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Penicillin Allergy De-labeling: Evaluating a Health System's Implementation of the PEN-FAST Tool within an Infectious Disease Clinic.

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Penicillin Allergy De-labeling: Evaluating a Health System's Implementation of the PEN-FAST Tool within an Infectious Disease Clinic

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The speaker and mentors have no actual or potential conflict of interest in relation to this presentation

Why the Term Penicillin Allergy is Misleading

- Estimated that ~10% of all US patients report an allergic reaction to a beta-lactam antibiotic
 - Approximately over 80% of these patients lose their sensitivity after 10 years
 - <1% of the whole population have a true IgE mediated allergy
- Excessively broad term as most agents may not have cross reactivity
 - Leading to an ***inappropriate antibiotic class allergy***

"Penicillins" refers to four general groups of antibiotics:

- Natural penicillins
- Anti-staph penicillins
- Aminopenicillins
- Anti-pseudomonal penicillins

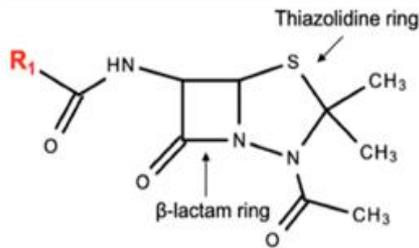
When patients report "penicillin allergy" they commonly refer to:

- Aminopenicillin
- Penicillin G
- Penicillin VK

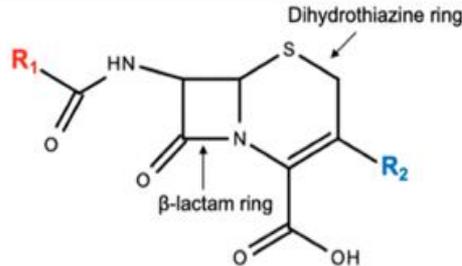


Side Chain Role in Drug Allergies

- Previously thought to be related to the core beta-lactam ring structure
 - Would confer reaction to **all** beta-lactam antibiotics
 - Beta-lactams are too small to bind to IgE
 - IgE mediated allergies occur via **R-1 side chains**
- Development of IgE antibodies to the **R-1 specific side chain structure**
 - Via protein binding



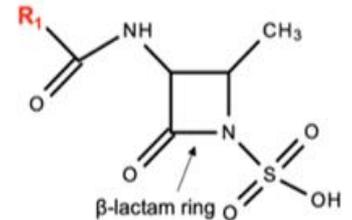
Penicillin Core Structure



Cephalosporin Core Structure



Carbapenem Core Structure



Monobactam Core Structure

Penicillin & Cephalosporin Cross Reactivity

- Cross reactivity stems from similar R-1 side chains
 - **Not** antimicrobial class
- Reported rates range ~**16% to 40%** in agents with **similar** side chains
- Antibiotics that have **unique** side chains are **not** cross allergic with other drugs
 - i.e. cefazolin & ceftaroline

(+) Known cross-reactive (X) Similar or same side chain	Penicillin	Amoxicillin	Ampicillin
Penicillin		+	+
Amoxicillin	+		+
Ampicillin	+	+	
Cephalexin	+	+	X
Cefazolin			
Cefuroxime			
Cefoxitin			
Ceftriaxone			
Cefotaxime			
Ceftazidime			
Cefepime			
Cefiderocol			

The Cost of Inappropriate Penicillin Allergies

Emergence of
*antibiotic
resistance*

Delays in
patient care

**Suboptimal
Antibiotic
Therapy**

Increased Healthcare Costs

- Skin test ordering
- Hospital readmissions & Increased length of stay
- Increased use of alternative agents



The Organization's Current Approach to Allergy De-Labeling

- Antibiotic Allergy Skin Testing
 - Specialized **2-Step Process**
 1. Intradermal Skin testing, if **negative**,
Followed by
 2. Oral challenge with a penicillin
 - i.e. amoxicillin ± clavulanic acid

- Historical practice at institution
 - Use is limited by cost & lack of a penicillin challenge

- Goal
 - Phase out completely with more clinically effective & cost saving methods

(+) Known cross-reactive (X) Similar or same side chain	Penicillin	Amoxicillin	Ampicillin
Penicillin		+	+
Amoxicillin	+		+
Ampicillin	+	+	
Cephalexin	+	+	X
Cefazolin			
Cefuroxime			
Cefoxitin			
Ceftriaxone			



What is the PEN-FAST Tool?

