



Impact of Penicillin Allergy Labels on Children Treated for Outpatient Respiratory Infections

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Background Penicillin allergy is the most common antibiotic allergy, yet most children labeled as allergic tolerate penicillin. The impact of inaccurate penicillin allergy labels (PALs) on pediatric outpatients is unknown. The objective of this study was to compare outcomes between children with and without a PAL after treatment for outpatient respiratory tract infections (RTI).

Methods: A retrospective, longitudinal birth cohort study was performed in children who received care in 90 pediatric primary care practices in Philadelphia and Houston metropolitan areas. Prescribing and clinical outcomes of children with a PAL at the time of an RTI were compared to non-allergic children, adjusting for potential confounders.

Results: Antibiotics were prescribed for 663,473 non-recurrent RTIs among 200,977 children. Children with a PAL (5% of cohort) were more likely than non-allergic children to receive broad-spectrum antibiotics (adjusted relative risk (aRR) 3.24, 95% CI 3.22–3.26) and second-line antibiotics (aRR 4.87, 95% CI 4.83, 4.89). Compared to non-allergic children receiving first-line antibiotics, children with a PAL were more likely to return with adverse drug events (aRR 1.28, 95% CI 1.18–1.39). There was no difference in treatment failure between groups (aRR 0.95, 95% CI 0.90–1.00).

Conclusions PALs lead to higher rates of broad-spectrum and second-line antibiotic prescribing in children treated for RTIs in primary care and contribute to unnecessary healthcare utilization through increased adverse events. Given the frequency of PALs, efforts to prevent inappropriate penicillin allergy labeling and promote de-labeling of existing inaccurate allergy labels may improve care of children treated for common bacterial infections.

Key Words. penicillin; allergy; antimicrobial stewardship.

Penicillin allergy is reported in 4–10% of children but over 95% of children labeled as penicillin allergic do not have an IgE-mediated hypersensitivity reaction on formal evaluation.[1–5] Instead, these children may have been labeled as allergic following symptoms related to a viral illness (e.g., rash), an antibiotic side effect (e.g., diarrhea), or a virus-drug interaction.[6] Prior studies, largely focused on adults and pediatric inpatients, report associations between penicillin allergy labels (PALs) and increased use of broad-spectrum antibiotics, *Clostridioides difficile* and vancomycin-resistant *Enterococcus* infections, increased cost and increased healthcare utilization, decreased survival in sepsis, and prolonged hospitalization.[7–13] However, the impact of PALs on clinical outcomes of pediatric

outpatients, a population that receives more antibiotics than any other group, remains unclear.

In 2019, more than 55 million outpatient antibiotic prescriptions were given to children in the United States.[14] Respiratory tract infections (RTIs) are the most common indication for antimicrobial prescribing in children, and penicillin antibiotics are considered first-line therapy for these infections by the Infectious Diseases Society of America and the American Academy of Pediatrics.[15–18] Recent studies have shown that approximately 20% of children receive second line antibiotics for RTIs, however the contribution of PALs to second-line antibiotic prescribing is less well understood.[19, 20] This study aimed to examine the effect of PALs on antibiotic prescribing and clinical outcomes in children diagnosed with acute RTIs in two large pediatric primary care networks that include urban, suburban, and rural populations of diverse race, ethnicity, and socioeconomic status: The Children's Hospital of Philadelphia (CHOP) Primary Care Network and the Texas Children's Pediatrics (TCP) network. Because first-line antibiotics are chosen to maximize efficacy and minimize adverse effects, we hypothesized that children with a PAL would receive more broad-spectrum and second-line antibiotics and would therefore experience more adverse drug effects, treatment failures,

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and serious infectious complications compared to non-labeled children prescribed first-line antibiotics for RTIs.

METHODS

Study Design

This retrospective longitudinal birth cohort study was conducted in the CHOP and TCP primary care networks.^[1] The CHOP and Baylor College of Medicine Institutional Review Boards for the Protection of Human Subjects granted a waiver of consent with approval of this study. The STROBE guidelines for reporting observational studies were followed.^[21]

Setting

The CHOP and TCP outpatient networks contain 90 affiliated pediatric primary care clinics that employ over 500 pediatricians and advanced practice providers in Pennsylvania, New Jersey, and Texas. In 2019 and 2020, these networks had over 3.7 million primary care encounters by over 700,000 children. Clinicians in both systems exclusively use the electronic medical record (EMR) EpiCare (Epic Systems, Inc; Verona, WI) for office and telephone encounter documentation and order entry.

