Published in final edited form as:

South Med J. 2017 March ; 110(3): 172–180. doi:10.14423/SMJ.0000000000000622.

Risk Factors for Outpatient Use of Antibiotics in Children with Acute Respiratory Illnesses

Sophie R. Zhao, MD, Marie R. Griffin, MD, MPH, Barron L. Patterson, MD, Rachel L. Mace, MD, Dayna Wyatt, RN, CCRP, Yuwei Zhu, MD, MS, and H. Keipp Talbot, MD, MPH

Departments of Medicine and Health Policy, Vanderbilt University Medical Center, the Department of Pediatrics, Monroe Carell Jr. Children's Hospital at Vanderbilt University, and the Department of Biostatistics, Vanderbilt University School of Medicine, Nashville, Tennessee

Abstract

Objectives—Antibiotics for acute respiratory illness (ARI) constitute most pediatric medication use and contribute to the emergence of antimicrobial resistance. We investigated antibiotic prescription risk factors for ARI in pediatric clinics and clinical follow-up in individuals prescribed and not prescribed antibiotics.

Methods—In this observational study, we enrolled children ages 2 to 17 years old presenting with ARI with fever to two academic pediatric primary care outpatient clinics during influenza season 2013–2014. We collected information on demographics, initial symptoms, medical conditions, laboratory tests, discharge diagnoses, treatments, and 30 days of follow-up medical encounters. Factors associated with antibiotic prescription receipt were evaluated using logistic regression.

Results—Of 206 consented and enrolled children, 59 (29%) were prescribed antibiotics, 51 of 59 (86%) for indicated diagnoses: 34 for streptococcal pharyngitis, 15 for acute otitis media (AOM), and 2 for pneumonia. Discharge diagnoses were the only factors independently associated with an antibiotic prescription. Of children prescribed/not prescribed an antibiotic, 17%/17% received follow-up telephone calls and 27%/17% had follow-up visits related to ARI within 30 days. Two children with AOM were prescribed a second antibiotic during follow-up, and one developed *Clostridium difficile* colitis. Eighteen of 206 (9%) additional children were prescribed antibiotics within 30 days for ARI symptoms, 17 for streptococcal pharyngitis, AOM, pneumonia, or sinusitis; one was prescribed antibiotics for influenza-like illness.

Conclusions—Among study children 2 to 17 years old with outpatient ARI, 29% were prescribed antibiotics at the initial visit and another 9% were prescribed antibiotics during the 30-day follow-up (most were for appropriate indications). Further decreasing antibiotic use in similar

Correspondence to Dr H Keipp Talbot, A2200 Medical Center North, Vanderbilt School of Medicine, 1161 21st Ave S, Nashville, TN 37232. keipp.talbot@vanderbilt.edu.

To purchase a single copy of this article, visit sma.org/smj-home. To purchase larger reprint quantities, please contact reprints@wolterskluwer.com.

M.R.G. has received research funding from MedImmune. H.K.T. has received research funding from MedImmune, AstraZeneca, Sanofi Pasteur, and Gilead Sciences, and has served as an advisor to Teva Pharmaceutical Industries, Novartis International AG, and VaxInnate. The remaining authors did not report any financial relationships or conflicts of interest.

settings will likely require wider implementation of watchful waiting for AOM, a change in guidelines for pharyngitis management, and/or reductions in these diseases.

Keywords

antibiotic prescriptions; pediatric acute respiratory illness

Antibiotics are the most widely used medication group in the worldwide pediatric population,¹ and approximately three-fourths of all outpatient antibiotic prescriptions to children are associated with acute respiratory illness (ARI).² As of 2011, more than 1 in 5 pediatric ambulatory visits resulted in an antibiotic prescription, resulting in nearly 50 million prescriptions written annually in the United States.³ Widespread antibiotic use contributes to the problem of growing selection pressure for drug-resistant bacterial strains.^{4,5} Antibiotic resistance in the United States costs an estimated \$20 billion/year in excess healthcare costs, \$35 billion in other societal costs, and more than \$8 million in labor productivity losses as a result of additional hospital days.^{6–8} To combat these trends, numerous public campaigns have been launched during the past decade to promote judicious prescription practice.^{6,9,10}

Because prescriptions for ARI constitute most pediatric antibiotic use, it is particularly concerning that antibiotics have been prescribed routinely for conditions for which there are no clear benefits, specifically viral respiratory illnesses.^{3,11,12} It is encouraging that outpatient antibiotic prescriptions for children have been on the decline,^{13–15} a result in part of the reduction in visits for otitis media (OM).¹⁶ Proposed causes for these trends, in addition to educational efforts, include the introduction of pneumococcal conjugate vaccines, provided routinely to infants and young children since 2000,¹⁷ and seasonal influenza vaccine recommendations being expanded to include healthy children¹⁸; however, misuse of broad-spectrum antibiotics is still of vital concern.^{16,19,20} In addition to the public health implications, antibiotic use can lead to direct adverse outcomes, including diarrhea, allergic urticaria, dermatitis, and unintentional overdoses, for the children receiving them.^{21–23}

We evaluated children who presented to two academic outpatient facilities with ARI, with respect to their clinical diagnoses, socioeconomic factors, and medical history, to better understand the factors associated with antibiotic prescribing for these children. In addition, we assessed follow-up telephone calls and return visits in the 30 days after the initial visit for those who were and were not prescribed antibiotics.

