



Penicillin Allergy: How Avoidance Leads to Adverse Clinical Outcomes

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Disclosures

- I have no actual or potential conflict of interest in relation to this presentation.
- Sanofi/Regeneron Advisory Board Participant
- Kalvista Advisory Board Participant
- Medical Advisor/Consultant for Noho Allergy (2021-present)

Objectives

- Review the clinical data on clinical decision making in patients with penicillin allergies
- Be able to identify which patients should have further evaluation after a drug-related adverse event

Case Presentation

DH is an 18 yo male with newly diagnosed syphilis.

SP is a 32 yo female that presents to the hospital for delivery of her 1st child and is GBS positive.

JC is a 63 yo male with a history of diabetes and ESRD s/p DDKT on chronic immunosuppression that presents with pneumonia.

All have a distant history of penicillin allergy.

Penicillin As First-Line Therapy

Organism	Examples
Group A <i>Streptococcus</i>	Pharyngitis, skin and soft tissue infections (cellulitis, erysipelas, pyoderma), necrotizing fasciitis, myositis, acute rheumatic fever, acute glomerulonephritis, pneumonia, postpartum endometritis, toxic shock syndrome, bacteremia
Group B <i>Streptococcus</i>	Meningitis, puerperal sepsis
Viridans group streptococci and <i>Streptococcus gallolyticus</i> (bovis)	Endocarditis
<i>Listeria monocytogenes</i>	Meningitis
<i>Actinomyces</i> spp	Cervicofacial, pelvic, and respiratory infections
<i>Cutibacterium acnes</i> (formerly <i>Propionibacterium acnes</i>)	Bone and joint and central nervous system shunt infections
<i>Staphylococcus aureus</i>	Skin and soft tissue, bone and joint, and respiratory tract infections ^a
<i>Pasteurella multocida</i>	Skin and soft tissue infections, bacteremia, and respiratory tract infections
<i>Neisseria gonorrhoeae</i>	Urethritis, epididymitis, pharyngitis, conjunctivitis, cervicitis, proctitis, disseminated disease (septic arthritis, endocarditis)
<i>Neisseria meningitidis</i>	Meningitis
<i>Treponema pallidum</i> (syphilis)	Primary syphilis (chancre), secondary syphilis (rash, condylomata lata), tertiary syphilis (aortitis), meningitis

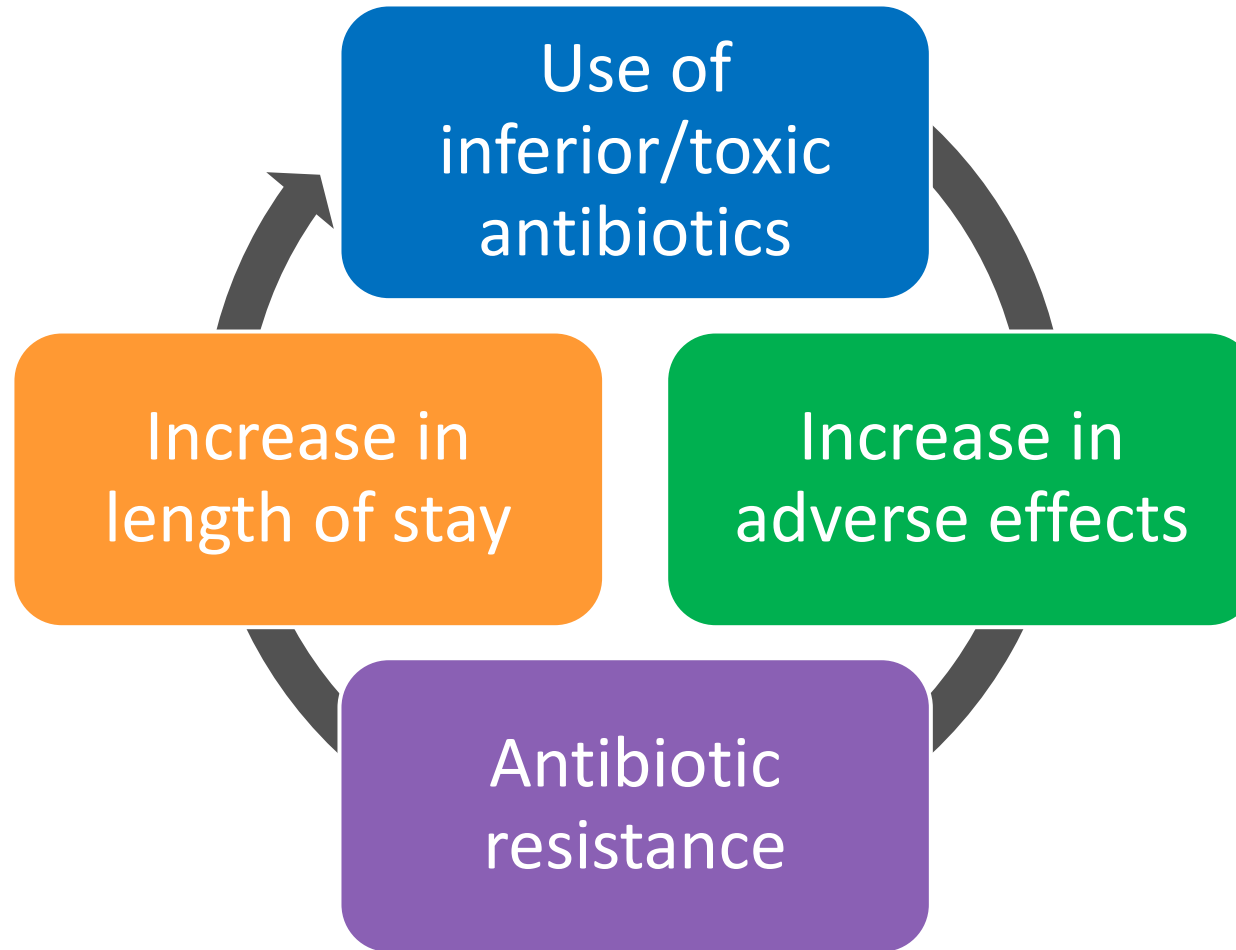
Penicillin Allergy Labels

- 8-10% of the US population carries a history of penicillin allergy
 - >95% will tolerate penicillin use after evaluation
 - Family history does not increase risk
- Waning sensitivity to penicillin
 - 50% lose sensitivity by 5 years
 - 80% lose sensitivity by 10 years
- Subsequent penicillin use after negative testing does not increase risk of sensitization

Sogn DD, Evans R, Shepherd GM, et al. *Ann Intern Med.* 1992.
Gadde J, Spence M, Wheeler B, et.al. *JAMA.* 1993.
Macy E, Contreras R. *J Allergy Clin Immunol.* 2014.
Solensky R, Earl HS, Gruchalla, RS. *Arch Intern Med,* 2002.
Dorman SM, Seth S, Khan DA. *J Allergy Clin Immunol Pract,* 2018.



Effects of Penicillin Allergy Label



Choosing Wisely Campaign



An initiative of the ABIM Foundation

American Academy of Allergy, Asthma & Immunology



Five Things Physicians and Patients Should Question

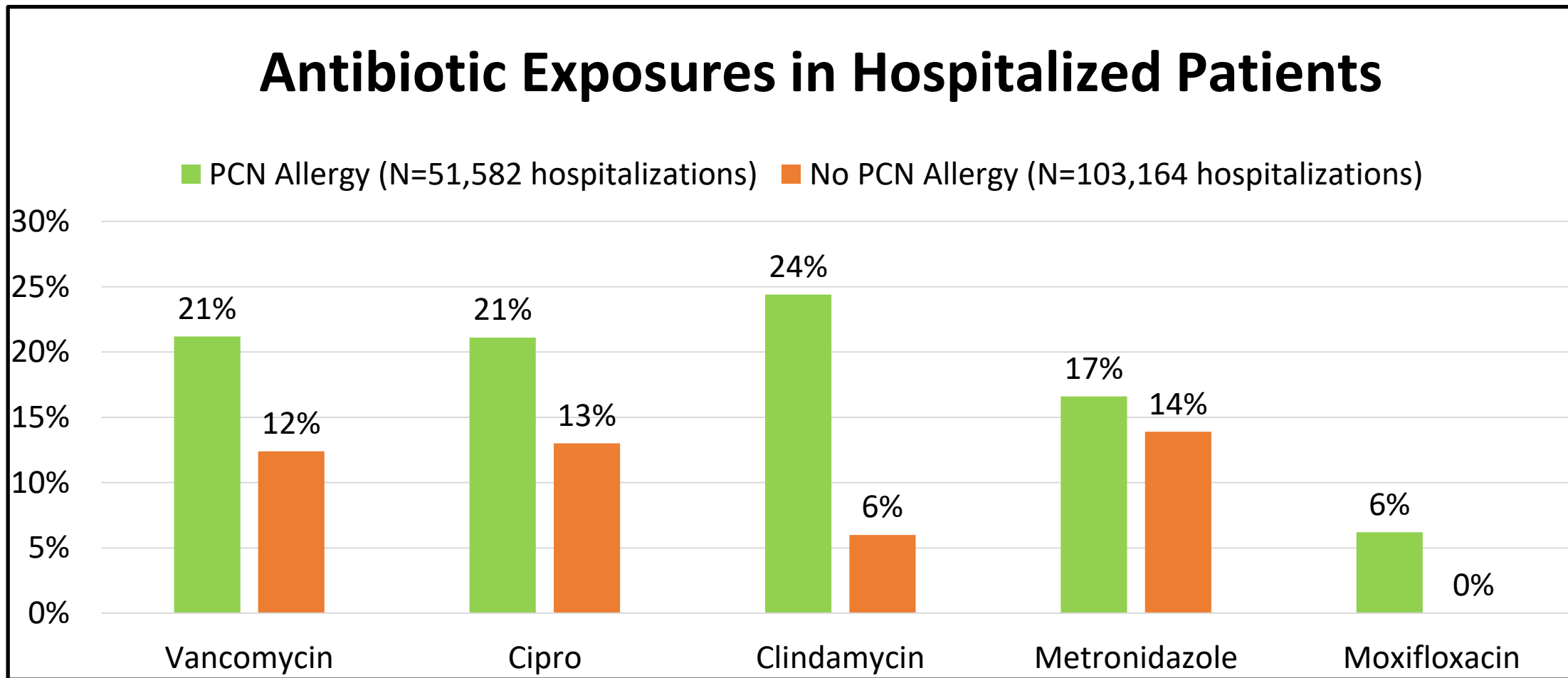
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Don't overuse non-beta lactam antibiotics in patients with a history of penicillin allergy, without an appropriate evaluation.

