



# Contribution of Penicillin Allergy Labels to Second-Line Broad-Spectrum Antibiotic Prescribing for Pediatric Respiratory Tract Infections

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## ABSTRACT

**Introduction:** Antibiotic allergies are overdiagnosed. This may lead to unnecessary use of second-line broader-spectrum agents in place of narrower-spectrum guideline-recommended first-line therapies especially for uncomplicated respiratory tract infections. The extent to which this occurs for children with respiratory tract infections is unknown.

**Methods:** We included outpatient encounters for patients < 18 years with acute respiratory

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tract infections (sinusitis, bronchitis, bronchiolitis, upper respiratory tract infection, pharyngitis, otitis media). Patients were classified as penicillin allergic based on the presence of an allergy label in the electronic medical record. First-line guideline-recommended antibiotics included penicillin, amoxicillin or amoxicillin-clavulanate; all others were considered second line. The percentage of patients treated with first-line versus second-line antibiotics was compared between those with and without penicillin allergy. Additionally, we calculated the contribution of penicillin allergy to overall use of second-line antibiotics.

**Results:** Among 17,578 eligible encounters for respiratory tract infections, 1332 (8%) included patients with a penicillin allergy label. Overall, second-line antibiotics were prescribed in 15% of encounters. Second-line antibiotics were prescribed in 91% of encounters for penicillin-allergic patients, compared with 8% of encounters for non-allergic patients ( $P < 0.001$ ). Patients with penicillin allergy labels accounted for 47% of all second-line antibiotic prescriptions.

**Conclusion:** In a large population of pediatric outpatient encounters for acute respiratory tract infections, patients labeled with a penicillin allergy accounted for nearly half of second-line antibiotics, which are often broader spectrum. Efforts to de-label children with penicillin allergies have the potential to reduce broader-spectrum antibiotic use.

**Keywords:** Allergy; Antibiotic; Pediatrics

### Key Summary Points

#### Why carry out this study?

Antibiotic allergies are common and often over-diagnosed, especially for penicillin.

As a result, patients with allergy labels often receive broader-spectrum antibiotics that may not be necessary.

The objective was to assess the contribution of penicillin allergy to broad-spectrum antibiotic use in children with respiratory tract infections.

#### What was learned from the study?

In the study population, patients with penicillin allergy were responsible for nearly half of broader-spectrum antibiotic prescriptions.

Allergy delabeling interventions have the potential to reduce broad-spectrum antibiotic use in pediatrics.

## INTRODUCTION

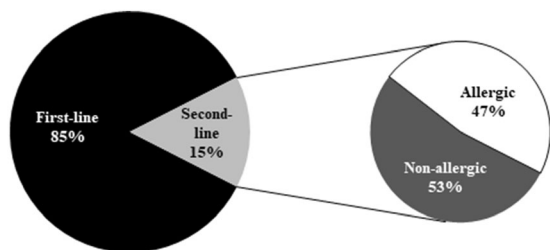
Inappropriate antibiotic prescribing contributes to avoidable adverse events and antibiotic-resistant infections. Although national guidelines recommend narrower-spectrum beta-lactam antibiotics—for example, amoxicillin and penicillin—as first-line agents for most uncomplicated bacterial acute respiratory tract infections (ARTIs) in children, use of second-line antibiotics for these conditions is common and these alternatives are often broader spectrum [1]. One important clinical scenario that may justify the use of second-line broader-spectrum antibiotics instead of first-line therapy is when a patient is allergic to penicillin. However, there is growing evidence that penicillin allergy labels are often inaccurate and that patients labeled as penicillin-allergic are more likely to receive

second-line antibiotics and to experience inferior clinical outcomes compared with non-allergic patients [2, 3]. Since second-line agents are not more effective for children with respiratory tract infections than first-line therapies and cause more adverse drug events, minimizing their unnecessary use is a core component of antibiotic stewardship [4]. The extent to which patients with penicillin allergy labels contribute to use of second-line antibiotics in outpatient pediatrics has not been quantified.

## METHODS

We examined outpatient encounters by patients < 18 years of age in eight primary care and four urgent care clinics in the University of Utah Health System between October 1, 2014, and June 30, 2018. These clinics are located in Salt Lake City, UT, and surrounding communities. Encounters were included if the patient was prescribed systemic antibiotics and received a diagnosis of an ARTI based on International Classification of Diseases, Clinical Modification, 10th Revision codes adapted from a prior study [1]. ARTIs were defined as sinusitis, bronchitis, bronchiolitis, upper respiratory tract infection, pharyngitis and otitis media. Patients were classified as penicillin-allergic based on the presence of an allergy listed in the allergy field of the electronic medical record. We considered penicillin allergy to encompass penicillin and penicillin derivatives (e.g., amoxicillin). Encounters by patients who had been prescribed antibiotics within the prior 30 days were excluded, since a recent antibiotic exposure could justify use of an alternative agent. We classified first-line antibiotics as penicillin, amoxicillin and amoxicillin–clavulanate based national guidelines for pediatric upper respiratory tract infections including otitis media, sinusitis and pharyngitis [5–7]. All other antibiotic classes (e.g., cephalosporins and macrolides) were considered second-line antibiotics.

