MASSACHUSETTS GENERAL HOSPITAL
RHEUMATOLOGY, ALLERGY AND IMMUNOLOGY

Updates on the Drug Allergy Practice Parameters

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Learning Objectives

- Upon completion of this learning activity, participants should be able to identify key drug allergy practice parameter updates

- Upon completion of this learning activity, participants should be able to employ drug challenges safely across clinical settings

- Upon completion of this learning activity, participants should be able to describe the rationale for, and approaches to, penicillin allergy de-labeling

Drug Allergy Parameter Update

- Last parameter published 2010
- Next parameter will update ~ 14 sections
- Currently drafted and being revised based on comments from AAAAI/ACAAI/JTFPP
- All recommendations in this presentation should be considered as *preliminary*
- Expected publication in 2022

Drug Allergy Parameter Update: Key Updates

- Antibiotic: de-emphasis on skin testing and increased role for drug challenge
- Administration of beta-lactams in those with penicillin and cephalosporin allergies: Risk stratify based on anaphylactic history
- New recommendations for approach to sulfonamide antibiotic allergy
- New recommendation for 2-step challenge rather desensitization for those with aspirin allergy with acute cardiovascular disease

David Khan (Chair)

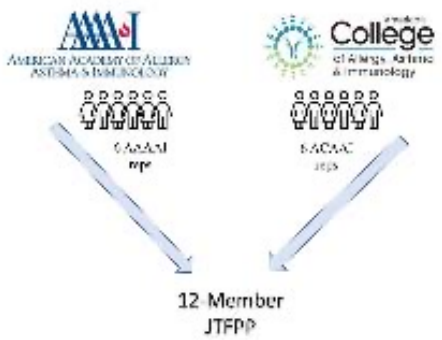
Aleena Banerji

Kim Blumenthal

Elizabeth Phillips

Roland Solensky

Drew White



David Golden
David Stukus

Drug Allergy Workgroup

Drug Allergy Parameter Update

- **Diagnostic Tests**
  - Drug challenge procedures
  - Delayed reaction testing
  - Pharmacogenomics

- **Antibiotic Updates**
  - Penicillins
  - Cephalosporins
  - Carbapenems
  - Monobactams
  - Sulfonamides
  - Fluoroquinolones
  - Macrolides

- **Other Updates**
  - NSAID Hypersensitivity
    - Aspirin challenge for acute cardiovascular disease
  - Chemotherapeutics
  - Biologics
  - Excipients

Drug Allergy Parameter Update

- **Diagnostic Tests**
  - **Drug challenge procedures**
  - Delayed reaction testing
  - Pharmacogenomics

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  - **Penicillins**
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  - **Fluoroquinolones**
  - **Macrolides**

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  - Biologics
  - Excipients

Drug Challenge: 1 or 2 Step Preferred

Consensus Based Statement	Strength of Recommendation	Certainty of Evidence
We suggest that when the clinical probability of a drug allergy is low, in patients without contraindications for a drug challenge, that it be performed with a 1- or 2-step drug challenge.	**Conditional**	**Low**

Iammatteo M et al. *J Allergy Clin Immunol Pract.* 2016

Open Drug Challenge Protocols for Immediate Reactions

	Dose	Observation
1-Step	1 tab or Full PO/IV /IM/SC dose	30-60 min
2-Step	Step 1:¼ tab PO or 1/10th IV/IM/SC dose	30-60 min
	Step 2: 1 tab or Full PO/IV /IM/SC dose	30-60 min
Criteria for positive reaction	Urticaria, angioedema, exanthem, wheezing, hypoxia, hypotension, anaphylaxis	
Criteria for possible reaction	Flushing, vomiting, cough, abdominal cramping, persistent pruritus without rash, fever, mouth or eye soreness	
Doubtful reactions	Dizziness, tachycardia, subjective lip/tongue swelling, subjective throat tightness, lump in throat, dyspnea, transient pruritus without rash, headache	

Drug Challenge Considerations

- Patients deemed unlikely to be allergic to the drug
- Shared decision making may be used in patients with a higher pretest probability of true allergy or a history of more severe reactions when the benefit of drug therapy outweighs the risks
- For very low risk patients without significant comorbidities: Single full dose challenge (e.g., sulfonamide antibiotics & penicillins)
- Consider placebo-controlled challenges for possible or doubtful reactions to confirm or refute allergy

Drug Challenge Contraindications

Severe Cutaneous Adverse Drug Reactions	**Severe Drug Anaphylaxis**
SJS/TEN	
DRESS	**Organ Specific Drug Reactions**
AGEP	Cytopenias (anemia, neutropenia, leukopenia, thrombocytopenia)
	Drug induced liver injury
Drug-Induced Neutrophilic Dermatosis	Nephritis
Sweet's syndrome	Pneumonitis
	Meningitis
Drug-Induced Autoimmune Diseases	Pancreatitis
Bullous pemphigoid	
Pemphigus vulgaris	**Drug Induced Vasculitis**
Linear IgA bullous disease	Leukocytoclastic vasculitis
Drug induced lupus	Eosinophilic granulomatosis with polyangiitis
Other Cutaneous Drug Reactions	**ACE inhibitor angioedema**
Generalized bullous fixed drug eruption	
Exfoliative dermatitis	

Original Article

Differentiating Between β-Lactam-Induced Serum Sickness–Like Reactions and Viral Exanthem in Children Using a Graded Oral Challenge

Variable	Patients (n = 75)
Age at index reaction, median (IQR)	2.00 (1.20, 4.00)
Sex, n (% males)	35 (46.7)
Symptoms of index reaction, n (%)	
Pruritus (generalized)	31 (41.3)
Urticaria	48 (65.3)
Angioedema	26 (34.7)
Macular/papular rash	33 (44.0)
Gastrointestinal	8 (10.7)
Throat tightness	2 (2.7)
Breathing difficulties	3 (4.0)
Arthritis/arthralgia	75 (100)
Fever	30 (40.0)
Antibiotic type, n (%)	
Amoxicillin	66 (88.0)
Clavulin	5 (6.7)
Cefprozil	2 (2.7)
Cephalexin	2 (2.7)

Variable	n (%)
Challenge outcome	
Positive (immediate)	2 (2.7)
Positive (nonimmediate)	3 (4.0)
Negative	70 (93.3)

All positive challenge reactions were grade 1 reactions.

- Protocol: 10% dose then 20 min later 90% dose

Colli LD et al. *J Allergy Clin Immunol Pract.* 2021

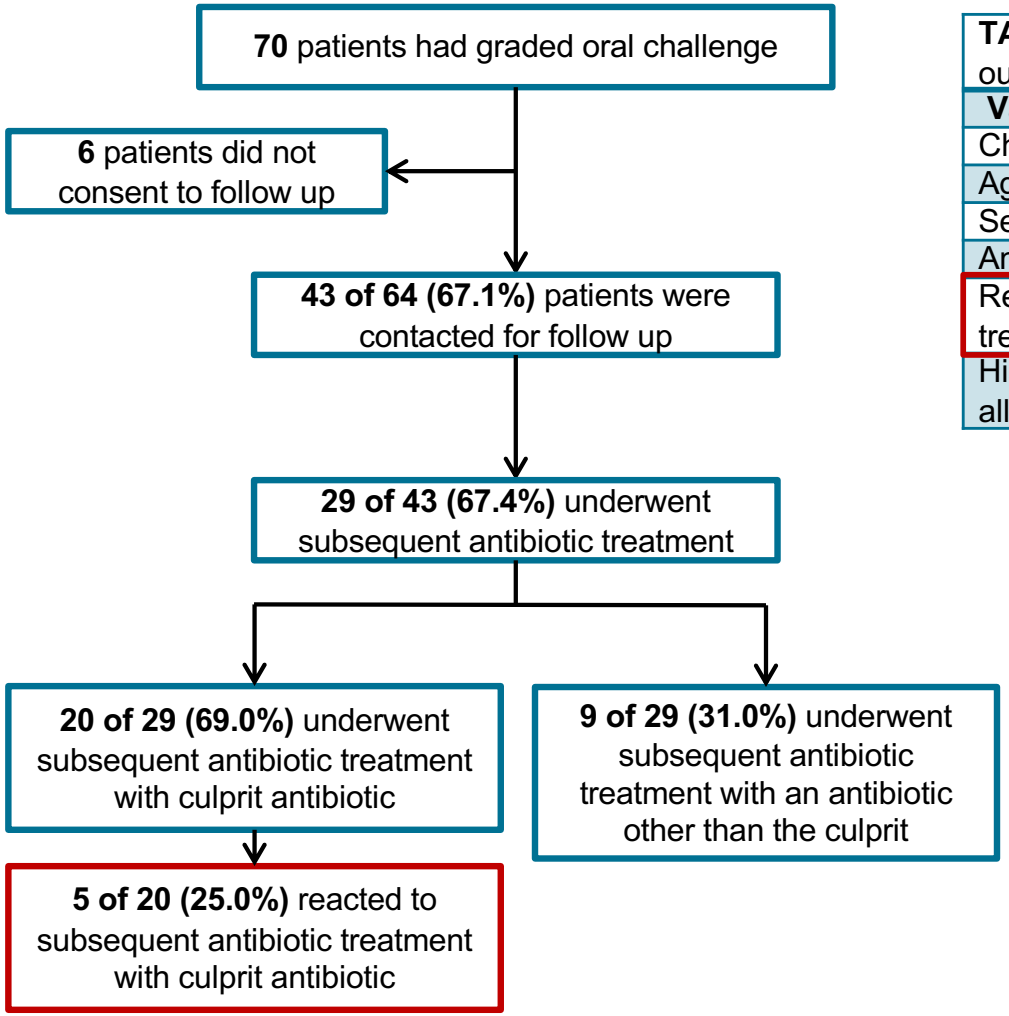


TABLE III. Factors associated with positive graded oral challenge outcome or positive subsequent reaction in pediatric patients