<https://www.choosingwisely.org>



Antibiotic Exposure



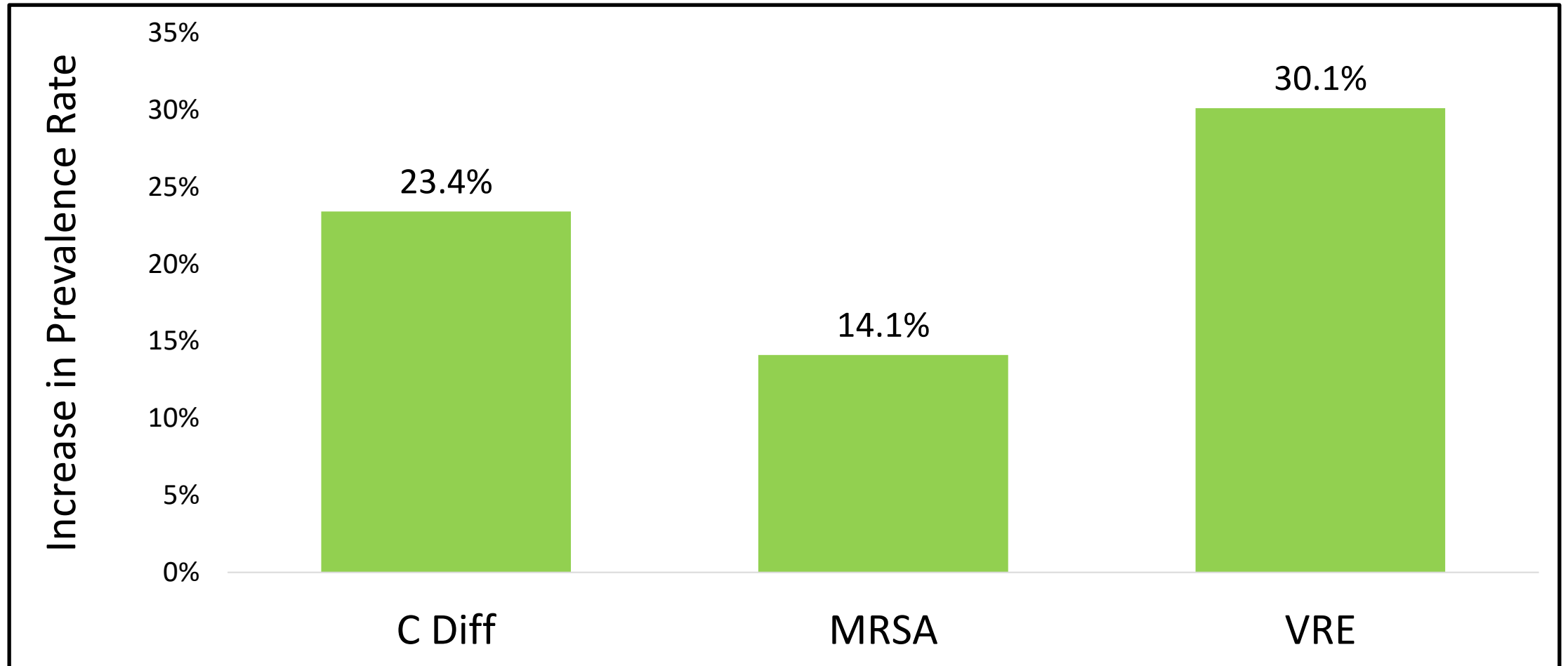
Outcomes: PCN Allergy Label

1. Higher rate of treatment failures
2. Increased prevalence of *Clostridium difficile*, MRSA, and VRE
3. Increased future healthcare utilization
 - Longer hospital length of stay
 - Higher rate of readmission
4. Increased healthcare dollars
5. Higher rates of surgical site infections

Macy E, Contreras R. *J Allergy Clin Immunol*, 2014.
Jeffres MD, et al. *J Allergy Clin Immunol*, 2016.
Picard M, et al. *J Allergy Clin Immunol Pract*, 2013.
Blumenthal KG, et al. *Clin Infectious Dis*, 2018.



C difficile, MRSA, and VRE

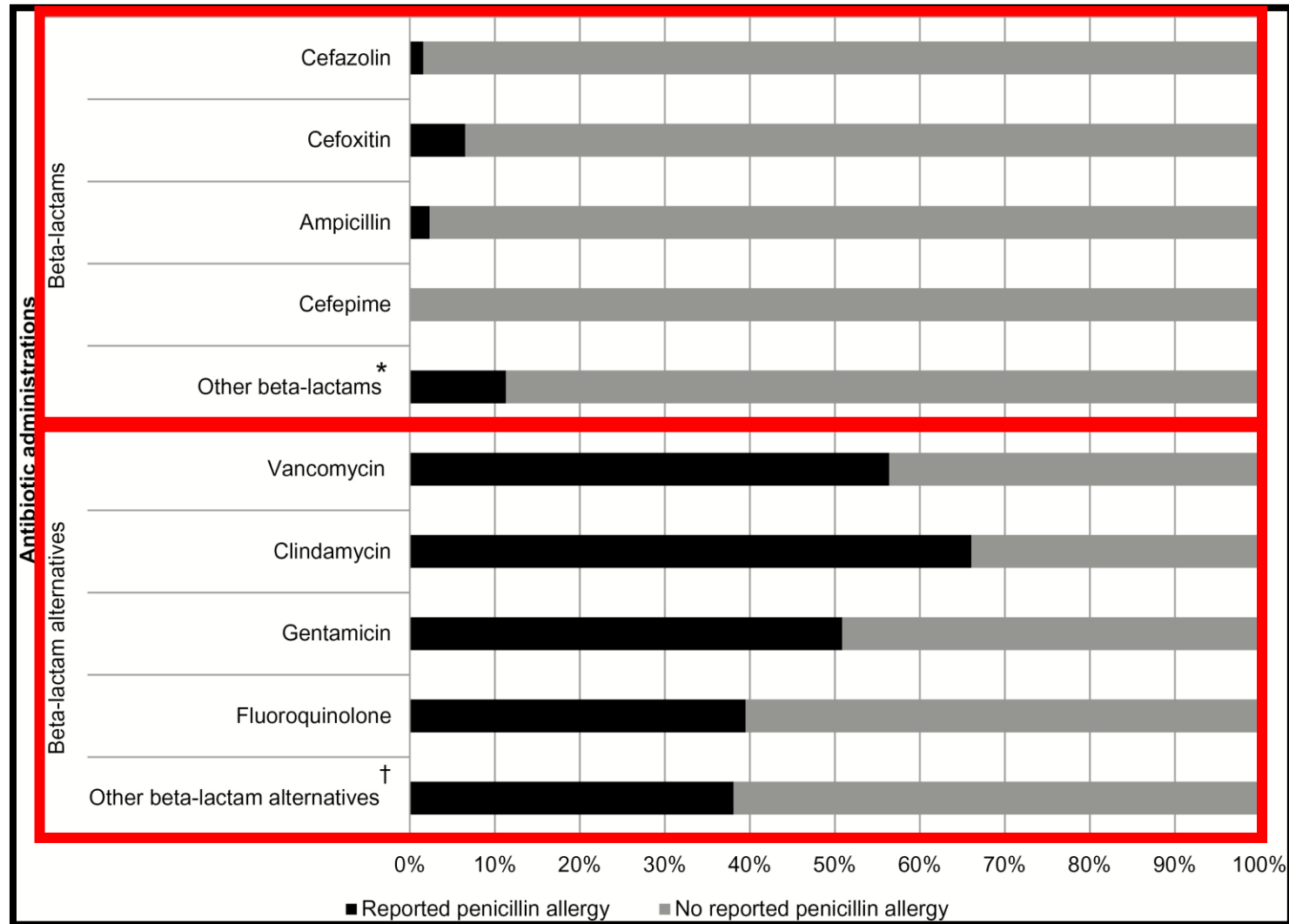


Macy E, Contreras R. *J Allergy Clin Immunol*, 2014.

