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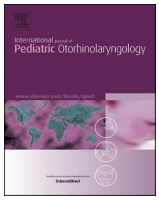

Clinical utility of an optical coherence tomography middle ear scope: Interim results of the modification of antibiotic treatment intervention in children (OTO-MATIC) pragmatic cluster randomized controlled trial (RCT)

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ABSTRACT

Objectives: To evaluate the impact of a novel Optical Coherence Tomography (OCT) otoscope on the number of antibiotic prescriptions written for pediatric patients presenting to a primary care office with ear-related complaints, compared to the Standard of Care (SOC), a traditional otoscope.

Study Design: Planned interim analysis of the One Year OTO-MATIC Randomized Controlled Trial (RCT), multicenter, real-world effectiveness study. Pediatric patients presenting with ear-related complaints were seen by a provider previously randomized into the SOC or Intervention arm. The primary outcome was reduced antibiotic prescriptions (clinician rate and number of rounds per patient) for Intervention participants compared to the SOC participants. Secondary outcomes included changes in treatment recommendations at Baseline Visit (BV), including singular versus multimodal treatments, and referrals to an otolaryngologist, specifically.

Results: At the time of the interim database lock, there were 248 participants enrolled across four sites and 16 providers who had completed the BV. Our results demonstrate that the OCT intervention reduced the odds of antibiotic prescribing by 50 % compared to the SOC (OR = 0.50, 95 % CI: 0.45–0.56). Additionally, providers in the Intervention group were significantly more likely to initiate a single therapeutic modality versus multiple, often disparate modalities (91.6 % vs. 73.8 %, $p < 0.001$, respectively).

Conclusions: Interim results suggest the OCT imaging technology (OtoSight, PhotoniCare) improves antibiotic stewardship with clinicians in the OCT arm having a reduced likelihood of prescribing antibiotics compared to the SOC arm. Overall, changes in provider prescribing patterns and therapeutic management of the patient are consistent with increased diagnostic certainty.

1. Introduction

Otitis media (OM) is one of the most common diagnoses in younger children worldwide and is the most common indication for antibiotic prescribing in children in the United States [1]. OM is characterized by viral or bacterial infection and inflammation in the middle ear. This infection results in accumulation of fluid known as Middle Ear Effusion (MEE), which can negatively impact hearing function if not effectively resolved. OM is classified based upon the severity, onset, duration, and infectious etiology. The main types of OM include: Acute OM (AOM), OM with effusion (OME), recurrent AOM (rAOM), Chronic OME (COME), or Chronic Suppurative OM (CSOM).

OM is a clinical diagnosis informed by symptoms reported and subjective signs found on physical examination (otoscopy), primarily the presence of MEE. The type of OM informs treatment recommendations. The accurate diagnosis of the presence, type, and duration of MEE is critical to the management of OM but is difficult to accurately detect and characterize in practice. Traditional otoscopy remains the gold standard

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for evaluation of OM, despite its notably low diagnostic accuracy in detecting and characterizing fluid, often hovering around 50 % in frontline providers [2].

The overuse of antibiotics has significant consequences to both children's health and public health in the US and worldwide [3], including antibiotic-resistant infections and changes in the microbiome that may place children at risk for future autoimmune diseases [4]. Antibiotic stewardship emphasizes the importance of diagnostic accuracy in order to promote the judicious prescription of antibiotics by providers and combat antibiotic resistance [5]. In the frontline care diagnosis and management of pediatric ear-related complaints, distinguishing between acute otitis media (AOM) and otitis media with effusion (OME) is critical for ensuring appropriate treatment and avoiding unnecessary antibiotic use. Proper characterization of MEE is essential, as AOM involves an active bacterial or viral infection, often with purulent effusion requiring antibiotics, whereas OME is typically a sterile fluid accumulation (or at least a fluid with only viral pathogens) that resolves without antibiotics. Misdiagnosis is common, with studies showing that even experienced clinicians may struggle to differentiate between these conditions based on otoscopic examination alone [6].

The American Academy of Pediatrics (AAP) identifies the presence of fluid as a primary criterion for diagnosing specific types of OM that warrant antibiotic treatment. However, the AAP also considers additional clinical signs, symptoms, and external factors, such as caregiver preference, in determining the appropriate use of antibiotics [7]. Optical Coherence Tomography (OCT) is a near-infrared imaging technique utilized by the OtoSight Middle Ear Scope (PhotoniCare, FDA-cleared Class II device as of 09/26/22; commercially available, see https://photoni.care/for more information). The OtoSight device uses both video and OCT technology to look at, and beyond, the tympanic membrane (see Fig. 1). When fluid is present, the OtoSight device can assess the density of MEE using Low-Coherence Interferometry, a non-scanning implementation of OCT, while also visualizing the ear canal and tympanic membrane in 2D and 3D [8]. With this technology, the OtoSight device can identify the presence and type of fluid with over 90.2 % and 80.1 % specificity respectively [9]. OCT technology has been proven to enhance diagnostic accuracy in past studies [9,10]. However, real-world evidence on how OCT technology impacts clinician behavior and therapeutic decision-making is lacking. This study investigates the device's impact on antibiotic prescribing patterns versus the Standard of Care (SOC), addressing an important knowledge gap in the literature.