- Standardized clinical decision tool
 - Predicts patients who are likely to test negative on a formal penicillin allergy skin test
 - Scores <3 share a negative predictive value of 96% in positive skin tests
- Widely studied & validated within clinical trials evaluating its translation to skin tests
 - A point of care tool to identify inappropriately labeled penicillin allergies
- **Available in online calculators**

PEN-FAST - Penicillin Allergy Risk

PEN	Penicillin allergy reported by patient	<input type="checkbox"/> If yes, proceed with assessment
F	Five years or less since reaction ^a	<input type="checkbox"/> 2 points
A	Anaphylaxis or angioedema	<input type="checkbox"/> 2 points
S	Severe cutaneous adverse reaction ^b	
T	Treatment required for reaction ^a	<input type="checkbox"/> 1 point
		<hr/>
		<input type="checkbox"/> Total points

Interpretation

Points	
<input type="checkbox"/> 0	Very low risk of positive penicillin allergy test <1% (<1 in 100 patients reporting penicillin allergy)
<input type="checkbox"/> 1-2	Low risk of positive penicillin allergy test 5% (1 in 20 patients)
<input type="checkbox"/> 3	Moderate risk of positive penicillin allergy test 20% (1 in 5 patients)
<input type="checkbox"/> 4-5	High risk of positive penicillin allergy test 50% (1 in 2 patients)

Support From Primary Literature

Evaluating the PEN-FAST Clinical Decision-making Tool to Enhance Penicillin Allergy De-labeling. *JAMA Intern Med.* (2023)

Outcomes Evaluated	PEN-FAST scores were compared with positive skin test results and direct oral penicillin challenges to stratify risk of a positive result: <ul style="list-style-type: none">• Sensitivity, specificity, NPV, and positive likelihood ratio (PPV)	
Key Points	Majority of US patients have a low-risk penicillin allergy	NPV: ~96% & PPV: 4% (PEN-FAST Scores <2)
	Immune mediated reaction rates were similar between both groups	Future studies should focus on direct challenges in low-risk patients
	Validated PEN-FAST score correlation with anticipated skin test results	Confirms that low risk patients would be ideal candidates to undergo a DOPC



Assessment Question #1

According to clinical trials, a negative predictive value of 96% was associated with what PEN-FAST score?

- a) ≤ 1
- b) ≤ 2
- c) ≤ 3
- d) ≤ 4

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According to clinical trials, a negative predictive value of 96% was associated with what PEN-FAST score?

a) ≤ 1

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c) $\leq 3^{**}$

d) ≤ 4

**Typo in “ \leq ” question answers, correct symbol is “ $<$ ”

Assessment Question #2

A 58-year-old patient reports an allergy to amoxicillin in childhood with a reaction of hives where he was then switched to a different antibiotic. If a skin test was performed today, what risk category of a positive skin test result would this patient fall based on the PEN-FAST?

- a) Very low risk
- b) Low risk
- c) Moderate risk
- d) High risk

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	OR	
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Purpose

Evaluate the number of patients with a penicillin allergy within the organizations patient population who can become de-labeled to optimize efforts related to:

- Antimicrobial stewardship
- Costs related to skin testing

Parkview Health Infectious Disease

- Not-for-profit, community teaching health system
 - Provides services to Northeast Indiana & Northwest Ohio
 - Two clinics located in Northeast Indiana
- Both clinics see ~700 patients/month on average
- Onsite ID clinical pharmacist at each clinic



Design

- Single center, retrospective cohort
 - Adopted based on previous clinical trials