Reddy V, Baman NS, Whitener C, Ishmael FT, *J Allergy Clin Immunol*, 2013.

Blumenthal KG, et al. *BMJ*, 2018.

Surgical Site Infections



When controlled for surgery type, age, sex, race, American Society of Anesthesiologists class, procedure duration, and wound class



51% increased risk
of a SSI in patients
that have a PCN
allergy label (p<0.04)

Anesthesiologist Perspective

- Up to 60% of anesthesiologists will not give β -lactam antibiotics to penicillin-allergic patients
 - Medical-legal concerns
- Studies have supported:
 - Penicillin allergy evaluation prior to surgery
 - Cefazolin without prior evaluation/testing (in penicillin allergic patients)
 - OHSU Perioperative Antibiotic Protocol: Cefazolin as first-line for penicillin allergic patients (unless anaphylaxis documented)

Savic LC, et al. *Br J Anes*, 2019.

Beltran RJ, et al. *J Pediatr Surg*, 2015.

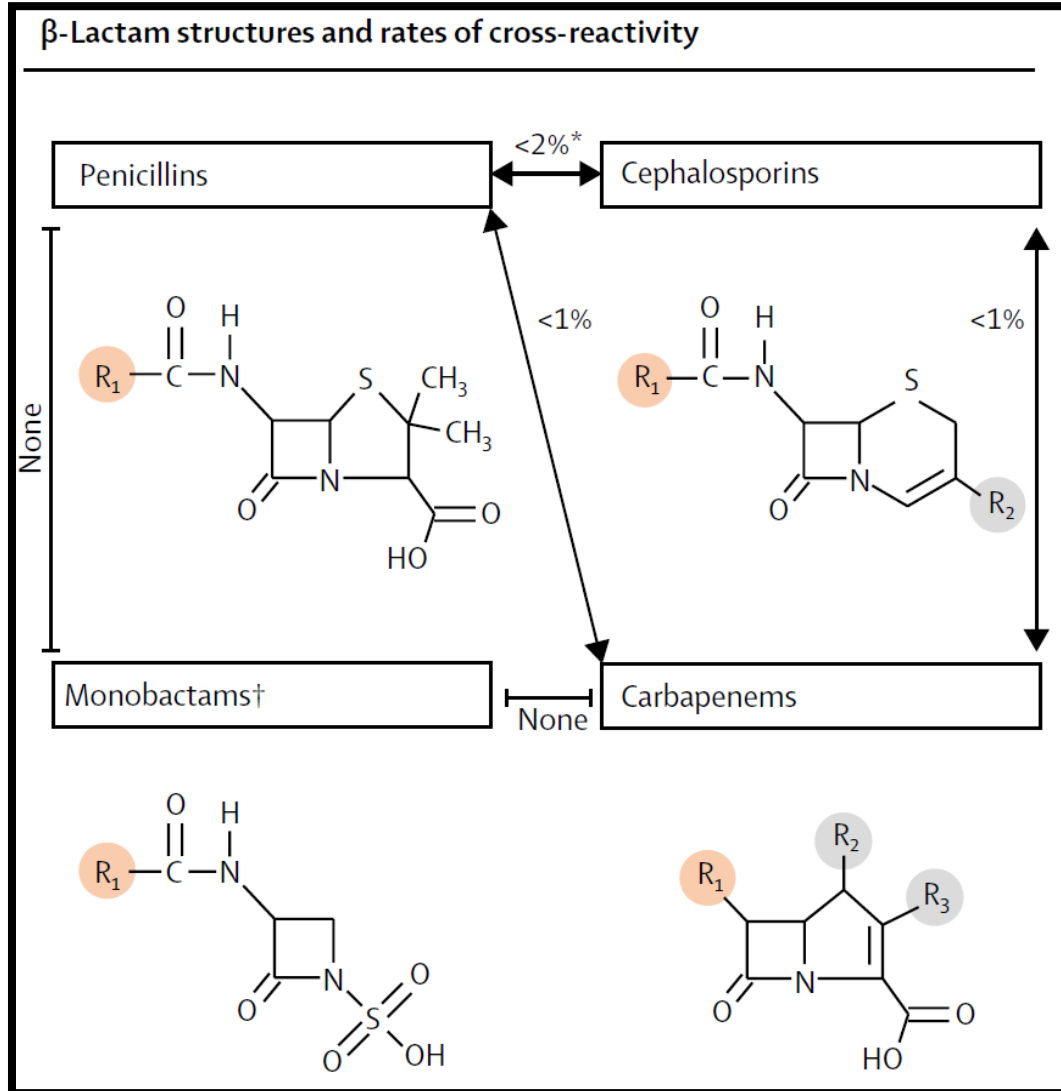
Haslam S, et al. *Iowa Orthop J*, 2012.

Goodman EJ, et al. *J Clin Anaesth*, 2001.

Kuruvilla M, et al. *J Allergy Clin Immunol Pract*, 2019.



Penicillin Cross-Reactivity




- Historically, cross-reactivity has been overestimated
- Recent meta-analysis (PCN Allergic)
 - Aminocephalosporins: 16.5%
 - Intermediate-similarity-score: 5.6%
 - Low-similarity-score: 2.11%
- R1 and R2 side chains

Blumenthal KG, et al. *Lancet*, 2019.


Picard M, et al. *J Allergy Clin Immunol Pract*, 2019.

Penicillin Cross-Reactivity

Cephalosporin		Type of penicillin allergy			
Generation	Name	n/N	 IgE	T-cell	
			AR in % (95% CI)	n/N	AR in % (95% CI)
First	Cephalexin	40/310	12.9 (9.6-17.1)	57/383	14.9 (11.7-18.8)
	Cefadroxil	75/287	26.1 (21.4-31.5)	20/270	7.4 (4.8-11.2)
	Cephalothin	8/128	6.3 (2.7-11.9)	1/56	1.8 (0.3-11.6)
	Cefazolin	0/47	0.0 (0.0-7.5)	1/26	3.8 (0.0-19.6)
	Cefatrizine	NA	NA	1/56	1.8 (0.3-11.6)
	Cephaloridine	0/17	0.0 (0.0-19.5)	NA	NA
	Second	Cefamandole	22/418	5.3 (3.5-7.9)	1/56
	Cefaclor	41/282	14.5 (10.9-19.2)	49/397	12.3 (9.5-16.0)
	Cefuroxime	7/490	1.1 (0.2-5.8)	7/423	0.5 (0.0-8.0)
	Cefprozil	NA	NA	3/39	7.7 (1.6-20.9)
Third	Cefpodoxime	NA	NA	1/71	1.4 (0.0-7.6)
	Ceftazidime	2/433	0.3 (0.0-4.7)	NA	NA
	Cefotaxime	5/380	1.3 (0.6-3.1)	0/56	0.0 (0.0-6.4)
	Cefixime	0/39	0.0 (0.0-9.0)	2/285	0.7 (0.2-2.8)
	Ceftriaxone	12/474	2.5 (1.4-4.4)	1/367	0.2 (0.0-9.5)
	Ceftibuten	NA	NA	0/153	0.0 (0.0-2.4)
Fourth	Cefepime	1/285	0.3 (0.0-10.3)	NA	NA

Picard M, et al. *J Allergy Clin Immunol Pract*, 2019.