Methods

Institutional review board approval from the Vanderbilt University human research protection program was obtained for both the parent surveillance study and for our chart review study. Datasets were stored in REDCap,²⁵ a secure and deidentified database supported by the academic institution.

Participant Enrollment

Participants in the study were children ages 2 to 17 years enrolled in an ongoing multicenter influenza surveillance study during the 2013–2014 influenza season. The participants presented to a pediatric clinic at one of two outpatient sites. Enrollment took place between December 2013 and April 2014 from 8 AM to 4 PM, Monday through Friday, and from 8 AM to 12 PM on Saturdays. Trained staff reviewed the appointment schedule to identify eligible participants, and the child and his or her parents/guardians were approached to provide informed consent and assent. Inclusion criteria included acute respiratory symptoms; oral temperature 100.0°F (37.8°C) at study visit, or history of fever reported by parents, or use of an antipyretic before study visit; symptom onset <5 days before study visit; and no receipt of an antiviral drug for influenza or influenza vaccination during the 14 days before enrollment.

Demographic and Clinical Information

Enrollment Visit—In the parent multicenter observational study, funded by MedImmune²⁴ and performed to assess influenza vaccine effectiveness, a standardized survey pertaining to the child's medical history, seasonal influenza vaccine status, social and economic background, and presenting symptoms was administered to the parent/guardian. Medical notes on the visit, including records of any laboratory tests performed, medications prescribed, and discharge diagnoses, were collected in a standardized format using a chart review of the electronic medical record system. Confirmatory influenza testing via reverse transcriptase polymerase chain reaction was completed after the visit in a research laboratory, and the results were not available to the providers at the time of the visit. A small number of providers ordered rapid influenza diagnostic tests in the clinics.

30-Day Follow-up—We collected additional data, which was confined to one academic institution in the same city with two outpatient clinics. A chart review for the 30-day period after the enrollment visit was conducted to evaluate how many times the participants called or made return visits for problems related to the original ARI or new ARI symptoms. Multiple telephone calls and visits were collapsed into their respective categories—in other words, we made no distinction between making one telephone call and, for example, three telephone calls in our analyses.

Telephone calls and return visits were documented as being the result either of continuing or new ARI symptoms or a possible medication reaction (eg, rash, diarrhea, difficulty breathing). We also documented whether the child was instructed to make a return visit, and if a return visit was made, the facility visited, medications prescribed, laboratory tests completed, and discharge diagnoses as noted in the clinical notes or discharge summary.

Two independent reviewers separately reviewed the charts of the entire participant pool of 206 children. Any discrepancies between the reviews were noted and reconciled between the reviewers after a second round of chart review together.

Statistical Analysis

Descriptive summaries of the participant population were performed. Pearson χ^2 or Wilcoxon rank sum test were used to compare groups with or without antibiotic prescriptions at the enrollment visit or patients with or without return visit in terms of demographic and clinical characteristics. A two-sided $P < 0.05$ indicated statistical significance. All of the analyses were completed using STATA/IC 13 (StataCorp, College Station, TX). Our study used data collected for the parent study. (Additional data collection and analysis for the substudy was not funded by MedImmune.)

Risk Factors for Antibiotic Prescription

To evaluate factors associated with receiving antibiotics at the enrollment visit, we used a multivariable logistic regression model. Because of potential diagnostic overlap, discharge diagnoses of viral illness, influenza, and other upper respiratory illness (URI) were combined into one category. Low count caused bronchiolitis/bronchitis (one participant), acute asthma exacerbation (two participants), and wheezing (one participant) to be combined into the category of lower respiratory tract illnesses. The diagnoses of allergic rhinitis, croup, tonsillitis, other respiratory tract illnesses, paroxysmal coughing, respiratory syncytial virus, and sinusitis were dropped from the regression model because none of the participants with these primary diagnoses were prescribed antibiotics. The diagnosis of cough was dropped because of low count. Other covariates entered into the regression model included clinic site, insurance type, race, influenza vaccination in the 2013–2014 flu season before enrollment visit, and chronic illnesses. A secondary logistic regression was performed in which the discharge diagnoses were grouped into either “probably appropriate” (streptococcal pharyngitis, acute OM [AOM], and pneumonia/pneumonitis, and sinusitis) or “probably inappropriate” (viral illness, influenza, URI, bronchiolitis, acute asthma exacerbation, wheezing, allergic rhinitis, cough, croup, tonsillitis, paroxysmal coughing, and respiratory syncytial virus). Pneumonia was diagnosed when a radiologist-read chest radiography indicated pathologic findings. We relied on clinical diagnoses of sinusitis. The preliminary analysis did not show age to be an independent risk factor for antibiotic prescription and this variable was removed from the final model.