2. Methods

2.1. Study design

The OTO-MATIC study is a pragmatic real-world, cluster-randomized controlled trial (RCT) investigating the effectiveness of OCT in the frontline diagnoses and management of pediatric OM. Pragmatic trials combine real-world evidence with randomization to evaluate interventions in real-world settings, prioritizing generalizability and applicability by using broad inclusion criteria, flexible protocols, and routine clinical practices. In contrast, traditional randomized controlled trials (RCTs) focus on internal validity, often employing strict eligibility criteria, highly controlled environments, and standardized interventions to minimize bias. In addition, pragmatic clinical trials emphasize research questions that are important to decision makers such as providers, patients, payers and policymakers, including investigation of the clinical and non-clinical effectiveness of new diagnostic and therapeutic tools across multiple real-world settings [11]. Cluster randomization was chosen to reduce contamination and Hawthorne bias by assigning providers, rather than participants, to intervention or SOC, preventing behavioral changes from a provider switching between interventions throughout the trial. The protocol was reviewed and approved by a centralized International Review Board (IRB), as well as local IRBs for specific sites when required. This study is registered on ClinicalTrials.

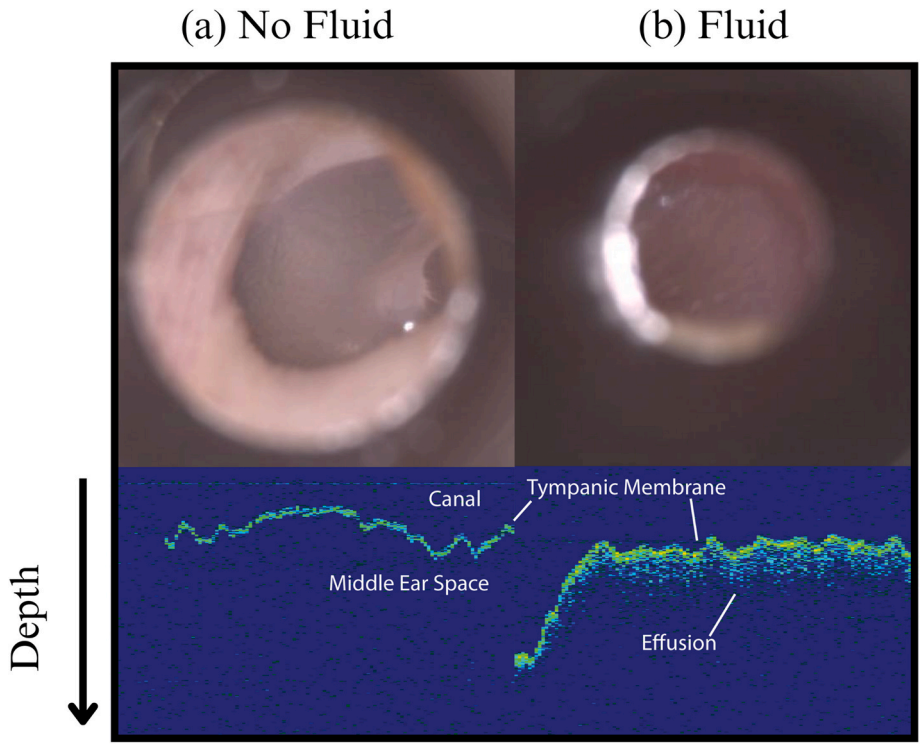

Fig. 1. Optical Coherence Tomography (OCT) imaging of the middle ear under different conditions. (a) No-fluid case, imaged using a standard speculum tip, showing a clear middle ear space. (b) Fluid-present case, imaged using a pediatric speculum tip, revealing a hyperreflective effusion behind the tympanic membrane. The lower panel illustrates the corresponding OCT depth profiles, with labeled structures including the ear canal, tympanic membrane, and middle ear space. The presence of effusion is evident in the fluid-filled case.

gov (NCT06285812).

2.2. Sites

Sites were recruited through both existing relationships and new investigator outreach. Multiple institutions expressed interest and were considered to participate in the study, and all interested institutions completed a feasibility assessment. The feasibility assessment included relevant study questions such as type of facility, location of facility, number of pediatric patients seen, and research capabilities. A variety of healthcare settings act as the frontline caregivers for children presenting with ear-related complaints (i.e., primary care, Ear, Nose, and Throat (ENT) specialists, urgent care facilities), which was a requirement to participate in this study. In alignment with pragmatic RCTs, a variety of different types of institutions were contracted. Based on the assessment answers, some sites were deemed as ineligible or not a good fit for the study. Eligible sites were contracted to participate in the study.

There were five healthcare sites in the United States included in the study, although only four of the five sites are included in this analysis due to the timing of the database lock and data availability. Each site contributed the following number of participants to this analysis: Site 1 = 20 participants, Site 2 = 56 participants, Site 3 = 80 participants, and Site 4 = 92 participants.

2.3. Participants

Pediatric patients between the ages of 6 months and 17 years and 364 days were eligible for the study based on the following inclusion criteria: (1) pediatric participants who (2) presented for an office visit with ear-related complaint potentially indicative of OME or AOM (i.e., otalgia, hearing difficulty, speech development delay, disequilibrium, signs of infection such as fever or discharge, or prodromal upper respiratory tract illness) and (3) whose parents or legally responsible guardians signed an informed consent. Pediatric participants who met any of the following exclusion criteria were not enrolled: (1) participants whose parent/guardian did not speak the language of their clinician; (2) participants who were enrolled in another clinical trial; (3) participants with signs of severe chronic illness (e.g., immunodeficiencies, congenital heart disease, encephalopathies, pulmonary diseases other than asthma, and any other anatomical disorders of the ear, nose and throat that would affect their ability to undergo an otoscopy exam. The requirement for the language of the patient and provider to match was established to minimize the risk of information bias; that is, to ensure clear communication, minimizing the risk of misinterpretation that could lead to discord between the provider's assessment, recommended treatment, and the patient's compliance and follow-up care. Before seeing patients, facility-employed researchers would screen the visit schedule of study providers to identify potentially eligible patients based on the age criteria and reason for visit. At the time of the visits for potentially eligible patients, the researchers would approach patients and their legally authorized representatives (LAR) to assess their interest in participating in the study. If interested in participating in the study, patients and/or LARs were provided with either written or verbal informed consent. Patients with the ability to give assent completed written or verbal assent./. Eligible and interested patients were enrolled in the study by trained site staff.

