



# Reported Knowledge and Management of Potential Penicillin Allergy in Children

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The authors have no conflicts of interest to disclose.

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Received for publication November 19, 2018; accepted January 16, 2019.

## ABSTRACT

**BACKGROUND:** Pediatric emergency medicine (PEM) and primary care provider (PCP) providers are the most likely physicians to initially label a child as allergic to penicillin. Differences in knowledge and management of reported penicillin allergy between these 2 groups have not been well characterized.

**METHODS:** A cross-sectional, 20-question survey was administered to PEM and PCPs to ascertain differential knowledge and management of penicillin allergy. Knowledge regarding high- and low-risk symptoms for true allergy and extent of history taking regarding allergy were compared between the 2 groups using *t* tests, Chi-square, and Wilcoxon tests.

**RESULTS:** In total, 182 PEM and 54 PCPs completed the survey. PEM and PCPs reported that 74.1 ± 19.5% and 69.0 ± 23.8% of patients with remote low-risk symptoms of allergy could tolerate penicillin without an allergic reaction. PEM and PCPs incorrectly identified low-risk symptoms of allergy as high-risk, including vomiting with medication administration and delayed skin rash. PCPs took more detailed allergy

histories when compared with PEM providers. In total, 143 (78.5%) of PEM providers and 51 (94.4%) PCPs were interested in using a penicillin allergy questionnaire to segregate children into high- or low-risk categories.

**CONCLUSIONS:** Most pediatric providers believe that children with a remote history of low-risk allergy symptoms could tolerate penicillin without an allergic reaction; however, this is infrequently acted upon. Both PEM and PCP providers were likely to classify low-risk symptoms as high-risk and infrequently referred children for further detailed allergy assessment. Both groups were receptive to decision support measures to facilitate improved penicillin allergy classification and labeling and support antibiotic appropriateness in their patients.

**KEYWORDS:** general pediatrics; pediatric emergency department; penicillin allergy

**ACADEMIC PEDIATRICS** 2019;19:684–690

## WHAT'S NEW

After surveying providers, we found that the majority are interested in using a questionnaire that could categorize penicillin allergy risk level. This may lead to new locations of testing for penicillin allergy that may increase how we delabel children.

PENICILLIN ALLERGY FREQUENTLY is diagnosed at an early age and is the most common medication allergy, reported in 5% to 20% of patients who present for medical care.<sup>1-7</sup> Clinical providers often rely on patient report of allergy when making treatment decisions, which directly affects selection of first-line antibiotics for common childhood infections.<sup>8-11</sup> Since the likelihood of a serious or immunoglobulin E (IgE)-mediated reaction to penicillin in the presence of self-reported allergy is exceedingly low, the majority of patients could tolerate the medication without having an allergic reaction.<sup>12-16</sup> Therefore, many

children are being denied appropriate therapy due to an ill-defined penicillin allergy.<sup>7</sup> In addition, although it is recommended to undergo a detailed historical assessment and allergy testing as appropriate in the presence of a reported allergy, most children do not undergo this detailed assessment, and they remain labeled with a poorly defined drug allergy into adulthood. As a result, misattribution of penicillin allergy in adults significantly increases hospital length of stay and the development of hospital-acquired infections, leading to increased morbidity and mortality.<sup>17</sup> It is therefore particularly important to appropriately characterize as many children labeled as penicillin allergic as possible to prevent increased costs and complications such as increased morbidity and mortality in subsequent years.

In a previous investigation, our study team used a survey administered in the pediatric emergency department and found that 76% of families who self-report penicillin allergy actually report low-risk symptoms that likely do

not correlate with true allergy.<sup>1</sup> Subsequently, we used the standard 3-tier testing method for 100 children with parent-reported, low-risk penicillin allergy symptoms and determined that 100% were negative for true allergy.<sup>18</sup> Therefore, identification of children at low risk for true penicillin allergy by using a survey has the potential to detect patients able to tolerate an oral penicillin challenge, but these studies do not offer insight into pediatric providers' knowledge and management of children with reported penicillin allergy. A previous study by Puchner and Zacharisen<sup>19</sup> demonstrated marked variability in how reported penicillin allergy altered the care of patients and that increased provider education on penicillin allergy was needed. The study did not provide comprehensive information on how pediatric providers manage a reported penicillin allergy.