30-Day Follow-up

Descriptive summaries of follow-up calls and return visits were performed. The relation between having been prescribed antibiotics and follow-up/return visits was evaluated using bivariate analyses (Pearson χ^2). Participants who did and did not make return visits were characterized by age, sex, race/ethnicity, clinic site, insurance, chronic illnesses, and diagnosis at the initial visit. Logistic regressions on the risk factors for all and for AOM return visits were performed. The covariates in the models included clinic site, insurance type, race/ethnicity, and chronic illnesses. Characteristics of all of the participants who did not receive antibiotics at the initial visit but returned to receive antibiotics at follow-up were described.

Results

There were 219 eligible children who were approached; 206 (94%) were consented and enrolled in the parent study. All of the children in the study received their primary care at the academic hospital. There were 130 (63%) children enrolled in pediatric on-campus clinics, which include continuity clinics for pediatric residents, and have a high proportion of children enrolled in Medicaid. There were 76 (37%) children enrolled at off-campus pediatric and adolescent clinics, which were staffed primarily by attending physicians with more privately insured patients. Descriptive summaries of the participant characteristics are presented in Table 1; 49% of the participants were male, 52% were non-Hispanic white, 39% were non-Hispanic African American, 6% were Latino, 4% were Asian, and 1% was other race. A total of 50% had public insurance, 47% had private insurance, and 3% had both types. Twenty-six percent of the children had one or more chronic illnesses. Seventy-four percent of the children received influenza vaccination during the 2013–2014 flu season. Seven children had a rapid influenza test completed in the clinic (three positive and four negative results). Of the three children testing positively, two were diagnosed as having influenza and one as having viral illness.

Race/ethnicity, clinic site, and insurance type were found to be significantly different between those prescribed and not prescribed antibiotics on bivariate analyses (Table 1), but none were independently associated with antibiotic prescriptions in the multivariate analysis. Children who were prescribed antibiotics were less likely than those not prescribed to have reported headaches and vomiting. Having one or more chronic illnesses was not associated with differences in receiving antibiotics. The children who were prescribed antibiotics were less likely than those not prescribed to have been diagnosed as having influenza, URI, pharyngitis, and viral illness and more likely to have been diagnosed as having AOM, pneumonia/pneumonitis, and streptococcal pharyngitis. Lastly, no participant was prescribed both antivirals and antibiotics at this visit.

Fifty-nine (29%) children were prescribed oral antibiotics at their initial visit, 51 (86%) of these for indicated diagnoses: 34 for streptococcal pharyngitis, 15 for AOM, and 2 for pneumonia. Fourteen of 206 children (7%) were prescribed antiviral medications. Of the children who received antibiotics, 76% received penicillin, 12% azithromycin, 3% cephalosporins, 3% fluoroquinolones, 2% sulfa drugs, and 2% clindamycin. Nine (4%) additional children with pharyngitis at the initial visit and who had a negative streptococcal rapid antigen detection test (RADT) were prescribed antibiotics (100% penicillin) when their culture tested positive (counted as “pharyngitis/not prescribed antibiotics” in Table 1).

Risk Factors for Prescription of Antibiotics

Risk factors for being prescribed an antibiotic at the initial visit are presented in Table 2. All 15 patients with a diagnosis of AOM and both children diagnosed with pneumonia were prescribed antibiotics. The only other factor that was independently associated with receiving antibiotics was a diagnosis of streptococcal pharyngitis. A secondary analysis using the classification of “probably appropriate” compared with the “probably not appropriate” grouping of the primary diagnosis demonstrated similar results; here, having an appropriate discharge diagnosis was the only factor independently associated with receiving

an antibiotic (odds ratio 286.05, 95% confidence interval 71.13–1150.38). Further subset analyses separating those who were and were not diagnosed as having streptococcal pharyngitis did not identify significant risk factors for antibiotic prescription in either group. Additional analysis excluding the diagnosis of streptococcal pharyngitis as a covariate identified the diagnoses of URI and influenza/viral illness as independent negative predictors of receiving antibiotics.

Follow-up Patterns

The follow-up patterns of participants are described in the Figure. Of the 59 children who were prescribed antibiotics, 17% (n = 10) made follow-up telephone calls and 27% (n = 16) made at least one return visit. In comparison, of the 147 children who were not prescribed antibiotics, 17% (n = 25) made follow-up telephone calls and 17% (n = 25) made at least 1 return visit. Having an antibiotic prescribed at the enrollment visit was significantly associated with return clinic visits, and only 2 of 16 return visits were made to check for resolution of AOM. Two children (3%) who were prescribed antibiotics returned to the emergency department (ED); one with AOM returned with AOM and one with viral illness returned with vomiting. Nine children (6%) not prescribed antibiotics returned to the ED: two with pneumonia, one with AOM, one with streptococcal pharyngitis, three with viral syndrome, one with influenza, and one with continued ARI symptoms and diabetic ketoacidosis was subsequently hospitalized. Adverse gastrointestinal effects were reported in 4 of 59 (7%) children prescribed antibiotics (3 telephone calls, 1 return visit) and 1 of 14 (7%) children prescribed oseltamivir (1 telephone call and 1 return visit).