Variable	Univariate	Multivariate
Challenge outcome	OR (95% CI)	OR (95% CI)
Age at index reaction	1.00 (0.98, 1.02)	1.00 (0.97, 1.02)
Sex (male)	0.96 (0.82, 1.12)	0.97 (0.83, 1.14)
Antibiotic type--amoxicillin	1.05 (0.84, 1.30)	1.09 (0.87, 1.37)
Reaction within 4-6 d of treatment	1.18 (1.00, 1.39)	1.20 (1.01, 1.42)
History of parental drug allergy	1.03 (0.86, 1.23)	1.04 (0.87, 1.25)

Challenges may be considered for SSLR, however 25% may have benign symptoms with subsequent course

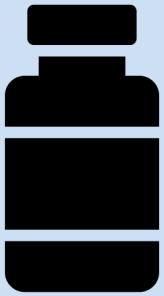
Colli LD et al. *J Allergy Clin Immunol Pract.* 2021

Placebo Challenges for Subjective Reactions or Multiple Drug Intolerance

Consensus Based Statement	Strength of Recommendation	Certainty of Evidence
We suggest that placebo-controlled drug challenges be considered in patients with a history of primarily subjective symptoms and/or multiple reported drug allergies.	**Conditional**	**Low**

Nocebo Effect

- The nocebo effect is the onset of untoward reactions following the administration of an indifferent substance.



- Beta-lactam challenge, ~200 patients in US, **8%** reacted to placebo
- Placebo reactors commonly female and with more drug allergy labels

Iammatteo *J Allergy Clin Immunol Pract*. 2019

Determinants of nocebo effect during oral drug provocation tests

S. Bavbek[a,*], Ö. Aydın[a], Z.Ç. Sözener[a], S. Yüksel[b]

137/228 (60%) had reactions to placebo

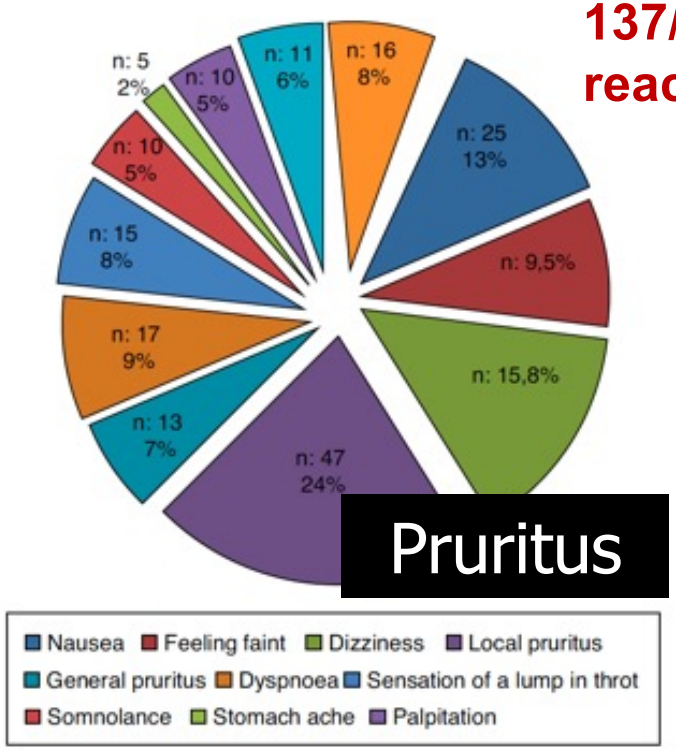


Figure 2 Subjective findings with placebo.

12% of nocebo reactions were objective

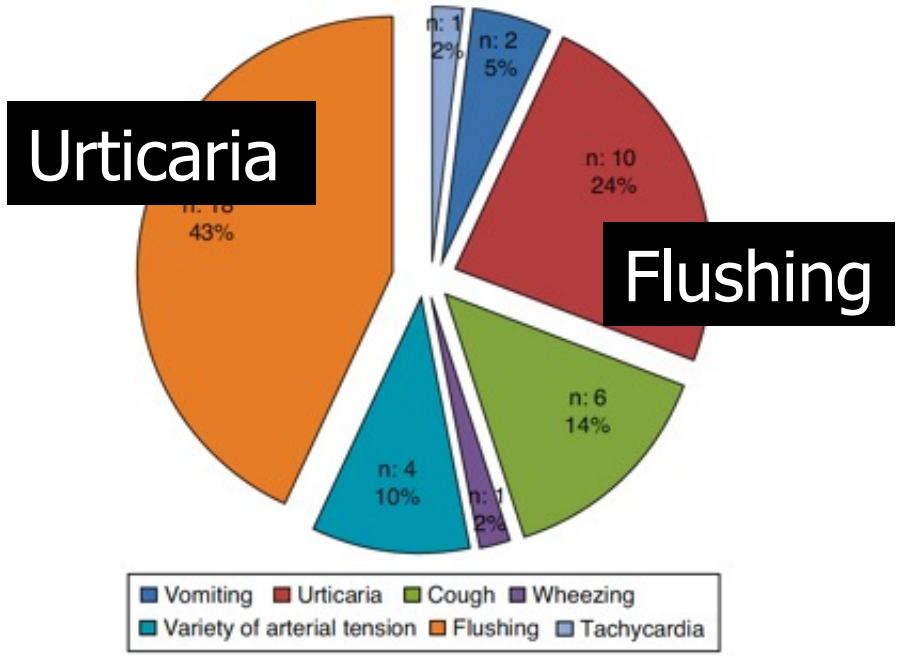
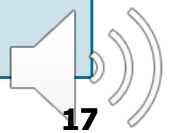


Figure 1 Objective findings with placebo.

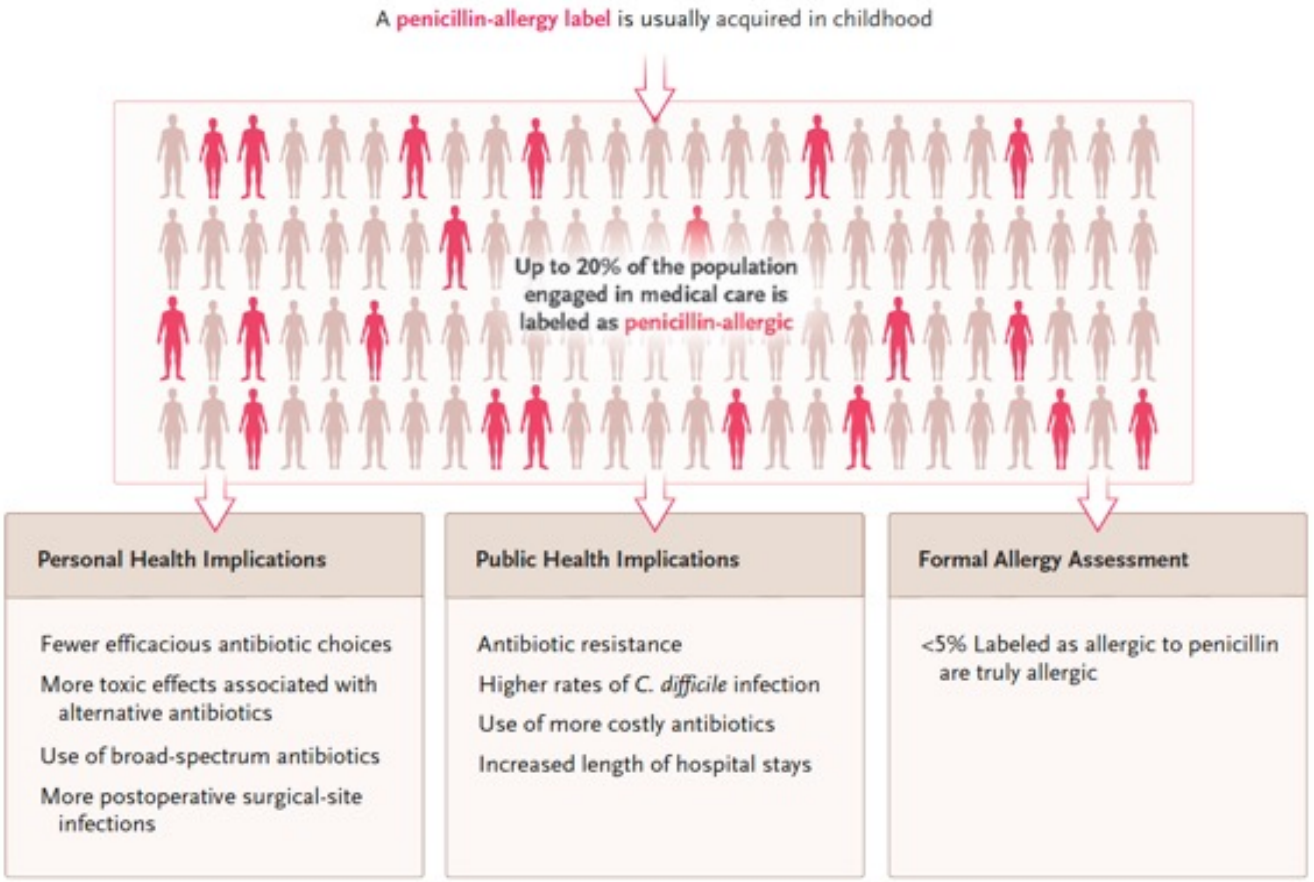
Bavbek S et al. *Allergol Immunopathol (Madr).* 2015