The objective of this study was to evaluate the knowledge and management of self-reported penicillin allergy by pediatric emergency medicine (PEM) providers within the American Academy of Pediatrics (AAP) Section of Emergency Medicine Survey Listserv and primary care providers (PCPs) within the Children's Medical Group (CMG) of Wisconsin. Our hypotheses were 1) that greater than 75% of both PEM and PCP providers would know that a child presenting with a remote (>6 months) history of low-risk reaction with penicillin administration would tolerate the medication without an immediate IgE-mediated allergic reaction and 2) that PCPs would manage the report of penicillin allergy differently than PEM providers by taking a more in-depth patient allergy history and being more interested in potentially delabeling children as penicillin allergic. These results have potential to inform the development of more personalized, innovative, effective, and evidence-based interventions to improve the administration and prescription of penicillin in both acute and primary care settings.

## METHODS

### STUDY DESIGN

This was a cross-sectional voluntary survey of 2 groups of deidentified pediatric physicians. The study was approved by the hospital's institutional review board. The 2 groups included 1) PEM physicians (members of the AAP Section on Emergency Medicine Survey LISTSERV) and 2) PCPs (pediatricians associated with the Children's Hospital of Wisconsin CMG). The PEM physicians were sent an electronic survey via REDCap (Research Electronic Data Capture) between December 2017 and February 2018, with 3 automated reminders. Once a member completed the survey, they were no longer distributed the survey to ensure that the survey was taken only once. The CMG pediatricians, who staff 26 pediatric clinics, were sent the same electronic survey via REDCap in March and April of 2018.<sup>20</sup> All members of this group were sent the electronic survey twice but encouraged to only fill out the survey once.

### SURVEY DEVELOPMENT

The 5-minute, 20-question REDCap based survey was rigorously developed using a multistep process that included methodology described by Burns et al.<sup>21</sup> The primary investigator generated items that created the initial survey after comprehensive literature review. Study team members, which included 3 experts in PEM and an expert in allergy and immunology, reviewed the items for content. Items were intended to assess provider knowledge and management of children with reported penicillin allergy. The initial survey was 27 questions in length; after revisions based on content and question structure, item reduction resulted in 22 items.

The revised survey was reviewed by a different 5-member panel that included experts in PEM, allergy, and infectious diseases. A modified Delphi approach was used to rank relevance of questions and perform further item reduction. Following this process, survey questions were reduced to an updated version that consisted of 20 items. Feasibility and readability were pilot tested among 28 physicians representing the target audience and was further refined for clarity and ease of administration.

The final survey included 20 items driven by case vignettes; item types included multiple choice, Likert-type, and free-text questions ([Appendix](#)). Domains assessed included physician knowledge and management of reported penicillin allergy, hypothetical approaches related to penicillin delabeling, and provider demographics.

With regards to physician knowledge, providers were asked to label a reported symptom as high or low risk for true allergy. Symptom responses were dichotomized and arranged in no particular order after consultation with an allergist before giving providers the survey. The survey included 9 low-risk allergy symptoms and 8 high-risk allergy symptoms. The designation of risk level was based on the reported organ system involved and the potential for severe IgE-mediated reaction; this designation was consistent with our previous studies.<sup>1,18</sup> In order for a particular provider group to be deemed as having correctly identified and designated a symptom as low risk, greater than 50% of the group had to consider it low risk. In order for a particular provider group to be deemed as having correctly identified and designated a symptom as potentially high risk, less than 50% of the group had to consider it low-risk.

### DATA MANAGEMENT

Data were collected and managed using REDCap, hosted at the Medical College of Wisconsin.

