# Delinking Cephalosporin Cross Sensitivity Alerts in Patients with Penicillin Allergy Labels

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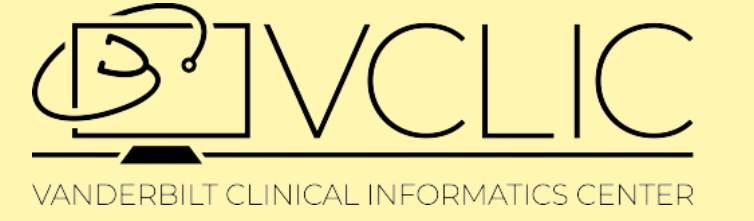
Background

- Penicillin allergies and penicillin allergy labels (PALs) in the electronic health record (EHR) are frequently misdiagnosed and/or inaccurate.
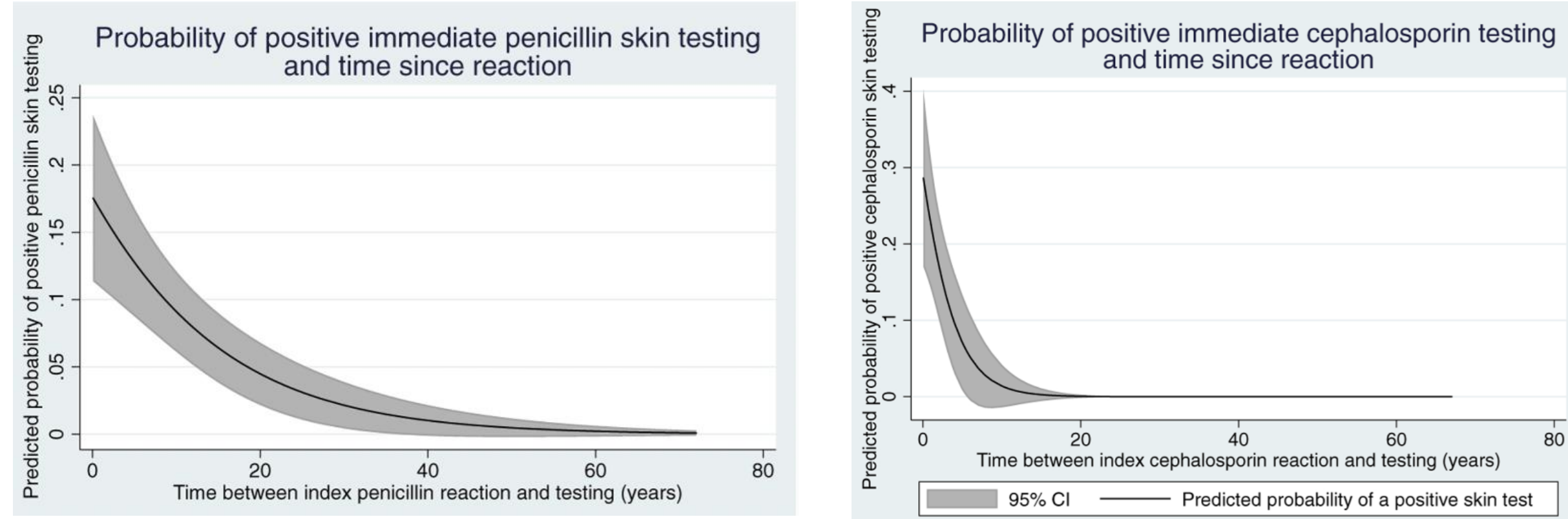

Fig 1. Probability of positive immediate hypersensitivity skin testing in patients with immediate reaction history (top: penicillins, bottom: cephalosporins)[1]