Penicillin Allergy

Consensus Based Statement	Strength of Recommendation	Certainty of Evidence
We recommend that a proactive effort should be made to delabel a penicillin allergy, if appropriate.	**Strong**	**Moderate**
We recommend against testing in patients with a history inconsistent with penicillin allergy (such as headache or family history of penicillin allergy), but a 1-step amoxicillin challenge may be offered to patients who are anxious or request additional reassurance to accept the removal of a penicillin allergy label.	**Strong**	**Moderate**
We suggest penicillin skin testing for patients with a history of anaphylaxis or a recent reaction suspected to be IgE mediated.	**Conditional**	**Low**



Why Penicillin Allergy Labels Matter



Castells MC, Khan DA, Phillips EC *NEJM*. 2019

Original Article

The Effect of Penicillin Allergy Testing on Future Health Care Utilization: A Matched Cohort Study

Eric Macy, MD, MS[a], and Yu-Hsiang Shu, MS, PhD[b] *San Diego and Pasadena, Calif*

Beta-Lactam Alternatives	Evaluated (n=308)	Not Evaluated (n=1,251)	P-Value
Cotrimoxazole	21.1	23.7	0.36
Clindamycin	14.6	32.5	<0.001
Macrolide	31.5	41.8	0.001
Tetracycline	24.0	19.2	0.07
Quinolone	31.5	30.7	0.84
Vancomycin	4.5	6.6	0.22
Aminoglycoside	11.0	14.6	0.12

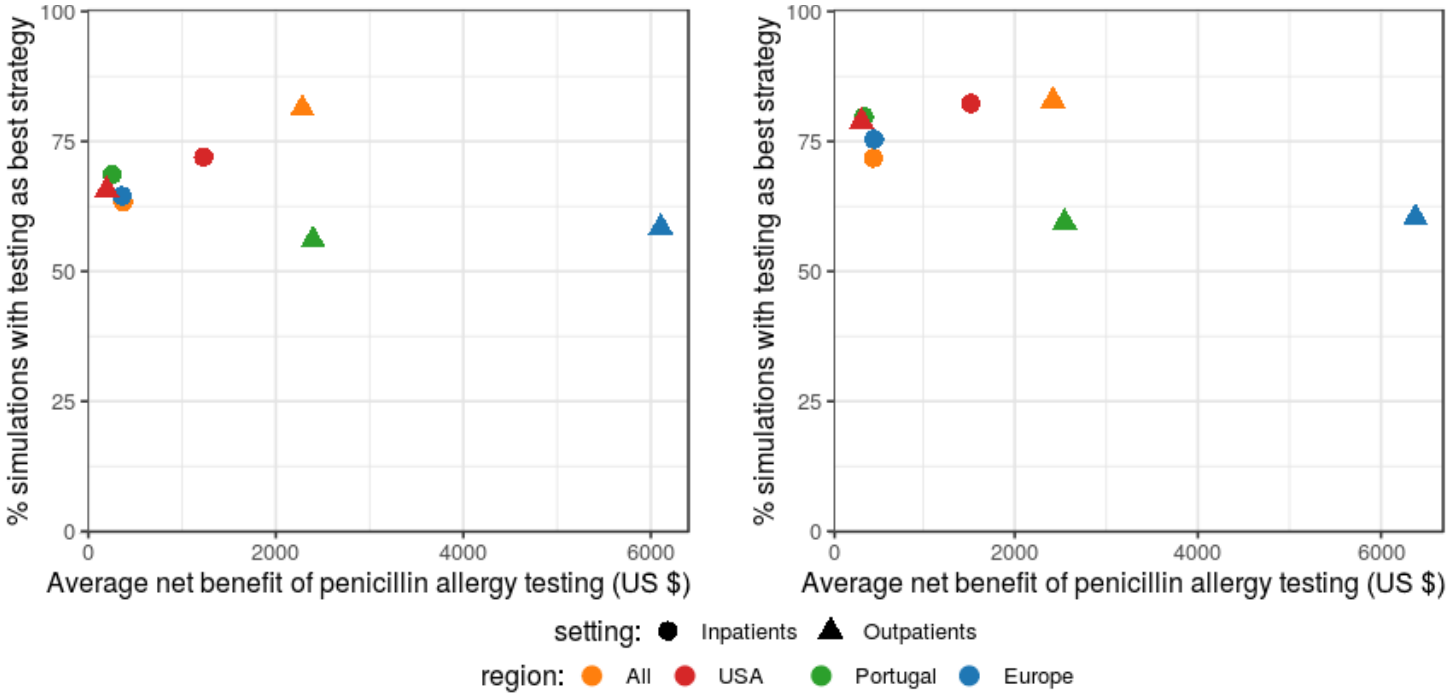
Macy *J Allergy Clin Immunol Pract.* 2017

Penicillin Allergy Testing Is Cost-Saving: An Economic Evaluation Study

Bernardo Sousa-Pinto,[1,2,3] Kimberly G. Blumenthal,[4,5] Eric Macy,[6] Ana Margarida Pereira,[1,2] Luís Filipe Azevedo,[1,2] Luís Delgado,[2,3] and João Almeida Fonseca[1,2]

Skin Testing & Drug Challenge Testing:
Savings $554 for inpatients and $2,745 for outpatients

Drug Challenge Testing Alone:
Savings of $616 for inpatients and $3,051 for outpatients



Sousa-Pinto *Clin Infect Dis.* 2020

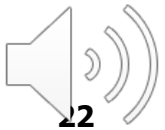
Methods to De-label Penicillin Allergy

Setting	Method	Comment
Outpatient	Referral based skin test and challenge	With or without minor determinant mixture
	Direct challenge	Low risk histories
	Protocol driven	Allergy clinic
		Other clinics
Inpatient	Allergy consultation	Least efficient
	Proactive testing protocol	Pharmacists or other healthcare providers
	Intensive care unit testing	Skin testing
	Emergency Department	Skin testing or direct challenge by non-allergy specialists or other healthcare providers

Khan DA *Allergy Asthma Proc.* 2020

Consensus Based Statement

Consensus Based Statement	Strength of Recommendation	Certainty of Evidence
We recommend against penicillin skin testing prior to direct amoxicillin challenge in pediatric patients with a history of benign cutaneous reaction (such as maculopapular rashes and urticaria).	**Strong**	**Moderate**
We suggest that direct amoxicillin challenge be considered in adults with distant and benign cutaneous reaction histories (such as maculopapular rashes and urticaria).	**Conditional**	**Low**

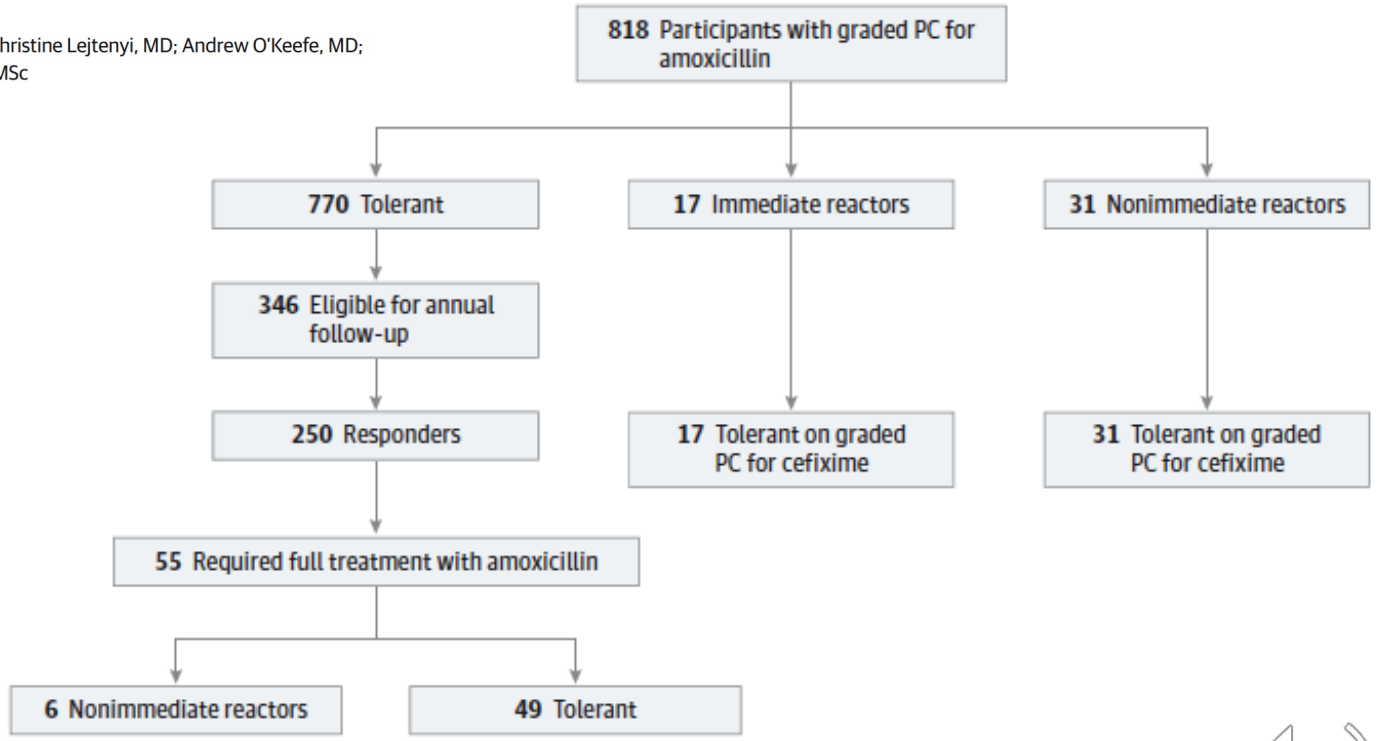


Original Investigation

Assessing the Diagnostic Properties of a Graded Oral Provocation Challenge for the Diagnosis of Immediate and Nonimmediate Reactions to Amoxicillin in Children

Christopher Mill, MPH; Marie-Noël Primeau, MD; Elaine Medoff, MD; Christine Lejtenyi, MD; Andrew O'Keefe, MD; Elena Netchiporouk, MD; Alizee Dery, BSc; Moshe Ben-Shoshan, MD, MSc

94% passed challenge



Mill C et al. *JAMA Pediatr.* 2016

CME Review

Who needs penicillin allergy testing?