### STUDY POPULATION/SAMPLE

Based on past experience with surveys from both groups, we anticipated a 50% response rate from the PEM physician survey LISTSERV of 462 members (231 participants) and a 30% response rate from CMG physicians from a LISTSERV of 120 members (36 participants).

These response rates would allow comparisons between PEM and PCP responses between the 2 groups.

### DATA ANALYSIS

Demographic data including sex, type of clinical practice setting, residency type, and years since completing training were summarized using descriptive statistics. PEM and CMG responses were compared using *t* tests for continuous responses, Chi-square tests for categorical responses (exact tests for low counts), and Wilcoxon tests for ordinal responses. Analyses were completed using SAS V9.4 (SAS Institute, Cary, NC).

## RESULTS

During the study period 182 (42.7%) of 426 PEM and 54 (45.0%) of 120 PCP providers completed the survey. In total, 175 (96.2%) of PEM respondents worked in a children's emergency department (ED) or urgent care, 167 (91.8%) referred to their practice type as academic, 150 (82.4%) had completed a PEM fellowship, and 94 (52.8%) were female (Table 1). The average time since training completion was  $14 \pm 10$  years. All pediatrician respondents completed pediatric residency and worked as general academic pediatricians; 33 (63.4%) were female. The average time since training completion was  $13 \pm 9$  years.

### KNOWLEDGE OF REPORTED PENICILLIN ALLERGY

With regard to penicillin allergy knowledge,  $74.1 \pm 19.5\%$  and  $69.0 \pm 23.8\%$  of PEM and PCP providers, respectively, knew that children with remote, low-risk allergy symptoms could tolerate a penicillin antibiotic. The 2 groups were in agreement on risk designation in 8

of 9 low-risk allergy symptoms (Fig. 1A). The only low-risk symptom in which there was statistically significant disagreement was pruritis greater than 2 hours after medication administration. However, when the list of low-risk allergy symptoms was reviewed, the 2 groups correctly identified a symptom as low risk in 4 of 9 symptoms. For high-risk allergy symptoms, the 2 groups were in agreement on risk designation in 7 of 8 high-risk allergy symptoms (Fig. 1B). The only high-risk symptom in which there was statistically significant disagreement was presence of abdominal pain immediately after giving the medication. When the high-risk symptoms were reviewed, the 2 groups correctly identified a symptom as high risk in 8 of 8 symptoms.

### MANAGEMENT OF REPORTED PENICILLIN ALLERGY

When evaluating management (Fig. 2), PCPs more frequently inquired about the time since allergic reaction/age at which reaction occurred ( $P = .003$ ), whether the allergy was diagnosed by a health care provider ( $P = .019$ ), and when symptoms developed relative to antibiotic exposure ( $P = .049$ ). Symptom assessment between PEM and PCP groups occurred with similar frequency.