2.4. Randomization

This pragmatic study randomized providers rather than patients to reflect real-world clinical settings. Prior to participant enrollment, each study provider was randomized into either the SOC or Intervention group by research personnel. For sites with two study providers, one provider was randomized into each group (SOC group and OCT group). When sites had more than 2 study providers, clusters were randomized using a stratified randomization approach to ensure balance across key characteristics. Within each stratum, a random number sequence was used to randomize clusters as 1's (Intervention) or 2's (SOC). Randomizing providers instead of patients was done to reduce contamination in the usual practice group by preventing providers from switching between intervention and usual care practices. Additionally, providers could not "choose" which participants received the intervention vs SOC, which would introduce risk of selection bias. The consort diagram for the RCT can be found in Fig. 2. Enrollment began when the first site was onboarded in January 2024 and was ongoing at the time of this analysis because the enrollment goal had not yet been met.

2.5. Intervention

Otoscopic assessments were performed at the sites for both the SOC and Intervention groups at the Baseline Visit (BV). The SOC group's otoscopic assessment was performed using a traditional otoscope, following best practice guidelines. The Intervention group's otoscopic assessments were performed by trained providers using the OCT device, with exam data stored in a secure cloud database. The presence of fluid, either bilaterally or unilaterally, was recorded for each group (SOC and OCT). All providers, regardless of study arm, received standardized training on best practices for otoscopic assessment, the interpretation of otoscopic findings, and national prescribing guidelines for otitis media, including antibiotic stewardship principles. This training ensured that both SOC and OCT providers were equally informed about evidence-based treatment recommendations and the role of MEE in clinical decision-making. For providers in the Intervention group, additional in-person or remote training sessions were conducted on OCT device operation and result interpretation. Company representatives were always available to answer questions and to provide assistance with device-related concerns.

2.6. Outcomes and other variables

Assessments were conducted at the BV for all outcomes. Assessments include the otoscopic assessments as well as the completion of various case report forms (CRFs). CRFs completed at the BV include Demographics & Medical History CRF, Ear Exam CRF, Encounter Related CRF, and the Otitis Media Outcomes-22 (OMO-22). These CRFs gather information relating to subjects' medical history (Demographics & Medical History CRF), clinical findings from the ear exam (Ear Exam CRF), diagnoses such as the presence of fluid (Ear Exam CRF), diagnoses (Ear Exam CRF), recommended treatment (Encounter Related CRF), and quality of life (OMO-22). Longer term follow-up is underway and will include in-person visits and remote 6-month and 12-month follow-up visits. While some data on in-person follow up visits were collected at the time of the database lock, there was not enough to produce significant results at the time of database lock. All outcome data was collected electronically and securely transferred to an electronic database capture (EDC) for storage and management. Data integrity was ensured through systematic review and verification by a Senior Clinical Research Manager. Important variables in the causal pathway were included in analyses, including the presence of fluid in one or both ears; baseline provider attitudes and behaviors around antibiotic prescribing; provider rates of recommending watchful waiting as well as other treatment options, which included measures such as ear wax removal, additional prescriptions, antibiotic injections, and over-the-counter prescriptions.

2.7. Primary outcome

The primary outcome for the study was a decrease in the rate of clinician antibiotic prescriptions in pediatric patients presenting with ear-related pain who were evaluated with the OCT otoscope as compared to the SOC. Total projected enrollment for the RCT was 300 participants (150 per arm) based on sample size calculations to detect an absolute reduction in provider antibiotic prescribing rates of 15 % at