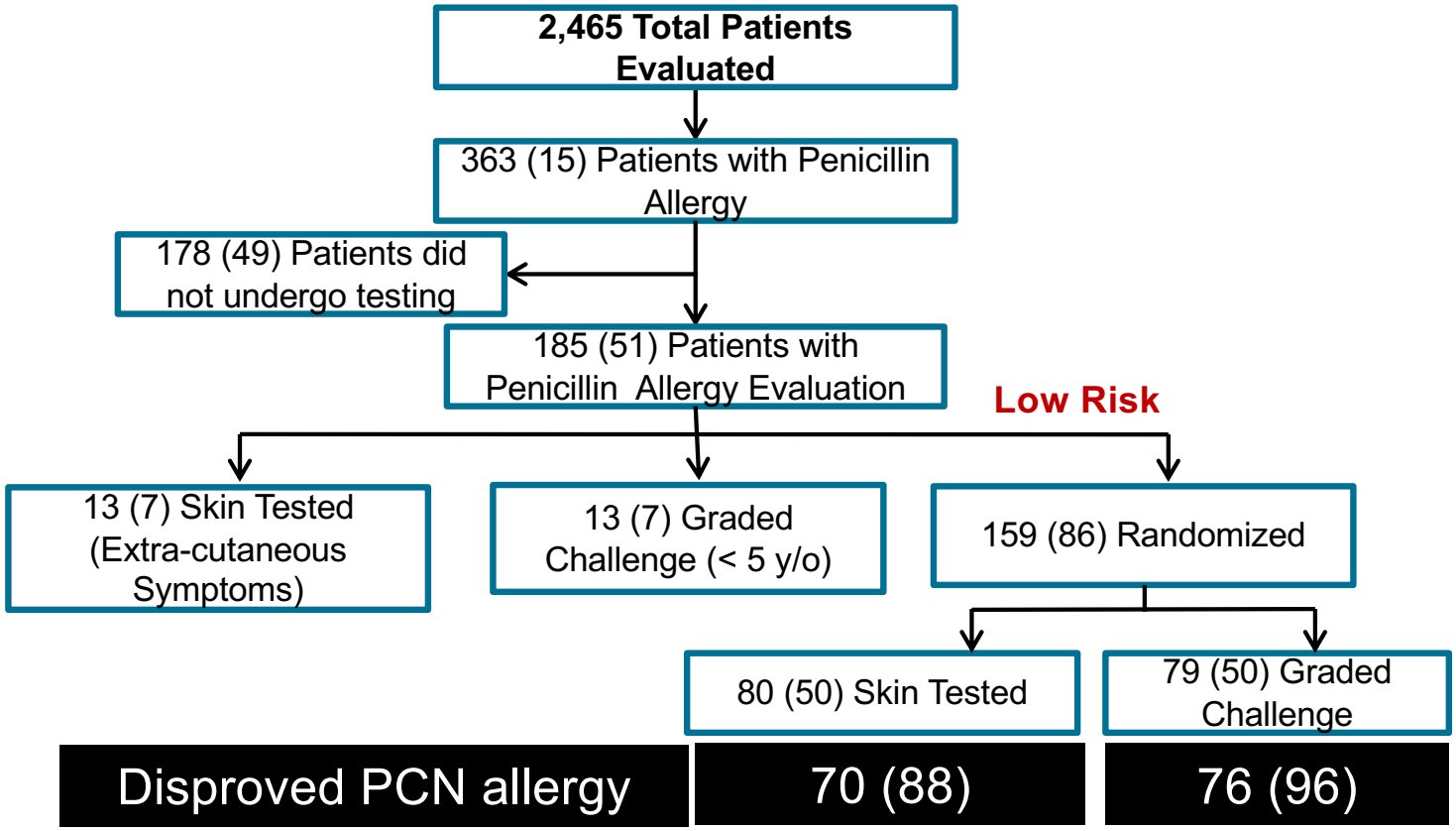
Eric Macy, MD, MS*; David Vyles, DO, MS†

No. of Patients	Age Groups	Country	Immediate-Onset Positive	Delayed-Onset Positive
818	Children	Canada	17 (2.1%)	31 (3.5%)
328	Adults	United States	5 (1.5%)	0 (0%)
130	Children	Canada	3 (2.3%)	5 (3.8%)
155	Children and adults	United States	1 (0.6%)	3 (1.9%)
732	Children	Spain	6 (0.8%)	29 (4.0%)
617	Children (n=435) and adults (n=207)	Israel	9 (1.5%)	1 day: 24 (19.0%); 5 day: 30 (6.1%)
519	Children and adults	United States	1 (0.2%)	8 (1.6%)
3,299			**42 (1.3%; 95%CI 0.9-1.7%)**	**130 (3.9%; 95% CI 3.3-4.7%)**

Macy *Ann Allergy Asthma Immunol.* 2018

Original Article

Comparing Direct Challenge to Penicillin Skin Testing for the Outpatient Evaluation of Penicillin Allergy: A Randomized Controlled Trial



Mustafa *J Allergy Clin Immunol Pract*. 2019

Prolonged Penicillin Challenges Not Needed

Consensus Based Statement	Strength of Recommendation	Certainty of Evidence
We recommend against the routine use of prolonged (multi-day) challenges in the evaluation of penicillin allergy.	**Strong**	**Low**

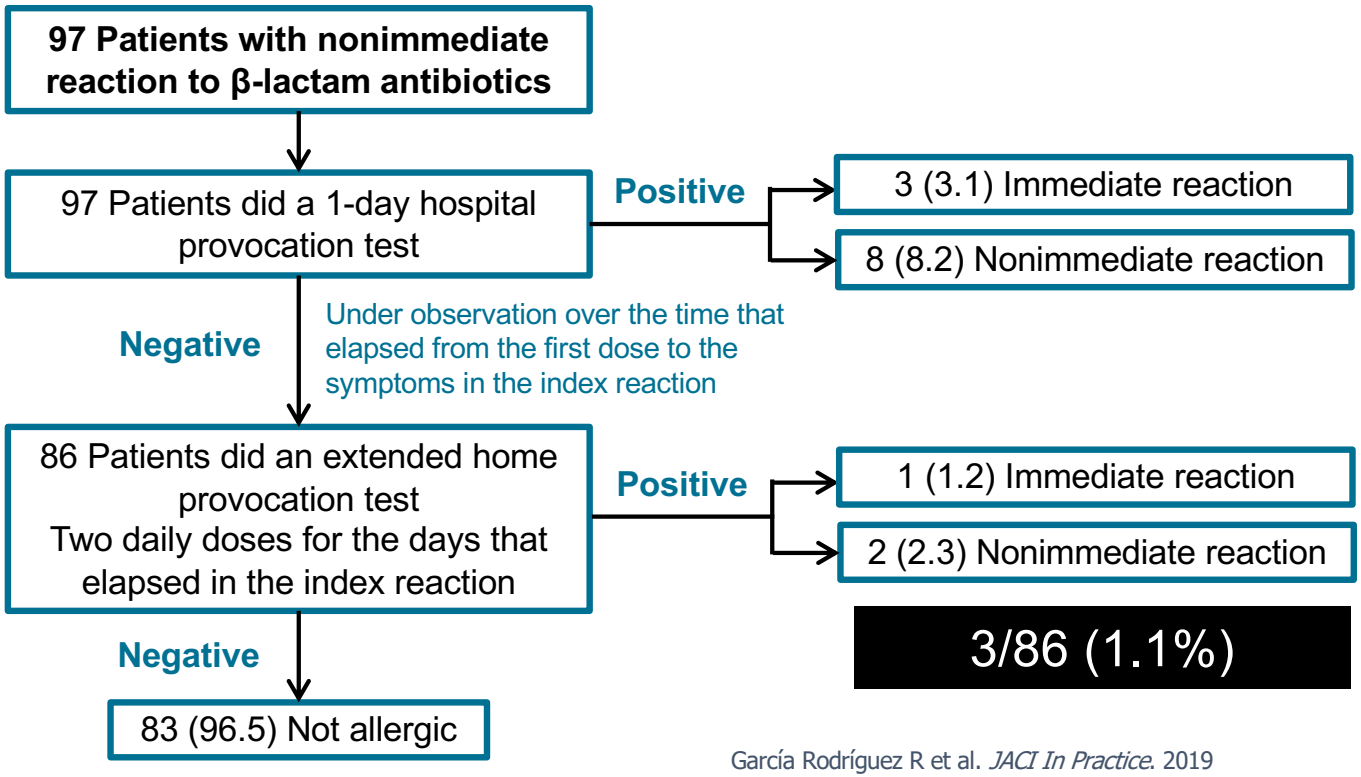
Are Extended Multiday Penicillin Challenges Necessary?