Inclusion Criteria	Exclusion Criteria
<ul style="list-style-type: none">• ≥ 18 years of age• Documented penicillin class or drug allergy	<ul style="list-style-type: none">• Documented incomplete PEN-FAST score due to no penicillin allergy

Outcomes

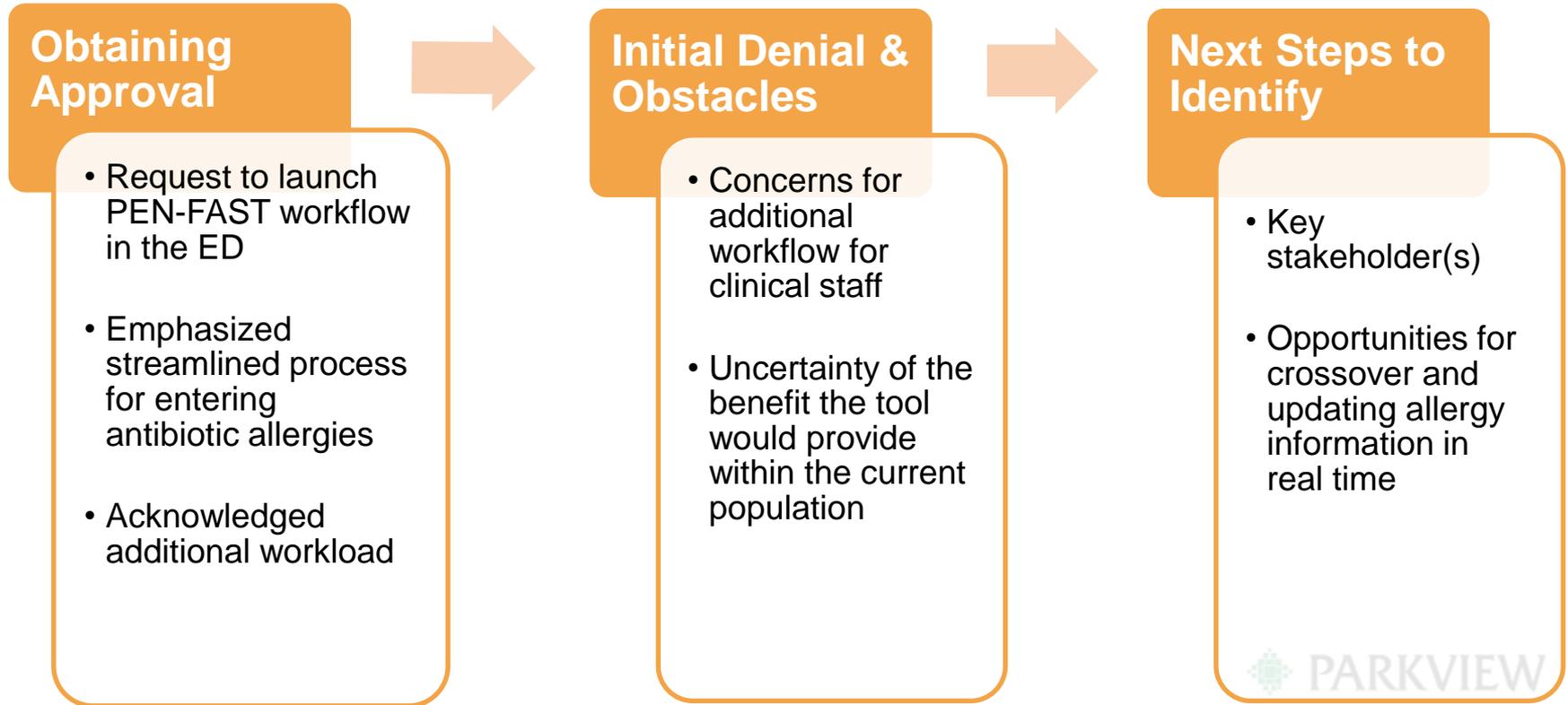
Primary