Penicillin/Cephalosporin Cross-Reactivity



		Penicillin					1st	2nd	3rd			4th	5th	Sid	Carb Mon								
		Penicillin G/V	Oxacillin	Nafcillin	Amoxicillin	Ampicillin	Piperacillin	Cephalexin	Cefazolin	Cefoxitin	Cefotetan	Cefuroxime	Cefdinir	Cefixime	Cefpodoxime	Ceftazidime	Ceftriaxone	Cefepime	Ceftaroline	Ceftolozane	Cefiderocol	Imipenem	Aztreonam
Penicillin	Penicillin G/V	Black	Red	Red	Red	Red	Red	O	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Oxacillin	Red	Black	Red	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Nafcillin	Red	Red	Black	Red	Red	Red	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Amoxicillin	Red	Red	Red	Black	Red	Red	O	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Ampicillin	Red	Red	Red	Red	Black	O	X	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Piperacillin	Red	Red	Red	Red	Black	O	O	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
1st	Cephalexin	O	Green	Green	O	X	O	Black	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Cefazolin	Green	Green	Green	Green	Green	Green	Black	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
2nd	Cefoxitin	Green	Green	Green	Green	Green	Green	Green	Black	X	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Cefotetan	Green	Green	Green	Green	Green	Green	Green	Black	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green
	Cefuroxime	Green	Green	Green	Green	Green	Green	Green	X	Black	Green	O	O	O	O	Green	Green	Green	Green	Green	Green	Green	Green
3rd	Cefdinir	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Black	X	O	O	O	O	Green	Green	Green	Green	Green	Green
	Cefixime	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Black	X	O	O	O	O	O	O	Green	Green	Green	Green
	Cefpodoxime	Green	Green	Green	Green	Green	Green	Green	Green	Green	O	O	O	Black	O	X	X	O	O	Green	Green	Green	Green
	Ceftazidime	Green	Green	Green	Green	Green	Green	Green	Green	Green	O	O	O	O	Black	O	O	O	O	O	X	Green	X
4th	Ceftriaxone	Green	Green	Green	Green	Green	Green	Green	Green	Green	O	O	O	X	O	Black	X	O	O	Green	Green	Green	Green
	Cefepime	Green	Green	Green	Green	Green	Green	Green	Green	O	O	O	O	X	O	X	Black	O	O	Green	Green	Green	Green
5th	Ceftaroline	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	O	O	O	O	O	Black	O	Green	Green	Green	Green
	Ceftolozane	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	O	O	O	O	O	O	O	Black	O	O	Green	O
Siderophore	Cefiderocol	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	X	Green	Green	Green	O	Black	Green	Green	X
Carbapenem	Imipenem	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	O	Black	Green
Monobactam	Aztreonam	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	Green	X	Green	Green	Green	O	X	Green	Black	Green

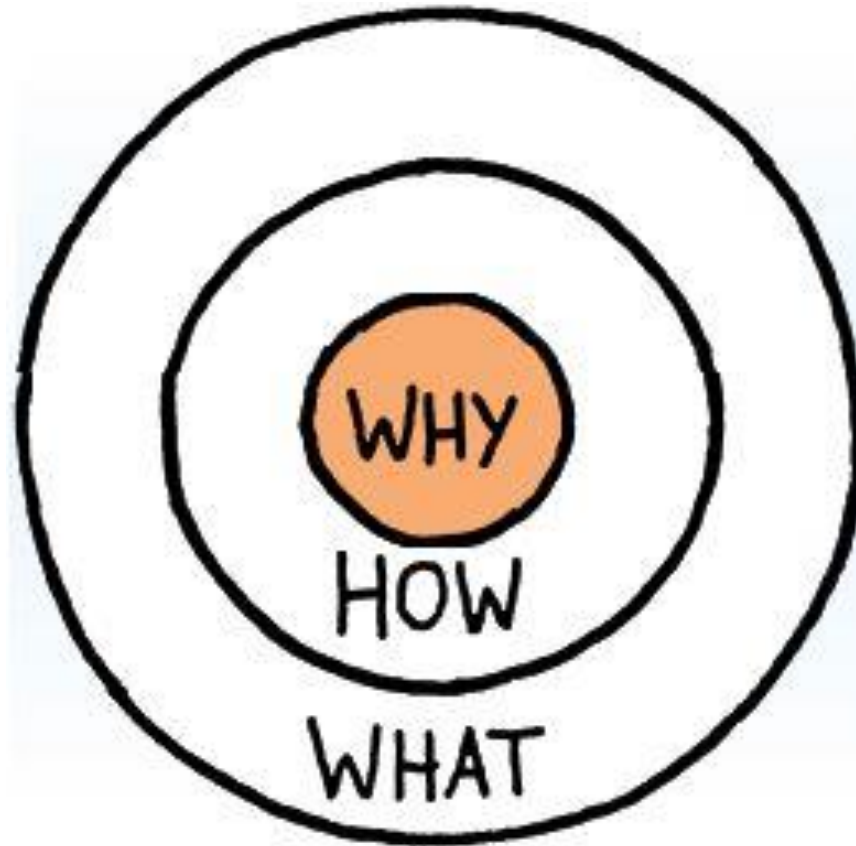
Do not prescribe. Theoretical or clinical evidence of cross reactivity

Considered safe to prescribe.

O Similar R-1 side chain

X Identical R-1 side chain

Golden Circle



<https://medium.com/@JyotiMotwani/find-your-why-applying-sineks-golden-circle-to-your-career-2a4328437f2a>

How Should We Test Patients?

- Inpatient vs Outpatient?
- Skin Testing vs Direct Provocation Challenge?
- Allergist vs Non-allergist?

Inpatient vs Outpatient Evaluation

Traditionally, penicillin allergy evaluation has occurred in the outpatient setting

Outpatient:

- Allergists primary practice in the outpatient setting
- Can perform multiple evaluations simultaneously
- Difficult to schedule testing

Hospitalized patients:

- Incidence of penicillin allergy is higher (up to 15%)
- Older, more ill and greater need for antibiotics
- Testing could alter antibiotic therapy immediately

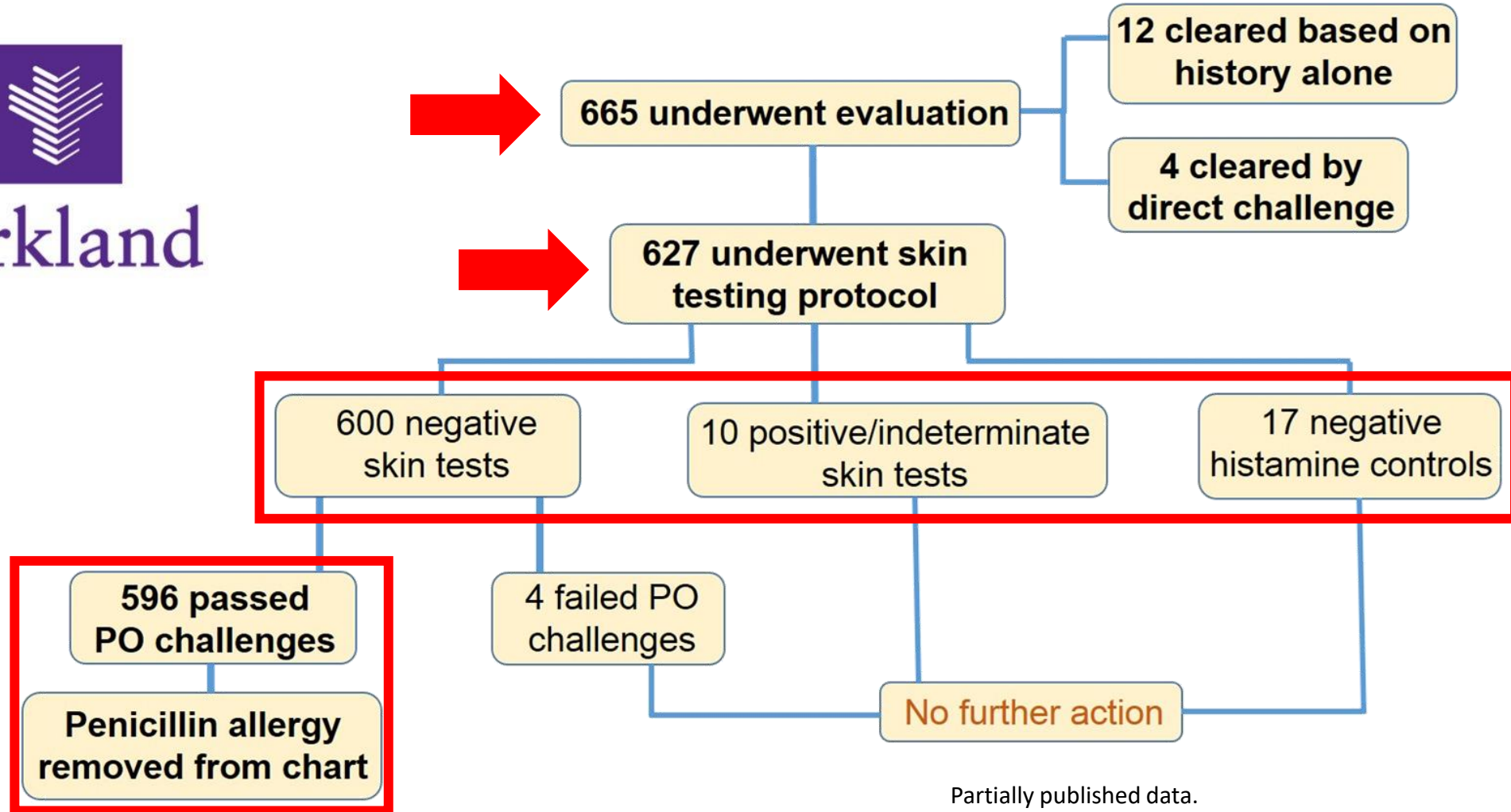
Penicillin Skin Testing

- Modified protocol
 - Skin prick and intradermal testing
 - Penicilloyl-polylysine
 - Penicillin G
 - Observed (graded) oral amoxicillin challenge
- NPV of 97-100%
 - PPV not well established