- European studies
  - Oral challenges 3-10 days
  - Delayed reactions 5-12%
  - Most self-reported, almost all mild and easily treated

- US Studies
  - Full therapeutic courses after negative tests
  - Delayed reactions 0-2%

Original Article

Provocation Tests in Nonimmediate Hypersensitivity Reactions to β-Lactam Antibiotics in Children: Are Extended Challenges Needed?



García Rodríguez R et al. *JACI In Practice*. 2019

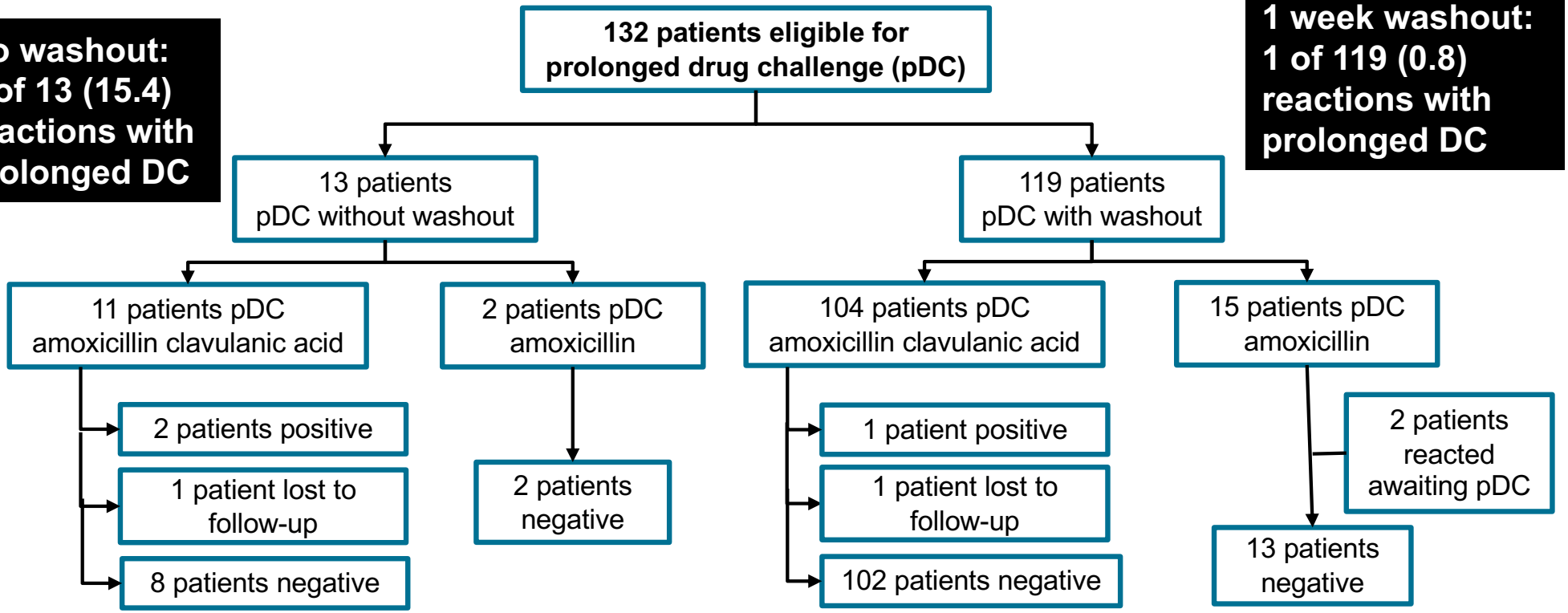
Delayed reactions occurred **6 hrs to 7 days** from initial challenge

Original Article

The Limited Value of Prolonged Drug Challenges in Nonimmediate Amoxicillin (Clavulanic Acid) Hypersensitivity

No washout: 2 of 13 (15.4) reactions with prolonged DC

1 week washout: 1 of 119 (0.8) reactions with prolonged DC

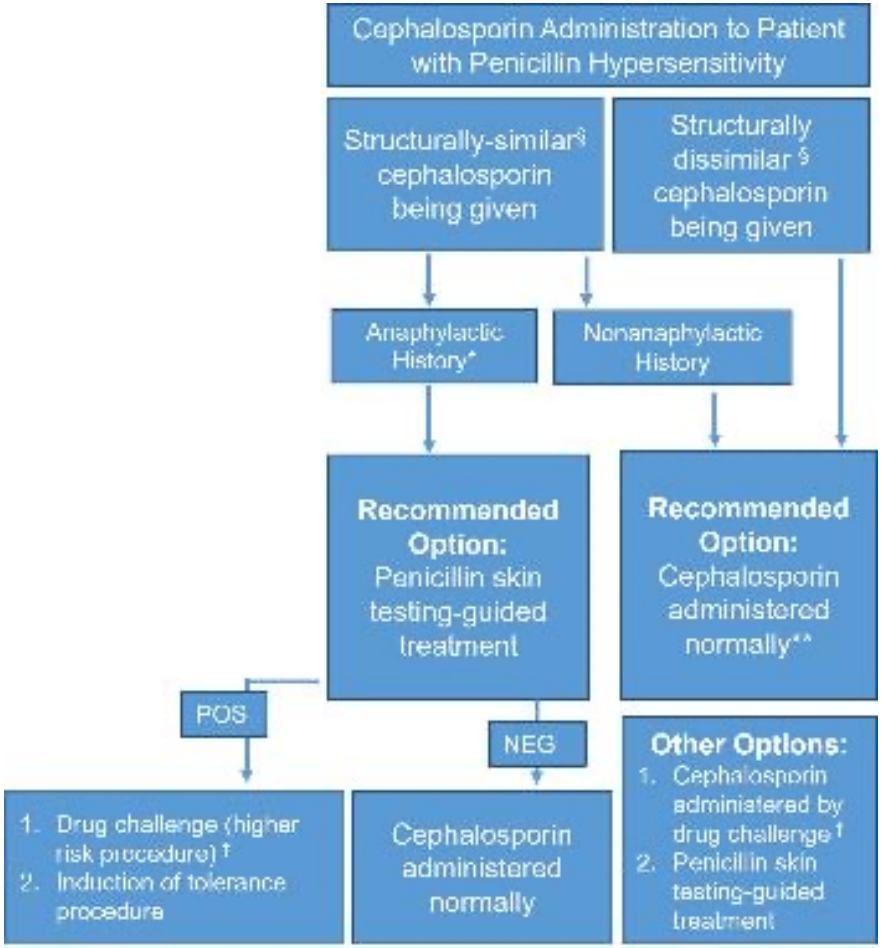


Van Gasse AL et al. *JACI In Practice*. 2019

Use of Cephalosporins in Penicillin Allergy

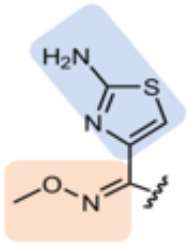
Consensus Based Statement	Strength of Recommendation	Certainty of Evidence
We suggest that for patients with an unverified non-anaphylactic penicillin allergy, a cephalosporin can be administered without testing or additional precautions.	Conditional	Moderate
We suggest that for patients with a history of anaphylaxis to penicillin, a non-cross–reactive cephalosporin can be administered without prior testing.	Conditional	Moderate

Cephalosporins Administration with History of Penicillin Allergy



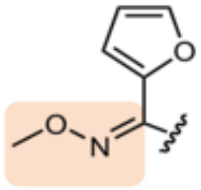
Cephalosporin Allergy Based on R1 Side Chain

Group 1



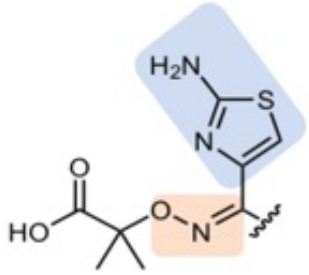
Ceftriaxone, Cefotaxime, Cefepime
Cefpodoxime, Cefditoren
(may cross-react with Groups 2&3)

Group 2



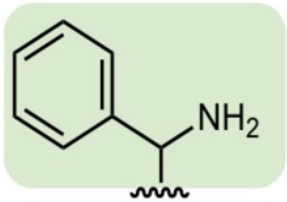
Cefuroxime
(may cross-react with groups 1&3)

Group 3



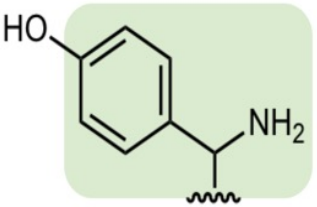
Ceftazidime, aztreonam
(may cross-react with groups 2&3)