- Number of patients classified as “Very low & low risk”
 - PEN-FAST score <3

Secondary

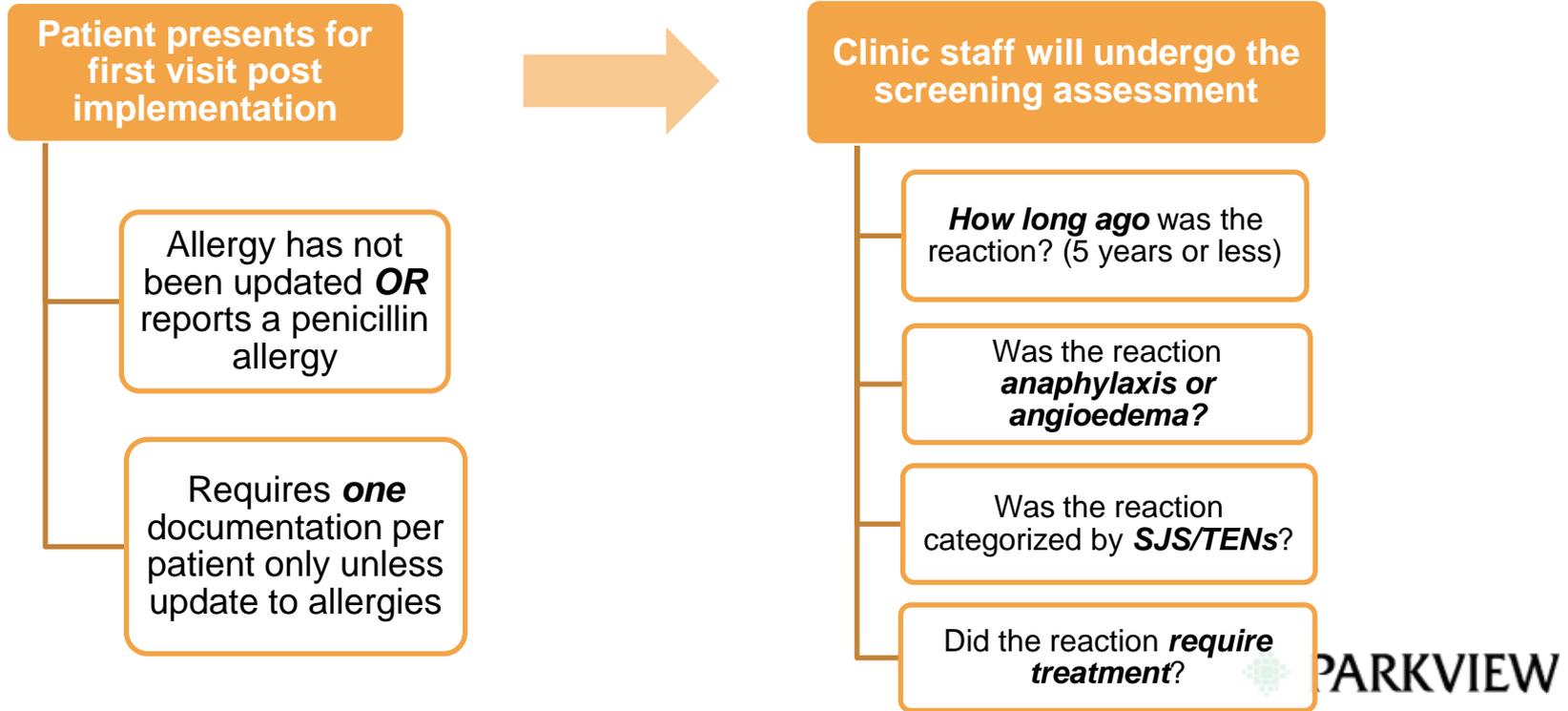
- Number of:
 - Oral penicillin challenge post-documentation
 - Skin test use pre-documentation
 - Documented allergies with:
 - Severity
 - Specified reaction
 - As a non-penicillin allergy