Of the children who received an antibiotic prescription at the initial visit, 7 (12%) were prescribed another antibiotic at the return visit, including 3 children with AOM at both the initial and return visits (one of whom later developed *Clostridium difficile* colitis); 3 children with streptococcal pharyngitis, and 1 child with wheezing/possible pneumonia. Of the 147 children who were not prescribed antibiotics at the initial visit, 9 (6%) with pharyngitis were prescribed an antibiotic when their cultures tested positive for group A streptococcus, and an additional 9 (6%) received antibiotics during a return visit. The nine children who were prescribed antibiotics after a positive culture were counted as having received antibiotics previously in the follow-up analyses. These nine children made return visits within a median of 9 days (interquartile range 5–15). Eight (89%) of these children were originally diagnosed as having URI or viral illness. Two children were diagnosed as having pneumonia at 3 and 4 days after the initial visit. Two children were diagnosed as having streptococcal pharyngitis at 14 and 15 days, 2 with AOM at 8 and 29 days, and 1 each with sinusitis and bacterial conjunctivitis. One child was diagnosed as having allergic rhinitis, returned in 5 days, and was diagnosed as having viral illness and was prescribed antibiotics.

The characteristics of the children who did and did not make return visits are summarized in Table 3. Of the 206 children, 41 (20%) returned to the clinic or ED within 30 days of the initial visit. A greater proportion of the children who returned were non-Hispanic white, seen at the off-campus clinic, had private insurance, and were diagnosed as having AOM at the initial visit. Of the 41 children who made return visits, 7 (17%) were diagnosed as

having viral illness; 7 (17%) as having URI; 7 (17%) as having streptococcal pharyngitis; 5 (12%) as having AOM; 2 (5%) as having pneumonia; 6 (15%) collectively as having acute asthma exacerbation, conjunctivitis, or vomiting; and 24 (59%) as having other diagnoses.^A Fifteen (37%) of the children who returned were diagnosed as having streptococcal pharyngitis or AOM at the initial visit and had already been treated with antibiotics. We were unable to identify factors associated with return visits.

Discussion

Physicians in our study rarely prescribed antibiotics for diagnoses of low clinical indication (eg, nonspecific URIs, viral illnesses, influenza). Eighty-six percent ($n = 51$) of children prescribed an antibiotic had a diagnosis of streptococcal pharyngitis, AOM, or pneumonia/pneumonitis. In the univariate analyses children who were non-Hispanic white or Asian, who had private insurance, and who were examined at the off-campus clinic site were likely to be prescribed antibiotics. These factors were no longer statistically significant in the multivariate analysis, however, suggesting that some of the differences were explained by differences in discharge diagnoses. Only 1 of 24 children diagnosed as having viral illness and 2 of 64 children diagnosed as having URI received antibiotics.

All of the children in the study diagnosed as having AOM received antibiotics at the enrollment visit. For children younger than 2 years, there is good evidence that antibiotics (specifically, amoxicillin clavulanate) help to reduce the time to resolution of symptoms and overall symptom burden in AOM.²⁶ In older children, however, the benefits of antibiotic treatment for AOM are less clear.^{27–29} In children 2 years or older with nonsevere unilateral AOM, the American Academy of Pediatrics guidelines offer the grade B recommendation to either prescribe antibiotic therapy or observe with plans for close follow-up; specifically: “a mechanism must be in place to ensure follow-up and begin antibiotic therapy if the child worsens or fails to improve within 48 to 72 hours of onset of symptoms.”²⁸ In our study, none of the clinicians chose to use the “watchful waiting” strategy recommended by these guidelines. The desire to reduce follow-up visits, patient volume, legal concerns,³⁰ and constraints of daily practice³¹ has been found to influence physicians’ antibiotics prescribing behavior. It is noteworthy that of the 15 children in our study who were prescribed antibiotics for AOM, 40% ($n = 6$) made a return visit within 30 days.

A high proportion of antibiotic use in our population was for streptococcal pharyngitis. There were 65 and 10 children diagnosed as having pharyngitis at initial and follow-up visits, respectively. Of these, 72% ($n = 47$) of the initial cases and 70% ($n = 7$) of the follow-up cases tested positive for group A streptococci (GAS) via RADT or follow-up culture. GAS pharyngitis generally accounts for 20% to 30% of cases of pharyngitis in children.³² Our study aimed to enroll only children with a history of fever, which may account in part for the higher than expected prevalence of GAS detections. The RADT is highly specific for GAS; a positive test can be considered equivalent to a positive throat culture and antibiotic therapy initiated without further microbiologic confirmation.³³ The threshold for treating

^AIn the sentence beginning “Of the 41 children who,” did children have multiple diagnoses? The list totals 58, not 41. If children did have multiple diagnoses, please rework sentence to reflect this fact.

with antibiotics is typically low once the diagnosis of GAS pharyngitis is established because of their important preventive role in the development of acute rheumatic fever and suppurative complications. Based on the Modified Centor Score,³⁴ febrile children 3 to 14 years old (score of 2) should receive antibiotics if the throat culture or RADT is positive; however, RADT does not effectively differentiate acutely infected patients from asymptomatic chronic carriers.³³ As such, it is possible that some of the children with positive RADT were GAS carriers with a different concurrent ARI instead of overt acute GAS pharyngitis.

