

## ABSTRACT (revised)

### Background:

Adverse reactions (AR) to antibiotics are common among outpatients, accounting for ~20% of drug-related AR visits to emergency rooms. Little is known about the prevalence of ARs among inpatients. This retrospective study describes patient-reported antibiotic allergies on admission, their effect on outcome, and ARs associated with antibiotic use in 6 acute care facilities of varying size and location.

### Methods:

Cross-sectional study using retrospective chart review of 1,200 adult inpatients (pts), hospitalized (>24hrs) in Veterans Affairs (n=1), teaching (n=2), non-teaching (n=3) hospitals, and receiving ≥1 antibiotic doses on 4 index dates corresponding to a random hospital day and chosen at equal intervals through a 1-year study period (9/2009-10/2010). Medical records were reviewed for antibiotic allergies on admission, demographics, comorbidities, diagnostics, duration and indication for prescribed antibiotics, treatment outcomes and ARs. Therapy failure was defined as lack of treatment response based on clinical evidence available in record. Proportions were compared using Pearson's  $\chi^2$  test.

### Results:

History of antibiotic allergies was present in 306/1,200pts (25.5%) that reported 429 allergies (83 to >1 antibiotic class). The most common allergies were to penicillins (185), sulfonamides (99) and cephalosporins (35). Rash was the most common prior adverse reaction (21% n=90), but 46% of prior adverse reactions were unknown (n= 196). One hundred seven pts (9%) received an antibiotic to which they had a prior documented allergy. Pts with prior allergies had higher odds for therapy failure (OR = 1.4, p = 0.08) than non-allergic patients. New ARs were noted for 147/1,200 study pts (12%), including diarrhea (8%), nausea (1.3%), hepatic or renal failure (1.3%), and rash (0.6%). Patients with new ARs had increased odds of therapy failure (OR 1.68, p = 0.02).

### Conclusion:

Patient-reported antibiotic allergies in inpatients are common and may limit optimal treatment, though specific allergies are often unconfirmed. New adverse reactions occur in 12% of inpatients and are associated with treatment failure. Improved documentation of antibiotic allergies could minimize risk of treatment failure and ARs.

## OBJECTIVES

- Describe the prevalence of prior antimicrobial allergies in hospitalized patients requiring antibiotics
- Describe the prevalence of new adverse reactions amongst hospital patients receiving antibiotics
- Estimate the clinical consequences of prior allergies and new adverse drug reactions in hospitalized patients requiring antibiotics

## METHODS

**Population:** inpatients at Veterans Affairs (n=1), teaching (n=2), non-teaching (n=3) hospitals;  
**Study period:** 4 index dates chosen at equal intervals b/n 9/2009 - 10/2010 (11/20, 2009; 2/10, 2010; 10/20, 2010, 8/10, 2010)

**Include** patients with active order for antibiotic prescription on index date  
**Exclude** ambulatory (LOS <24 hrs), pediatric (age <18yrs) and psychiatric admissions

**Enroll 1,200 charts** (50 per date per facility)  
**Review:**  
Patient history and allergies  
Indications, start/stop dates for <9 Rxs  
<6 admission ICD9 codes (Charlson comorbidity score)  
Microbiology reports (14d window)  
Radiology reports (3d window)  
Infection parameters (fever and WBC)