Intervention Early Phases – Aug 2023



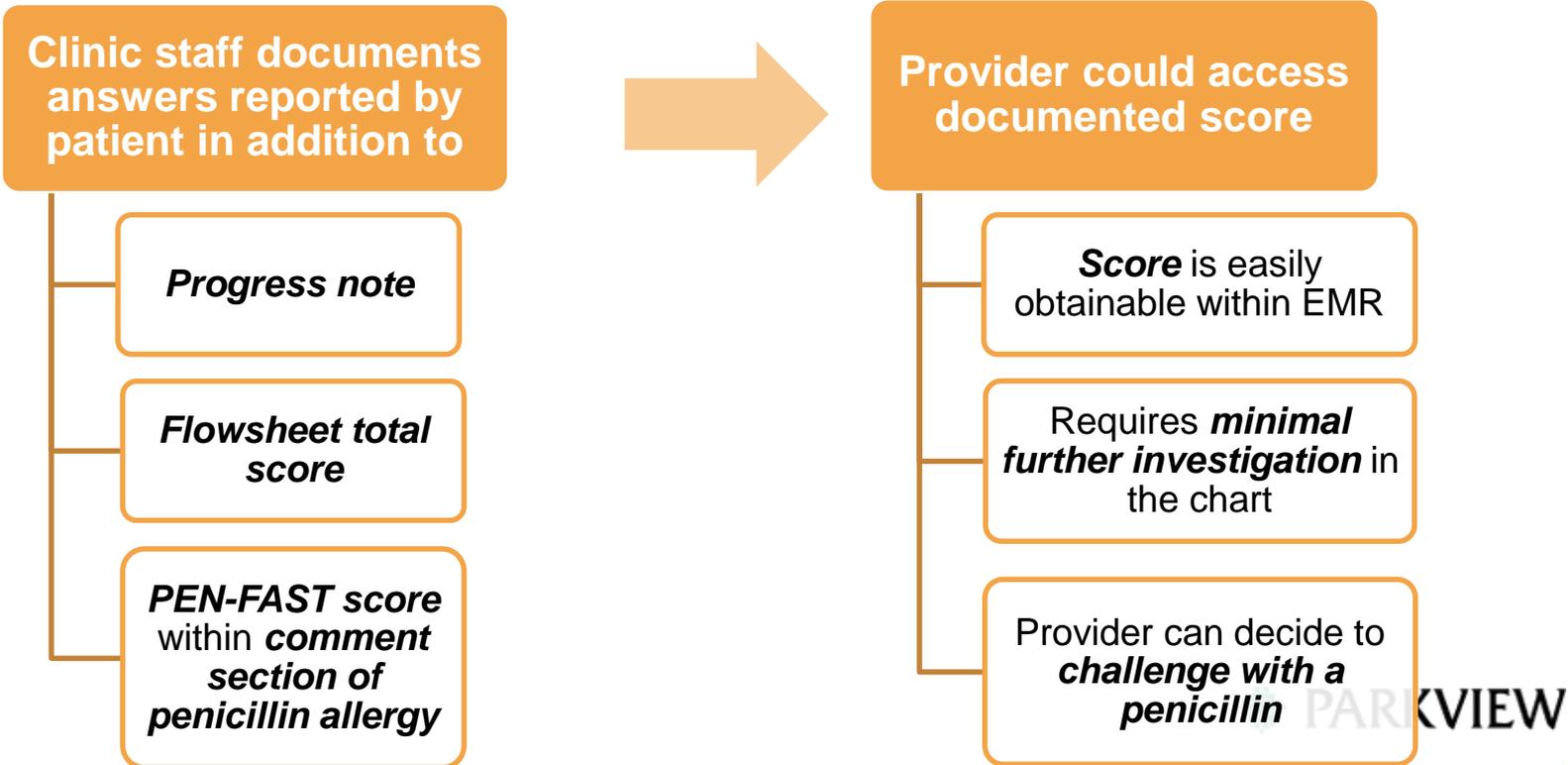
Clinic Workflow Education

- Timeframe: November 2023 – February 2024



Clinic Workflow Education cont.