- Many EHRs include clinical decision support (CDS) recommending cephalosporin avoidance due to potential cross-reactivity.
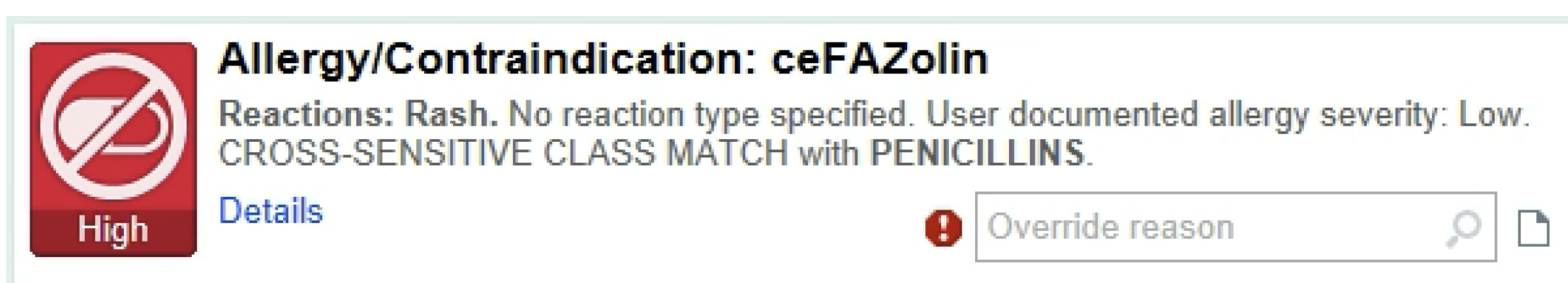

Fig 2. EHR allergy warning for cephalosporin order in patients with PAL

- Though cross sensitivity may occur in select penicillins and cephalosporins, **PALs shouldn't rule out cephalosporin administration[2]**.
- Inaccurate PALs = negative patient outcomes from riskier alternatives[3].
- **Objective: Evaluate existing EHR alert recommending cephalosporin avoidance in PAL patients and determine its patient impact.**

Methods

- **Alert logs, medication orders, and outcomes** extracted from Epic's Clarity database for alerts triggered by cephalosporin orders in Vanderbilt University Medical Center (VUMC) inpatients with and without PALs admitted from ~ 2021 - 2023.

Fig 3. Data pipeline

- Descriptive analysis performed using RStudio to evaluate alert usage and outcomes in patients administered cephalosporins vs non cephalosporin non penicillin alternatives featuring:
  - Stratification by prior tolerance
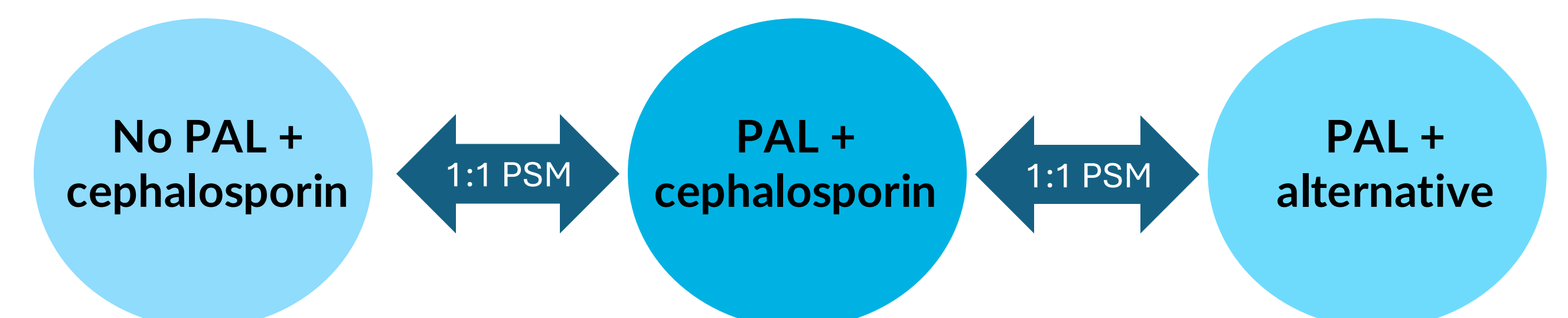 - Propensity Score Matching (PSM)

Fig 4. PSM groups, matched on Elixhauser score, ICU and surgical admission.

