in the Higher Intensity arm) left their practices during the study leaving 38 clinicians who all completed the follow-up survey and interview. Most clinicians were female (n=30, 78%) and MD/DO physicians (n=25, 66%) with 8 median years in practice (IQR 4,14; range 1-40). Clinician demographics were similar across arms and between those who did and did not participate in the study.

Parent-Child Dyads

Figure 1 illustrates the flow of parent-child dyads from pre-screening through the two-week follow-up visit. Table 2 displays demographics for the 1599 dyads included in the primary

Table 2: Parent and Patient Demographics (N = 1599)

		Higher Intensity	Lower Intensity
Gender of Parent			
	Female	584 (83.9%)	764 (84.6%)
Ethnicity of Parent			
	Hispanic	129 (18.5%)	171 (18.9%)
Race of Parent			
	Asian	13 (1.9%)	10 (1.1%)
	Black	90 (12.9%)	104 (11.5%)
	White	537 (77.2%)	721 (79.8%)
	Multi-Racial	15 (2.2%)	24 (2.7%)
	Other	10 (1.4%)	13 (1.4%)
	Chose not to answer	31 (4.5%)	31 (3.4%)
Preferred Language			
	Spanish	41 (5.9%)	60 (6.6%)
Education			
	Less than High School	38 (5.5%)	49 (5.4%)
	High School degree or GED	151 (21.7%)	183 (20.3%)
	Some College	228 (32.8%)	335 (37.1%)
	Secondary Degree	196 (28.2%)	240 (26.6%)
	Post Secondary Degree	79 (11.4%)	94 (10.4%)
	Other/Unknown	4 (0.6%)	2 (0.2%)
Patient Age			
	1	249 (35.8%)	307 (34.0%)
	2	126 (18.1%)	172 (19.0%)
	3	104 (14.9%)	145 (16.1%)
	4	96 (13.8%)	136 (15.1%)
	5	121 (17.4%)	143 (15.8%)
Patient Sex			
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Patient Diagnosis			
	Viral URI / Pharyngitis / OME	352 (50.6%)	440 (48.7%)
	Strep Throat	20 (2.9%)	16 (1.8%)
	AOM	126 (18.1%)	162 (17.9%)
	Sinusitis	2 (0.3%)	4 (0.4%)
	Pneumonia	6 (0.9%)	13 (1.4%)
	Multiple or Other Diagnosis	190 (27.3%)	268 (29.7%)

analysis. Demographic characteristics of parents and children were similar among those exposed to the Higher or Lower Intensity intervention. Spanish speaking parents and those who had more

education were more likely to complete the two-week assessment, no other differences were observed. Missing survey responses were rare overall (<1% for all variables) and did not exhibit any systematic patterns so we did not impute values.

Fidelity Assessment

Analysis of 141 visit audio recordings confirmed a similar mean duration of visits (Higher = 11.7 vs. Lower = 10.2 minutes) and no evidence of contamination between arms. Compared to Lower Intensity clinicians, Higher Intensity clinicians consistently delivered more of the communication content they were taught in training and no Higher Intensity materials were used in sessions conducted by Lower Intensity clinicians .

Primary Outcome: Inappropriate Antibiotic Prescribing

A total of 429 (26.8%) patients received an antibiotic prescription with 139 (32.4%) meeting criteria for being inappropriate (Table 3). The most common reasons for an antibiotic to be considered inappropriate were being prescribed for a presumed bacterial ARTI that did not meet diagnostic criteria (n=109; 78.4%) and prescribing a broad-spectrum antibiotic for a child without a penicillin allergy (n=24; 17.3%). The rate of inappropriate prescriptions among all enrolled patients in each arm was similar among Higher Intensity (54 of 696; 7.8%) and Lower

Table 3: Chi-Square Comparison of Overall & Inappropriate Antibiotic Prescribing (N = 1599).