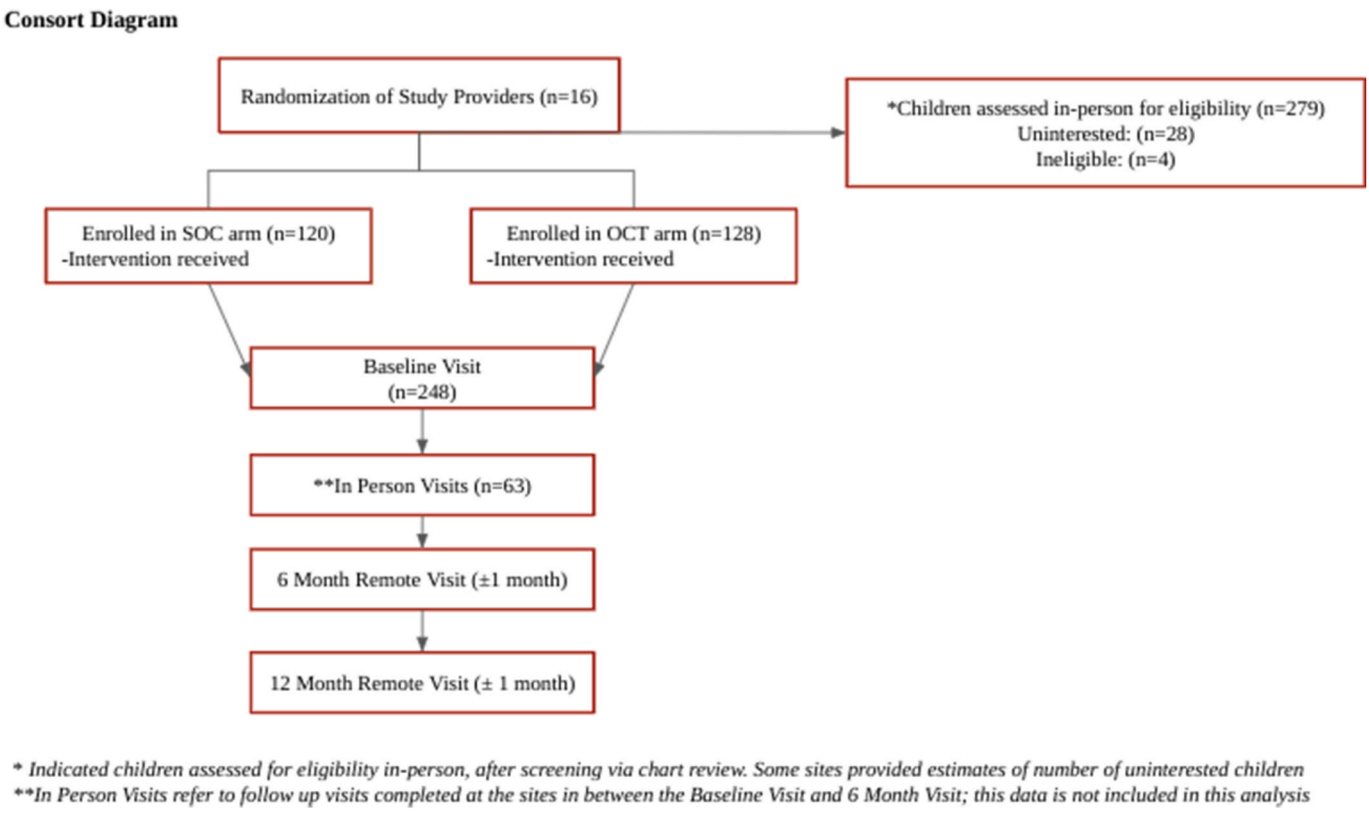

Fig. 2. Consort diagram.

baseline based on reductions observed in other antimicrobial stewardship interventions [9] and assuming 80 % power and an allocation ratio of 1:1.

2.8. Secondary outcome

The secondary outcome for the study was the proportion of patients who received a singular versus multimodal therapeutic approach, assessing whether the use of OCT influenced provider confidence in selecting a single treatment modality compared to standard otoscopy. To evaluate the secondary outcome of singular versus multi-modal therapeutic approaches, treatment decisions were categorized based on whether patients received a single intervention (e.g., antibiotics alone, watchful waiting alone) or multiple concurrent treatments (e.g., antibiotics combined with another intervention). Treatment data were collected at the time of clinical decision-making and categorized into predefined therapeutic groups.

The distinction between singular vs. multi-modal treatments provided insights into diagnostic certainty, with singular treatment decisions suggesting higher confidence in diagnosis. This analysis was designed to address uncertainty regarding whether the Intervention improved diagnostic certainty and reduced the therapeutic odyssey.

2.9. Statistical analysis

This intent-to-treat (ITT) interim analysis was completed in alignment with the protocol to assess the statistical strength of the primary outcome data collected from 248 participants and to inform decisions on potential early trial termination or sample size adjustments based on effectiveness. Based on the results of this analysis, the enrollment number could be modified if necessary. Data collected included patient and provider demographics, patient medical history, provider experience and prescribing patterns at study initiation as well as findings from the otoscopic exam. All data was entered and stored in a centralized electronic database.

An analysis of potential confounders was conducted both theoretically, using a causal diagram to identify key confounders and their relationships, and empirically, by assessing baseline characteristics, performing statistical adjustments, and evaluating the impact of covariates on the estimated treatment effect. Causal diagrams play a critical role in epidemiology and clinical studies by visually representing the relationships between variables, clarifying assumptions, identifying potential confounders, and improving the accuracy of causal inference in multivariate statistical model building. A visual depiction of the relationship between the different variables analyzed (intervention, fluid presence, diagnosis, provider, and site) with regards to antibiotic prescribing is provided in Fig. 3. This causal diagram guided the creation of statistical models used to analyze the relationship between the intervention and primary outcome of antibiotic prescribing patterns. Unmeasured confounding is always a potential limitation in any study but as an RCT, we took pains to minimize confounding by site by adjusting for site differences in the multivariable analysis. To compare responses by treatment arm, the chi-square test was used for categorical variables unless a cell count was <5, wherein Fisher's exact test was used. To compare continuous variables, the Mann-Whitney test was used. Provider responses regarding their demographics were described and compared similarly.

To evaluate the primary outcome at the provider level, a stepwise logistic regression model was constructed. Independent variables included: intervention arm, the proportion of patients treated with watchful waiting, the proportion of patients receiving other treatments, the presence of fluid in either ear, and demographic variables. Other treatments consisted of three primary categories: (1) Medications in addition to antibiotic prescription, including Ceftriaxone injection, Steroids, and OTC medications such as allergy and antihistamines; (2) Physical intervention such as ear flushing and cerumen removal, and (3) Treatment escalation such as indication for tonsillectomy or ear tube insertion.