- Tests for significant differences in outcomes:
  - Length of stay (LOS): t test of means
  - Surgical Site Infections/*C. difficile*/anaphylaxis: χ^2 contingency

Results

Clinician Responses to PAL Cross Sensitivity Alert When Ordering Cephalosporins*

Top override reasons: **"benefit outweighs risk" (66.3%)**, "does not apply to patient" (10.6%), "per protocol" (9.1%), and "inaccurate warning" (4.5%)
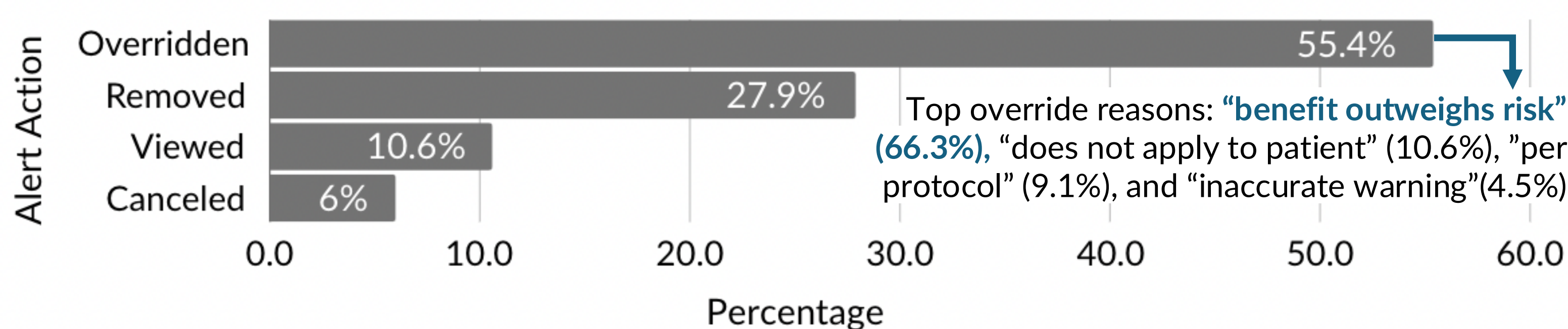
Fig 5. Clinician actions and override reasoning for cephalosporin allergy alert
*response data includes inpatient AND outpatient contexts

Sample Characteristic	Group 1. No PAL + Cephalosporin Administration	Group 2. PAL + Cephalosporin Administration	Group 3. PAL + Alternative Administration
PSM Matched Group Size*	N= 90995	N= 5061	N= 2396
% Readmission**	14.6% [b]	42.4% [ax]	62.3% [y]
Average LOS	4.35 days [b]	5.02 days [ax]	7.50 days [y]
Median LOS	1 day [b]	3 days [ax]	5 days [y]
% SSI	1.65% [b]	1.21% [ax]	2.64% [y]
% C. diff	0.508% [a]	0.613% [ax]	0.626% [x]
% Anaphylaxis	0.033% [a]	0.071% [ax]	0.129% [x]