	Any Antibiotic prescribed			Inappropriate antibiotic prescribed		
	n	Freq (%)	P value	n	Freq (%)	P value
Study Arm			0.291			0.244
Higher	696	196 (28.2%)		696	54 (7.8%)	
Lower	903	233 (25.8%)		903	85 (9.4%)	
Site			0.630			0.455
Private Practice	1292	350 (27.1%)		1292	109 (8.4%)	
Academic	307	79 (25.7%)		307	30 (9.8%)	
Clinician Type			0.129			0.572
MD/DO	907	230 (25.4%)		907	82 (9.0%)	
CPNP/APRN	692	199 (28.8%)		692	57 (8.2%)	

Intensity (85 of 903; 9.4%) clinicians. Inappropriate antibiotic prescribing also did not vary significantly based on study site or clinician type. In the unadjusted GLMM, we found that the odds of receiving inappropriate antibiotic treatment for the Higher Intensity arm did not vary significantly when compared to the Lower Intensity arm (odds ratio [OR] = 1.09; 95% confidence interval [CI]: 0.56, 2.10; ICC = 0.11; Table 4).

[a] *Adjusting for intervention arm, clinician type, practice type, and clinician years of experience.*

Table 4: Odd Ratios of Receiving Inappropriate Antibiotic (N = 1599).

	UNADJUSTED				ADJUSTED [a]			
		95% CI				95% CI		
	OR	Lower	Upper	P Value	OR	Lower	Upper	P Value
Intervention Arm								
Higher Intensity (versus Lower)	1.09	0.56	2.10	0.81	0.99	0.52	1.89	0.98
Clinician type								
CPNP/APRN (versus MD/DO)	1.24	0.63	2.44	0.53	1.29	0.67	2.46	0.45
Practice Type								
Academic (versus private)	1.21	0.63	2.30	0.56	1.13	0.60	2.16	0.70
Clinician years of experience								
10+ years (versus <10 years)	1.40	0.73	2.66	0.31	1.42	0.73	2.77	0.30

Heterogeneity of Treatment Effect

After adjusting for clinician type, clinic setting, and clinician experience there was still no significant intervention effect (AOR = 0.99; 95% CI: 0.52, 1.89). However, the interaction of the treatment arm and clinician type was significant in the adjusted GLMM model (AOR = 0.12; 95%: 0.04, 0.37; see Supplemental Table 1). Specifically, the MD/DO clinicians in the Higher Intensity intervention were less likely to prescribe an inappropriate antibiotic than MD/DO clinicians in the Lower Intensity intervention arm. The reverse was true for the CPNP/APRN clinicians. No interaction between intervention and gender or location was observed. No

interaction between treatment and any of the parent-patient dyad variables (i.e., patient age or sex, parent education level, race/ethnicity, preferred language, relationship to patient or insurance type) was observed.

Secondary Outcomes

Revisits and Adverse Drug Reactions: Approximately 12% of patients had a return visit within two weeks of their index visit. The rate of revisits did not vary between patients seen by Higher or Lower Intensity clinicians (12.2% vs. 11.9%, p = 0.879). Adverse reactions to the prescribed antibiotic were similar across arms (16.5% vs. 12.8%, p = 0.27). (Antibiotic prescription rates for different ARTI diagnoses are presented by arm in Supplemental Table 2.)

Shared Decision-Making: Parents' CollaboRATE ratings were extremely high overall (likely evidencing a ceiling effect) and similar across Higher and Lower Intensity arms (median 9.0 [IQR: 8.7, 9.0] vs. 9.0 [IQR: 8.3, 9.0], p = 0.85).

Quality of Parent–Clinician Communication and Visit Satisfaction: Parent rated satisfaction with their clinician's communication during the visit (median 5 [IQR: 5, 5] vs. 5 [IQR: 5, 5], p = 0.20) and their overall visit satisfaction (median 5 [IQR: 5, 5] vs. 5 [IQR: 5, 5], p = 0.38) were also very high overall and similar between arms.

Clinician Satisfaction and Feasibility

Most clinicians (84%) reported being "very satisfied" with the program, thought it would be "very" (71%) effective in reducing inappropriate prescribing and all would recommend it to other clinicians.

Parent Satisfaction

The majority of parents who completed the two-week follow-up survey (N=1337) reported being "very" (92%) satisfied with the program and 93% reported that they would recommend it to others.