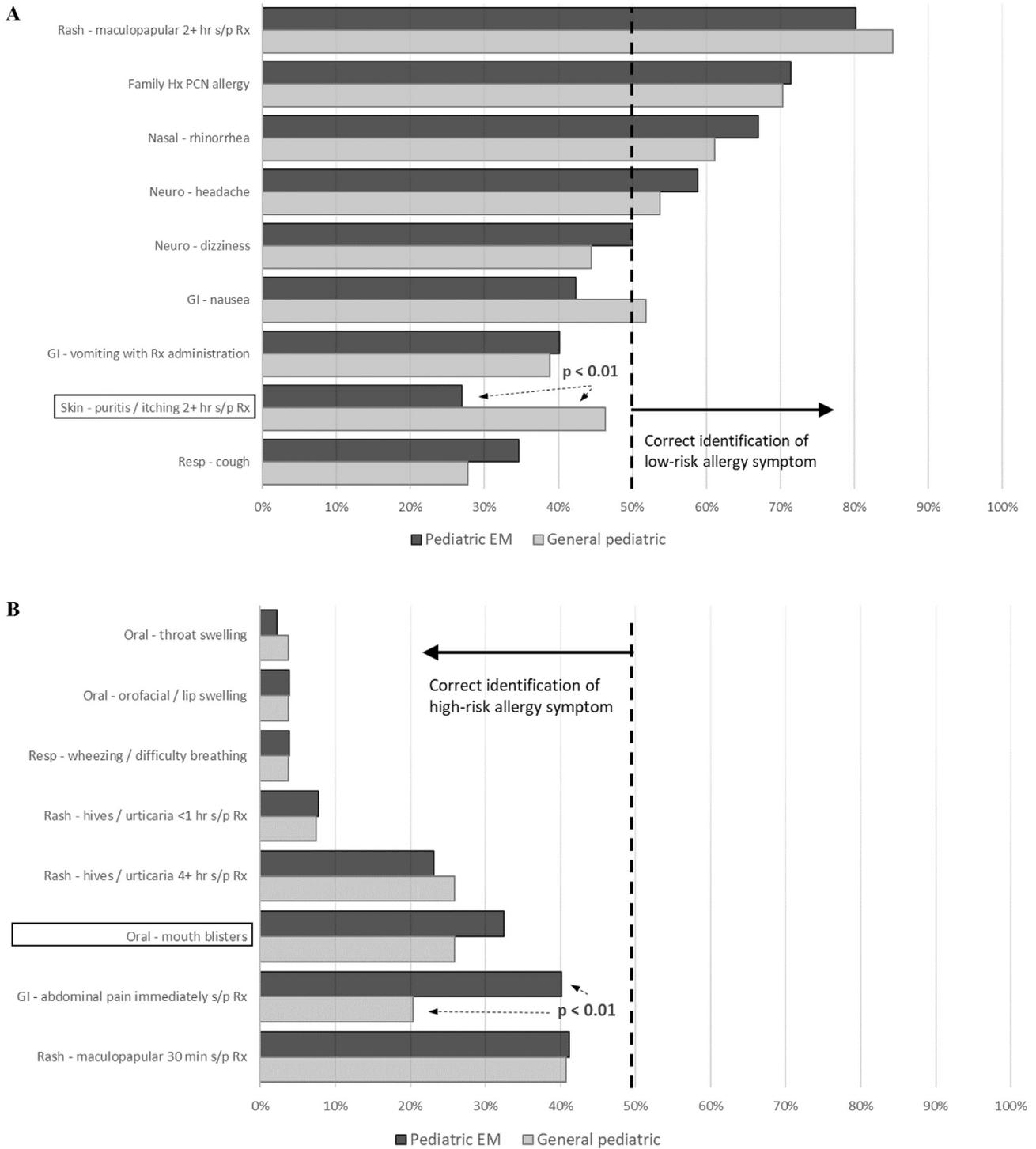
When choosing an alternative antibiotic for penicillin allergy in a child with otitis media, 148 (81.3%) of PEM and 53 (98.1%) of PCP providers reported that they use a cephalosporin as their primary alternate antibiotic ( $P = .01$ ). Many PEM providers 31 (17.1%) indicated they may use a macrolide antibiotic in the presence of a reported penicillin allergy.

The majority of PEM and PCP physicians reported interest in using a survey to identify low-risk children, although interest was greater among PCPs (94.4%) versus

**Table 1.** Characteristics of PEM and PCP Providers

	PEM n = 182	PCP n = 54	P Value
Clinical practice setting, n (%)			
Children's ED/UC	175 (96.2)		
General ED/UC	5 (2.7)		
Missing	2 (1.1)		
PCP clinic	0 (0.0)	54 (100.0)	
Clinical practice type, n (%)			
Private practice	13 (7.1)		
Academic	167 (91.8)	54 (100.0)	
Missing	2 (1.1)		
Residency completed, n (%)			
Pediatrics	176 (96.7)	54 (100.0)	
Emergency medicine	3 (1.6)		
Other	3 (1.6)		
Emergency medicine fellowship completed, n (%)			
Yes	150 (82.4)		
No	23 (12.6)		
Currently in fellowship	7 (3.8)		
Missing	2 (1.1)		
Years since training completion, $\pm$ SD	$14.4 \pm 10.0$	$13.1 \pm 9.5$	.435
Female, n (%)	94 (52.8)	33 (63.4)	.174

PEM indicates pediatric emergency medicine; PCP, primary care providers; ED, emergency department; UC, urgent care; and SD, standard deviation.