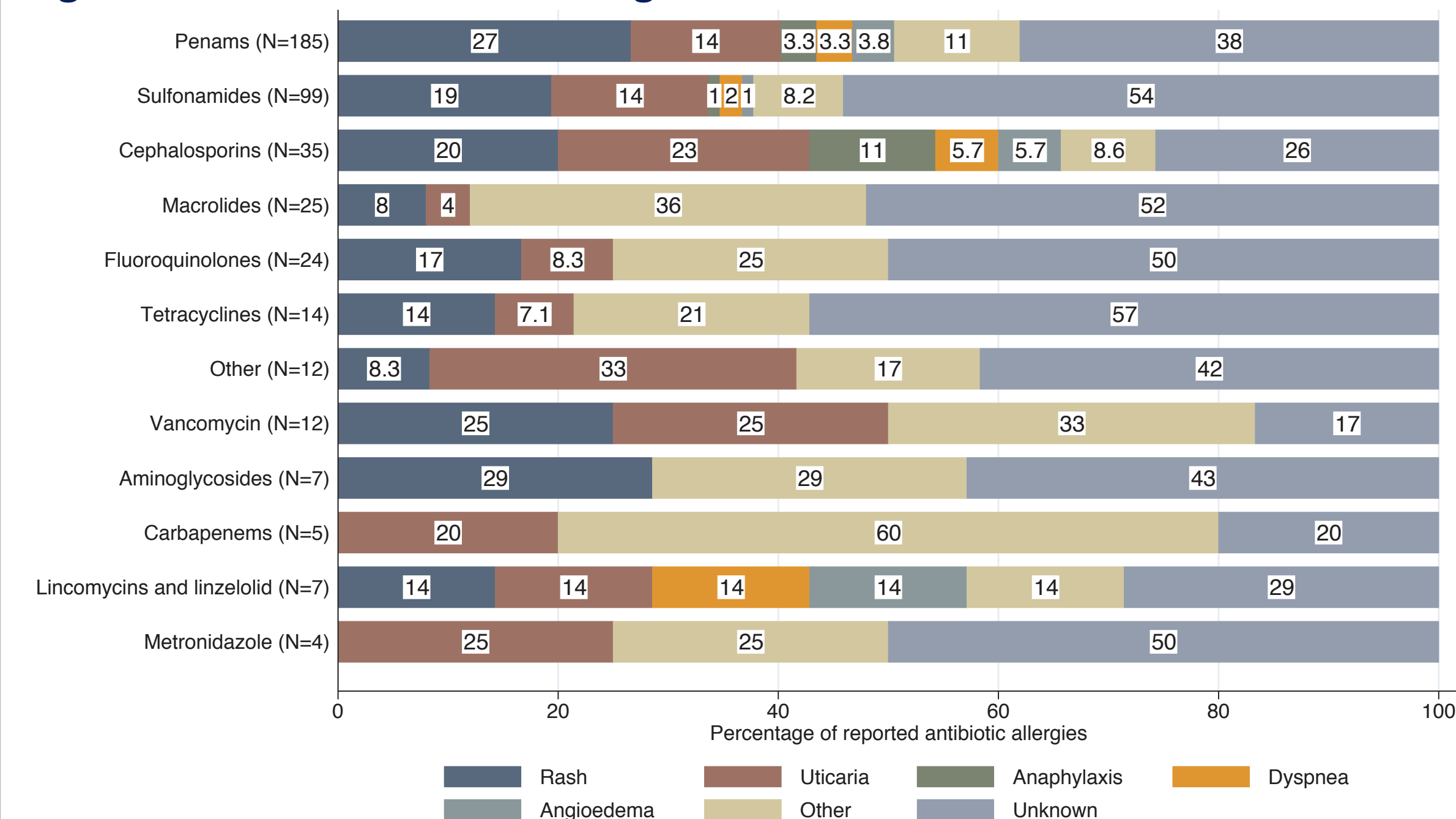
## RESULTS

**Table 1: Over 25% of Patients Reported Preexisting Antibiotic Allergies; 43% were to Penicillins**

Allergies per patient	N	(%)
<b>Total</b>	<b>1,200</b>	<b>(100)</b>
None reported	894	(74.5)
1	223	(18.6)
2	57	(4.8)
3	15	(1.3)
>3	11	(0.9)
<b>Antibiotics</b>		
<b>Total</b>	<b>429</b>	<b>(100)</b>
Penicillins	185	(43.1)
Sulfonamides	99	(23.1)
Cephalosporins	35	(8.2)
Macrolides	25	(5.8)
Fluoroquinolones	24	(5.6)
Tetracyclines	14	(3.3)
Vancomycin	12	(2.8)
Other	12	(2.8)
Aminoglycosides	7	(1.6)
Lincomycins and oxazolidinones	7	(1.6)
Carbapenems	5	(1.2)
Metronidazole	4	(0.9)
<b>Reported reactions</b>		
Unknown	180	(42.2)
Rash	90	(21.1)
Other	63	(14.8)
Urticaria	61	(14.3)
Anaphylaxis	11	(2.6)
Dyspnea	11	(2.6)
Angioedema	11	(2.6)