Study Population

To establish a group of children who were likely to get the majority of their care in network, Children in the CHOP and TCP healthcare networks were included in the birth cohort only if they were (1) born between January 1st 2010 and June 30th 2020, (2) seen by a CHOP or TCP primary care pediatrician (PCP) within the first fourteen days of life, and (3) had at least two additional PCP visits in the first year of life. In subsequent years of life, children were censored if they did not have at least one PCP encounter per year from ages one to four years and at least one PCP encounter every two years after four years of age; the censor date was the date of the child's last qualifying PCP visit. Basic demographics were obtained for each patient, and the following data from each healthcare visit were extracted from the EMR: encounter date, ICD-10 codes [International Classification of Diseases, 10th edition], clinic location, clinician name, insurance payer, and medications prescribed. The date of data extraction was November 12, 2020 for TCP and December 13, 2020 for CHOP clinics. Electronically extracted data, including the timing of placement of a PAL, were validated by manual chart review of 50 charts in each health systems EMR.

Exposure

The exposure of interest was presence of a PAL at the time a child was prescribed an antibiotic for an RTI. PALs were defined as EMR documentation of allergy to a penicillin or penicillin derivative, including penicillin, amoxicillin, ampicillin,

amoxicillin/clavulanate, ampicillin/sulbactam, piperacillin/tazobactam, oxacillin or nafcillin. RTIs were defined as primary care encounters with an ICD-10 code for acute otitis media (AOM), sinusitis, group A Streptococcal pharyngitis, or community acquired pneumonia (CAP) (Supplementary Table 1). These infections were chosen because they are frequently presumed to be bacterial in etiology and the majority of children with these infections receive an antibiotic. RTIs within 30 days of an antibiotic prescription were excluded from analysis as antimicrobial selection may have been affected by prior prescriptions.

Outcomes

The following five outcomes were independently assessed for each non-recurrent RTI: (1) Receipt of a second-line antibiotic per AAP or IDSA guidelines, including antibiotics other than amoxicillin or amoxicillin/clavulanate for AOM or acute bacterial sinusitis, antibiotics other than amoxicillin or azithromycin for CAP, and antibiotics other than amoxicillin or penicillin for group A Streptococcal pharyngitis.^[15–18] (2) Receipt of a broad-spectrum antibiotic, defined as an antibiotic other than penicillin or amoxicillin. (3) Adverse drug events, defined as encounters with an ICD-10 code for anaphylaxis (within seven days of RTI), Steven's Johnson Syndrome, unspecified allergic reaction, unspecified rash, urticaria, candidiasis, diaper dermatitis, diarrhea, nausea/emesis (within 30 days of RTI), and *Clostridioides difficile* infection (within 90 days of RTI). (4) Treatment failure, defined as primary care encounters between two and 14 days after receipt of an antibiotic prescription for a non-recurrent RTI with the same RTI diagnosis, a different antibiotic prescribed, and absence of an ICD-10 code for adverse events as defined for outcome (3). (5) Serious infectious complications within the subsequent 30 days of an RTI, defined as an ICD-10 code for mastoiditis, orbital cellulitis, intracranial abscess, retropharyngeal abscess, peritonsillar abscess, empyema and pleural effusion (Supplementary Table 1).

For second-line and broad-spectrum antibiotic use, PAL status at time of RTI diagnosis was the primary exposure of interest. For adverse drug events, treatment failure and infectious complications, children with a PAL at the time of an RTI were compared to non-allergic children who received a first line antibiotic. Encounters of children who eventually became labeled as penicillin-allergic (pre-allergic encounters) and non-allergic children receiving second-line antibiotics were excluded from the non-allergic group (Figure 1).