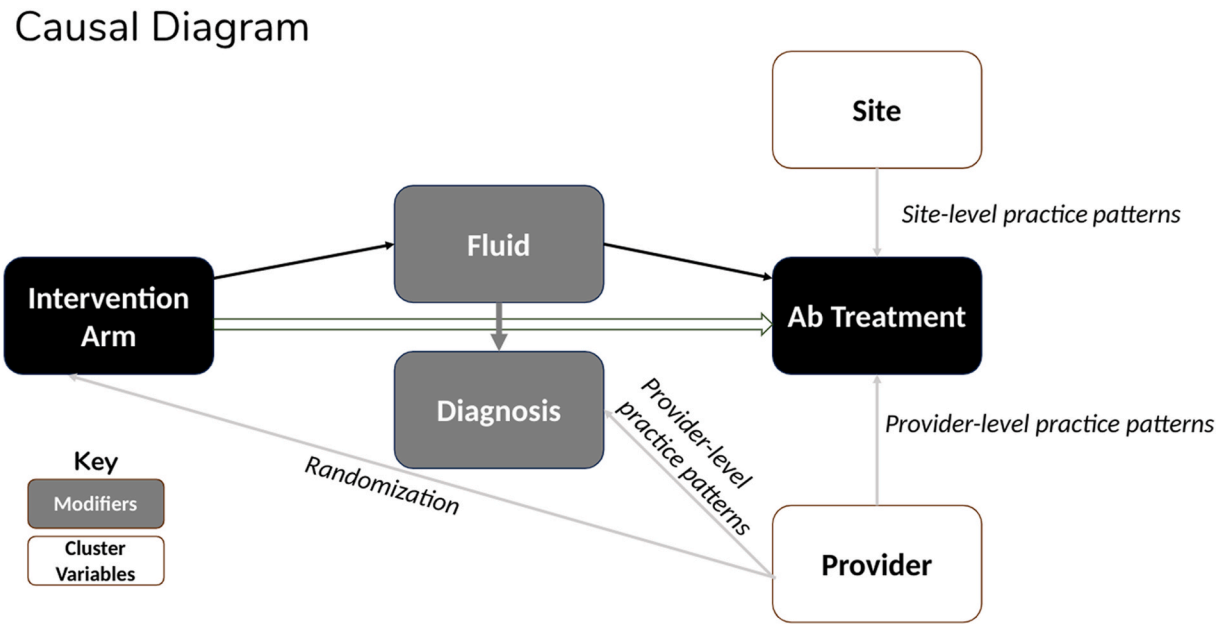

Fig. 3. Causal diagram.

The statistical analysis for the secondary outcome of singular versus multi-modal treatments first utilized descriptive statistics to summarize categorical treatment variables and assess differences between intervention arms. Chi-square tests were used to compare proportions of treatment choices, including antibiotic prescribing and alternative therapeutic options, across groups. P-values were reported to determine statistical significance, with a threshold of $p < 0.05$ considered significant.

To further assess the impact of the OtoSight intervention on antibiotic prescribing patterns, a patient-level multinomial logistic regression model was used to evaluate the association between the intervention and singular antibiotic use versus multi-modal treatment decisions. The model accounted for site, fluid presence, and provider clustering to control for variations in prescribing behavior. "Antibiotics only" was set as the reference category, allowing comparisons between single and combined treatment approaches. Predictive margins were estimated to calculate the percentages of each treatment decision, accounting for important clinical and provider-related variables.

All analyses were done using Stata/MP 18.0 for Windows (StataCorp. Stata Statistical Software: Release 18; 2023. College Station, TX: StataCorp LLC).

Table 1
Provider demographics.

Treatment	OCT		SOC		
	n = 9	%	n = 7	%	p-value
Provider Sex					
Female	6	66.7	5	71.4	1.000
Male	3	33.3	2	28.6	
Age					
Median [IQR]	37	[34, 41]	38	[33, 48]	1.000
Years Since Graduation					
Median [IQR]	13 [6, 14]		6 [3, 31]		0.958
Specialty					
Family Practice	2	22.2	2	28.6	
Pediatrician (or Pediatrician & Internist)	5	55.6	4	57.1	1.000
Otolaryngology	1	11.1	0	0.0	
Nursing	0	0.0	1	14.3	
How many children have you seen in the previous 4 weeks with RAOM or OME					
Median [IQR]	12 [10, 20]		10 [10, 12]		0.450

3. Results

Four sites and 16 providers were included in the analysis and data on provider demographics, experience and prescribing patterns were analyzed. A total of 248 participants were enrolled at the time of the interim analysis data lock; 128 were in the Intervention arm and 120 participants were in the SOC arm. There were no participants excluded due to protocol deviation. Since the analysis focuses on Baseline data, there were no recorded losses to follow-up and follow-up data is not reported. Both Patient-Level and Provider-Level results are presented.

3.1. Provider-level descriptive statistics

The interim data shows no statistically significant differences between the providers in the SOC group as compared to the intervention group with regard to age, sex, experience, and specialty (see 6.1 Table 1), eliminating any concerns about ineffective randomization and potential confounding. Additionally, clinician attitudes and practices around antibiotic prescribing were examined at baseline. There were no statistically significant differences in the influence of patient medical history and other patient factors, physical exam parameters, or caregiver concerns that could have explained the observed differences in post-interventional treatment decisions (section 7.1 Table S1).

3.2. Patient-level descriptive statistics

The SOC and OCT groups had very similar patient-level demographics (see 6.2 Table 2), suggesting that randomization at the provider level resulted in comparable patient populations, with no observed statistically significant differences between groups with regards to age, race, and sex.

Regarding the ear exam, the only statistically significant findings are that the SOC group had more patients presenting with symptoms of fluid drainage (otorreah) and loss of balance than the OCT group (14.2 % vs 6.3 %, p-value = 0.039 and 5.8 % vs 0.8 %, p-value = 0.031 respectively, see 6.2 Table 2). We have analyzed whether otorrhea patients require a

Table 2
Patient demographics and baseline visit findings.