It also is possible that antibiotics could prevent complications from ARIs. In a large-scale retrospective cohort study, Petersen et al³⁵ found that serious complications (defined as mastoiditis after AOM, peritonsillar abscess after sore throat, and pneumonia after URI) were rare and that the number needed to treat with antibiotics to prevent these complications was large; the exception was in patients with chest infections, for whom the risk of pneumonia is relatively high.³⁵

Our study was not designed to evaluate the benefit of prophylactic antibiotics. Two children who did not receive antibiotics at the initial visit returned within 5 days with pneumonia, and two children who did not receive antibiotics at the initial visit returned at 7 and 29 days and were diagnosed as having AOM. Overall, the number of return visits and the need for subsequent antibiotics were low in those not initially treated, and it is uncertain whether the subsequent visits for pneumonia or AOM could have been prevented had the children been given antibiotics at the initial visit.

It is unclear why a higher proportion of children who were prescribed antibiotics made return clinic visits. In a previous study, it was reported that children who were prescribed antibiotics for a respiratory illness returned almost twice as often for a second unplanned visit,³⁶ and that such prescribing behavior may in fact encourage clinic visits for subsequent episodes,³⁷ intensify pressure on clinicians to prescribe,³⁸ and increase overall antibiotic usage. It is unclear whether the increase in return visits in our study was the result of the prescription of antibiotics, differences in the underlying ARIs, or in characteristics of the children and/or their caregivers. Of the 41 children who made return visits, 15% (n = 6) were diagnosed as having AOM or pneumonia.

Our study has several important limitations. First, although our dataset contains a rich variety of participant characteristics and medical/laboratory findings, the study was not powered to show statistical significance in many of the findings. Second, our study was built within an influenza surveillance study; it is possible that providers altered their behavior based on the knowledge that their prescribing patterns would be monitored and preferentially chose diagnoses to justify antibiotic use. This use of diagnosis to justify antibiotic usage would overestimate the appropriate use of antibiotics. Lastly, this study may not be generalizable for the following reasons: this is an observational study in one academic setting, our study population does not include children younger than 2 years, we did not capture children with afebrile ARIs, physician diagnoses were not standardized or validated across providers, and we did not capture children who may have sought follow-up care in other healthcare systems.

Our findings indicate that the clinical practice of prescribing antibiotics for pediatric ARI within our study population was usually appropriate. To further reduce overall antibiotic use, interventions will need to be directed at diagnoses for which the majority of the antibiotics were prescribed—streptococcal pharyngitis and AOM. For streptococcal pharyngitis, the ability to identify carriage compared with infection and/or to identify infections unlikely to result in complications could limit antibiotic use for this indication. For AOM, declines in antibiotic use will require greater use of watchful waiting, increased routine vaccination against respiratory pathogens such as pneumococcus and influenza, and/or development of new vaccines for other pathogens that result in AOM. In general, the establishment of clinical practice guidelines and antibiotic stewardship programs with regular provider feedback also may improve antibiotic prescribing.

References

1. Chai G, Governale L, McMahon AW, et al. Trends of outpatient prescription drug utilization in US children, 2002–2010. *Pediatrics*. 2012; 130:23–31. [PubMed: 22711728]
2. Nash DR, Harman J, Wald ER, et al. Antibiotic prescribing by primary care physicians for children with upper respiratory tract infections. *Arch Pediatr Adolesc Med*. 2002; 156:1114–1119. [PubMed: 12413339]
3. Hersh AL, Shapiro DJ, Pavia AT, et al. Antibiotic prescribing in ambulatory pediatrics in the United States. *Pediatrics*. 2011; 128:1053–1061. [PubMed: 22065263]
4. Besser RE. Antimicrobial prescribing in the United States: good news, bad news. *Ann Intern Med*. 2003; 138:605–606. [PubMed: 12667034]
5. Jenkins SG, Farrell DJ. Increase in pneumococcus macrolide resistance, United States. *Emerg Infect Dis*. 2009; 15:1260–1264. [PubMed: 19751588]
6. Centers for Disease Control and Prevention. Antibiotic resistance threats in the United States. 2013. <http://www.cdc.gov/drugresistance/threat-report-2013>. Updated July 17, 2014. Accessed April 2, 2015
7. Smith R, Coast J. The true cost of antimicrobial resistance. *BMJ*. 2013; 346:f1493. [PubMed: 23479660]
8. World Health Organization. Antimicrobial resistance: global report on surveillance. <http://www.who.int/drugresistance/documents/surveillancereport/en>. Published 2014. Accessed December 29, 2016
9. Preventing Emerging Infectious Diseases. Addressing the Problem of Antimicrobial Resistance: A Strategy for the 21st Century. Centers for Disease Control and Prevention; Atlanta: 1998.
10. Infectious Diseases Society of America. Spellberg B, Blaser M, et al. Combating antimicrobial resistance: policy recommendations to save lives. *Clin Infect Dis*. 2011; 52(Suppl 5):S397–S428. [PubMed: 21474585]
11. Gonzales R, Malone DC, Maselli JH, et al. Excessive antibiotic use for acute respiratory infections in the United States. *Clin Infect Dis*. 2001; 33:757–762. [PubMed: 11512079]
12. Gaur AH, Hare ME, Shorr RI. Provider and practice characteristics associated with antibiotic use in children with presumed viral respiratory tract infections. *Pediatrics*. 2005; 115:635–641. [PubMed: 15741365]
13. Lee GC, Reveles KR, Attridge RT, et al. Outpatient antibiotic prescribing in the United States: 2000 to 2010. *BMC Med*. 2014; 12:96. [PubMed: 24916809]
14. Sarpong EM, Miller GE. Narrow-and broad-spectrum antibiotic use among US children. *Health Serv Res*. 2015; 50:830–846. [PubMed: 25424240]
15. Frenk SM, Kit BK, Lukacs SL, et al. Trends in the use of prescription antibiotics: NHANES 1999–2012. *J Antimicrob Chemother*. 2016; 71:251–256. [PubMed: 26462985]
16. Grijalva CG, Nuorti JP, Griffin MR. Antibiotic prescription rates for acute respiratory tract infections in US ambulatory settings. *JAMA*. 2009; 302:758–766. [PubMed: 19690308]

