RESEARCH LETTER

Multisite Oral Amoxicillin Challenges During Pediatric Emergency Department Visits

Approximately 10% of children seen in pediatric emergency departments (PEDs) present with a parent-reported allergy to a penicillin family antibiotic,[1] which results in adverse health outcomes and increased costs to families and health care systems.[2-4]

Supplemental content

Delabeling a penicillin allergy through a direct oral challenge (DOC) in low-risk populations has positive health implications.[5,6] This study implemented a penicillin allergy delabeling program across 3 sites to evaluate differences in allergy risk level designation, clinician and family willingness to proceed with DOC, and results of a DOC.

Methods | This cohort study enrolled children aged 2 to 16 years with a parent-reported penicillin allergy presenting to 1 of 3 urban Midwest teaching PEDs within a Pediatric Emergency Care Applied Research Network node between March 2019 and November 2020 and data were analyzed between November 25, 2020, and December 11, 2020. The study was approved by the hospitals' institutional review boards and the STROBE reporting guideline was used. Parents completed a penicillin allergy symptom questionnaire, with children having a low-risk or high-risk based on symptoms.[1] DOC eligibility was based on previously developed criteria.[6] Families completed written consent for DOC and clinicians were approached for approval of amoxicillin administration.

Data were managed using REDCap. Descriptive statistics were used to summarize patient demographic, allergy questionnaire, and oral challenge data. Analysis of variance, Kruskal-Wallis, Pearson χ^2 tests, and Fisher exact tests were used based on data distribution. SAS version 9.4 (SAS Institute) with a 2-sided significance level of $P < .05$ was used for all analyses.

Results | Among the 3 sites, 1189 parents were approached, and 372 (31%) questionnaires were completed (mean [SD] age, 9.03 [4.40] years; 191 [51.6%] were boys). After applying exclusion criteria and getting approval from clinicians, 117 participants completed the DOC (**Figure**). Significant differences were found among respective sites A, B, and C for low-risk designation (57%, 69%, and 46%; $P < .001$), family interest in the DOC (87%, 75%, and 58%; $P < .02$), and clinician willingness to proceed with DOC (85%, 94%, and 56%; $P < .001$). Physicians elected not to proceed to DOC 19 times, with the most frequent reason being time constraints. Patient demographic characteristics are summarized in the **Table**.