A sub analysis comparing broad-spectrum, second-line, adverse events, and treatment failure by RTI type was performed. In addition, a secondary analysis categorizing the adverse events as hypersensitivity (anaphylaxis, unspecified allergic reaction, unspecified rash and urticaria) or non-hypersensitivity, (nausea/emesis, *Clostridioides difficile*

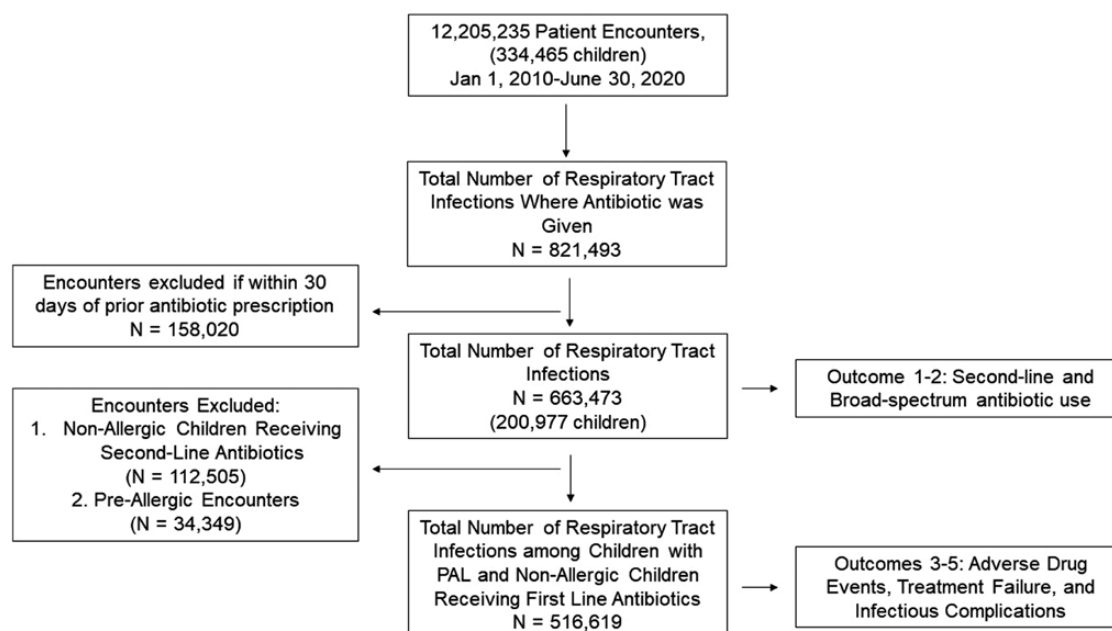


Figure 1. Study flow diagram.

infection, diarrhea, candidiasis and diaper dermatitis) was also performed.

Statistical Methods

A modified Poisson regression was used to estimate the relative risk and confidence intervals with robust variance estimates.[22] The outcomes of interest included second-line and broad-spectrum antibiotic prescribing, adverse events, treatment failure, and infectious complications for penicillin-allergic and non-labeled groups. Adjusted risk differences between penicillin-allergic or non-labeled groups were calculated based on the modified Poisson models and by holding all other covariates at their means. Covariates were selected *a priori* due to potential confounding of the association between penicillin allergy labeling and antibiotic prescribing and included: age at infection, sex, chronic condition, insurance payer, race/ethnicity, primary clinic, and number of healthcare encounters by the age of 2 years. Race/ethnicity were self-reported in the EMR and were then classified into the following groups: Hispanic, non-Hispanic Black, non-Hispanic White, Asian or Pacific Islander and other/missing. Chronic condition was dichotomized as a yes/no variable based on the presence of a complex condition from the patient's problem list using the pediatric complex conditions classification system 2 diagnoses codes.[23] Children with at least one encounter using government insurance were classified as having government insurance. Primary clinic was defined as the first primary care clinic where a patient was seen. All analyses were performed using Stata 16 software (StataCorp. 2021. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC). A two-sided 5% significance level was used for all statistical inferences.

RESULTS

Study Population

The birth cohort encompassed a total of 12,205,235 health-care encounters from 334,465 children over 1.4 million-person years. Overall, 18,015 (5%) children were labeled as penicillin allergic, and 2,329 (14%) were de-labeled during the study period. Additional demographics of all children in the birth cohort are described elsewhere.[1] The demographics of 200,977 children with at least 1 antibiotic prescription for an RTI are shown in Table 1; 16,775 (8%) children had an active penicillin allergy label at the time of an RTI.