Lettering indicates statistically significant differences in outcome
*PSM Matching applied between Group 1/Group 2 and Group 2/Group 3
** %readmitted within 30 days
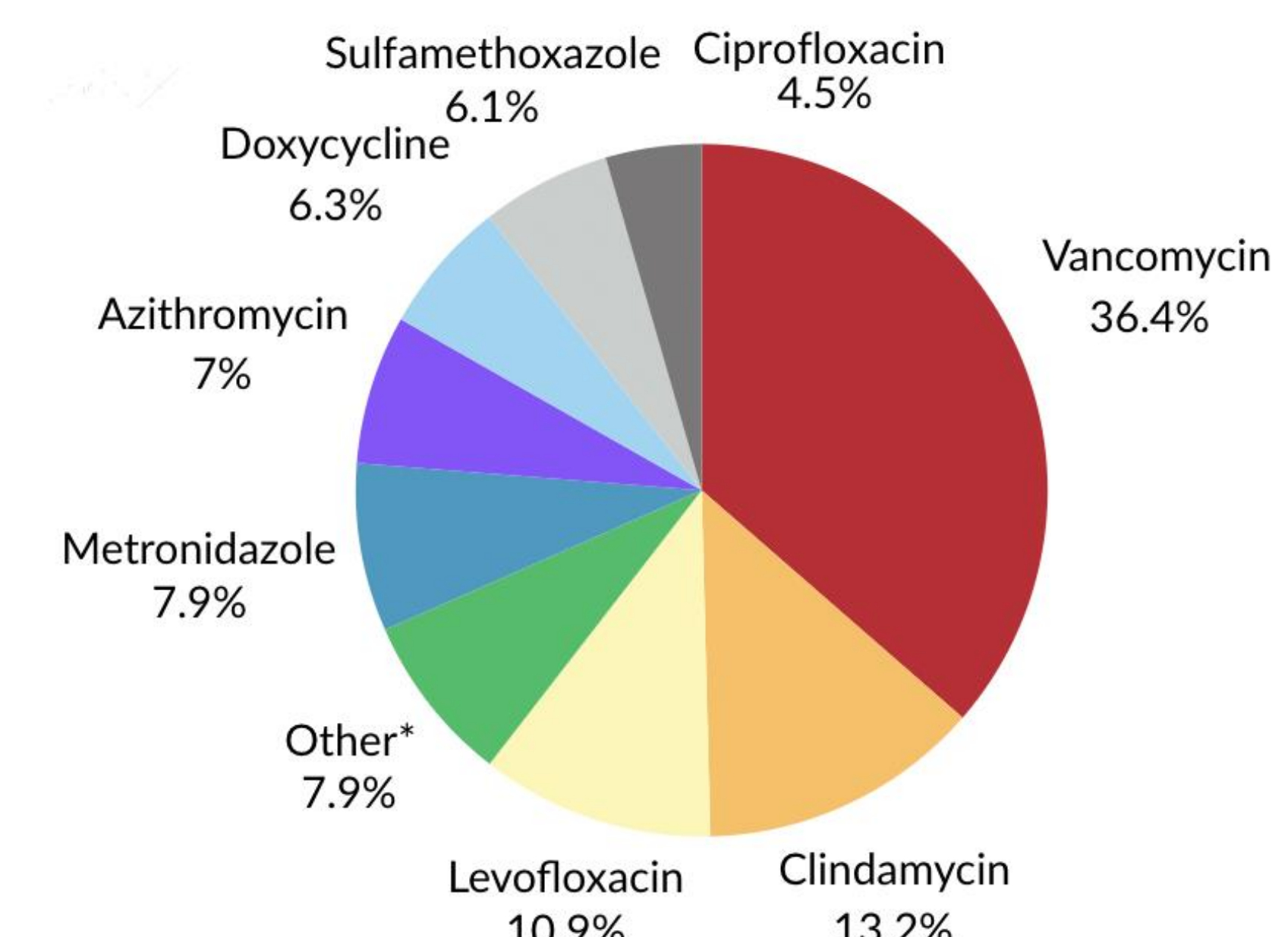Table 1. Outcomes of Unique Patient Records Triggered by Cephalosporin Orders