DISCUSSION

This randomized comparative effectiveness trial comparing two feasible interventions for enhancing parent-clinician communication found no evidence of a difference in inappropriate antibiotic prescriptions. Inappropriate antibiotic prescribing was lower than recently published estimates of inappropriate prescribing in the US Midwest (14.3%),[38] which have been on the decline especially among pediatricians.[39] Nevertheless, it was still higher than findings from other successful intervention studies (rates from 1.5% - 3.9%).[15,40] In the main outcome analysis, the odds of receiving an inappropriate antibiotic did not vary significantly between the Higher and Lower Intensity arms, even after adjusting for clinician type, clinic setting, and clinician experience.

Secondary outcomes of revisits and adverse reactions did not vary between patients seen by Higher or Lower Intensity clinicians. These findings indicate that there is no evidence that one of the interventions presented a greater risk to patients than the other. Parent ratings of shared decision making, satisfaction with quality of parent-clinician communication and visit satisfaction were all very high and similar between arms. Ceiling effects on the measures were apparent and likely reduced our ability to observe any true differences between arms. Nevertheless, these findings indicate that both interventions were highly satisfactory to parents.

In this study, Higher Intensity MD/DO clinicians were significantly less likely to prescribe inappropriate antibiotics than their MD/DO counterparts in the Lower Intensity arm. The reverse was true for the CPNP/APRN clinicians. The reasons for this difference among MD/DO clinicians are unclear and we likely have too few CPNP/APRN clinicians to draw any

definitive conclusions about this subgroup, but there is data to support the notion that CPNP/APRN are simply more likely to adhere to guidelines[41] so the educational training provided in both arms was likely sufficient to ensure similar low rates of inappropriate prescribing among CPNP/APRNs. Future studies should continue to explore difference in response to intervention between different types of clinicians.

The lack of a statistically significant or clinically meaningful main effect may indicate that shared decision-making and the other communication factors targeted by the Higher Intensity intervention were not as strongly related to inappropriate prescribing as had been expected. This may indicate a cultural shift in parental expectations and/or clinician comfort in withholding unnecessary antibiotics, challenging the relevance of early literature to the social and communication dynamics at play today. It may be that the antibiotic education training for clinicians in both arms and study video that significantly reduced parents' desires for an antibiotic[22] might have been enough to make a meaningful impact on prescribing. Other recent studies have found success focusing on clinician education about appropriate antibiotic prescribing and the effects of peer comparison.[37,40] Clinician education interventions may be sufficient to yield long-term benefits, as parental expectations for antibiotics continue to decrease from an overall cultural shift or from exposure to a high-quality parent education video like the one used in this study.

LIMITATIONS

The overall low rate of inappropriate antibiotic prescribing across interventions and sites is encouraging, but our design did not allow us to draw conclusions about the role of either intervention in these lower rates compared to usual care. Future studies should target settings

with high rates of inappropriate prescribing. Higher Intensity intervention clinicians may not have been given a sufficient "dose" of the training. Lack of a control group or baseline antibiotic prescribing information limits our ability to understand how the rates of inappropriate prescribing we observed in the two intervention arms differs from usual practice at the study sites.

CONCLUSION

Implementing evidence-based clinician and parent interventions to improve antibiotic prescribing can be acceptable to clinicians and parents and feasible in both academic and private pediatric outpatient settings. Clinician education coupled with high-quality parent education delivered via video may be sufficient to yield low inappropriate antibiotic prescribing rates.

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Author Contributions

Dr. Goggin conceptualized, designed and oversaw the study, designed and implemented the parent education and clinician communication training, designed and directed all study procedures and materials, directed the data analysis and interpretation of results, drafted the initial manuscript, and reviewed and revised the manuscript.

Dr. Hurley contributed to the design of the study, facilitated recruitment, intervention delivery and data collection, contributed to data analysis and interpretation of results, led qualitative data analysis and interpretation of results, drafted sections of the initial manuscript, and critically reviewed the manuscript for important intellectual content.

Dr. Lee contributed to the design of the study, conducted the data analysis, contributed to the interpretation of results, drafted sections of the initial manuscript, and critically reviewed the manuscript for important intellectual content.