<https://www.medscape.com/viewarticle/871833>

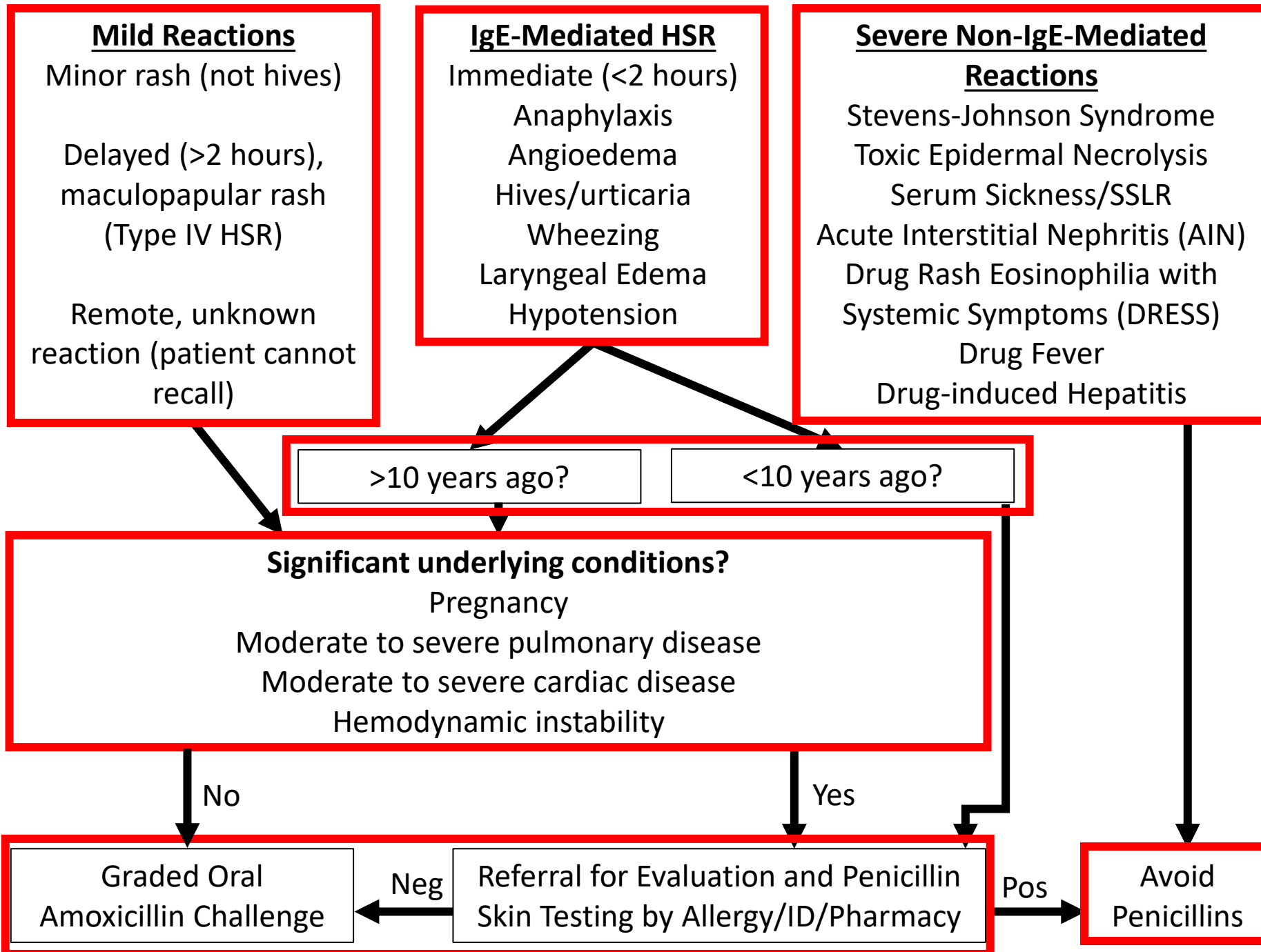
Penicillin Testing (Inpatient)



Partially published data.
Lutfeali S, et al. *J Allergy Clin Immunol Pract.* 2021.

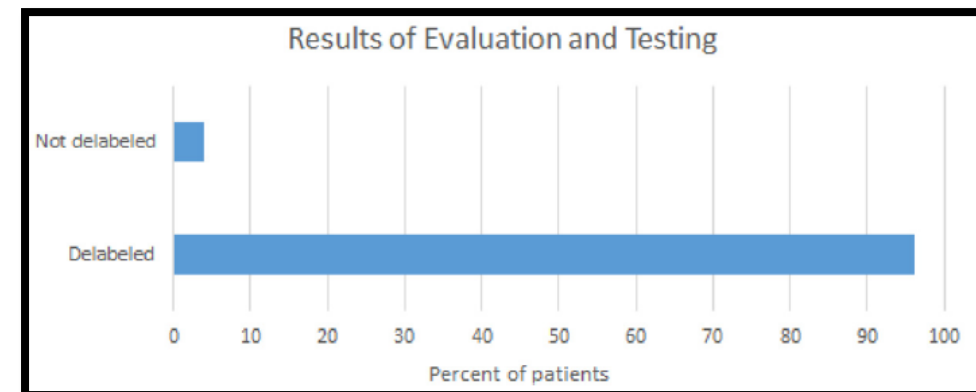
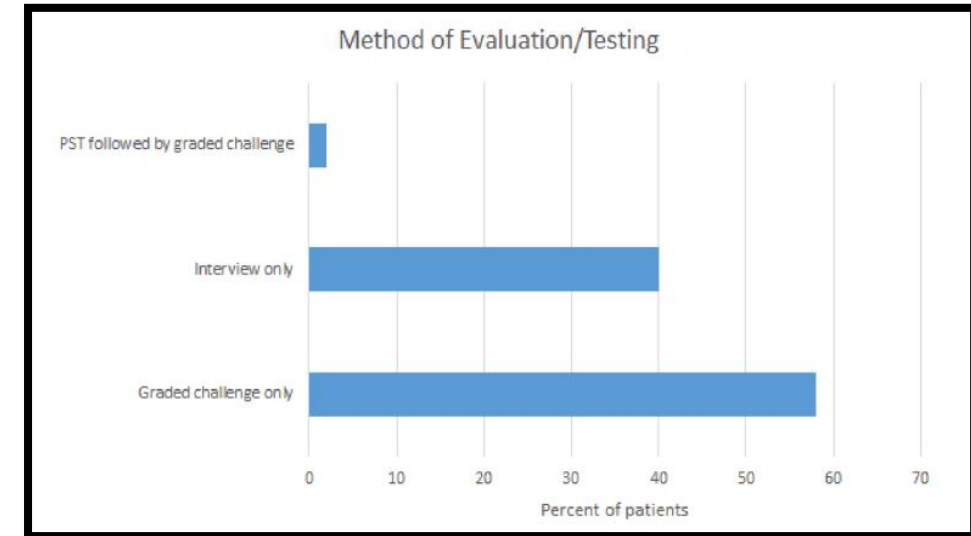


