# BEST PRACTICES AWARD

Antibiotic Use in Patients with Documented **B-lactam Allergies:** Impact of an Antibiotic Side-Chain-Based Cross-Reactivity Chart Combined with Enhanced Assessment

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#### Introduction

#### **Healthcare Facility**

- 548-bed community teaching hospital
- 5-hospital network in Southeast Michigan
- 93-member non-profit corporate system (Trinity Health) in

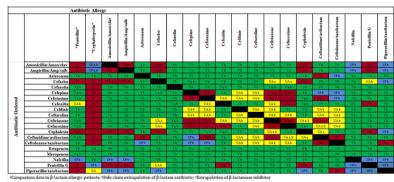
## Background

- B-lactam antibiotics with dissimilar R-group side chains are associated with low cross-reactivity.
- The myths surrounding the incidence and reporting of β-lactam allergies, and the cross-reactivity of B-lactam antibiotics, may lead to use of non-B-lactam alternative antibiotics which have been associated with less efficacy (e.g., increased surgical site infections), and increased adverse events including Clostridioides difficile infections (CDI))

# Description of the Program

- A multi-disciplinary team at our hospital implemented an institutional approach for antibiotic management of patients with B-lactam allergies in October 2014.
- Strategies included enhanced allergy assessment, and the use of an internally developed, literature-based, antibiotic sidechain-based cross-reactivity chart to guide prescribing (Figure 1).
- Pharmacists actively intervened to assess for previous tolerance of β-lactams, ensure compliance with chart recommendations, and communicate with prescribers when warranted.

## Figure 1: Institutional Cross-Reactivity Chart



#### Experience with the Program

## Methods

- We describe the impact of the cross-reactivity chart in combination with enhanced allergy assessment, antimicrobial stewardship, and pharmacy processes to optimize B-lactam use for patients with pneumonia and surgical prophylaxis.
- Impact was determined by assessing antibiotic use and associated outcomes in patients with B-lactam allergies in quasi-experimental pre-post study designs.
- Propensity-weighted scoring analyses compared categorical and continuous outcomes.
- Interrupted time-series analysis further analyzed key outcomes.

#### Experience with the Program (continued)

#### Surgical Prophylaxis<sup>1</sup>

- A total of 2,208 adult surgical patients were included
  - 1,119 historical cohort
  - 1.089 intervention cohort
- There was a significant difference in the number of patients who received an alternative antibiotic between the historical and intervention cohorts (84.9% vs. 15.1%, p < 0.001) (Figure 2).
- The use of preferred B-lactams significantly improved in all patient allergy types and across all procedure groupings.
- There was no change in the rate of allergic reactions between cohorts (0.5% vs. 0.3%; p = 0.323).
- There were significant increases in the patients who received recommended antibiotic:
  - timing (93.7% vs. 95.9%; p = 0.003)
  - selection (92.6% vs. 96.2%, p < 0.001)
  - duration (98.3% vs. 99.2%; p = 0.05)

## Table 1. Surgical Prophylaxis Outcomes by Cohort (Unadjusted and Propensity Score-Weighted)

				PS
	Historical	Intervention		weighted
Variable <sup>a</sup>	(n=1119)	(n=1089)	P value	P value
Categorical Outcomes				
Received Beta-lactam	950 (84.9)	164 (15.1)	< 0.001	< 0.001
Alternative				
SSI	24 (2.1)	15 (1.4)	0.227	0.093
Any Allergic Reaction to Surgical	6 (0.5)	3 (0.3)	0.507	0.323
Prophylaxis				
Readmission	88 (7.9)	69 (6.3)	0.189	0.035
Readmission with SSI <sup>b</sup>	13 (14.8)	9 (13)	0.938	0.765
In-hospital Mortality	4 (0.4)	8 (0.7)	0.36	0.269
30-day Mortality	12 (1.1)	14 (1.3)	0.789	0.957
Infection Related 30-day	2 (0.2)	4 (0.4)	0.446	0.665
Mortality				
Nephrotoxic Prophylaxis	414 (37)	96 (8.8)	< 0.001	< 0.001
Acute kidney injury	37 (3.3)	32 (3)	0.712	0.622
Nephrotoxic Prophylaxis <sup>e</sup>	16 (43.2)	5 (15.6)	0.026	0.011
HO-CDI	2 (0.2)	1 (0.1)	> 0.999	0.557
Continuous Outcomes <sup>d</sup>				
Inpatient Costs (\$)	16063	16922	0.125	0.367
	(12725)	(12873)		
LOS (days)	3.6 (3.4)	3.6 (3.6)	0.977	0.317