A total of 821,493 RTIs resulted in an antibiotic prescription; 663,473 of these occurred >30 days from a prior antibiotic prescription and were included in the analysis for second-line and broad-spectrum antibiotic prescribing. AOM was the most common RTI (521,756, 79%), and 35,771 (5%) of all RTIs occurred in children with an active PAL. After excluding encounters of non-allergic children receiving second-line antibiotics and pre-allergic encounters, 516,619 RTIs were assessed for adverse events, treatment failure, and infectious complications (Figure 1).

Second-line and Broad-spectrum antibiotic use

Children diagnosed with non-recurrent RTI received a second-line or broad-spectrum antibiotic in 150,195 (23%) and 213,036 (32%) of 663,473 RTIs, respectively. Despite only making up 5% of the cohort, children with a PAL accounted for 22% of the second-line antibiotics prescribed. Among non-allergic children, the most commonly prescribed antibiotics

Table 1. Demographic characteristics of 200,977 children in birth cohort with at least 1 antibiotic prescription for a respiratory tract infection.

Demographic	Penicillin Allergic 16,775 (8%)	Penicillin Non Allergic 184,202 (92%)
Sex		
Female	7,732 (46%)	88,681 (48%)
Male	9,043 (54%)	95,521 (52%)
Race/Ethnicity		
Asian or Pacific Islander	937 (6%)	10,342 (6%)
Non-Hispanic Black	1,431 (8%)	27,230 (15%)
Hispanic	2,987 (18%)	40,612 (22%)
Non-Hispanic White	10,124 (60%)	91,140 (49%)
Other/Missing	1,296 (8%)	14,878 (8%)
Government Insurance	4,365 (26%)	59,170 (32%)
Chronic Medical Condition	1,227 (7%)	13,526 (7%)
Organization		
CHOP	7,013 (42%)	63,225 (34%)
TCP	9,762 (58%)	120,977 (66%)
Median time in birth cohort, years (IQR)	5.3 (3.1-7.5)	5.6 (3.4-7.8)
Median number of primary care healthcare encounters by 2 years of age (IQR)	21 (17, 27)	18 (13-22)
Median Age of RTI, years (IQR)	1.9 (1.1, 3.5)	1.7 (0.9-3.1)
Total Number of non-recurrent RTI	70,120	593,353
Acute Otitis Media	53,575 (76%)	468,064 (79%)
Group A Strep Pharyngitis	6,840 (10%)	52,816 (9%)
Sinusitis	6,568 (9%)	48,305 (8%)
Community Acquired Pneumonia	2,437 (3%)	19,706 (3%)
>1 RTI diagnosis	700 (1%)	4,462 (1%)
Median Number of RTI (IQR)	6 (4-9)	5 (3-7)
Median Age of PAL placement years (IQR)	1.3 (0.9-2.3)	NA

were penicillin or amoxicillin (71%) followed by third generation cephalosporins (15%). Children with a PAL at the time of RTI were most commonly prescribed third-generation cephalosporins (64%) and macrolides (27%) (Figure 2), although 3% of children with a PAL received a penicillin antibiotic. Children with an RTI and active PAL were more likely than those without a PAL to receive second-line (adjusted relative risk (aRR) 4.87 [95% CI 4.83, 4.89], 66.1% predictive risk difference) and broad-spectrum (aRR 3.24 [95% CI 3.22, 3.26], 60.0% predicted risk difference, Table 2) antibiotics. In a sub

analysis by RTI type, Streptococcal pharyngitis had the highest predicted risk difference for receipt of a broad-spectrum and second-line antibiotic and CAP had the lowest (Table 2).

Adverse Events, Treatment Failure and Infectious Complications

Adverse drug events, treatment failure, and infectious complications were evaluated among 516,619 non-recurrent RTIs. Adverse drug events occurred following 8,736 encounters (2%) and children with a PAL at the time of RTI were more likely to have an adverse drug event compared to non-allergic