- Timeframe: November 2023 – February 2024



Baseline Characteristics

- **Majority of patients had a primary problem of:**
 - Osteomyelitis
 - HIV
- Most patients had a concurrent antibiotic allergy
- **50%** of performed skin tests were **unread**

Table 1. Baseline Characteristics (n = 148 patients)	
Infectious Disease Problem	# of Patients (%)
Osteomyelitis	26 (18%)
HIV	23 (16%)
Hepatitis C	10 (7%)
Cellulitis/Diabetic Foot Infection	8 (5%)
Bacteremia	8 (5%)
Recurrent UTI's	7 (5%)
Endocarditis	7 (5%)
Additional Antibiotic Allergies	# of Patients (%)
Cephalosporin	32 (22%)
Miscellaneous Antibiotics	63 (43%)

Primary Outcome

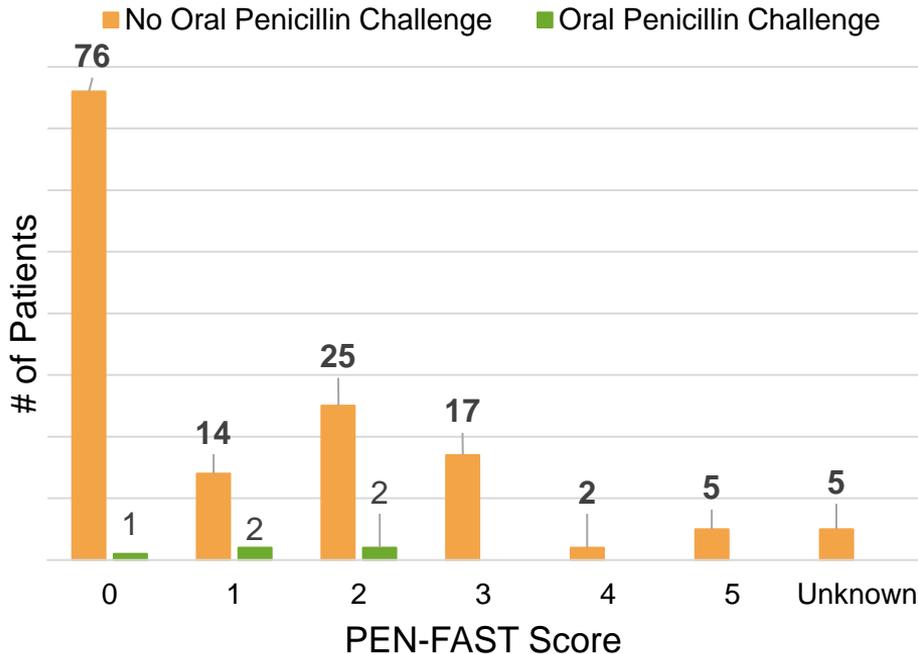
- A large majority of the organization's patient population would qualify to become “de-labeled”
 - 81% of patients had a PEN-FAST score <3
- Majority of patients could theoretically tolerate a penicillin challenge

Table 2. Proportion of Patients Stratified by PEN-FAST Score (n = 148)

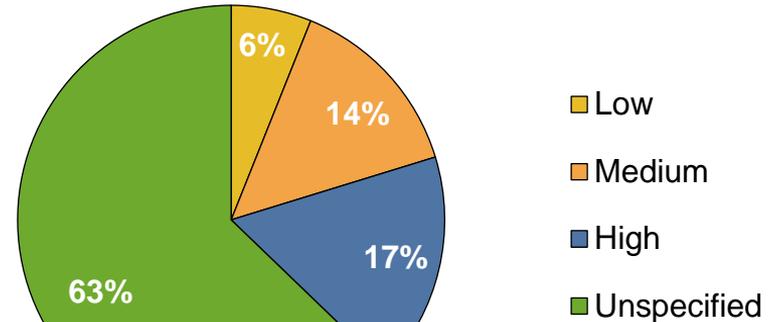
PEN-FAST Score	# of Patients (%)
Unknown	5 (3%)
0	77 (52%)
1	16 (11%)
2	27 (18%)
3	17 (11%)
4	2 (1%)
5	5 (3%)