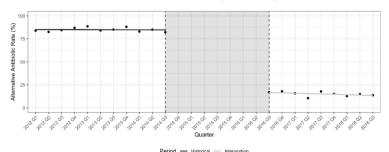
Abbreviations: PS, propensity score; SSI, surgical site infection; HO-CDI, healthcare facility-onset *Clostridioides difficile* infection; LOS, length of stay

\*Data are no. (%) unless otherwise specified.

Analysis performed on the subset of patients with acute kidney injury (Historical Cohort N = 37, Intervention Cohort N = 32).

Data are summarized with mean (standard deviation) unless otherwise specified

## Figure 2. Interrupted Time-Series Analysis of Non-B-lactam Alternative Antibiotic Use for Surgical Prophylaxis



#### Experience with the Program (continued)

### Pneumonia<sup>2</sup>

- A total of 341 and 623 patient encounters were included in the historical and intervention pneumonia cohorts, respectively.
- There was a significantly greater use of B-lactams in the intervention cohort (70.4% vs 89.3%; p < 0.001) (Figure 3).
- Decreased use of alternative therapy (58.1% vs. 36%; p < 0.001).
- There was no difference in:
  - overall allergic reactions between cohorts (2.4% vs. 1.6%; p = 0.738)
  - reactions caused by B-lactams (1.3% vs. 0.9%; p = 0.703)
- There was a significant increase in both inpatient mortality (0% vs. 6.4%; p < 0.001) and 30-day mortality (2.4% vs. 14.3%; p < 0.001).
  - There was no difference in β-lactam or alternative therapy use between cohorts in patients who experienced mortality at 30-days.
  - No inpatient deaths were attributed to an allergic reaction.
- · Healthcare facility-onset CDI decreased between cohorts (1.2% vs. 0.2%; p = 0.032).

Table 2. Outcomes by Pneumonia Cohort

	Historical	Intervention		PS weighted
Variable	(n=341)	(n=623)	P value	P value
Categorical outcomes	(11-342)	(11-02-5)	, value	1 value
Received β-lactam	240 (70.4)	556 (89.3)	< 0.001	< 0.001
Allergy Type	, ,	, ,		
Drug intolerance	n = 19	n = 45		
Received β-lactam	17 (89.5)	41 (91.1)	> 0.999	
Mild reaction	n = 69	n = 148		
Received β-lactam	54 (78.3)	137 (92.6)	0.005	
Type I HSR	n = 120	n = 262		
Received β-lactam	68 (56.7)	225 (85.9)	< 0.001	
Unknown allergy	n = 130	n = 161		
Received β-lactam	100 (76.9)	148 (91.9)	< 0.001	
Type II-IV HSRs	n = 3	n = 7		
Received β-lactam	1 (33.3)	5 (71.4)	0.5	
Readmission	50 (14.7)	102 (16.4)	0.546	0.806
In-hospital mortality	0 (0)	40 (6.4)	< 0.001	< 0.001
Received β-lactam	-	37 (92.5)	-	
Received alternative therapy	-	34 (85)	-	
30-day mortality	8 (2.3)	89 (14.3)	< 0.001	< 0.001
Received β-lactam <sup>a</sup>	7 (87.5)	80 (89.9)	> 0.999	
Received alternative therapy <sup>a</sup>	8 (100)	79 (88.8)	> 0.999	
HO-CDI	4 (1.2)	1 (0.2)	0.056	0.032
ontinuous outcomes, median (IQR)				
Inpatient costs, \$b	7921 (4611,	7454 (4624,	0.524	0.303
	14600)	13431)		
Antibiotic days of therapy	8 (5, 13)	8 (5, 12)	0.98	0.9
Antibiotic duration, days	5 (3, 8)	5 (3, 7)	0.426	0.62
Antibiotic cost per patient day, \$	68 (28, 143)	76 (36, 153)	0.029	0.1
oata are no. (%) unless otherwise specified				

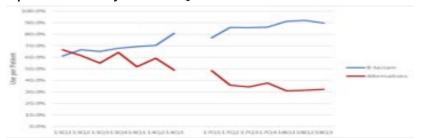
Total are no. (30) unless otherwise spectned.