We compared the percentage of patients with and without penicillin allergy who received second-line antibiotics. We used a chi-square test to compare proportions between



**Fig. 1** Contribution of penicillin allergy labels to second-line antibiotic prescribing. (Left) Proportion of all antibiotics that were first-line guideline recommended (penicillin, amoxicillin, amoxicillin-clavulanate) versus second line. (Right) Proportion of second-line antibiotics that were for penicillin-allergic versus non-allergic patients

groups. We used multivariable logistic regression to determine the independent association between penicillin allergy and second-line antibiotic use while controlling for patient age, gender and ARTI diagnosis. Additionally, we determined the percentage of second-line prescriptions that were associated with a penicillin allergy label. All analyses were performed using RStudio 1.1.463 (R version 3.5.2). This study received approval from the University of Utah Institutional Review Board (Fig. 1).

## RESULTS

We identified 17,578 eligible encounters for respiratory tract infections among 14,029 unique patients that received antibiotics for ARTI during the study period; 1332 encounters (8% of all encounters) included patients with a penicillin allergy label, and these patients accounted for 1067 patients (8% of all patients) in the cohort. The median age was 6 years in the allergic group and 5 years in the non-allergic, and 51% were male in both groups. The most common diagnosis was acute otitis media (46% of all encounters), followed by pharyngitis (33%). Overall, second-line antibiotics were prescribed in 15% of encounters. The most commonly prescribed second-line antibiotics were cephalosporins (61% of second-line antibiotics, 86% third-generation) and macrolides (36%). Amoxicillin or amoxicillin-clavulanate was prescribed for 116/1332 (9%)

encounters for penicillin-allergic patients. Second-line antibiotics were prescribed in 91% of encounters for penicillin-allergic patients compared with 8% of encounters for non-allergic patients ( $P < 0.001$ ). After adjusting for age and diagnosis, the odds of receiving a second-line antibiotic were 137 (95% CI 112–169) for patients with penicillin allergy compared to non-allergic patients. Collectively, encounters for patients with penicillin allergy labels accounted for 47% of second-line antibiotics prescribed in all encounters.

## DISCUSSION

This study compared outpatient antibiotic prescribing patterns for ARTIs between children with and without penicillin allergy and quantified the contribution of penicillin allergy labels to second-line, broader-spectrum antibiotic prescribing in a large health network. The study had three main findings. First, approximately 8% of children diagnosed and treated for ARTIs were labeled as penicillin-allergic—a prevalence similar to that found in studies of adults [8, 9]. Second, penicillin-allergic patients were much more likely than non-allergic patients to receive second-line broader-spectrum antibiotics. Third, despite accounting for < 10% of all visits, penicillin-allergic patients accounted for nearly half of all second-line antibiotic prescriptions for ARTI.

Collectively, these findings suggest that interventions designed to improve initial allergy assessment/documentation in the electronic medical record and to de-label penicillin-allergic patients have the potential to reduce unnecessary second-line broader-spectrum antibiotic use in outpatient pediatrics [10]. Such interventions are important, as broader-spectrum antibiotics may be associated with higher rates of adverse drug events and antibiotic resistance compared to narrow-spectrum agents. Additionally, because the prevalence of penicillin allergy in this cohort of children is similar to that reported in adults, our findings suggest that many penicillin allergy labels are likely assigned during childhood. Furthermore, the fact that 9% of patients labeled as penicillin

allergic nonetheless received a penicillin derivative indicates that clinicians may already be aware that some allergy labels are incorrect. As such, allergy de-labeling interventions targeted toward children have the potential to limit cumulative exposure to broader-spectrum antibiotics throughout a patient's life.

Our study has limitations. First, because the study was conducted in one regional healthcare network, the results may not be generalizable to other populations outside of the Salt Lake City region or University of Utah care network. Of particular note, the use of second-line agents in our sample was less frequent than in the US as a whole [1]. As a result, the potential impact of de-labeling strategies may be greater in other regions. We were unable to distinguish individual cases in which second-line antibiotic use was prescribed because of factors other than penicillin allergy (e.g., patient or provider preferences). Additionally, we relied on allergies reported in the medical record but could not verify the type of reaction or accuracy of the allergy label.

## CONCLUSIONS

Notwithstanding these limitations, our study demonstrates that penicillin allergy labels are an important contributor to second-line broader-spectrum antibiotic selection in outpatient pediatrics. Allergy de-labeling should be emphasized as part of outpatient stewardship interventions in pediatrics.

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**Data Availability.** The datasets generated during and/or analyzed during the current study are not publicly available due to privacy protections at the University of Utah.

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