Ms. Bradley-Ewing and Ms. Bickford contributed to the design of all aspects of the study, co-led the engagement with the Community Advisory Board and critically reviewed the manuscript for important intellectual content.

Ms. Pina, and Ms. Donis De Miranda contributed to the design study procedures, conducted recruitment and data collection, conducted the analysis and interpretation of qualitative results, drafted sections of the initial manuscript, and critically reviewed the manuscript for important intellectual content.

Drs. Yu, Weltmer, Linnemayr, and Butler contributed to the design of the study and critically reviewed the manuscript for important intellectual content.

Drs. Newland and Myers designed the study, designed and implemented the ARTI diagnosis and treatment training, conducted the blind review of the EMR, and critically reviewed the manuscript for important intellectual content.

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Figure 1: Parent-child Dyads Enrollment

Competing Interest Statement: The authors have no conflicts of interest relevant to this article to disclose.

Data Sharing Statement: Deidentified data limited to visit-based inappropriate prescribing rates, patient characteristics, and dummy variables for clinic site will be shared. No protected health information will be shared. Data will be provided as a comma-separated values file with a data dictionary defining all variables included in the file and will be transferred via a secure file transfer protocol after establishing a data use agreement. No additional data or codes will be made available. The data will be made available after publication of the primary studies to researchers who provide a detailed methodologically sound proposal. Proposals should be submitted to Dr. Goggin (kgoggin@cmh.edu).

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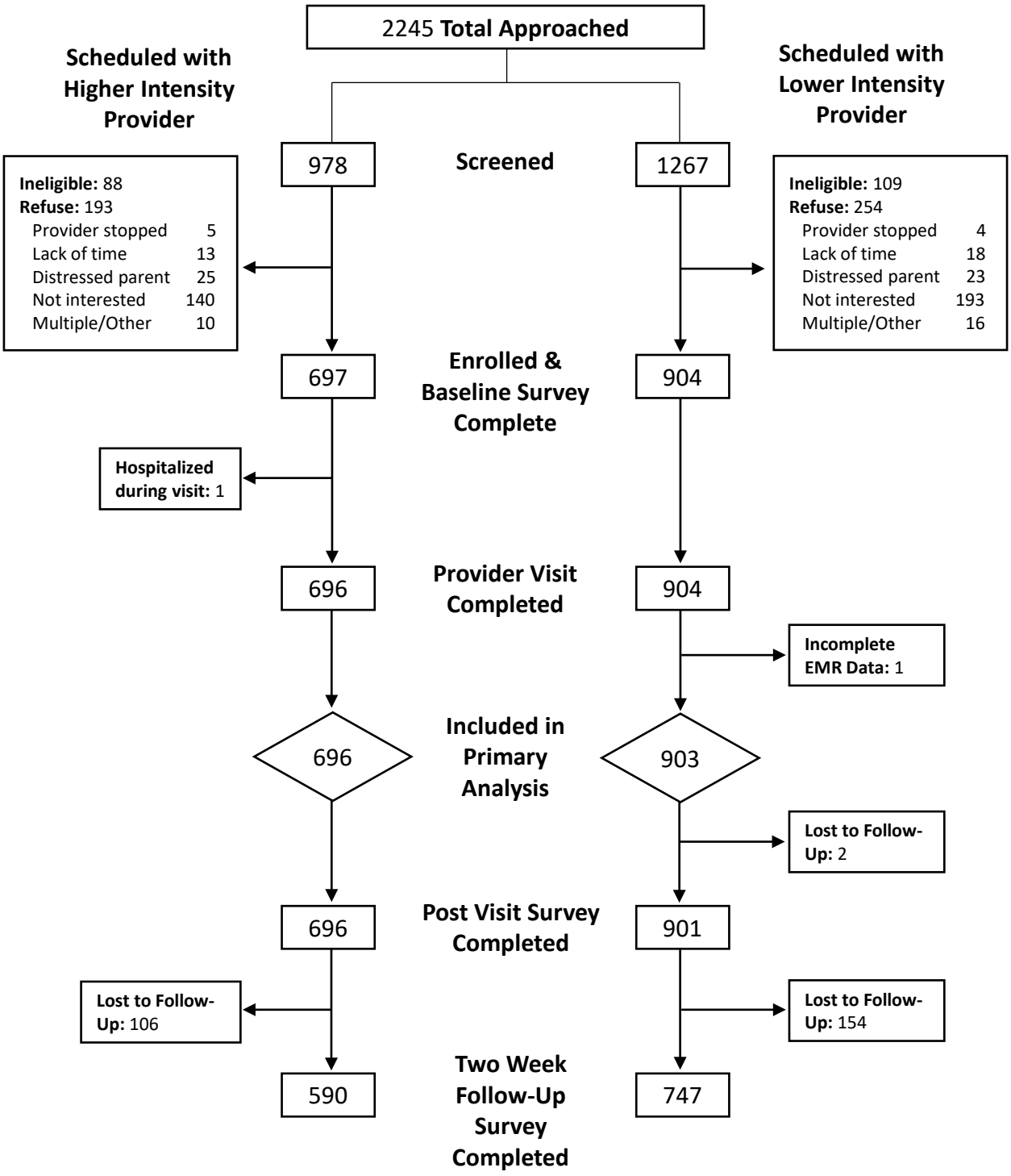
Figure 1: Parent-Child Dyads Enrollment