Figure. Patient Flow Diagram

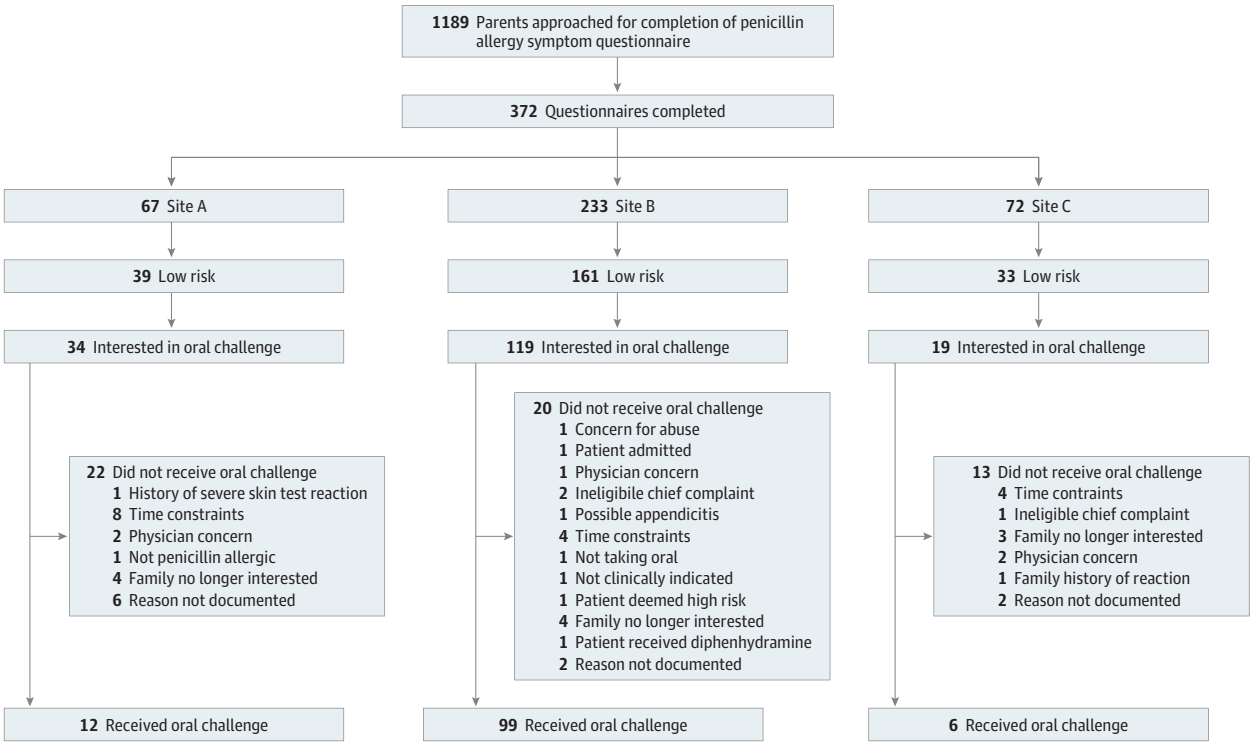

Table. Demographic Characteristics of Study Participants

Variable	No. (%)				*P* value
	Total (N = 372)	Site A (n = 67)	Site B (n = 233)	Site C (n = 72)	
Age					
Age y, mean (SD)	9.03 (4.40)	9.88 (4.38)	9.02 (4.38)	8.27 (4.41)	.01
Missing	1	0	0	1	
Gender					
Boys	191 (51.6)	31 (46.3)	126 (54.3)	34 (47.9)	.40
Girls	179 (48.4)	36 (53.7)	106 (45.7)	37 (52.1)	
Missing	1	0	0	1	
Race and ethnicity[a]					
African American	79 (21.5)	14 (20.9)	42 (18.3)	23 (32.4)	NA
American Indian or Alaska Native	2 (0.5)	0	1 (0.4)	1 (1.4)	NA
Asian	1 (0.3)	0	1 (0.4)	0	NA
Hispanic	49 (13.4)	3 (4.5)	44 (19.2)	2 (2.8)	NA
Multiracial	17 (4.6)	3 (4.5)	11 (4.8)	3 (4.2)	NA
White	213 (58)	46 (68.7)	126 (55)	41 (57.7)	NA
Other	6 (1.6)	1 (1.5)	4 (1.7)	1 (1.4)	NA
Missing	4	0	3	1	NA

Abbreviation: NA, not applicable.

[a] Race and ethnicity were assessed to help define the demographic characteristics of the population in this study and were self-reported. Race choices were consistent with National Institutes of Health race categories. If a family felt they did not fit these categories, then the term *other* was an option and was not broken down further.

Discussion | We used an allergy questionnaire to categorize risk as low or high, administer a DOC, and delabel 98% of reported penicillin allergy, supporting the safe and effective use of DOC in low-risk patients.[1]

We found significant variation among sites in the designation of risk level. Differences may be explained by several reasons. First, site B enrolled the largest volume of patients and differences may have leveled off with higher enrollment at other sites. Second, sites A and C used research staff to complete questionnaires through a tablet-based process. Site B used nursing staff questionnaire administration via an electronic medical record (EMR) based process; this variability may have skewed the risk-level designation. This study is limited in its generalizability as the questionnaire administration differed between sites.

There were significant differences in family interest in receiving the DOC among sites, including fear of a severe allergic reaction and time constraints. Severe reaction to amoxicillin is exceedingly rare and should a reaction occur, the PED is an exceptionally safe place to treat any reaction.[6] We also identified differences in clinician willingness to proceed with DOC. Process improvements to optimize efficiency in drug ordering, dispensing, and administration once a patient has been identified as a candidate for DOC are necessary for success.

A penicillin delabeling program using a DOC may be effective in the PED. DOC may be best suited for children in need of acute antibiotics. Integration through a standardized EMR-based process is the next step toward expansion of addressing the problem of overreported penicillin allergy. This could include better prevention of allergy labels and a more streamlined process for allergy testing referrals.