**Figure 1.** (A) Low-risk allergy symptom identification. (B) High-risk allergy symptom identification.

PEM providers (78.5%) ( $P = .03$ ). When asked about the number of children needed to tolerate an oral challenge, PCPs reported lower numbers required ( $P < .01$ ), with the plurality of PCPs reporting 100 versus 1000 for PEM providers (Table 2).

**DISCUSSION**

In this study, we surveyed both PEM and PCP providers to determine current knowledge and management

of self-reported penicillin allergy. Our results showed that both PEM and PCP physician groups were knowledgeable about low-risk symptoms for true penicillin allergy, and that most of these children can likely tolerate penicillin without having a true IgE-mediated allergic reaction. In general, both groups of physicians agreed on their categorization of allergy symptoms but often incorrectly identified a single symptom as high risk when it was in fact low risk. Significant differences in the management of a reported penicillin allergy were found between groups in

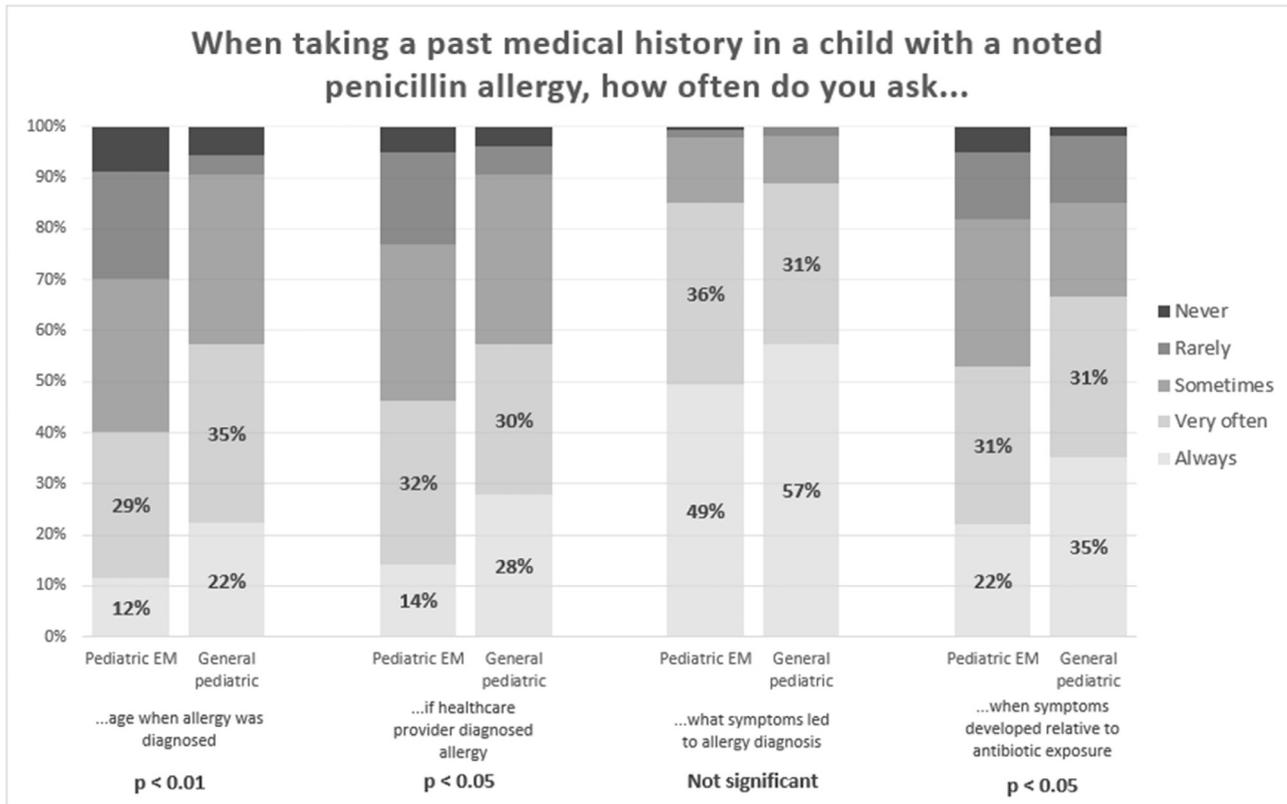


Figure 2. Medical history in a child with reported penicillin allergy.

Table 2. PEM and PCP Provider Differences

“Assume a valid questionnaire could identify children at low-risk for true penicillin allergy. How many children labeled as low-risk by questionnaire would have to tolerate oral penicillin without a reaction before you would elect to routinely treat with penicillin prescriptions for home use?”

Number of children	PEM-CRC	CMG	P Value
100	41 (23%)	25 (48%)	<.01
500	53 (30%)	11 (21%)	
1000	69 (39%)	13 (25%)	
2000	4 (2.2%)	2 (3.8%)	
>3000	9 (5.1%)	1 (1.9%)	

PEM indicates pediatric emergency medicine; PCP, primary care provider; CRC, Collaborative Research Committee; and CMG, Children’s Medical Group.

allergy history ascertainment, antibiotic prescription in patients with reported allergy, interest in using an allergy questionnaire as a decision support strategy that could segregate patients into high/low-risk groups, and the number of patients who would be needed to be challenged after questionnaire segregation to feel comfortable prescribing a penicillin to a patient with reported allergy.

Previously, our group developed an ED-based penicillin allergy questionnaire that determined 76% of children with reported symptoms of allergy to penicillin are actually not representative of a true IgE-mediated reaction.<sup>1</sup> These symptoms most often include delayed maculopapular rash and represent an adverse but not necessarily