Supplemental Table 1: Regression Analyses of Treatment Arm Interaction.

	UNADJUSTED				ADJUSTED			
			95% Confidence Interval				95% Confidence Interval	
Treatment Arm Interaction Term	**OR**	**p-value**	**Lower**	**Upper**	**OR**	**p-value**	**Lower**	**Upper**
Site (ref= private practice)	1.73	0.404	0.48	6.25	1.87	0.325	0.54	6.53
Clinical type (ref= CPNP/APRN)	0.13	0.001	0.04	0.44	0.12	<0.001	0.04	0.37
Clinical years of experience (ref= <10 years)	0.61	0.462	0.16	2.27	0.66	0.543	0.18	2.49
Parent preferred language (ref= English)	1.09	0.906	0.25	4.89	1.13	0.871	0.25	5.03

Supplemental Table 2: Antibiotic Prescription Rates for Different ARTI Diagnoses by Arm.

	Lower Intensity			Higher Intensity		
	Denom	Treated	% Treated	Denom	Treated	% Treated
Provider Diagnosis						
Viral URI	376	4	1.1%	317	0	0.0%
Pharyngitis	51	5	9.8%	26	1	3.8%
Strep Throat	16	16	100.0%	20	17	85.0%
AOM	162	157	96.9%	126	125	99.2%
OME	13	0	0.0%	9	3	33.3%
Sinusitis	4	4	100.0%	2	2	100.0%
Pneumonia	14	14	100.0%	6	6	100.0%
2+ Diagnoses	58	33	56.9%	68	40	58.8%
Other Dx	210	1	0.5%	122	2	1.6%
	904	234	25.9%	696	196	28.2%

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	4-5
	2b	Specific objectives or hypotheses	5
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	5
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	N/A
Participants	4a	Eligibility criteria for participants	6
	4b	Settings and locations where the data were collected	5
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	6-9
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	9-10
	6b	Any changes to trial outcomes after the trial commenced, with reasons	N/A
Sample size	7a	How sample size was determined	11
	7b	When applicable, explanation of any interim analyses and stopping guidelines	N/A
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	6
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	6
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	6
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	6
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those	9

		assessing outcomes) and how	
	11b	If relevant, description of the similarity of interventions	8-9
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	9-11
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	10-11
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	11-12
	13b	For each group, losses and exclusions after randomisation, together with reasons	11-12
Recruitment	14a	Dates defining the periods of recruitment and follow-up	2,6
	14b	Why the trial ended or was stopped	11
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	11-12,Table 2
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	Fig 1, Table 3
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	12-14
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	12-14
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	12-14
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	N/A
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	16
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	14-16
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	14-16
Other information			
Registration	23	Registration number and name of trial registry	1,3
Protocol	24	Where the full trial protocol can be accessed, if available	Ref 18
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	1, 18

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.