Delinking Cephalosporin Cross Sensitivity Alerts in Patients with PAL

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Background

- Most patients with a penicillin allergy label (PAL) in their electronic health record (EHR) are not truly allergic .
  - **< 5%** of PALs are verified via allergy testing[1].
  - Many penicillin and cephalosporin (a closely related antibiotic) allergies diminish over time[2].

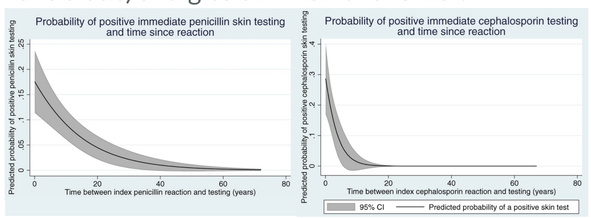


Fig 1. Probability of obtaining positive immediate hypersensitivity skin testing in patients with an immediate reaction history (left: penicillins, right: cephalosporins)[2]

- Misdiagnosed PALs = negative patient outcomes as alternatives have greater risks and side effects[4].
- Risk stratification model was developed to identify low-risk patients who would benefit from PAL delabeling post oral challenge[3]. But EHRs also recommend cephalosporin avoidance due to potential cross sensitivity.

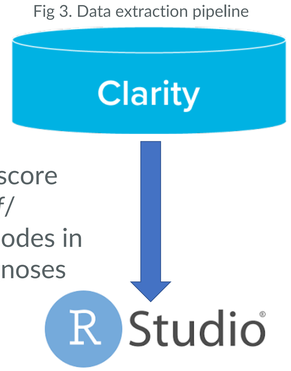
Fig 2. EHR allergy warning for cephalosporin order in patients with PAL

- Though cross sensitivity may occur between penicillins and cephalosporins with similar side chains, **PALs should not rule cephalosporin administration**[5].
  - Evidence suggests **cross reactivity ≤ 1%**[6]
- **Objective: evaluate cephalosporin alerts in patients with PAL to implement an appropriate intervention.**

Methods

- 63,474 alerts in Vanderbilt's EHR from 07/01/21-07/16/23 for patients with PALs in inpatient setting extracted from Epic's Clarity database.
- Outcomes stratified by Elixhauser score
- Surgical site infections (SSIs)/*C. diff*/ anaphylaxis identified via ICD-10 codes in problem list/encounter/billing diagnoses ≤ 30 days post alert.
- Tests for significant differences in outcomes:
  - Length of stay (LOS)- t test of means
  - SSI/C. diff/anaphylaxis- χ^2 contingency

Fig 3. Data extraction pipeline



Results

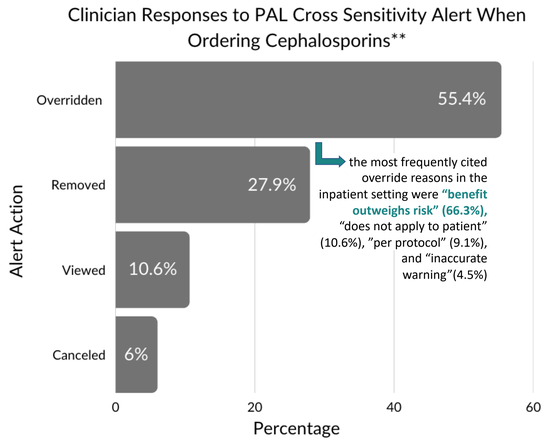
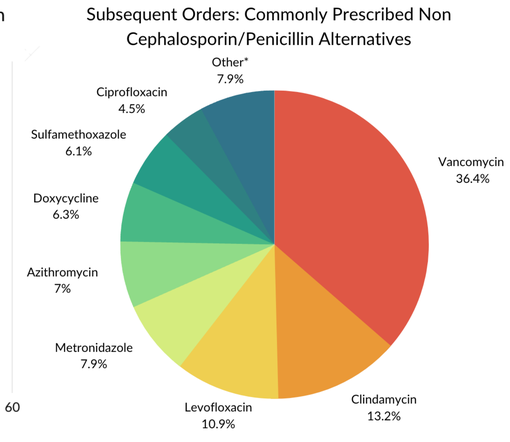


Fig 4. Clinician actions and override reasoning for cephalosporin allergy alert
**response data includes inpatient AND outpatient contexts