David Vyles, DO, MS
George Hoganson, MD
Constance McAneney, MD
Mariana Castells, MD, PhD
Elizabeth J. Phillips, MD
Alexis Visotcky, MS
David C. Brousseau, MD, MS

Author Affiliations: Medical College of Wisconsin, Milwaukee (Vyles, Visotcky, Brousseau); Washington University School of Medicine, St Louis, Missouri (Hoganson); Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio (McAneney); Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts (Castells); Vanderbilt University School of Medicine, Nashville, Tennessee (Phillips).

Accepted for Publication: July 12, 2023.

Published Online: October 2, 2023. doi:10.1001/jamapediatrics.2023.3659

Corresponding Author: David Vyles, DO, MS, Department of Pediatrics, Children's Corporate Center, Medical College of Wisconsin, 999 N 92nd St, Ste 550, Milwaukee, WI 53226 (dvyles@mcw.edu).

Author Contributions: Dr Vyles had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.
Concept and design: Vyles, Hoganson, Castells, Phillips, Brousseau.
Acquisition, analysis, or interpretation of data: Vyles, Hoganson, McAneney, Castells, Visotcky.
Drafting of the manuscript: Vyles, Hoganson, McAneney, Castells.
Critical review of the manuscript for important intellectual content: Vyles.
Statistical analysis: Visotcky, Brousseau.
Administrative, technical, or material support: Hoganson, Brousseau.
Supervision: Vyles, Hoganson, Castells, Phillips.

Conflict of Interest Disclosures: Dr Phillips reported personal fees from Verve, Janssen, UpToDate, AstraZeneca, and Biocryst, and grants from NIH and NHMRC outside the submitted work. No other disclosures were reported.

Funding/Support: Nodal Pilot Award from Hospitals of Midwest Research Node (HOMERUN) of the Pediatric Emergency Care Applied Research Network (PECARN): U03MC22684 (Dr Vyles) Emergency Medical Services for Children/Maternal and Child Health Bureau of the Health Resources and Services Administration.

Role of the Funder/Sponsor: The funding organizations had no role in the design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Data Sharing Statement: See the Supplement.

1. Vyles D, Chiu A, Simpson P, Nimmer M, Adams J, Brousseau DC. Parent-reported penicillin allergy symptoms in the pediatric emergency department. *Acad Pediatr*. 2017;17(3):251-255. doi:10.1016/j.acap.2016.11.004

2. MacLaughlin EJ, Saseen JJ, Malone DC. Costs of beta-lactam allergies: selection and costs of antibiotics for patients with a reported beta-lactam allergy. *Arch Fam Med*. 2000;9(8):722-726. doi:10.1001/archfami.9.8.722

3. Vyles D, Chiu A, Routes J, et al. Antibiotic use after removal of penicillin allergy label. *Pediatrics*. 2018;141(5):e20173466. doi:10.1542/peds.2017-3466

4. Blumenthal KG, Lu N, Zhang Y, Li Y, Walensky RP, Choi HK. Risk of methicillin resistant *Staphylococcus aureus* and *Clostridium difficile* in patients with a documented penicillin allergy: population based matched cohort study. *BMJ*. 2018;361:k2400. doi:10.1136/bmj.k2400

5. Mustafa SS, Conn K, Ramsey A. Comparing direct challenge to penicillin skin testing for the outpatient evaluation of penicillin allergy: a randomized controlled trial. *J Allergy Clin Immunol Pract*. 2019;7(7):2163-2170. doi:10.1016/j.jaip.2019.05.037

6. Vyles D, Chiu A, Routes J, et al. Oral amoxicillin challenges in low-risk children during a pediatric emergency department visit. *J Allergy Clin Immunol Pract*. 2020;8(3):1126-1128.e1. doi:10.1016/j.jaip.2019.09.022

Early Childhood Education and Midlife Ideal Cardiovascular Health in a Prospective Urban Cohort

Early childhood programs show promise in reducing cardiovascular risks and combating racial and income disparities.[1-3] However, most previous studies had small sample sizes, unreplicable program elements, retrospective designs, and measurement problems.[1] In a study of the Child-Parent Centers (CPC) program, preschool was associated with lower 30-year Framingham risk scores by age 37 years.[1] Generalizability to broader cardiovascular health is unknown. This cohort study assessed whether preschool is associated with long-term cardiovascular health measured by the American Heart Association (AHA) Ideal Cardiovascular Health Index (iCVH)[4] and whether educational attainment accounts for this association.