allergic reaction. An important finding within this study was that there was general agreement on allergy symptom categorization between the 2 groups of physicians but that both groups often categorized a low-risk symptom as high-risk. Physicians from both groups correctly identified the following symptoms as low risk: a maculopapular rash occurring greater than 2 hours after antibiotic administration, isolated family history of penicillin allergy, rhinorrhea, and headache. However, misclassification of symptoms occurred for itching greater than 2 hours after med administration, isolated cough, and vomiting while administering the medication. Each of these is low risk but was identified as high risk by most providers. These findings support the need for greater education of low-risk symptoms for penicillin allergy and need for dissemination on a larger scale. Modalities such as a decision tool that can stratify patients into categories capable of identifying low-risk patients who could be tested to determine true allergy status could be helpful to these providers.

One key aspect of this study was to evaluate how both PEM and PCP providers ask about a reported penicillin allergy. PCPs were more likely to ask important questions about age at which a child was diagnosed with penicillin allergy, who diagnosed the allergy, and the tempo of which allergy symptom(s) developed in relationship to antibiotic dosing. Several potential explanations exist for these differences. First, the perceived time constraints in the ED may focus PEM providers on treating acute illness and therefore do not prioritize questioning an allergy within the medical record. PCPs, while still time

constrained, may have increased opportunities during well-child visits to discuss the patient's allergy history. Second, PCPs develop long-standing relationships with patients that PEM providers do not, possibly favoring a more vested interest and potential desire to delabel a patient as penicillin allergic for the duration of their clinical care. Lastly, in the pediatric ED, children may be brought in by providers (grandparents, relatives, etc) with incomplete health information that may lead to an inability to rule out high or low risk allergy symptom questions that depend on historical recall.