Fig 6. Commonly prescribed penicillin-cephalosporin alternatives
*Other medications include Rifaximin (1.29%), Meropenem (1.09%), Linezolid (0.79%), and <0.50% each of remaining medications.
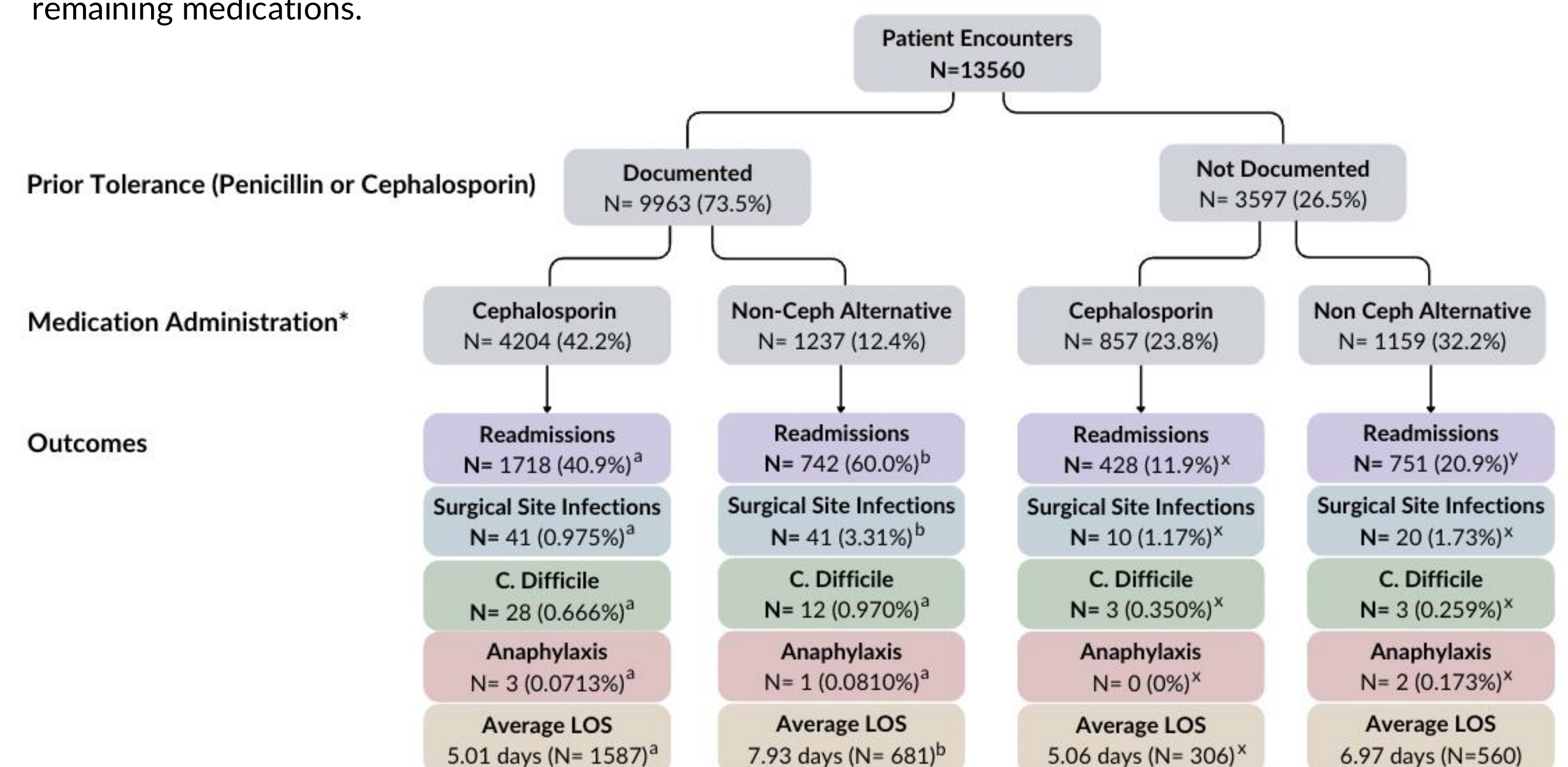

Fig 7. Flow chart of patient outcomes partitioned by prior tolerance and cephalosporin or alternative administration
* Medication Administration excludes patients administered both a cephalosporin and an alternative

Discussion

- Clinicians frequently override current alert knowing the benefits of prescribing cephalosporins over alternatives outweigh risks.
- For most outcomes and groups with a significant sample size, **patients not administered cephalosporin in the presence of a PAL fared worse.**
- Limitations: generalizability limited to patients in Vanderbilt's EHR system; outcomes limited to those encoded in EHR.
- **Conclusion: existing cephalosporin warning for patients with PAL may be more harmful than beneficial to clinicians and patients.**

Future Plans

- Improve alert specificity for high-risk patients and treatments.
- Automate penicillin risk score calculations using EHR notes.

References

1..Stone CA Jr, et al. Testing Strategies and Predictors for Evaluating Immediate and Delayed Reactions to Cephalosporins. J Allergy Clin Immunol Pract. 2021 Jan;9(1):435-444.e13. doi: 10.1016/j.jaip.2020.07.056. Epub 2020 Aug 19. PMID: 32822918; PMCID: PMC7855229.
2. McCoy AB, et al (2022). Informatics-Enabled Penicillin Allergy Risk Stratification and De-Labeling [Conference presentation]. XGM 2022, Verona, Wisconsin, United States.
3. Yuson CL, et al. 'Cephalosporin allergy' label is misleading. Aust Prescr. 2018 Apr;41(2):37-41. doi: 10.18773/austprescr.2018.008. Epub 2018 Apr 3. Erratum in: Aust Prescr. 2018 Dec;41(6):205. PMID: 29670309; PMCID: PMC5895476.