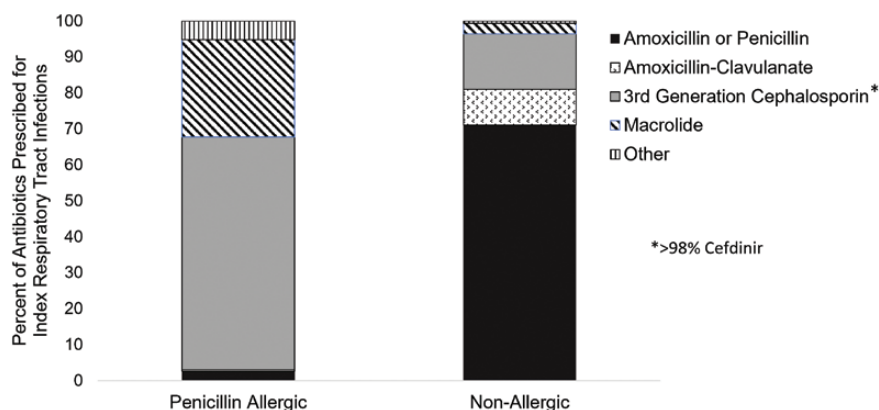


Figure 2. Composition of antibiotic prescribing for respiratory tract infections by antibiotic class among children with and without penicillin allergy labels.

Table 2. Adjusted relative risk, predicted risk and risk differences for outcomes of interest based on modified Poisson regression.

Outcome	Adjusted Relative Risk [95% CI]*	Predicted Risk % [95% CI]**		Predicted Risk Difference % [95% CI]
		Penicillin Allergic at Encounter	Non-Allergic at Encounter	
Second-Line Antibiotics	4.87 [4.83-4.89]	83.3 [82.8, 83.7]	17.2 [17.1, 17.3]	66.1 [65.7, 66.4]
AOM	4.78 [4.74-4.82]	80.4 [79.8-81.0]	16.8 [16.7-16.9]	63.6 [63.1-64.1]
CAP	6.59 [6.11-7.10]	43.9 [41.0-46.8]	6.66 [6.34-6.98]	34.7 [34.7-41.8]
Sinusitis	4.54 [4.44-4.65]	84.1 [82.6-85.6]	18.5 [18.2-18.8]	65.6 [64.4-66.8]
Strep Pharyngitis	7.34 [7.17-7.52]	91.9 [91.0-92.8]	12.5 [12.2-12.8]	79.4 [78.8-80.0]
Broad-Spectrum Antibiotics	3.24 [3.22, 3.26]	86.8 [86.4, 87.2]	26.8 [26.7, 26.9]	60.0 [59.7, 60.3]
AOM	3.11 [3.09-3.13]	83.8 [83.3-84.3]	26.9 [26.8-27.1]	56.9 [56.5-57.2]
CAP	2.41 [2.35-2.48]	89.6 [87.5-91.8]	37.1 [36.5-37.8]	52.5 [51.0-54.0]
Sinusitis	2.56 [2.51-2.60]	86.9 [85.6-88.2]	33.9 [33.5-34.3]	53.0 [52.1-53.9]
Strep Pharyngitis	7.34 [7.17-7.52]	91.9 [91.0-92.8]	12.5 [12.2-12.8]	79.4 [78.8-80.0]
Adverse Drug Event	1.28 [1.18, 1.39]	1.5 [1.4-1.7]	1.2 [1.2, 1.2]	0.3 [0.2, 0.4]
AOM	1.29 [1.18-1.42]	1.75 [1.58-1.91]	1.35 [1.31-1.39]	0.4 [0.27-0.52]
CAP	1.38 [0.85-2.26]	1.14 [0.59-1.68]	0.82 [0.62-1.02]	0.32 [-0.03-0.66]
Sinusitis	1.10 [0.78-1.55]	0.78 [0.52-1.04]	0.71 [0.60-0.81]	0.07 [-0.08-0.23]
Strep Pharyngitis	1.68 [1.30-2.17]	1.26 [0.95-1.57]	0.75 [0.67-0.84]	0.51 [0.28-0.73]
Treatment Failure	0.95 [0.90, 1.00]***	3.1 [2.9, 3.2]	3.2 [3.2, 3.3]	0.1 [0.1, 0.3]
AOM	0.96 [0.90-1.02]	3.70 [3.48-3.92]	3.86 [3.79-3.92]	-0.16 [-0.47-0.0]
CAP	0.86 [0.60-1.24]	1.60 [1.04-2.2]	1.8 [1.60-2.1]	-0.20 [-0.56-0.1]
Sinusitis	0.96 [0.72-1.29]	0.91 [0.69-1.23]	0.99 [0.89-1.10]	-0.08 [-0.20-0.13]
Strep Pharyngitis	1.07 [0.84-1.36]	1.31 [1.01-1.62]	1.23 [1.12-1.33]	0.08 [-0.11-0.29]