OHSU Penicillin Allergy Evaluation Protocol

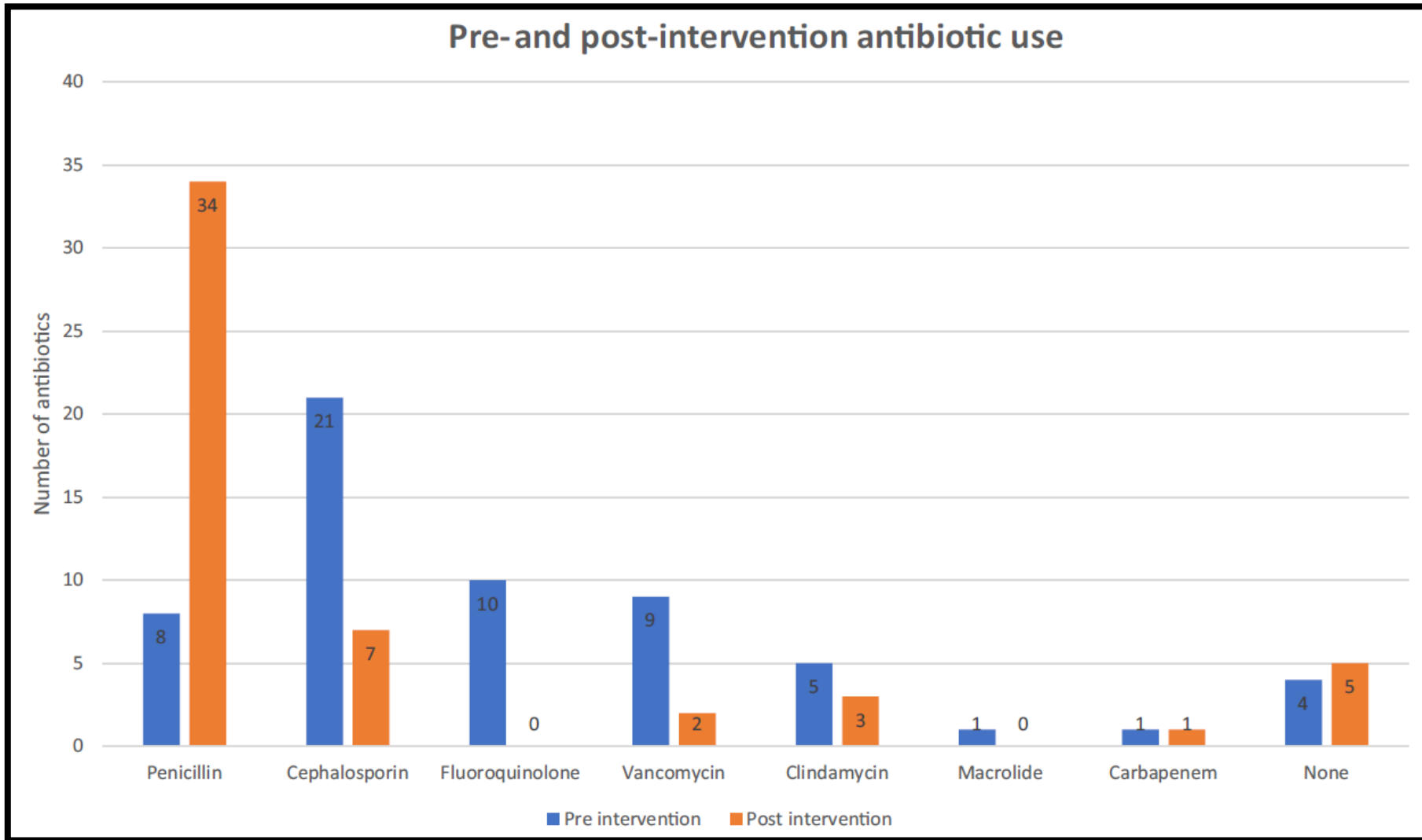


OHSU Inpatient Penicillin Allergy Service

- Inpatient Allergy Pharmacist
 - Natural partners in antimicrobial stewardship
 - Experienced in acquiring medication and allergy histories
 - Can advise primary services on optimal post-test antibiotics
- Screening Protocol
 - Inpatient consultation
 - EMR screening
 - Broad-spectrum antibiotic use
 - High-risk comorbidities



Direct Challenge (Inpatient Evaluation)



Risk Stratifying PCN Allergy Patients

- No consensus with high variability between studies
 - Time since reaction
 - Symptoms (cutaneous only)
 - Severity of reaction
- UK Tertiary Center Study – Multivariate regression analysis
 - Self reported history of anaphylaxis
 - Patients' recall of index penicillin
 - Time of less than 1 year since index reaction

Allergist or Non-Allergist?

- Both should be involved!
- Lower risk patients -> Can be Performed by Non-Allergists
 - Penicillin Allergy Toolbox
 - Evaluation and Management of Penicillin Allergy: A Review
 - Shenoy ES, Macy E, and Rowe T.
 - *JAMA*. 2019;321(2):188-199.
- Higher risk patients -> Allergist

Who/When Should We Be Evaluating?

Everyone!

- High risk patients and high utilizers of the healthcare system
 - Chronic disease (CF, diabetes, COPD, asthma)
 - Immunosuppressed (chemotherapy, autoimmune, transplant)
 - Immunodeficient (HIV, primary immunodeficiency)
 - Malignancy
- Key Opportunities
 - Perioperative
 - Inpatient
 - Pretransplant evaluation (BMT and solid organ)
 - Preconception planning/pregnancy

Take Home Points

1. Always question penicillin allergy labels
2. Penicillin allergy labels can drastically alter clinical outcomes and lead to increased healthcare utilization
3. Performing inpatient and/or outpatient penicillin evaluations (history, testing) is safe and reliable in removing penicillin allergy labels
4. Cross-reactivity between penicillin and cephalosporins is low, especially in patients with unconfirmed penicillin allergies

Questions?



Drug Allergy Clinic
Allergy and Immunology

- Acknowledgements
 - Inpatient Drug Allergy
 - YoungYoon Ham, PharmD
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 - Kendall Tucker, PharmD
 - Diana Yu, PharmD
 - Outpatient Drug Allergy
 - Karen Anstey, MD
 - Jordana Brown, MS2



How Common are Adverse Drug Events?

Allergy Label

- 36% of patients have a listed allergy in their EMR
 - 43% of these had multiple allergies
 - 4-7% have MDIS
- Risk factor: Drug exposure

Adverse Drug Events (ADEs)

- Adverse drug events occur in up to 25% of prescriptions
 - 13% of these were serious
- Allergic reactions (immunologically mediated) account for only 5-10% of all ADEs

Variety of Drug Hypersensitivities

Examples of Drug Allergies		
IgE-mediated	Pneumonitis	Urticaria multiforme
Hemolytic anemia	AIN	Erythema multiforme
Thrombocytopenia	Drug-induced lupus	AGEP
Granulocytopenia	FDE	Infusion reactions
Serum sickness	Contact dermatitis	Atopic dermatitis
Serum sickness-like	Acne	Angioedema
Vasculitis	Photosensitivity	IgE-mediated anaphylaxis
Arthus reaction	SDRIFE	Non-IgE-mediated anaphylaxis
DRESS	Drug exanthema	IgG-mediated anaphylaxis
SJS	Drug fever	MRGPRX2-mediated
TEN	Bullous pemphigoid	Pemphigus vulgaris

Treatment Failure with Alternative Antibiotics

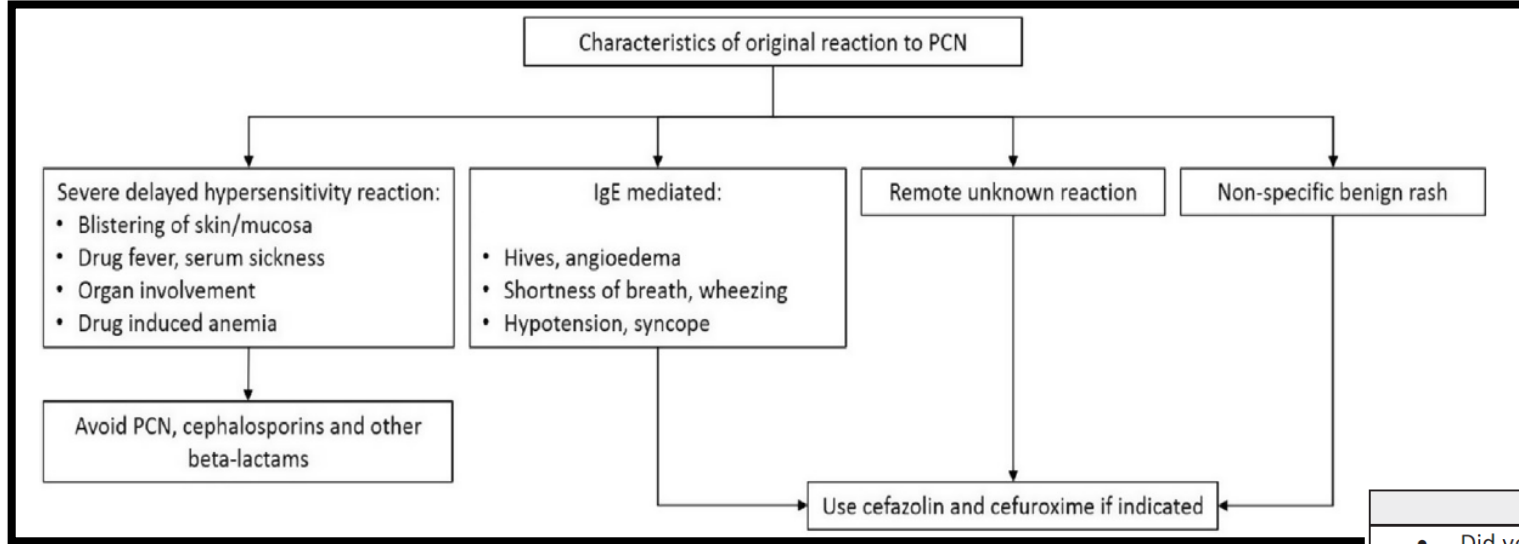
- GNB bacteremia (Jeffres et al.)
 - Non- β -lactam failure rate: 39%
 - β -lactam failure rate: 27%
- MSSA bloodstream infections (McDanel et al.)
 - β -lactams had a 35% lower mortality rate for definitive treatment compared to vancomycin

Surgical Site Infections

- Canadian study (2017-2018)
- 369 SSIs from 3,589 surgeries
 - Similar comorbidities, ASA physical status classification, surgical specialty, wound classification, and duration of surgery
- Results
 - Without β -lactam allergy: 154/3,220 (4.8%)
 - With β -lactam allergy: 27/369 (7.3%)
- 30-day SSI risk: aOR 1.61 (p=0.03)