17. Pavia M, Bianco A, Nobile CG, et al. Efficacy of pneumococcal vaccination in children younger than 24 months: a meta-analysis. *Pediatrics*. 2009; 123:e1103–e1110. [PubMed: 19482744]
18. Osterholm MT, Kelley NS, Sommer A, et al. Efficacy and effectiveness of influenza vaccines: a systematic review and meta-analysis. *Lancet Infect Dis*. 2012; 12:36–44. [PubMed: 22032844]
19. Vaz LE, Kleinman KP, Raebel MA, et al. Recent trends in outpatient antibiotic use in children. *Pediatrics*. 2014; 133:375–385. [PubMed: 24488744]
20. Hicks LA, Bartoces MG, Roberts RM, et al. US outpatient antibiotic prescribing variation according to geography, patient population, and provider specialty in 2011. *Clin Infect Dis*. 2015; 60:1308–1316. [PubMed: 25747410]
21. Bourgeois FT, Mandl KD, Valim C, et al. Pediatric adverse drug events in the outpatient setting: an 11-year national analysis. *Pediatrics*. 2009; 124:e744–e750. [PubMed: 19786435]
22. Shehab N, Patel PR, Srinivasan A, et al. Emergency department visits for antibiotic-associated adverse events. *Clin Infect Dis*. 2008; 47:735–743. [PubMed: 18694344]
23. Zed PJ, Black KJ, Fitzpatrick EA, et al. Medication-related emergency department visits in pediatrics: a prospective observational study. *Pediatrics*. 2015; 135:435–443. [PubMed: 25647671]
24. Caspard H, Gaglani M, Clipper L, et al. Effectiveness of live attenuated influenza vaccine and inactivated influenza vaccine in children 2–17 years of age in 2013–2014 in the United States. *Vaccine*. 2016; 34:77–82. [PubMed: 26589519]
25. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)—a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform*. 2009; 42:377–381. [PubMed: 18929686]
26. Hoberman A, Paradise JL, Rockette HE, et al. Treatment of acute otitis media in children under 2 years of age. *N Engl J Med*. 2011; 364:105–115. [PubMed: 21226576]
27. Hersh AL, Jackson MA, Hicks LA, et al. Principles of judicious antibiotic prescribing for upper respiratory tract infections in pediatrics. *Pediatrics*. 2013; 132:1146–1154. [PubMed: 24249823]
28. Lieberthal AS, Carroll AE, Chonmaitree T, et al. The diagnosis and management of acute otitis media. *Pediatrics*. 2013; 131:e964–e999. [PubMed: 23439909]
29. Coker TR, Chan LS, Newberry SJ, et al. Diagnosis, microbial epidemiology, and antibiotic treatment of acute otitis media in children: a systematic review. *JAMA*. 2010; 304:2161–2169. [PubMed: 21081729]
30. Watson RL, Dowell SF, Jayaraman M, et al. Antimicrobial use for pediatric upper respiratory infections: reported practice, actual practice, and parent beliefs. *Pediatrics*. 1999; 104:1251–1257. [PubMed: 10585974]
31. Mainous AG 3rd, Hueston WJ, Love MM. Antibiotics for colds in children: who are the high prescribers? *Arch Pediatr Adolesc Med*. 1998; 152:349–352. [PubMed: 9559710]
32. Wessels MR. Clinical practice. Streptococcal pharyngitis. *N Engl J Med*. 2011; 364:648–655. [PubMed: 21323542]
33. Bisno AL. Acute pharyngitis. *N Engl J Med*. 2001; 344:205–211. [PubMed: 11172144]
34. McIsaac WJ, Kellner JD, Aufricht P, et al. Empirical validation of guidelines for the management of pharyngitis in children and adults. *JAMA*. 2004; 291:1587–1595. [PubMed: 15069046]
35. Petersen I, Johnson AM, Islam A, et al. Protective effect of antibiotics against serious complications of common respiratory tract infections: retrospective cohort study with the UK General Practice Research Database. *BMJ*. 2007; 335:982. [PubMed: 17947744]
36. Pichichero ME, Green JL, Francis AB, et al. Outcomes after judicious antibiotic use for respiratory tract infections seen in a private pediatric practice. *Pediatrics*. 2000; 105(4):753–759. Pt 1. [PubMed: 10742316]
37. Rovers MM, Glasziou P, Appelman CL, et al. Antibiotics for acute otitis media: a meta-analysis with individual patient data. *Lancet*. 2006; 368:1429–1435. [PubMed: 17055944]
38. Macfarlane J, Holmes W, Macfarlane R, Britten N. Influence of patients' expectations on antibiotic management of acute lower respiratory tract illness in general practice: questionnaire study. *BMJ*. 1997; 315:1211–1214. [PubMed: 9393228]