*Other medications include Rifaximin (1.29%), Meropenem (1.09%), Linezolid (0.79%), and the following (<0.50% each): Rifampin, Nitrofurantoin Macrocrysta Gentamicin, Tobramycin, Fosfomycin Tromethamine, Dapsone, Methenamine Hippurate, Bacitracin, Ertapenem, Erythromycin, Minocycline, Moxifloxacin, Neomycin, Fidaxomicin, Erythromycin Ethylsuccinate, Clarithromycin, Trimethoprim, Ethambutol, Zithromax Z-Pak Oral. Xifaxan, Tetracycline, Tedizolid, Isoniazid, Uribel, Imipenem-Cilastatin-Relebactam, Methenam, Erythromycin Stearate, Daptomycin, Amikacin, Methenamine Mandelate

Fig 5. Commonly prescribed non cephalosporin/penicillin alternatives

Cephalosporin vs Alternative Outcomes

Outcome	Ceph (Overall) n= 20363	Non Ceph Alternative (Overall) n= 12676	Ceph (Elixhauser <11) n= 19719	Non Ceph Alternative (Elixhauser <11) n= 11905	Ceph (Elixhauser 11-15) n= 640	Non Ceph Alternative (Elixhauser 11-15) n= 761	Ceph (Elixhauser >15) n= 4	Non Ceph Alternative (Elixhauser >15) n= 10
% Readmission***	29.95%	42.247%	30.05%	43.65%	26.88%	21.16%	0%	0%
Average LOS	6.88 days	11.7 days	6.44 days	10.7 days	13.9 days	23.0 days	16.0 days	16.8 days
Median LOS	4 days	6 days	4 days	6 days	11 days	17 days	16 days	20 days
% SSI	1.98%	3.66%	1.89%	3.62%	4.24%	4.37%	0%	0%
% C. diff	0.649%	0.805%	0.649%	0.820%	0.653%	0.529%	0%	0%
% Anaphylaxis	0.220%	0.0657%	0.0781%	0.0701%	4.08%	0%	0%	0%

*** % readmitted within 30 days

Table 1. Cephalosporin vs alternative group outcomes stratified by comorbidity score.
A significant difference was observed between the cephalosporin and non cephalosporin alternative group outcomes for average length of stay (t= -21.18, df= 12955, p < 2.2e-16), readmissions (X^2 = 520.79, df= 1, p < 2.2e-16), and surgical site infections (X^2 = 520.79, df= 1, p < 2.2e-16). No significant difference was observed between the two groups for C. diff outcomes. **A significant difference was observed in anaphylactic outcomes between the groups for patients with an Elixhauser score between 11-15, but not for those patients with an Elixhauser score <11.**

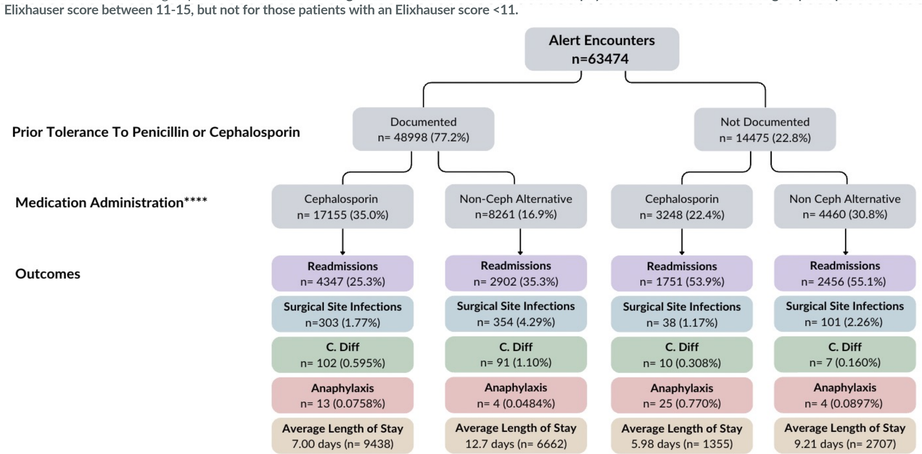


Fig 6. Flow chart of patient outcomes partitioned by prior tolerance and cephalosporin/alternative administration
**** Medication Administration excludes patients administered both a cephalosporin and an alternative

Discussion

- Clinicians frequently override current alert knowing the benefits of prescribing a cephalosporin over an alternative outweigh risks.
- For most outcomes and comorbidity scores with a significant sample size, **patients not administered a cephalosporin in the presence of a PAL had much worse outcomes.**
- **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 Works

- Case match and analyze outcomes for patients without PALs who are administered cephalosporins to establish a control group.
- Intervention design: customize alert for subset of high-risk patients/cephalosporins.

Acknowledgements

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