Secondary Outcomes

Penicillin Challenges By PEN-FAST Score (n = 148)



Current Severity Documentation of Penicillin Allergies (n = 148)



Secondary Outcomes

Cefazolin Skin Test Results By PEN-FAST Scores
(n = 148)

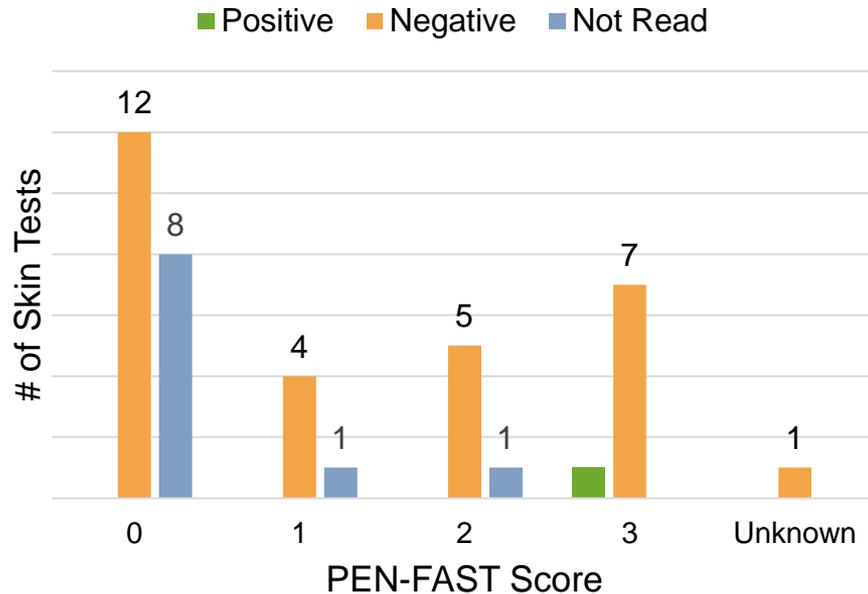


Table 3. Skin Test Usage and Results By PEN-FAST Score

PEN-FAST Score	Skin Test Result	
	Negative	Not Read
0	12	8
1	4	1
2	5	1
3	1	0
Skin Test	Documented Tests (n)	Unread Results (n; %)
Cefazolin	40	10 (25%)
Ceftriaxone	4	1 (25%)

Secondary Outcomes

Allergy Severity Documentation by Antibiotic Class
(n = 148)

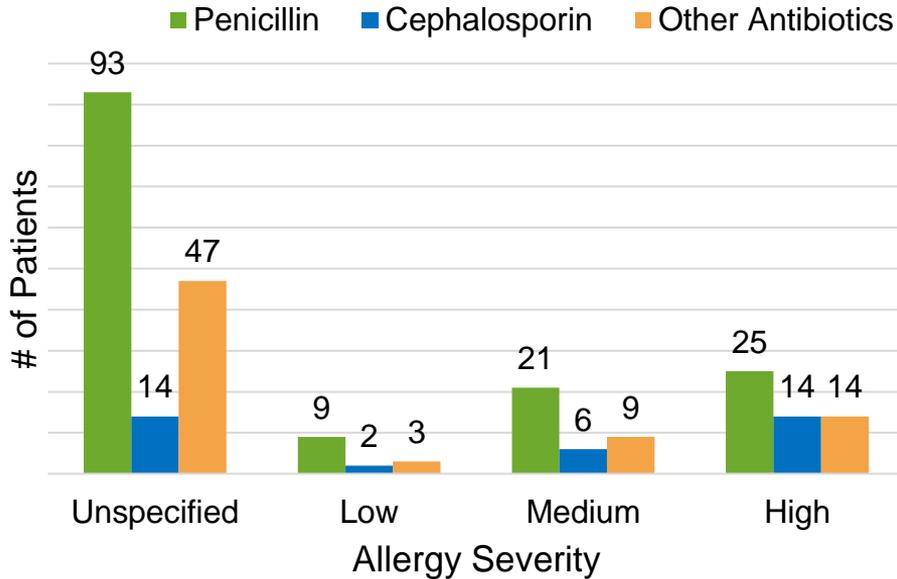


Table 4. Proportion of Patients with Concurrent Antibiotic Allergies and Documented Reactions
(n = 148)