PEM and PCP providers also differed in their choice of alternate antibiotics for reported penicillin allergic children, with PCPs reporting greater use of cephalosporins. One possible explanation could be that PEM providers are caring for a subset of higher-acuity patients in which a non-beta lactam antibiotic would potentially be an acceptable primary treatment option (atypical pneumonia) and therefore they would have prescribed it regardless of allergy. Regardless of which alternate antibiotic is chosen, we have previously shown that the prescription of second-line agents, specifically third-generation cephalosporins, leads to increased costs for patients, and other studies have shown that alternate antibiotics to preferred penicillins increase hospital lengths of stay along with morbidity and mortality for patients.<sup>8-11,15,22</sup> All of these findings support the need to develop and implement processes within pediatric emergency departments and primary care clinics to identify and delabel children with reported penicillin allergy who are not truly allergic. Identification and delabeling patients with low-risk penicillin allergy symptoms would lead to increased health care savings and decrease the development of antibiotic-resistant organisms.

Evidence has shown that most patients have histories of penicillin allergy that are low risk and could tolerate a penicillin without a true allergic reaction. For parents who report penicillin allergy to PEM or PCP providers, we are missing a substantial opportunity to appropriately classify children with reported penicillin allergy and are putting them at risk for inferior individual and public health outcomes as well as increased health care costs. With this in mind, we posed 2 hypothetical management questions to survey participants. We found that PCPs were more interested than PEM providers in using a survey that would provide decision support to appropriately label children with penicillin allergy. Furthermore, PCPs needed fewer patients to complete an oral challenge to feel comfortable prescribing penicillin to a patient with reported allergy. One explanation for this finding could be that because PCPs have increased engagement with their own patients and they have more commonly faced the challenge of prescribing an alternative and potentially inferior and costlier antibiotic for what was thought to be an incorrect allergy diagnosis. In addition, PEM providers may be more risk-averse due to fear of legal action in a patient they do not follow on a regular basis. Broader education of both PEM and PCP providers along with the implementation of a

time efficient decision support tool to increase knowledge of low-risk symptoms and facilitate correct labeling of low-risk children with penicillin allergy would likely lead to the decreased use of alternate antibiotics and improved antibiotic appropriateness and health care outcomes.

#### LIMITATIONS

This study has several limitations. First, response rates were low for both groups, which may have led to an inaccurate representation of collective PEM and PCP provider survey responses. Second, we surveyed members of the AAP Section on Emergency Medicine Survey LISTSEV and CMG as proxies for PEM and PCP providers. Although these groups may not generalize to all PEM and PCP providers, past AAP Section on Emergency Medicine Listserv surveys have been seen as representative of PEM providers,<sup>23</sup> but CMG practices are only representative of a single group of primary care physicians, which may differ from a broader national group. Lastly, there was also a slight difference in survey methodology, with PEM providers unable to receive the survey again after it was completed once whereas PCPs who had completed the survey could have received it again. PCPs were instructed to complete the survey only once, and it is unlikely they would have forgotten in so short a time period.

#### CONCLUSIONS

The majority of both PEM and PCP providers were in agreement that children with a remote history of penicillin allergy could likely tolerate the medication without an allergic reaction. Both groups incorrectly identified low-risk symptoms as high-risk symptoms, indicating the need for improved education on symptom identification. PCPs tended to ask penicillin allergy history questions much more often when compared with PEM providers. Although taking a penicillin allergy history may seem unimportant to a PEM provider, each chance to discuss likely incorrect labels should be viewed as an opportunity to improve antimicrobial stewardship. There is great interest among both groups of providers in using a questionnaire to differentiate children with low-risk symptoms for true penicillin allergy who could tolerate an oral challenge. Implementing and integrating a pediatric penicillin allergy decision support mechanism into both a PEM and PCP provider setting can help optimize antibiotic prescribing and contribute to improved antimicrobial stewardship and substantial health care savings.

#### SUPPLEMENTARY DATA

Supplementary data related to this article can be found online at <https://doi.org/10.1016/j.acap.2019.01.002>.

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