## RESULTS (continued)

**Figure 1: Over 40% of Prior Allergic Reactions Are of Unknown Presentation**



**Table 2: 147 Patients (12.2%) Had New Adverse Events Associated with Antibiotic Therapy; Over 60% of New Adverse Events Were Gastro-intestinal**

New Adverse Reactions	N (%)
Total	147 (12.2)
Diarrhea	84 (7.0)
Nausea	16 (1.3)
Rash	7 (0.6)
Renal failure	8 (0.7)
Hepatic failure	7 (0.6)
Systemic reaction	3 (0.2)
C. difficile	14 (1.2)
Other	6 (0.5)

**Table 3: Univariate Analysis of Variables Associated with New Adverse Reactions to Antimicrobials**

Variable	Value	Total (%) 1,200(100)	Had Adverse Reaction (%) 147(12)	No Adverse Reaction (%) 1053(88)	OR	[95% Conf.Interval]	p-value
Patient age	<50 years	279(23)	44(16)	235(84)			0.111
	51-65 yr.	363(30)	40(11)	323(89)	0.66	[0.418-1.048]	
	66-75 yr.	209(17)	29(14)	180(86)	0.86	[0.518-1.429]	
	>75 yr	344(29)	34(10)	310(90)	0.59	[0.363-0.945]	
ICU admission	no	834(70)	86(10)	748(90)			0.002
	yes	366(30)	61(17)	305(83)	1.74	[1.221-2.479]	
Immuno-compromised	no	1050(88)	121(12)	929(88)			0.042
	yes	150(12)	26(17)	124(83)	1.61	[1.013-2.558]	
Received outpatient antibiotic (<30d prior)	no	780(65)	78(10)	702(90)			0.001
	yes	300(25)	55(18)	245(82)	2.02	[1.389-2.938]	
Charlson comorbidity score	None (0)	692(58)	77(11)	615(89)			0.324
	Mild (1-5)	224(19)	33(15)	191(85)	1.38	[0.89-2.14]	
	Severe (>5)	284(24)	37(13)	247(87)	1.90	[0.787-1.819]	
Isolated ESKAPE pathogen	no	959(80)	107(11)	852(89)			0.021
	yes	241(20)	40(17)	201(83)	1.59	[1.068-2.351]	
Recorded prior allergies	no	888(74)	105(12)	783(88)			0.437
	yes	311(26)	42(14)	269(86)	1.16	[0.793-1.709]	
Received antibiotic despite documented cross-allergy	no	1151(96)	137(12)	1114(88)			0.075
	yes	49(4)	10(20)	39(80)	1.90	[0.926-3.888]	
Therapy failure	no	723(83)	99(14)	624(86)			0.021
	yes	152(17)	32(21)	120(79)	1.68	[1.078-2.62]	
Broad-spectrum or restricted abx	no	788(66)	84(11)	704(89)			0.02
	yes	412(34)	63(15)	359(85)	1.51	[1.065-2.149]	
Undocumented indication	no	998(83)	123(12)	875(88)			0.898
	yes	200(17)	24(12)	176(88)	0.97	[0.608-1.546]	

**Table 4: Select Univariate Analysis of Variables Associated With Treatment Failure (N=131); Prior Allergies Associated with Worse Outcomes**

Variable	Patients with treatment failure (%)	OR	[95% CI]	p-value
Recorded allergies	50 (21)	1.409	[0.966 - 2.055]	0.074
Adverse drug reaction	32 (24)	1.681	[1.078 - 2.620]	0.021
Received antibiotic despite documented (cross)allergy	6 (24)	1.523	[0.598 - 3.879]	0.375

**Treatment failure** defined as lack of treatment response to the index or concurrent therapy, based on clinical evidence available throughout treatment (e.g. persistence of fever, abnormal WBC count, other infectious symptoms), and including death or transition to palliative care.

## CONCLUSIONS

- Preexisting allergies to antibiotics are common in hospital patients requiring antibiotic treatment
- Preexisting allergies to antibiotics are associated with a trend towards worse clinical outcomes after treatment with antibiotics
- Amongst hospital patients treated with antibiotics, new adverse drug reactions are associated with worse clinical outcomes

## REFERENCES

1. Shehab, N., Patel, P. R., Srinivasan, A., & Budnitz, D. S. (2008). Emergency department visits for antibiotic-associated adverse events. *Clin Infect Dis*, 47(6), 735-43.

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