Preoperative Antibiotic ^a	All (n = 3,589), No. (%)	No Reported β -Lactam Allergy (n = 3,220), No. (%)	Reported β -Lactam Allergy (n = 369), No. (%)
Cefazolin ^b	3,217 (89.6)	3,074 (95.5)	143 (38.8)
Ampicillin	10 (0.3)	10 (0.3)	0 (0.0)
Ceftriaxone	35 (1.0)	35 (1.1)	0 (0.0)
Ertapenem	1 (0.0)	0 (0.0)	1 (0.3)
Meropenem	2 (0.1)	1 (0.0)	1 (0.3)
Piperacillin-Tazobactam	50 (1.4)	47 (1.5)	3 (0.8)
Ciprofloxacin ^b	20 (0.6)	7 (0.2)	13 (3.5)
Clindamycin ^b	197 (5.5)	5 (0.2)	192 (52.0)
Metronidazole ^b	915 (25.5)	840 (26.1)	75 (20.3)
Gentamicin ^b	13 (0.4)	0 (0.0)	13 (3.5)
Vancomycin ^b	12 (0.3)	4 (0.1)	8 (2.2)
None or not documented	66 (1.8)	62 (1.9)	4 (1.1)

Support of Cephalosporin Use

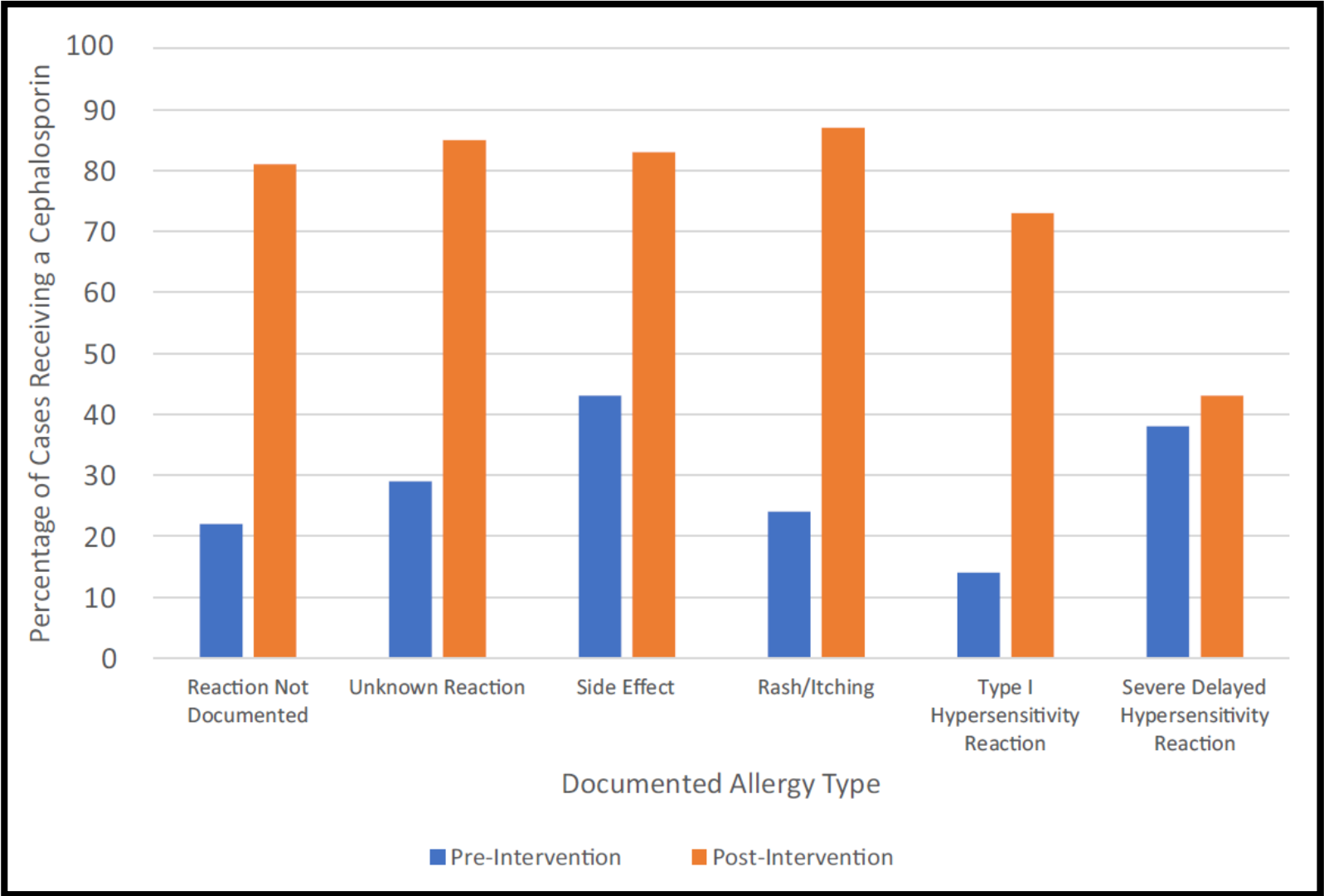


Penicillin Allergy Assessment

- Did you have a severe skin reaction involving blisters on your skin and shedding or detachment of your skin? (SJS/TEN)
- Were you told you had Stevens -Johnson Syndrome (SJS) or Toxic Epidermal Necrolysis (TEN)?
- Did you have liver injury or hepatitis caused by the medication?
- Did you have kidney injury, nephritis or acute renal failure caused by the medication (acute interstitial nephritis)?
- Were you told you had hemolytic anemia caused by the medication? (Low hemoglobin or hematocrit or "blood counts" counts caused by penicillin)
- Did you have painful swollen joints caused by the medication (serum sickness)?
- Were you diagnosed with "drug fever"? (A fever caused by the antibiotic that developed about a week after starting the medication and then went away when you stopped the antibiotic?)
- Did you have a severe reaction involving the inside of your mouth, eye, or genital ulcers?

Kuruvilla M, et al. *J Allergy Clin Immunol Pract*, 2020.

Cephalosporin Preoperative Use



Kuruvilla M, et al. *J Allergy Clin Immunol Pract*, 2020.



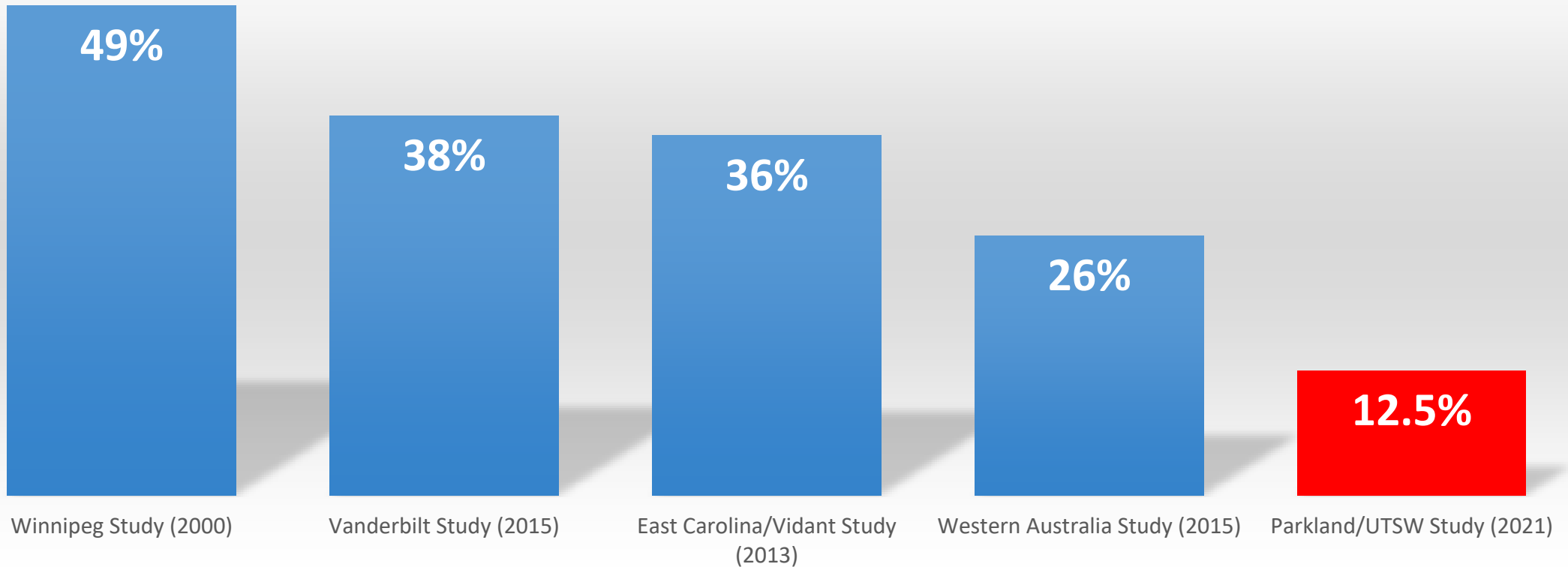
Direct Provocation Testing

Outcome	Penicillin SPT	DC	Difference
Patients	80	79	
PST Positive/DC fail, n (%)	10 (12.5)	3 (3.8)	8.7% ($P = .079$)
PST Negative/DC pass	70 (87.5)	76 (96.2)	
Time (min)			
Mean \pm SD	72.7 \pm 5.3	66.7 \pm 4.8	6.0 ($P < .001$)
Median (IQR)	73.5 (68.8-75.3)	66.0 (62-70)	7.5 ($P < .001$)
Cost			
Each	\$393.66	\$53.66	\$340.00
Total	\$29,092.80	\$4,239.14	\$24,853.66

- DC reactions were all minor cutaneous reactions
- False positive results from SPT

Mustafa SS, et al. *J Allergy Clin Immunol Pract*, 2019.
 Mill C, et al. *JAMA Pediatr*, 2016.