Key Points

- Most of the children in our study received antibiotics for appropriate indications.
- Lack of an antibiotic prescription did not increase the risk for return visits.
- Further decreasing antibiotic use in similar settings will likely require wider implementation of watchful waiting for acute otitis media, change in guidelines for pharyngitis management, and/or reductions in these diseases.

Fig.

Follow-up telephone calls and return visits. *a*, Descriptive summaries of follow-up telephone calls within 30 days of the initial visit and bivariate analyses between the groups of participants who were and were not initially prescribed antibiotics. *b*, Descriptive summaries of return visits within 30 days of the initial visit and bivariate analyses between the groups of participants who were and were not initially prescribed antibiotics. All *P* values calculated by Pearson χ^2 . *Significant at $P < 0.05$. abx, antibiotics; ARI, acute respiratory illness; ED, emergency department.

Table 1

Descriptive summaries and bivariate analyses

	No. participants, N = 206	Prescribed antibiotics, n = 59	Not prescribed antibiotics, n = 147	P
	No. (%) ^a	No. (%) ^b	No. (%) ^b	
Age, y	5 (4) ^c	5 (3) ^c	5 (5) ^c	0.50 ^a
Male sex	101 (49)	31 (31)	70 (69)	0.52
Race/ethnicity				<0.01*
Non-Hispanic white	107 (52)	36 (33)	71 (67)	
Non-Hispanic African American	80 (39)	17 (21)	63 (79)	
Hispanic/Latino	12 (6)	1 (8)	11 (92)	
Asian	9 (4)	7 (78)	2 (22)	
Pacific Islander	0	0	0	
Native American	0	0	0	
Other	2 (1)	0	2 (100)	
Clinic site				<0.01*
On campus	130 (63)	26 (20)	104 (80)	
Off campus	76 (37)	33 (43)	43 (57)	
Socioeconomic status				
Smoking in household	24 (12)	4 (17)	20 (83)	0.17
No. children in household	2[1, 2] ^c	2[1, 2] ^c	2 [1, 2] ^c	0.93 ^a
Insurance				0.01*
Public	103 (50)	20 (15)	83 (85)	
Private	97 (47)	36 (37)	61 (63)	
Both	6 (3)	3 (50)	3 (50)	
Influenza vaccination 2013–2014 season	153 (74)	44 (29)	109 (71)	0.95
Symptoms				
Cough	178 (86)	47 (26)	131 (74)	0.07
Fatigue	164 (80)	42 (26)	83 (74)	0.13
Congestion	159 (77)	43 (27)	116 (73)	0.35
Sore throat	125 (61)	24 (19)	68 (81)	0.04*
Irritability	113 (55)	17 (15)	49 (85)	0.36
Headache	92 (45)	29 (32)	84 (68)	0.45
Body aches	66 (32)	47 (71)	117 (29)	1.00
Nausea	55 (27)	17 (31)	38 (69)	0.66
Vomiting	53 (26)	8 (15)	45 (85)	0.01*
Wheezing	38 (18)	8 (21)	28 (79)	0.35
Diarrhea	36 (17)	11 (31)	27 (69)	0.96

	No. participants, N = 206	Prescribed antibiotics, n = 59	Not prescribed antibiotics, n = 147	<i>P</i>
	No. (%) ^a	No. (%) ^b	No. (%) ^b	
Medical history				
No. outpatient visits last year	2 [1, 3] ^c	2 [1, 3] ^c	2 [1, 2] ^c	0.19 ^a
1 chronic illnesses	53 (26)	12 (23)	41 (77)	0.26
Asthma	35 (16)	6 (17)	29 (83)	0.10
Blood disorder	3 (1)	1 (33)	2 (67)	0.86
Chronic lung disease	1 (0.5)	0	1 (100)	0.53
Diabetes mellitus	1 (0.5)	0	1 (100)	0.53
Heart disease	6 (3)	2 (33)	4 (67)	0.80
Immunodeficiencies	0	0	0	—
Kidney disease	2 (1)	0	2 (100)	0.37
Liver disease	1 (0.5)	0	1 (100)	0.53
Seizures	4 (2)	1 (25)	3 (75)	0.87
Severe obesity	0	0	0	—
Other chronic illnesses	11 (5)	6 (55)	5 (45)	0.05*
Primary diagnosis				
URI	62 (30)	2 (3)	60 (97)	0.00*
Streptococcal pharyngitis	38 (18)	34 (89)	4 (11)	0.00*
Pharyngitis	27 (13)	2 (7)	25 (93)	0.01*
Viral illness	24 (12)	1 (4)	23 (96)	0.01*
Influenza	15 (7)	0	15 (100)	0.01*
Acute otitis media	15 (7)	15 (100)	0	<0.01*
Fever ^A	6 (3)	1 (17)	5 (83)	0.51
None	6 (3)	1 (17)	5 (83)	0.51
Pneumonia/pneumonitis	2 (1)	2 (100)	0	0.03*
Allergic rhinitis	3 (1)	0	3 (100)	0.27
Acute asthma exacerbation	2 (1)	0	2 (100)	0.37
Croup	3 (1)	0	3 (100)	0.27
Tonsillitis	1 (0.5)	0	1 (100)	0.53
Bronchiolitis	1 (0.5)	1 (100)	0	0.11
Cough	1 (0.5)	0	1 (100)	0.53
Antiviral (oseltamivir) prescribed	14 (7)	0	14 (100)	0.01 [*]