Treatment	OCT		SOC		p-value
	n = 128	%	n = 120	%	
Patient Demographics					
Age, y, median (IQR)	6 [4, 10]		6 [3, 10]		0.591
Sex					
Male	63	49.2	62	51.7	
Female	65	50.8	58	48.3	0.889
Other (specify)	0	0.0	0	0.0	
Ethnicity					
Hispanic	22	17.2	9	8.5	**0.021**
Non-Hispanic	106	82.8	111	92.5	
Race					
White	90	70.3	80	66.7	0.923
Black or African American	28	21.9	32	26.7	
Asian	2	1.6	1	0.8	
Native Hawaiian or Other Pacific Islander	0	0.0	0	0.0	
Multiracial	6	4.7	5	4.2	
Other	2	1.6	2	1.7	
Type of Insurance at Baseline Visit					
Health Maintenance Organization (HMO)	54	42.2	35	29.2	**0.033**
Preferred Provider Organization (PPO)	37	28.9	31	25.8	0.636
Point of Service (POS)	1	0.8	2	1.7	0.612
Exclusive Provider Organization (EPO)	0	0.0	0	0.0	1.000
Health Savings Account (HSA)	1	0.8	1	0.8	1.000
Indemnity Plan	0	0.0	0	0.0	1.000
Medicaid	34	26.6	45	37.5	0.065
Unknown	4	3.1	0	0.0	0.123
Uninsured	3	2.3	0	0.0	0.248
Other	4	3.1	9	7.5	0.122
Attends in-person school or daycare	106	82.8	91	75.8	0.174
Exposure to second-hand smoke in the home	16	12.5	24	20	0.109
Heightened sensitivity to receiving ear exam	1	0.8	1	0.8	1.000
Cold or Flu in Past 6 Months	68	53.1	64	53.3	0.975
Respiratory disease	50	39.1	41	34.2	0.424
Sensorineural hearing loss (SNHL)	4	3.1	10	8.3	0.099
Allergies	45	35.2	54	45.0	0.114
Past anterior ear surgery	24	18.8	27	22.5	0.465
Vaccinations					
Hepatitis B (Hep B)	123	96.1	118	98.3	0.448
Rotavirus (RV)	122	95.3	110	91.7	0.243
Diphtheria, tetanus, and acellular pertussis (DTaP)	125	97.7	120	100.0	0.248
Fluid in the Ear at Baseline					
Fluid in either ear	86	67.2	77	64.2	0.616
Fluid in both ears (bilateral fluid)	52	40.6	46	38.3	0.712
Initial Complaint					
Unusual Irritability	18	14.1	22	18.3	0.361
Difficulty Sleeping/Staying Asleep	14	10.9	15	12.5	0.702
Tugging/Pulling at one or both ears	39	30.5	44	36.7	0.301
Fever	33	25.8	35	29.2	0.550
Fluid draining from ear/s	8	6.3	17	14.2	0.039
Loss of Balance	1	0.8	7	5.8	0.031
Hearing Difficulties	27	21.1	21	17.5	0.522
Ear Pain	93	72.7	94	78.3	0.300
Other (specify)	12	9.4	12	10.0	0.868
Primary Diagnosis (Baseline)					
AOM	55	43.0	47	39.2	
OME	14	10.9	26	21.7	
rAOM	3	2.3	0	0.0	
COME	11	8.6	6	5.0	0.183
Perforated TM and/or CSOM	7	5.5	8	6.7	
Normal Tympanogram	26	20.3	21	17.5	
Other (specify)	12	9.4	12	10.0	

separate group. Our statistical analysis shows no significant impact on treatment outcomes. Furthermore, there were no statistically significant differences in the presence or absence of fluid observed during the ear exam, or in the primary diagnoses at the BV between intervention arms.

3.3. Analysis of primary outcome

A stepwise logistic regression analysis was conducted to evaluate the association between the intervention and clinician antibiotic prescribing rates in pediatric patients with ear-related pain at the provider-level. The odds ratio of prescribing an antibiotic was estimated for the intervention group compared to the SOC referent group. Adjustments were made sequentially, beginning with site-level variation to account for differences in prescribing patterns across locations. Additional covariates were introduced to control for clinical decision-making factors, including the use of watchful waiting and other treatment modalities. Presence of fluid in the middle ear was incorporated as a key clinical determinant influencing antibiotic decisions. Demographic factors, such as race and age, were added in the final model to ensure broader consideration of patient-level characteristics. Confidence intervals and p-values were reported to determine statistical significance, with significance defined as $p < 0.05$.

Table 3 presents the results of the multivariable logistic regression analysis of the primary outcome. The initial model, adjusted only for site, shows an odds ratio (OR) of 1.05 (95 % CI: 0.50–2.23, $p = 0.890$), indicating no significant difference in antibiotic prescribing between intervention and SOC when only accounting for site-level variability. As additional clinical decision-making factors are introduced, the odds ratios remain below one, but none reach statistical significance in the intermediate models, suggesting that these alone do not fully explain the prescribing differences. However, when adjusting for site, watchful waiting, other treatments, and the presence of middle ear fluid, the odds ratio for the rate of antibiotic prescribing in the OCT group compared to the SOC group is 0.51 (95 % CI: 0.40–0.66, $p < 0.001$), indicating that clinicians in the OCT intervention group were significantly less likely to prescribe antibiotics compared to SOC. Adding race and age further strengthens this effect, with an odds ratio of 0.50 (95 % CI: 0.45–0.56, $p < 0.001$), suggesting that the intervention remained strongly associated with lower antibiotic prescribing even after accounting for demographic variations.