*Adjusted for sex, race/ethnicity, chronic condition, age at infection, payer type, primary clinic and number of health care encounters by 2 years of age

**At means.

*** $p = 0.067$.

children receiving a first line antibiotic (aRR 1.28 [1.18, 1.39], Table 2). In a sub analysis by RTI type, increased ADE occurred with AOM and Streptococcal pharyngitis but not CAP or sinusitis. Treatment failure occurred following 20,009 (4%) non-recurrent RTIs, but there was no statistically significant difference between children with PAL at the time of RTI and non-allergic groups (Table 2). Only 11 (0.002%) non-recurrent RTIs had serious infectious complications (Supplementary Table 2.)

In the secondary analysis, hypersensitivity adverse events occurred more often in children with a PAL at time of RTI than non-allergic children receiving a first line antibiotic (aRR 1.74 [1.54–1.96]. There was no difference in non-hypersensitivity adverse events between groups (aRR 1.05 [0.93–1.19]).

DISCUSSION

In this ten-year, birth cohort study of children with over 600,000 RTIs and associated antibiotic prescriptions in two of the largest pediatric primary care networks in the United States, those with a PAL at the time of RTI were more likely to receive second-line and broad-spectrum antibiotics and more likely to have an adverse drug event compared to non-allergic children receiving first-line antibiotics. There was no observed difference in the rate of treatment failure between labeled and non-labeled

children. Over 18,000 children in this birth cohort were labeled as penicillin allergic during the study period with 86% of these children retaining their PAL after placement through the study period and 35,000 RTIs encounters occurring in children carrying PALs. These findings highlight the need to scrutinize (and potentially “delabel”) those who have been assigned PALs and encourage more judicious assignment of allergy labels when evaluating a potential adverse drug reaction after antibiotic receipt.

Most children with PALs tolerate oral penicillin during drug provocation testing; however, referrals to allergy clinics are often limited by patient/family disinterest, time constraints from the referring provider or limited access to allergists.[3, 5, 6, 24] Consequently, PALs are perpetuated in the medical record, prompting physicians to avoid beta lactam antibiotics and instead prescribe alternative agents. Our study reports similar findings to a recent study of pediatric encounters for acute RTIs in children with a PAL, which also demonstrated increased exposure to broad-spectrum and second-line antibiotics compared to non-allergic children.[25] While other factors contributing to provider or patient preferences for antimicrobial selection in this study could not be distinguished, the findings were consistent with our results, particularly the increased use of third generation cephalosporins and macrolides among children with a PAL. Our study expanded upon this work in a larger, more diverse population and additionally examined

rates of adverse events and treatment failures. As antimicrobial stewardship efforts expand to the outpatient setting, addressing unconfirmed PALs in the community will be an important first step in combatting broad-spectrum and second-line antimicrobial use.[26]

The IDSA and the AAP have established treatment guidelines for the most common pediatric RTIs, acute otitis media, group A streptococcal pharyngitis, acute bacterial sinusitis and community-acquired pneumonia, and penicillin derivatives are considered first-line across all conditions.[15–18] Although these guidelines provide recommendations for use of second-line antibiotics for children with PALs, the impact of using these second-line antibiotics has not been clear. One study found that children prescribed broad-spectrum antibiotics for RTIs had higher rates of adverse drug events (4%) compared to those prescribed narrow-spectrum agents (3%).[27] However, penicillin allergy status at the time of these infections was not assessed. In our study, we similarly found that children with a PAL at the time of RTI were more likely to have return visits for adverse drug events compared to non-allergic peers who received first-line antibiotics.