Group 4



Ampicillin
Cefaclor
Cephalexin

Group 5



Amoxicillin
Cefadroxil
Cefprozil

Khan DA et al. *J Allergy Clin Immunol.* 2019

Original Article

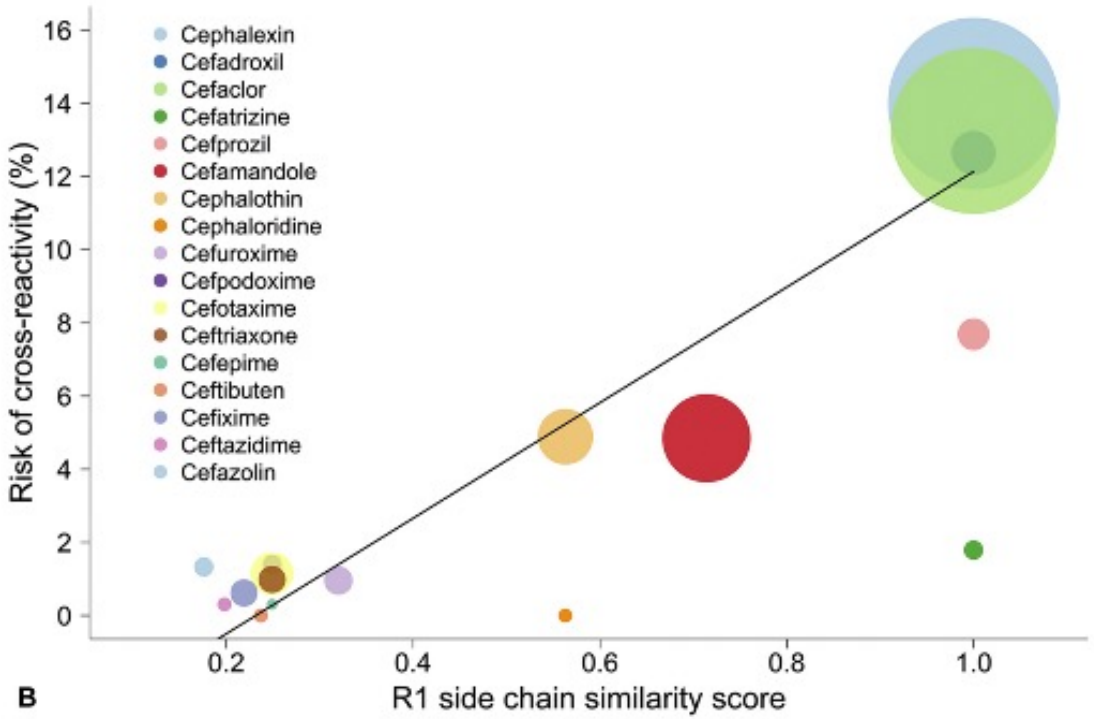
Cross-Reactivity to Cephalosporins and Carbapenems in Penicillin-Allergic Patients: Two Systematic Reviews and Meta-Analyses

Caveats of systematic review

- Almost all patients had confirmed aminopenicillin allergy (not penicillin allergy)
- 25 (89%) studies from Europe, 3 (11%) from Canada

If proven allergy to ampicillin:

- Risk of positive skin test to 1st /2ndgen aminocephalosporin is **16%**
- Risk of positive skin test to unrelated 2nd-4th generation is **2%**



Picard M et al. *JACI In Practice.* 2019

Original Article

Cross-Reactivity to Cephalosporins and Carbapenems in Penicillin-Allergic Patients: Two Systematic Reviews and Meta-Analyses

Generation	Name	No. of studies	n/N	AR in % (95% CI)
First	Cephalexin	8	97/693	14.00 (11.61-16.79)
	Cefadroxil	6	95/557	12.65 (5.85-25.26)
	Cephalothin	3	9/184	4.89 (2.56-9.13)
	Cefazolin	3	1/75	1.33 (0.19-8.86)
	Cefatrizine	2	1/56	1.79 (0.25-11.61)
	Cephaloridine	1	0/17	0.0 (0.0-19.5)
Second	Cefamandole	6	23/474	4.85 (3.25-7.20)
	Cefaclor	7	90/679	13.25 (10.91-16.02)
	Cefuroxime	14	16/984	0.96 (0.26-3.51)
	Cefprozil	1	3/39	7.69 (1.62-20.87)
Third	Cefpodoxime	1	1/71	1.4 (0.0-7.6)
	Ceftazidime	4	2/433	0.31 (0.02-4.72)
	Cefotaxime	4	5/436	1.15 (0.48-2.72)
	Cefixime	7	2/324	0.62 (0.15-2.43)
	Ceftriaxone	9	13/843	0.99 (0.25-3.87)
	Ceftibuten	3	0/153	0.0 (0.0-2.4)
Fourth	Cefepime	2	1/285	0.31 (0.01-10.32)

Picard M et al. *JACI In Practice.* 2019

JAMA Surgery | Original Investigation

Assessment of the Frequency of Dual Allergy to Penicillins and Cefazolin

A Systematic Review and Meta-analysis

Dual Allergy Results

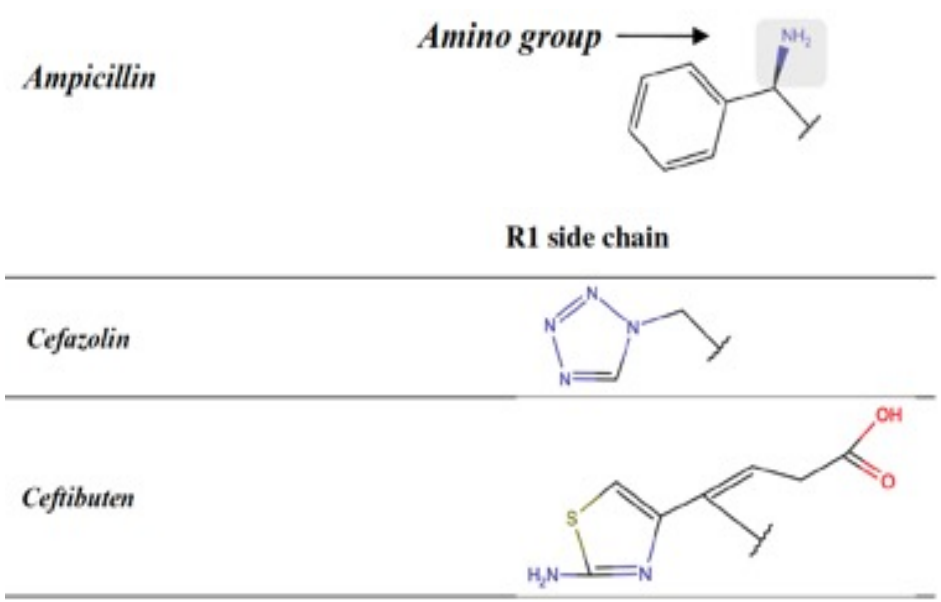
	Cohort	Surgical Patients	Penicillin Allergy History	
Index penicillin allergy	0.7% n=6001	0.7% n=3884	Self-reported	0.6% n=5487
Index cefazolin allergy	3% n=146	4.4% n=104	Confirmed	3% n=514

Sousa-Pinto, Blumenthal *JAMA Surg.* 2020

Original Article

Tolerability of Cefazolin and Ceftibuten in Patients with IgE-Mediated Aminopenicillin Allergy

- 131 subjects; 98.5% aminopenicillin allergy, 78% with anaphylaxis
- 130/131 had negative cefazolin/ceftibuten skin tests
  - 1 subject (outlier) had positive skin tests to all PCN reagents, cephalosporins, and carbapenems (beta lactam ring allergy)
- 129/130 agreed to cefazolin/ceftibuten challenges and did not have reactions

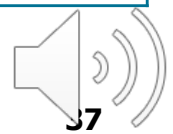


Cefazolin and ceftibuten R1 groups disparate from aminopenicillins

Romano A et al. *J Allergy Clin Immunol Pract*. 2020

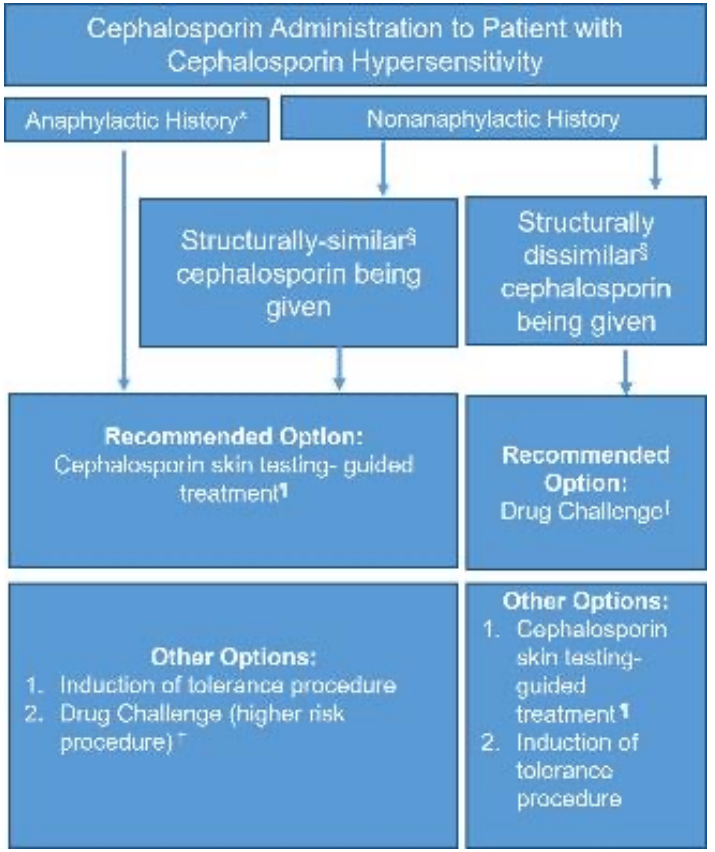
Cephalosporin and Penicillin Administration with History of Cephalosporin Allergy

Consensus Based Statement	Strength of Recommendation	Certainty of Evidence
We suggest that for patients with a history of non-anaphylactic cephalosporin allergy, direct challenges (without prior skin test) to cephalosporins with dissimilar side chains be performed to determine tolerance.	Conditional	Moderate
We suggest that for patients with a history of anaphylaxis to a cephalosporin, a negative cephalosporin skin test should be confirmed prior to administration of a parenteral cephalosporin with a non-identical R1 side chain.	Conditional	Low