3.4. Analysis of secondary outcome

Table 4 presents the unadjusted distribution of singular treatment decisions across OCT and SOC groups, highlighting differences in clinical management approaches. These results illustrate that providers in the OCT group were statistically significantly more likely to proceed with a singular therapeutic modality than SOC providers, (91.6 % versus

Table 3
Association between intervention and rate of clinician Antibiotic prescriptions in pediatric patients presenting with ear-related pain.

Odds Ratio of Prescribing an Antibiotic[a]	95 % CI	P-value	Adjusted for:
1.05	(0.50, 2.23)	0.890	Site
0.78	(0.37, 1.66)	0.524	Site; Watchful Waiting
0.76	(0.43, 1.35)	0.356	Site; Watchful Waiting; Other Treatments
0.51	(0.40, 0.66)	<0.001	Site; Watchful Waiting; Other Treatments; Presence of Fluid
0.50	(0.45, 0.56)	<0.001	Site; Watchful Waiting; Other Treatments; Presence of Fluid; Race; Age

[a] OCT intervention compared to SOC (referent).

Table 4
Singular treatment decisions (unadjusted raw data)[a].

Treatment	OCT		SOC		Total
	n = 120	%	n = 104	%	n = 224
Antibiotic Rx Only	58	48.3	43	41.3	101
Referral to ENT Only	1	0.0	0	0.0	1
Tympanostomy Tube Insertion Only	9	6.9	1	0.7	10
Glucocorticoid Ab Ear Drops Only	1	0.0	0	0.0	1
Watchful Waiting Only	26	21.7	33	31.7	59
Other Treatment Only	25	20.8	27	26.0	52
Subtotal for Singular Treatment Decisions	120	91.6	104	73.8	p < 0.001

Rx: Prescription; Ab: Antibiotics.
[a] This table presents the distribution of singular treatment decisions by treatment group. These raw frequencies do not account for covariates such as provider clustering, site differences, or patient characteristics, which are adjusted for and presented in Table 3.

73.8 %, $p < 0.001$). In addition, a shift in treatment patterns is evident, with OCT patients being more likely to receive definitive immediate interventions like antibiotics or tympanostomy tubes, whereas SOC patients were more likely to be placed under watchful waiting. The highly significant p-value ($p < 0.001$) indicates that these differences are unlikely due to chance, supporting the idea that OCT impacts clinical decision-making. While these raw frequencies illustrate general trends, our endpoint analysis adjusts for key covariates such as provider clustering, site effects, and patient characteristics, which influence clinical decision-making. These adjusted results, which better represent the overall effect of the intervention, are presented in Section 6.3 (Table 3).

As discussed in section 2.9 Statistical Analysis, a patient-level multinomial logistic regression model was conducted. The results of this multivariable model showed that SOC providers were 4.73 times more likely to prescribe antibiotics plus another treatment compared to OCT providers (RRR = 4.73, 95 % CI: 1.38–16.29, $p = 0.014$, results not presented in table), suggesting that OCT providers favored more singular treatment decisions. These results indicate that SOC providers prescribed antibiotics plus another treatment at an adjusted rate of 16.3 % in contrast to OCT providers who prescribed antibiotics plus another treatment at an adjusted rate of 4.6 %, reflecting a significantly lower likelihood of multimodal prescribing. These findings suggest that OtoSight was associated with a shift toward more singular treatment decisions, reducing reliance on combination therapies even after adjusting for key clinical and provider-related variables.

4. Discussion

Our results demonstrate that the OCT method may encourage more conservative and targeted antibiotic use through its ability to (1) more accurately detect the presence of fluid and (2) better characterize the type of fluid in the middle ear, which leads to better diagnostic certainty and improved antibiotic stewardship. In the fully adjusted model of the primary outcome, provider antibiotic prescribing rate, OCT was associated with a 50 % reduction in the odds of antibiotic prescribing compared to the SOC (OR = 0.50, 95 % CI: 0.45–0.56, $p < 0.001$), even after controlling for watchful waiting, other treatments, fluid presence, race, age, and site-level clustering. These findings suggest that OCT significantly influenced clinical decision-making, leading to more selective antibiotic use, reinforcing its potential role in improving antibiotic stewardship in pediatric ear infection management.

When controlling for differences between sites and the presence of fluid, the multinomial logistic regression model of the secondary outcome, singular antibiotic treatment versus multi-modal treatment, reveals key associations between the OCT device and pediatric care management compared to the SOC. Specifically, the multivariable modeling of the secondary outcome showed that SOC providers were nearly 5-times more likely than the OCT group to prescribe antibiotics in addition to other treatments versus antibiotics alone (OR = 4.73, 95 % CI: 1.37–16.29, $p = 0.014$). Controlling for fluid status is crucial because it directly addresses the primary indication for many treatments in OM. By doing so, we minimize confounding by indication bias, ensuring that differences in outcomes aren't driven by whether the patient had fluid present, but rather by the intervention itself.

The patient and provider level results demonstrate early clinical utility of the OCT otoscope by showing significant increases in the likelihood of patients evaluated with the SOC to receive antibiotic prescriptions (either alone or plus other treatments) compared to patients evaluated with the OCT otoscope. These results suggest that the OCT otoscope not only reduces antibiotic prescriptions but also increases provider confidence and diagnostic certainty. A specific example from the results helps to illustrate and support this: we found that 16.3 % of SOC providers initiated treatment of antibiotics plus glucocorticoid-antibiotic ear drops versus 0 % of OCT providers. Clinical guidelines for the use of glucocorticoid-antibiotic ear drops in children primarily focuses on conditions such as acute otitis externa (AOE, i.e., swimmer's ear) and CSOM where antibiotics would not be indicated. The higher rate of prescribing systemic antibiotics with glucocorticoid ear drops in the SOC group indicates diagnostic uncertainty and potentially unnecessary prescribing habits, likely caused by difficulty in visualizing the ear canal with a traditional otoscope.