Penicillin Relabel



Warrington RJ, Lee KR, McPhillips S. *Allergy Asthma Proc.* 2000;21(5):297-9.
Gerace KS, Phillips E. *J Allergy Clin Immunol Pract.* 2015;3(5):815-816.
Rimawi RH, Shah KB, Cook PP. *Journal of Hospital Medicine.* 2013;8:615-618.
Bourke J, Pavlos R, James I, et al. *J Allergy Clin Immunol Pract.* 2015;3:365-74.
Lutfeali S, et al. *J Allergy Clin Immunol Pract.* 2021; In Press.

Interventions to Maintain Penicillin Allergy Label Removal

1. Pharmacist counseling at the time of negative test
 - Active removal of allergy, procedure note documentation
2. Pharmacist counseling at post-discharge visit
 - Telephone call or face to face visit
3. Best practice advisory in the electronic medical record
 - Alerting providers to the negative penicillin allergy test result on attempt to add back allergy
4. Wallet card given to patient documenting negative testing
 - Given at time of negative test documentation

Wallet Card for Patient

ALLERGY INFORMATION

Name: _____

Date of Birth: _____

Allergies:

_____	_____
_____	_____
_____	_____
_____	_____
_____	_____

I am NOT Allergic to Penicillin

Penicillin Skin Testing (Prick and Intradermal) followed by an oral graded Amoxicillin Challenge was performed at Oregon Health and Science University (OHSU) on:

_____.

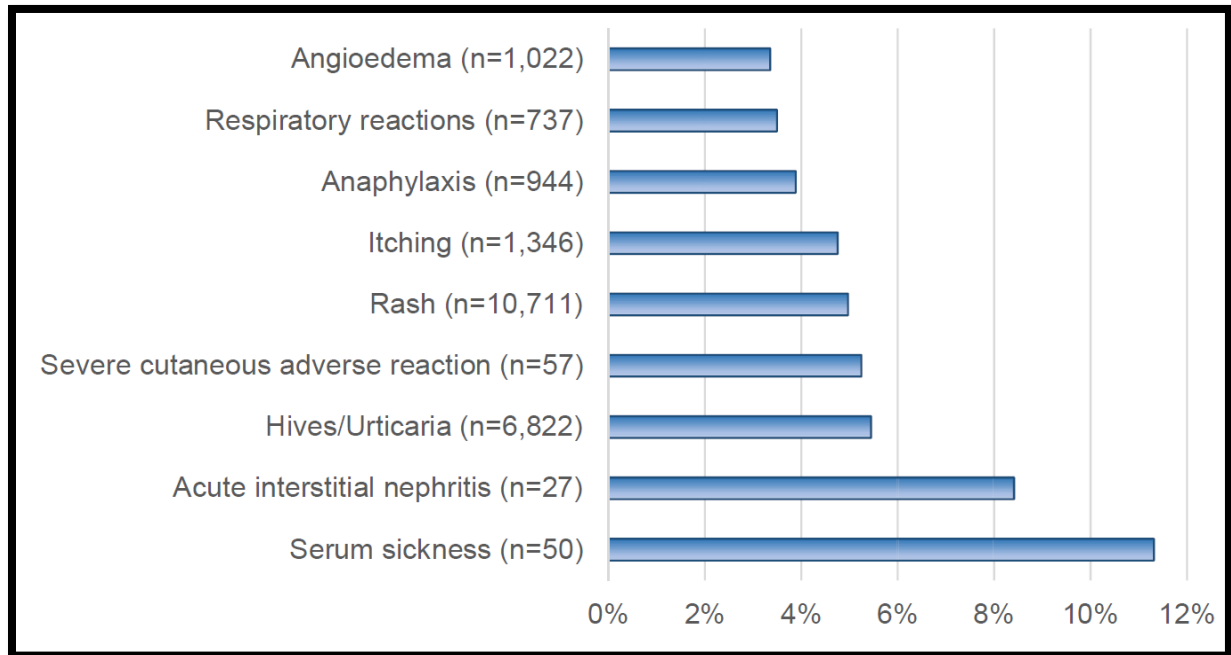
RESULTS: Negative (No Reaction)

Test performed by _____.



Cephalosporin Allergies

- Most commonly used antibiotic in US hospitals
- 1.3-1.7% of patients report ADRs to cephalosporins
- Can cause all types of HSRs
 - SSLR (11% of cases)
 - AIN (9% of cases)
 - SCAR (5% of cases)
 - Anaphylaxis (4% of cases)
- 60% of patients lose cephalosporin sensitivity after 5 years



Khan DA, et al. *J Allergy Clin Immunol Pract*, 2019.
Wong A, et al. *J Allergy Clin Immunol Pract*, 2019.
Blumenthal KG, et al. *J Allergy Clin Immunol Pract*, 2015.
Romano A, et al. *Allergy*, 2014.

Cephalosporin Testing

- Skin testing (prick and ID)
 - Limited data on sensitivity and specificity
 - False positive rate in healthy population (1421 patients): 5.2%
 - Perioperative anaphylaxis: Skin testing has high PPV
 - Danish study showed 7 of 7 patients had a positive DPT after positive skin test
 - Wide range of concentrations used
- Skin testing (delayed ID and patch)
- *In vitro* sIgE testing
 - Limited commercially availability and limited data
- Direct provocation testing

Classifying Adverse Drug Events

Type A Reactions

- Predictable – Due to known pharmacodynamics of the drug (dose-dependent)
- Based more on drug than host
- >85% of ADEs
- Examples
 - Sedation with diphenhydramine
 - Diarrhea with amoxicillin
 - Bleeding due to warfarin

Type B Reactions

- Unpredictable
- Based more on host than drug
- ~15% of ADEs
- Examples
 - Hypersensitivity reactions
 - Pseudoallergies

COVID-19 Vaccine Medical Exemption

CDC criteria for 'who should not get vaccinated'

- **If you have had a severe allergic reaction (anaphylaxis) or an immediate allergic reaction**, even if it was not severe, to any ingredient in an mRNA COVID-19 vaccine (such as polyethylene glycol, abbreviated as PEG), you should not get either of the mRNA COVID-19 vaccines, but may be eligible to receive the Johnson & Johnson vaccine.
- **If you have had a severe allergic reaction (anaphylaxis) or an immediate allergic reaction**, even if it was not severe, to any ingredient in the Johnson & Johnson/Janssen COVID-19 Vaccine (such as polysorbate), you should not get the J&J/Janssen COVID-19 Vaccine, but may be eligible to receive the mRNA COVID-19 vaccines.
- If you had a severe or immediate allergic reaction **after getting the first dose of an mRNA COVID-19 vaccine**, you should not get a second dose of either of the mRNA COVID-19 vaccines.
- A severe allergic reaction is one that needs to be treated with epinephrine, EpiPen or other medical care.
- An immediate allergic reaction means a reaction within 4 hours of exposure, including symptoms such as hives, swelling or wheezing (respiratory distress).

COVID-19 Vaccine Allergy

- Studies have shown no significant increased risk in patients with previous allergic history
 - Israeli study: 8102 individuals with allergic histories
 - 429 (5%) were “highly allergic”
 - 97.9% of patients had no immediate-type reaction
 - 1.4% had minor allergic symptoms
 - 0.7% had anaphylactic reactions
- Adverse Events after vaccination
 - Surveillance data of 8 US Health Plans (11,845,128 vaccine doses)
 - No signal for MI, Bell Palsy, cerebral venous sinus thrombosis, GBS, myocarditis/pericarditis, PE, CVA, and thrombocytopenia
- Previous history of Guillain-Barre Syndrome
 - Israeli study: 579 individuals with GBS history received the COVID vaccine
 - 1 (0.2%) patient had recurrence of lower extremity weakness for several weeks

Shavit R, et al. *JAMA Allergy*, Sept 2021.

Klein N, et al. *JAMA*, Sept 2021.

Ben David SS, et al. *JAMA Neurology*, Sept 2021.



COVID-19 Vaccine Allergy Evaluation

- Thorough history and reassurance
- Skin testing to PEG and Polysorbate-80
- Split-dose challenge in clinic
- Observed administration in clinic