Cephalosporin Administration with History of Cephalosporin Allergy

- Most data suggest that **90%** of cephalosporin allergy is due to R1 side chain
- Cephalosporin allergic patients typically tolerate other cephalosporins with disparate R1 side chains, especially if skin test negative
  - 102 cephalosporin allergic patients tolerated 326 challenges to skin test negative cephalosporins

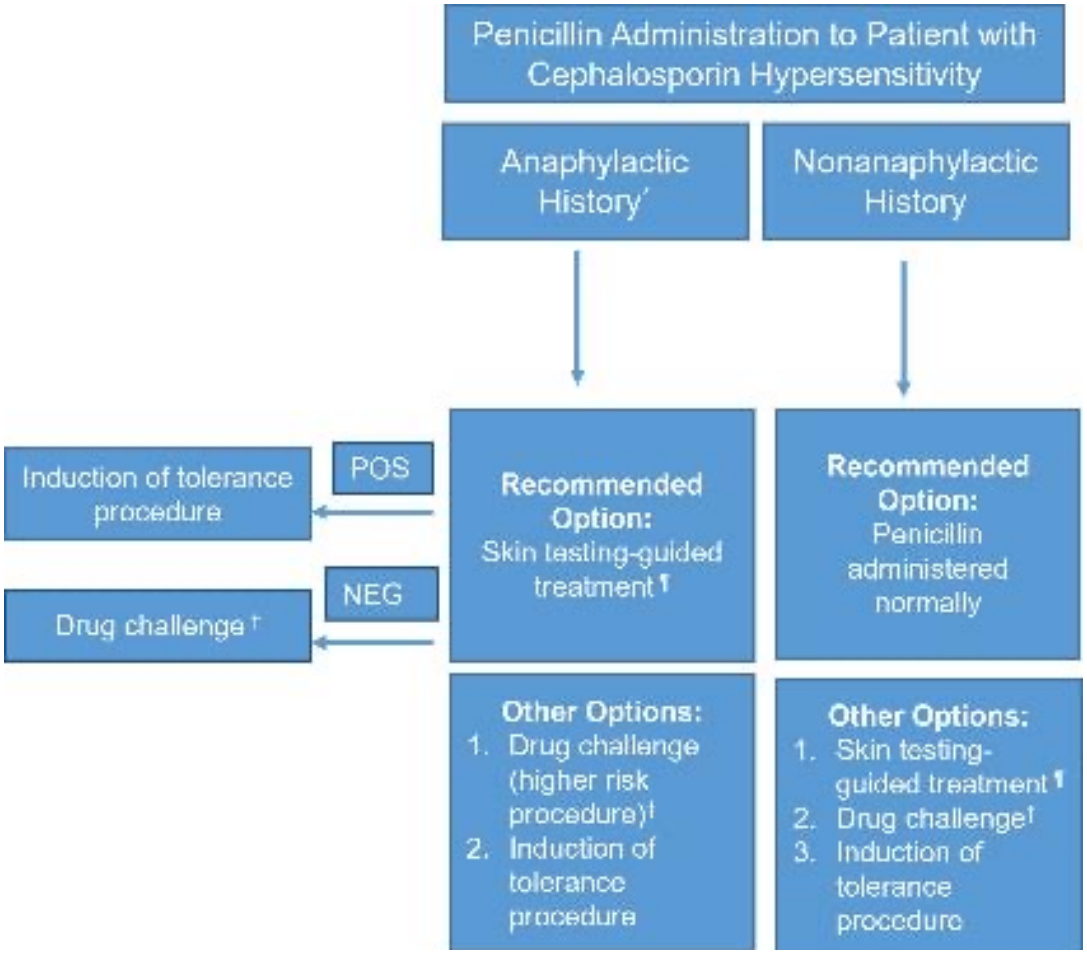


Romano A et al. *J Allergy Clin Immunol*. 2015

Penicillin Administration with History of Cephalosporin Allergy

Consensus Based Statement	Strength of Recommendation	Certainty of Evidence
We suggest against penicillin skin testing in patients with a non-anaphylactic history to cephalosporins prior to administration of penicillin therapy.	Conditional	Low
We suggest that in patients with a history of anaphylaxis to cephalosporins, penicillin skin testing and drug challenge should be performed prior to administration of penicillin therapy.	Conditional	Low

Penicillin Administration with History of Cephalosporin Allergy



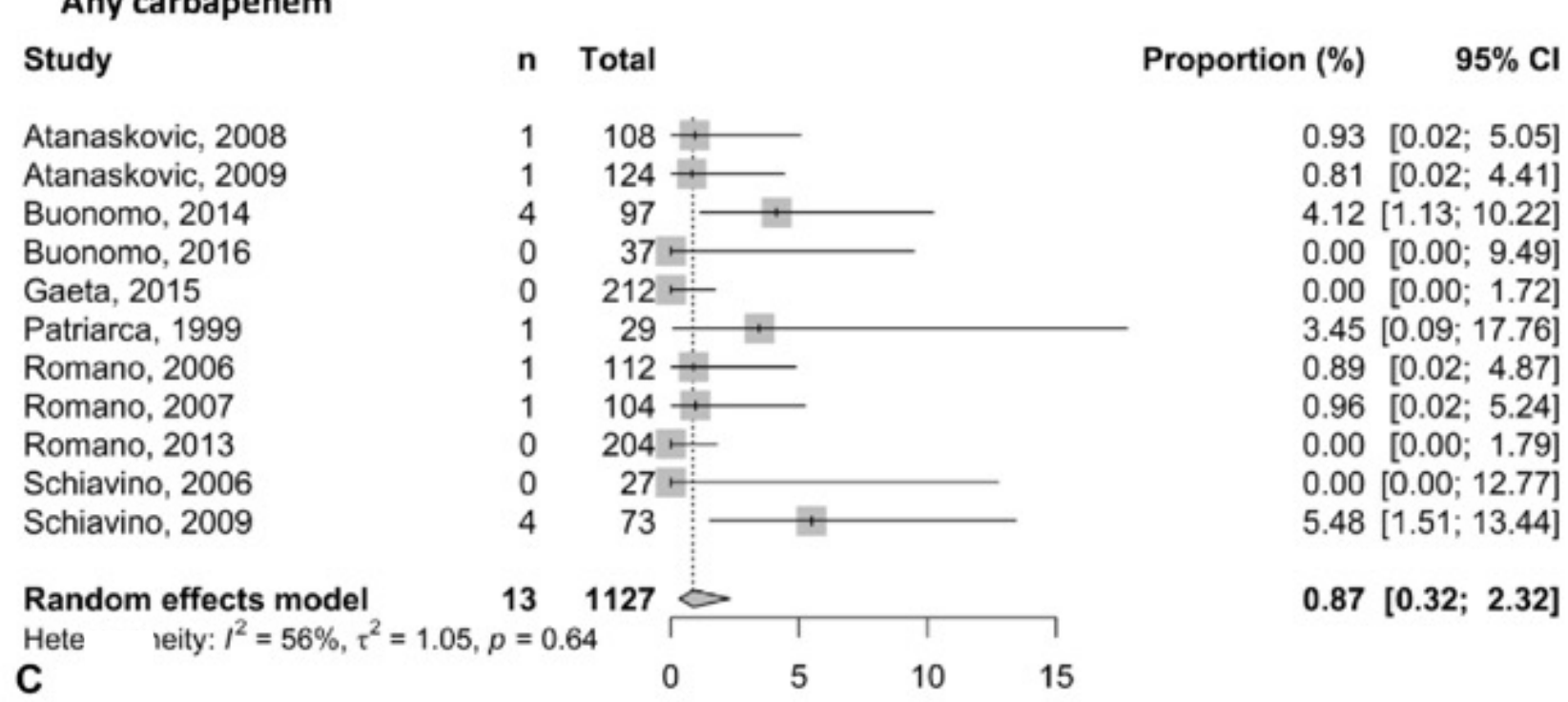
Carbapenem Administration in Penicillin or Cephalosporin Allergy

Consensus Based Statement	Strength of Recommendation	Certainty of Evidence
We recommend that in patients with a history of penicillin or cephalosporin allergy, a carbapenem may be administered without testing or additional precautions.	Strong	Moderate

Picard M et al. *JACI In Practice.* 2019

Original Article

Cross-Reactivity to Cephalosporins and Carbapenems in Penicillin-Allergic Patients: Two Systematic Reviews and Meta-Analyses



Picard M et al. *JACI In Practice.* 2019

Quinolone and Macrolide Allergy

Consensus Based Statement	Strength of Recommendation	Certainty of Evidence
We suggest using a 1- or 2-step drug challenge without preceding skin testing to confirm tolerance in patients with a history of non-anaphylactic reactions to fluoroquinolones or macrolides.	**Conditional**	**Low**

Doña I et al. In Drug Allergy Testing. Ed Khan DA, Banerji A. 2017
Kuruvilla M. In Drug Allergy Testing. Ed Khan DA, Banerji A 2017

Other antibiotics: Quinolones, Macrolides

Quinolone Allergy

- Incidence of immediate onset quinolone allergy is increasing
- First dose reactions due to MRGPRX2
- Delayed reactions to quinolones occur in 2-3%
- Skin testing not reliable due to high irritant potential of quinolones
- No clear patterns of cross-reactivity
- Drug challenges recommended for diagnosis

Macrolide Allergy

- Relatively uncommon
- Immediate and delayed reactions have been reported
- Anaphylaxis is rare
- Skin testing generally unreliable
- Patterns of cross-reactivity amongst macrolides variable
- Majority of patients are tolerant upon drug challenge