Our study has several notable strengths and limitations. Key strengths include its pragmatic design, characterized by an emphasis on real-world conditions and implementation of the intervention as it would be delivered in routine clinical practice, as well as a large overall sample size, objective outcomes, and multivariable statistical adjustments to minimize bias. Methods built into the design of traditional RCTs to minimize bias are often not appropriate in real-world pragmatic studies and statistical methods must be incorporated to minimize risk of bias. For example, in pragmatic trials where, in many cases, patients and providers must be aware of the intervention to ensure it is administered and used correctly, which renders participant and clinician blinding impractical. Additionally, interventions in pragmatic trials are often complex (e.g., surgery, behavioral therapies, or device use), further limiting the ability to mask treatment assignments.

Furthermore, we increased the generalizability of our findings by incorporating a diverse range of healthcare settings and providers, include primary care, group practices, and public health facilities. Providers who participated in this study include frontline pediatric medical professionals such as primary care physicians, pediatricians, ENT specialists who serve as frontline providers in their communities, and both family and pediatric nurse practitioners. Each site was assessed based on their function as front line care providers, meaning the first stop in care for patients. Thus, the inclusion of an ENT and nurse as part of the provider cohort was intentional to reflect the diversity of frontline providers who commonly evaluate and treat patients presenting with ear-related complaints. This approach enhances the generalizability of the study by making it representative of real-world care delivery settings, where patients are often seen by a variety of healthcare professionals. This diversity is critical for understanding the broader applicability of the intervention across different provider types and care contexts. Additionally, statistical adjustments were made during analysis to account for potential heterogeneity between sites and provider types, ensuring that the findings are robust and not biased by provider variation.

While the results support the adoption of the novel OCT otoscope, our analysis included multiple limitations. One limitation that is due to the nature of interim analyses, was the observation of differences in treatment arms that might be clinically meaningful, but did not attain statistical significance due to our limited sample size. For example, follow-up visit data on referral rates and adherence to treatment regimens was collected and analyzed with the baseline data. However, the

analyses were underpowered with wide confidence intervals due to the lack of available follow-up data at the time of the database lock. Next steps include the exploration of specialist referral rates, adherence to treatment plans and evaluation of the economic impact in future analyses that include more data. Since this study is limited to measuring rates of antibiotic prescription, medical resource utilization, and economic impact, future research studies should focus on the clinical outcomes of specific treatment decisions for the various diagnoses based upon the use of OCT compared to SOC.

Analysis of the Baseline provider and patient characteristics data did show a statistically significant difference between the Intervention and SOC group with regard to fluid drainage and loss of balance as initial complaints, raising concerns about potential clinical differences between the SOC and Intervention groups. However, additional analysis showed no significant effect on treatment outcomes, alleviating concerns about potential confounding. Regardless, this is an area worth exploring further.

Finally, we recognize that there is potential risk of Hawthorne bias, whereby clinicians change their behavior based on knowing they are being observed as part of a study. This risk is mitigated by cluster randomization at the provider level so providers utilizing SOC are not exposed to the new technology. However residual bias may exist. The most likely direction of that bias would be for SOC providers to become more conservative in their prescribing of antibiotics based on the study premise. If that were the case, this would result in a bias towards the null, meaning that our observed estimated differences between study arms would be an underestimate of the truth and the effect of OCT technology on antibiotic prescribing rates actually may be much stronger.

In conclusion, the focus of this interim analysis was to evaluate changes in provider prescribing practices and therapeutic regimen recommendations when utilizing a novel OCT otoscope versus the SOC. Our findings demonstrate the OCT otoscope significantly reduces the likelihood of prescribing antibiotics in conjunction with other treatments, mitigating the overuse of antibiotics, a critical component in combating antibiotic resistance. Additionally, the careful consideration of fluid status and site variability in this analysis highlights the importance of accounting for these factors when evaluating the effectiveness of new treatment methods. These results indicate a promising direction for the adoption of this novel OCT otoscope in clinical practice, where the use of optical diagnostics may offer adjuncts to traditional diagnostic methods to which remote-diagnosis (telemedicine) and/or artificial intelligence techniques may also be applied, potentially leading to more judicious use of antibiotics and improved patient outcomes.

Data availability statement

No data are available from this study due to Sponsor preference.

CRediT authorship contribution statement

April Zambelli-Weiner: Writing – review & editing, Writing – original draft, Supervision, Methodology, Conceptualization. **Brian H. Nathanson:** Writing – review & editing, Methodology, Formal analysis, Data curation. **Frank Calcagno:** Writing – review & editing, Investigation. **John Ansley:** Writing – review & editing, Investigation. **Karina Vattana:** Writing – review & editing, Investigation. **Bonnie Burnette-Vick:** Writing – review & editing, Investigation.

Declaration of competing interest

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GLOSSARY

AOM	Acute Otitis Media
BV	Baseline Visit
COME	Chronic Otitis Media with Effusion
CRF	Case Report Form
CSOM	Chronic Suppurative Otitis Media
LAR	Legally Authorized Guardian
MEE	Middle Ear Effusion
OCT	Optical Coherence Tomography
OM	Otitis Media
OME	Otitis Media with Effusion
rAOM	recurrent AOM
RCT	Randomized Control Trial
SOC	Standard of Care

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ijporl.2025.112356.

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