Supplemental content

Methods | From March 1 through June 30, 2023, we analyzed data from the Chicago Longitudinal Study, which tracks 989 children aged 3 to 4 years attending CPC preschool in 1983 to 1985 and a comparison group of 550 children who primarily attended usual early childhood education programs in randomly selected schools matched on poverty and neighborhood characteristics.[5] Survey and health examination data were approved by the institutional review boards of Northwestern University Feinberg School of Medicine and University of Minnesota, with written and oral informed consent. We followed the STROBE guideline.

The CPC provides comprehensive educational and family support services to counteract the effects of poverty (eMethods in Supplement 1).[1,5] After 1 to 2 years of part-day preschool, services are provided through third grade. The major long-term goal is educational attainment and greater well-being.

The iCVH is the sum of 7 positive, alterable cardiometabolic indicators and health behaviors predictive of long-term well-being (eg, healthy weight, nutrition, and blood pressure).[4] We aligned self-report indicators against AHA's criteria to obtain total scores from 0 to 7 (higher scores indicate greater risk) (eTable 1 in Supplement 1). Supporting validity, iCVH moderately correlated with Framingham risk score (r = −0.59) and in-person examination results (r = 0.67) and correlated as expected with self-rated health (r = 0.25).

Table 1. Characteristics of Children and Families at Follow-Up by Group

Characteristic[a]	Participants[b]		*P* value
	CPC program (n = 690)	Comparison (n = 352)	
Birth weight, mean (SD), lb	6.83 (1.26)	6.72 (1.25)	.18
Reside in neighborhood with ≥40% population at or below poverty level by age 5 y	389 (56.4)	132 (37.5)	<.001
Family risk index score by age 5 y, mean (SD)[c]	4.43 (14.03)	4.48 (14.54)	.66
Family risk index score squared	23.14 (1.64)	23.60 (1.72)	.46
Sex			
Men	305 (44.2)	178 (50.6)	.06
Women	385 (55.8)	174 (49.4)	
Race and ethnicity			
Black	642 (93.0)	332 (94.3)	.51
Hispanic and other[d]	48 (7.0)	20 (5.7)	
≥4 Family risk factors	493 (71.5)	251 (71.3)	>.99
Eligibility for subsidized meals	571 (82.8)	292 (83.0)	>.99
Single parent family status	520 (75.4)	270 (76.7)	.68
College attendance by parent	92 (13.3)	38 (10.8)	.28
Parent not employed fulltime or parttime	456 (66.1)	226 (64.2)	.58
Any child welfare case histories	22 (3.2)	15 (4.3)	.39
Chronic health condition by age 10 y	108 (15.7)	49 (13.9)	.52
Persons in original cohort with main outcome	690 (69.8)	352 (64.0)	.02
Persons in original cohort in interview at age 37 y	740 (74.8)	384 (69.8)	.03
Education by age 34 y (mediator), mean (SD), y[e]	13.00 (2.12)	12.34 (1.96)	<.001

Abbreviations: CPC, Child-Parent Centers; NA, not applicable.

[a] Except for chronic health conditions (retrospectively reported on the midlife survey), the baseline characteristics were measured up to age 3 years or closely to time of program enrollment. The 8 family risk factors include sociodemographic factors (eg, high school dropout, not employed, and family income near the poverty level) associated with lower child well-being.

[b] Unless otherwise indicated, data are expressed as number (percentage) of patients.

[c] Ranges from 0 to 7, with scores of 4 or greater indicating higher risk.

[d] Includes 1 non-Hispanic White patient.

[e] As the hypothesized mediator, educational attainment is shown for description only.