Doña I et al. In Drug Allergy Testing. Ed Khan DA, Banerji A. 2017
Kuruvilla M. In Drug Allergy Testing. Ed Khan DA, Banerji A 2017

Original Article

Clinical Characterization and Diagnostic Approaches for Patients Reporting Hypersensitivity Reactions to Quinolones

- Full diagnosis not possible in 442/612, but remaining 170 patients:
  - 128 were confirmed as having HSRs to quinolones
  - 42 as nonallergic (tolerant) to quinolones

- Confirmed hypersensitivity associated with:
  - History of anaphylaxis to moxifloxacin, OR=96
  - Reporting immediate reaction, OR 19
  - Ciprofloxacin is culprit, OR=0.11
  - Symptoms were MPE, FDE, urticaria or angioedema, OR=0.05

- Tolerance to alternative
  - 2/5 ciprofloxacin HSR tolerated levofloxacin
  - 3/5 levofloxacin HSR tolerated ciprofloxacin
  - 3/8 moxifloxacin HSR tolerated ciprofloxacin and 2/2 tolerated levofloxacin

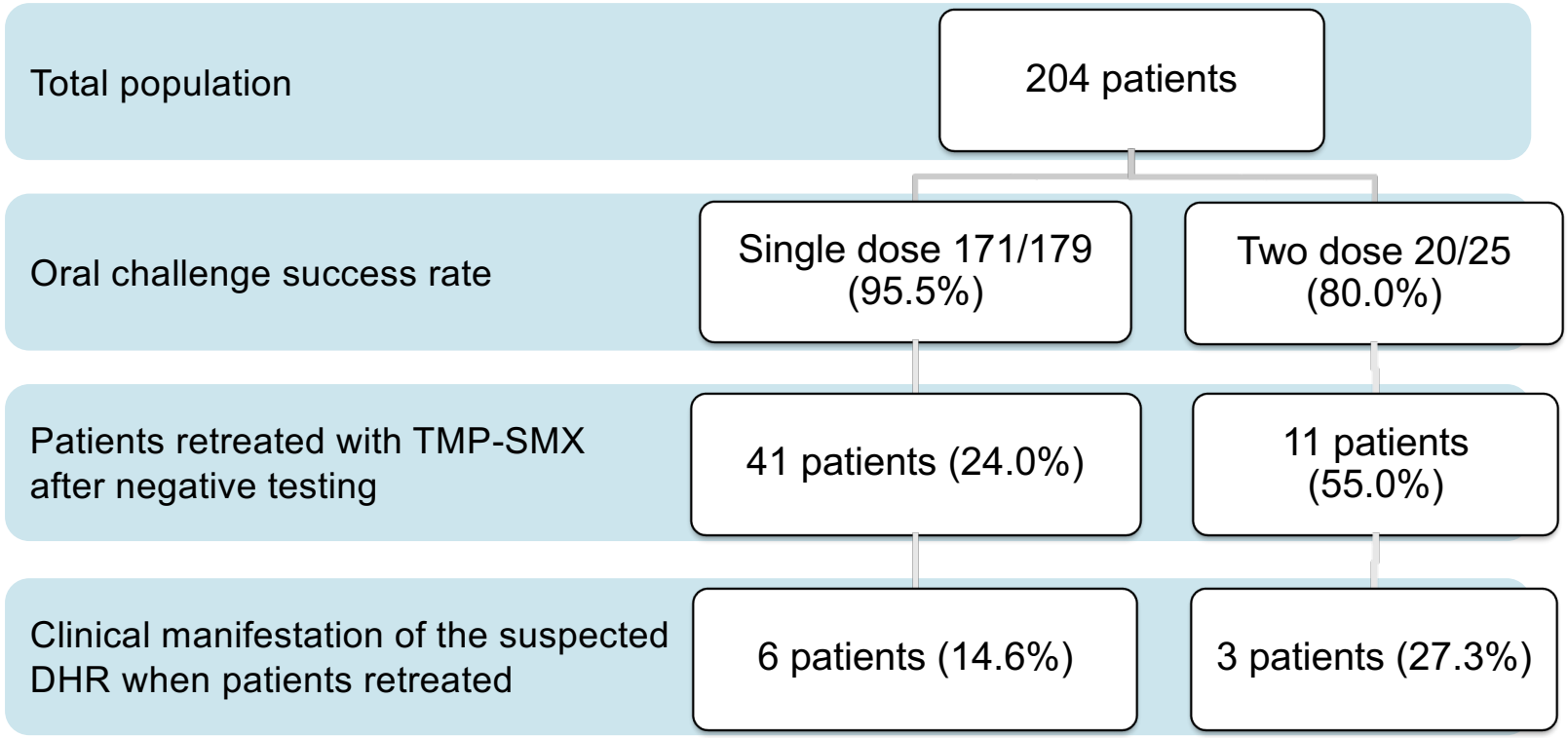
Doña I et al. *J Allergy Clin Immunol Pract*. 2020

Diagnosis of Sulfonamide Allergy

Consensus Based Statement	Strength of Recommendation	Certainty of Evidence
We suggest that for patients with histories of benign cutaneous reactions (e.g., maculopapular exanthem, urticaria) to sulfonamide antibiotics that occurred > 5 years ago, a full dose challenge with trimethoprim-sulfamethoxazole be performed when there is a need to delabel a sulfonamide antibiotic allergy.	**Conditional**	**Low**

Clinical Communications

Oral challenge with trimethoprim-sulfamethoxazole in patients with "sulfa" antibiotic allergy



Krantz *J Allergy Clin Immunol Pract*. 2019

Summary of Important Changes

1. Recommendation to define a positive skin test as a wheal that is ≥ 3 mm than the negative control for prick/puncture or intradermal tests accompanied by a ≥ 5 mm flare
2. Suggestion to use of 1- or 2-step drug challenges for low risk patients
3. Suggestion to use placebo challenges in patients with subjective symptoms or multiple reported drug allergies
4. Suggestion to consider dIDT and/or patch tests (PT) to identify culprit drugs for specific phenotypes of delayed drug reactions where the implicated agent is uncertain
5. Recognition that most pharmacogenetic associations identified to date are currently unlikely to translate into clinical practice
6. Recommendation for proactive penicillin allergy delabeling
7. Recommendation against multiple day challenges in evaluation of penicillin allergy
8. Recommendation against penicillin skin testing prior to direct amoxicillin challenge in low risk pediatric patients
9. Consideration for direct amoxicillin challenge in adults with low risk penicillin allergy histories
10. Recognition that patients with selective allergic reactions to piperacillin-tazobactam may be identified with skin tests to piperacillin-tazobactam and may tolerate other penicillins
11. Suggestion to perform direct challenge to cephalosporins with dissimilar side chains in patients with non-anaphylactic cephalosporin allergy
12. Suggestion to perform skin tests to parenteral cephalosporins (prior to challenge) with non-identical R1 side chains in patients with anaphylactic cephalosporin allergy
13. Specific guidance on administration of cephalosporins to patients with various phenotypes of penicillin allergy
14. Specific guidance on administration of penicillins to patients with various phenotypes of cephalosporin allergy
15. Suggestion to administer carbapenems without prior testing in patients with other beta-lactam allergies
16. Recommendation that allergists collaborate with hospitals and healthcare systems to implement beta-lactam allergy pathways to improve antibiotic stewardship outcomes

Summary of Important Changes

17. Suggestion to use a 1-step trimethoprim-sulfamethoxazole challenge rather than desensitization for low risk patients where there is a need to delabel sulfonamide allergy
18. Suggestion to use 1- or 2-step drug challenge for non-anaphylactic reactions to fluoroquinolones or macrolides without preceding skin testing
19. Recommendation against aspirin challenge to confirm a diagnosis of aspirin exacerbated respiratory disease (AERD) in cases of high diagnostic certainty based on history but that aspirin desensitization remains a therapeutic option when indicated
20. Suggestion for oral aspirin challenge only in patients where there is diagnostic uncertainty of AERD
21. Suggestion that cyclooxygenase 2 (COX-2) inhibitors may be used in any non-steroidal anti-inflammatory drug (NSAID) hypersensitivity phenotype when an NSAID is needed
22. Suggestion to use oral aspirin challenge in patients with NSAID-induced urticaria/angioedema to determine tolerance to other NSAIDs
23. Suggestion for 2-step aspirin challenge (not desensitization) for patients with a history of aspirin allergy in acute need of aspirin for cardiovascular disease
24. Suggestion that patients with non-immediate chemotherapy or biologic reactions be treated with slowed infusion rate, graded dose scalation, and/or pre-medications without desensitization
25. Suggestion that for patients with immediate reactions to taxanes, the severity of the initial reaction may assist in risk stratification and management
26. Suggestion that patients with non-immediate reactions to monoclonal antibodies (mAb) may be treated with a slowed infusion, graded dose escalation, and/or premedication without desensitization
27. Recognition that excipient allergy is very rare but may be considered in patients with anaphylaxis to ≥2 structurally unrelated products that share a common excipient

David Khan (Chair)

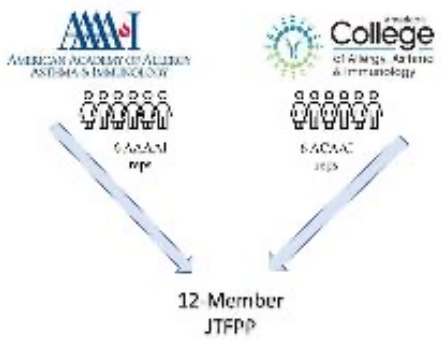
Aleena Banerji

Kim Blumenthal

Elizabeth Phillips

Roland Solensky

Drew White



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