Although the overall risk of an adverse event for a child receiving an antibiotic in this study was low (predicted risk 1.5% in PAL and 1.2% in non-allergic, predicted risk difference 0.3%) we believe this result is clinically meaningful for multiple reasons. First, prior studies have shown that the rate of adverse events identified after antibiotics is ten-fold higher when prospectively evaluated through patient survey as opposed to abstraction from ICD-10 codes, so our study likely underestimates the number of adverse drug events caused by PALs.[27] Second, with over 55 million outpatient antibiotic prescriptions given to children in the United States each year, the majority of which are for RTI, and with over 5% of children carrying a PAL in the outpatient setting, any increase in the rate of broad-spectrum antibiotic prescribing driven by PALs likely has a sizeable effect. Interestingly, the increased rate of return visits for adverse events among children with a PAL was driven primarily by hypersensitivity type symptoms as opposed to non-hypersensitivity symptoms, such as diarrhea, typically associated with broad-spectrum antibiotic use. These increased return visits occurred despite controlling for healthcare utilization and may indicate that children with a PAL are more likely to develop rashes during an infection or antibiotic exposure or have families who seek medical care when these adverse events occur. Future studies should further evaluate healthcare utilization of children with PALs.

We also hypothesized that children with PALs would have more treatment failures because of increased use of second-line antibiotics. In one study, rates of *Streptococcus pneumoniae* susceptibility were 89% for the first-line antibiotic (high-dose amoxicillin) but only 59% and 57% for cefdinir and azithromycin, respectively.[28] Oral third generation cephalosporins are relatively poorly absorbed, protein-bound, and

may lack optimal drug levels within the middle ear space.[29] Macrolide and clindamycin resistance has also been described in group A streptococcal isolates in children.[30] However, in this study, presence of a PAL was not associated with an increased risk of treatment failure. Although pediatricians commonly prescribe antibiotics for RTIs, these infections often resolve without antibiotic treatment, which could reduce the statistical power to detect differences in treatment failure related to antibiotic choice.[31] Second, because our definition of treatment failure required a change in antibiotic, prescribers for children with a PAL have fewer antibiotic options to choose from and thus may be less likely to change to a new antibiotic for those who return to clinic with lack of improvement. Future studies should examine this hypothesis and evaluate the effect of PALs on treatment outcomes in other pediatric infections, particularly those confirmed to be bacterial in nature.

The majority of work evaluating PALs in children have focused on inpatient and emergency department settings. Strengths of this study include its large sample size representing a diverse population of children aged 1–10 years from two parts of the United States, cared for in the outpatient setting. In addition, the development of a birth cohort using a common, comprehensive, electronic health record with established follow up allowed for controlling for confounders such as healthcare utilization not done in previous studies examining outpatient prescribing in children with PALs. To the best of our knowledge, this study was also the first to assess the impact of PALs on adverse events and treatment failures in pediatric outpatients. This study was limited by its retrospective nature and reliance on diagnostic codes (and thus subject to coding bias). Similarly, bacterial cultures were not used to confirm a bacterial etiology of RTIs, which may have led to failure to detect differences in treatment failure between groups. Additionally, any nuances that could further explain the reasons for return visits that we captured as treatment failure could not be elucidated. Furthermore, because medication data were based on dates of prescriptions, we could not establish whether a prescribed antibiotic was filled, taken correctly, and tolerated. We suspect, however, that such potential misclassification would be non-differential. Finally, we could not exclude that treatment failures or adverse drug events were managed in systems outside of the TCP and CHOP networks, and more severe reactions such as anaphylaxis may be more likely to be managed at an outside emergency department and not captured by our data. This limitation is likely minimized by the birth cohort study design, which selected for children most likely to stay within the CHOP and TCP networks for their acute care.

CONCLUSION

Children labeled as penicillin allergic at the time of an RTI were more likely to receive second-line and broad-spectrum

antibiotics and had increased return visits for hypersensitivity type adverse drug events. Treatment failure did not differ between groups and serious infectious complications were rare. These findings highlight that PALs are important targets for antimicrobial stewardship programs that desire to decrease broad-spectrum antibiotic use in the outpatient setting. Primary care physicians should also be aware that children with a PAL are more likely to return to clinic with an adverse event than children without PALs. Quality improvement efforts to prevent inappropriate labeling and promote de-labeling of children without true penicillin allergies should be top priorities for outpatient antimicrobial stewardship. Future work should examine the impact of PALs on other common pediatric infections and determine if appropriate PAL de-labeling is associated with improved patient-specific clinical outcomes, reduced healthcare overutilization, and costs.

Supplementary Data

Supplementary materials are available at the Journal of The Pediatric Infectious Diseases Society online (<http://jpids.oxfordjournals.org>).

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Potential conflicts of interest. All authors report no relevant conflicts of interest.

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