Abbreviations: HSR, hypersensitivity reactions; HO-CDI, healthcare facility-onset *Clostridioides difficile* infection; PS, propensity score.

Data are analyzed in patients with 30-day mortality (Historical Cohort n = 8, Intervention Cohort n = 89).

Data are analyzed in patients with available data (Historical Cohort n = 341, Intervention Cohort n = 529).

Figure 3. B-lactam vs. Non-B-lactam Alternative Therapy Use per Encounter by Calendar Ouarter



## Experience with the Program (continued)

Table 3. Allergic Reactions by Pneumonia Cohort

				P5 Weign
Variable <sup>a</sup>	Historical	Intervention	P value	P valu
Study cohort	n = 341	n = 623		
Any allergic reaction	8 (2.4)	10 (1.6)	0.573	0.73
Drug intolerance	3 (0.9)	0 (0)	0.044	0.02
Mild reactions	2 (0.6)	6 (1)	0.719	0.32
Type I-IV combined reactions	3 (0.9)	4 (0.6)	0.703	0.45
Type I HSR	1 (0.3)	1 (0.2)	> 0.999	0.52
Type II-IV HSR	2 (0.6)	3 (0.5)	> 0.999	0.61
Allergic reaction (excluding drug	5 (1.5)	10 (1.6)	> 0.999	0.78
intolerance reactions)				
Received β-lactam	n = 240	n = 556		
Reaction secondary to β-lactam use <sup>a, b</sup>	3 (1.3)	5 (0.9)	0.703	
Drug intolerance <sup>b</sup>	0 (0)	0 (0)		
Mild reactions <sup>b</sup>	0 (0)	4 (0.7)	0.322	
Type I-IV combined reactions	3 (1.3)	1 (0.2)	0.084	
Type I HSR <sup>b</sup>	1 (0.4)	0 (0)	0.302	
Type II-IV HSRb	2 (0.8)	1 (0.2)	0.218	
Received alternative therapy	n = 335	n = 586		
Reaction secondary to alternative use <sup>a, c</sup>	6 (1.8)	5 (0.9)	0.221	
Drug intolerance <sup>c</sup>	3 (0.9)	0 (0)	0.048	
Mild reactions <sup>c</sup>	2 (0.6)	2 (0.3)	0.625	
Type I-IV combined reactions	1 (0.3)	3 (0.5)	> 0.999	
Type I HSR <sup>c</sup>	0 (0)	1 (0.2)	> 0.999	
Type II-IV HSR <sup>c</sup>	1 (0.3)	2 (0.3)	> 0.999	
Allergic reactions secondary to alternative	3 (0.9)	5 (0.9)	> 0.999	
use (excluding drug intolerance				
reactions) <sup>a, c</sup>				
Data are no (%) unless otherwise specified				

Data are no. (%) unless otherwise specified. Abbreviations: HSR, hypersensitivity reactions: PSR, propensity score. "One allergic reaction was thought to be either from  $\beta$ -lactam or alternate therapy and included in both categories (Historical Cohort n =

. ata are analyzed in patients who received β-lactam antibiotics (Historical Cohort n = 240, Intervention Cohort n = 556). ata are analyzed in patients who received alternative antibiotics (Historical Cohort n = 335, Intervention Cohort n = 586

## **Discussion/Conclusion**

- Implementation substantially improved the prescribing of preferred B-lactam antibiotics without increasing allergic reactions.
- Active strategies incorporating side-chain-based allergy assessment, antimicrobial stewardship, and pharmacist review may be an inexpensive, effective, and deployable 'best practice' for pharmacies to incorporate into their suites of existing allergy stewardship strategies with the potential for wide-scale influential change.

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#### References

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