	# of Patients (n, %)
Concurrent Non-Penicillin Antibiotic Allergies	105 (71%)
Documented Reaction	121 (81%)

Discussion

- **Lack of oral penicillin challenges likely secondary to:**
 - *No indication* for antibiotic treatment with a penicillin
- **Indication for broader application outside ID clinic setting as majority of penicillin allergies are low risk and not documented correctly with current process**
 - Streamlined process could improve compliance
 - Application in these settings would allow for more opportunities for oral penicillin challenges
 - (i.e. family practice offices, inpatient)
- **Large amount of unread skin tests indicate current practice is not being utilized properly**
 - *Further indication* for implementing a more cost-effective alternative

Conclusion

- **Limitations**

- Partner relationships in trialing a new quality improvement initiative
- Timeline of collection conflicted with holiday clinic schedule
- Potential subjectivity in PEN-FAST question answers
 - Important to provide definitions

- **Next Steps**

- Implementation of the PEN-FAST in place of skin testing outside ID clinics \pm inpatient setting over a longer timeframe (>3 months)
- Focus on penicillin challenge to confirm specificity of assessment

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References

1. Is it really a penicillin allergy? - centers for Disease Control and ... Is It Really a Penicillin Allergy? Accessed March 5th, 2024. <https://www.cdc.gov/antibiotic-use/community/pdfs/penicillin-factsheet.pdf>.
2. Caruso C, Valluzzi RL, Colantuono S, Gaeta F, Romano A. β -Lactam Allergy and Cross-Reactivity: A Clinician's Guide to Selecting an Alternative Antibiotic. *J Asthma Allergy*. 2021;14:31-46. Published 2021 Jan 18. doi:10.2147/JAA.S242061
3. <https://www.mdpi.com/2226-4787/7/3/103>
4. De Rosa M, Verdino A, Soriente A, Marabotti A. The Odd Couple(s): An Overview of Beta-Lactam Antibiotics Bearing More Than One Pharmacophoric Group. *International Journal of Molecular Sciences*. 2021; 22(2):617. <https://doi.org/10.3390/ijms22020617>. Accessed March 5th, 2024.
5. Beta-Lactam Allergy Tip Sheet Hypersensitivity Type, Mechanism, and Clinical Manifestations. https://www.unmc.edu/intmed/_documents/id/asp/clinicpath-beta-lactam-cross-reaction-tip-sheet.pdf
6. Liu MY, McCoul ED, Brooks EG, Lao VF, Chen PG. Inaccurate penicillin allergy labels: Consequences, solutions, and opportunities for rhinologists. *Int Forum Allergy Rhinol*. 2023;13(6):973-978. doi:10.1002/alr.23173
7. Stone CA Jr, Trubiano J, Coleman DT, Rukasin CRF, Phillips EJ. The challenge of de-labeling penicillin allergy. *Allergy*. 2020;75(2):273-288. doi:10.1111/all.13848
8. Trubiano JA, Vogrin S, Chua KYL, et al. Development and Validation of a Penicillin Allergy Clinical Decision Rule. *JAMA Intern Med*. 2020;180(5):745-752. doi:10.1001/jamainternmed.2020.0403
9. Su C, Belmont A, Liao J, Kuster JK, Trubiano JA, Kwah JH. Evaluating the PEN-FAST Clinical Decision-making Tool to Enhance Penicillin Allergy Delabeling. *JAMA Intern Med*. 2023;183(8):883-885. doi:10.1001/jamainternmed.2023.1572