All *P* values calculated by Pearson χ^2 test, except those denoted by ^a, which were calculated by Wilcoxon rank sum test. Boldface type indicates statistical significance. URI, upper respiratory illness.

^aPercentages calculated from column total.

^bPercentages calculated from row total.

^cMedian value [25th percentile, 75th percentile].

^{*}Significant at $P < 0.05$.

^AEntries “Fever” and “None” have the same values. OK or error? Please clarify. (OR is “none” a subcategory of “Fever”?)

Table 2

Logistic regression of risk factors for antibiotic prescription (N = 189)

Risk factors for antibiotic prescription	OR (95% CI)	P
Off-campus vs on-campus clinics	1.47 (0.27–8.10)	0.66
Private vs public insurance	2.40 (0.46–12.53)	0.27
African American vs non-African American race	0.40 (0.08–2.05)	0.27
Chronic illnesses	3.90 (0.74–20.40)	0.11
Influenza vaccination 2013–2014 season	0.52 (0.13–2.18)	0.37
Primary diagnosis		
Streptococcal pharyngitis	137.97 (12.85–1481.48)	<0.01*
Acute otitis media	— ^a	
Pharyngitis	1.08 (0.08–13.96)	0.95
Fever	2.40 (0.11–53.23)	0.58
Pneumonia	— ^b	
URI, influenza, viral illness	0.33 (0.03–4.03)	0.38
LRTI except pneumonia	4.40 (0.12–160.63)	0.42

Boldface type indicates statistical significance. CI, confidence interval; LRTI, lower respiratory tract illnesses; OM, otitis media; OR, odds ratio; URI upper respiratory illness.

^a100% of participants with primary diagnosis of OM were prescribed antibiotics; 15 participants dropped.

^b100% of participants with primary diagnosis of pneumonia/pneumonitis were prescribed antibiotics; 2 participants dropped.

*Significant at $P < 0.05$.

Table 3

Participants who did and did not make return visits

	No. (%) ^a		<i>P</i>
	Did make return visits, n = 41	Did not make return visit, n = 165	
Age, y	5[2, 6] ^b	5[3, 7] [*]	0.15 ^c
Sex			0.46
Male	18 (44)	83 (50)	
Female	23 (56)	82 (50)	
Race/ethnicity			0.04[*]
Non-Hispanic white	28 (68)	79 (48)	
Non-Hispanic African American	13 (32)	67 (41)	
Hispanic/Latino	0	12 (7)	
Asian	0	9 (5)	
Other	0	2 (1)	
Clinic site			0.01[*]
On campus	19 (46)	111 (67)	
Off campus	22 (54)	54 (33)	
Insurance			0.01[*]
Public	17 (41)	86 (52)	
Private	20 (49)	77 (47)	
Both	4 (10)	2 (1)	
1 chronic illnesses	14 (34)	39 (24)	0.17
Influenza vaccination 2013-2014 season	33 (81)	120 (73)	0.31
Diagnosis at initial visit			
URI	9 (22)	53 (32)	0.20
Streptococcal pharyngitis	9 (22)	29 (18)	0.52
Acute otitis media	6 (15)	9 (5)	0.04[*]
Viral illness	6 (15)	18 (11)	0.51
Pharyngitis	3 (7)	24 (15)	0.22
Influenza	2 (5)	13 (8)	0.51
None	2 (5)	4 (2)	0.40
Acute asthma exacerbation	1 (2)	1 (1)	0.28
Fever	1 (2)	5 (3)	0.84
Allergic rhinitis	0	3 (2)	0.27
Croup	0	3 (2)	0.62
Pneumonia/pneumonitis	0	2 (1)	0.48
Bronchiolitis	0	1 (1)	0.62

	No. (%) ^a		<i>P</i>
	Did make return visits, n = 41	Did not make return visit, n = 165	
Cough	0	1 (1)	0.62
Tonsillitis	0	1 (1)	0.53
Antibiotics prescribed at initial visit	16 (39)	43 (26)	0.10

All *P* values calculated by Pearson χ^2 test, except those denoted by ^c, which were calculated by Wilcoxon rank sum test. Boldface type indicates statistical significance. URI, upper respiratory illness.

^aPercentages calculated from column total.

^bMedian value [25th percentile, 75th percentile].

*Significant at *P* < 0.05.