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ACUTE KIDNEY INJURY IN PATIENTS TREATED WITH VANCOMYCIN AND PIPERACILLIN-TAZOBACTAM: A RETROSPECTIVE COHORT ANALYSIS

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THESIS

A thesis submitted in partial fulfillment of the
requirements for the degree of Master of Science in the
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at the University of Kentucky

By

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Lexington, Kentucky

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Lexington, Kentucky

2016

ABSTRACT OF THESIS

ACUTE KIDNEY INJURY IN PATIENTS TREATED WITH VANCOMYCIN AND PIPERACILLIN-TAZOBACTAM: A RETROSPECTIVE COHORT ANALYSIS

Empiric antimicrobial therapy often consists of the combination of Gram-positive coverage with vancomycin (VAN) and Gram-negative coverage, specifically an anti-pseudomonal beta-lactam, such as piperacillin-tazobactam (PTZ). Nephrotoxicity is commonly associated with VAN therapy; however, recent reports demonstrate increasing nephrotoxicity rates among patients treated with the combination of VAN and PTZ. This study evaluated the effect of the VAN/PTZ combination on acute kidney injury (AKI), as defined by the RIFLE criteria, compared to VAN and PTZ monotherapies.

Overall, 11,650 patients were analyzed, with 1,647 (14.1%) AKI cases occurring. AKI was significantly more frequent in the VAN/PTZ group (21%) compared to either monotherapy group (VAN 8.3%, PTZ 7.8%, $p<0.001$ for both). Combination therapy was independently associated with higher AKI odds compared to monotherapy with either agent (aOR=2.03; 95% CI 1.74-2.39; aOR=2.31; 95% CI 1.97-2.71, for VAN and PTZ, respectively). Receipt of concomitant nephrotoxic drugs were independently associated with increased AKI rates, as were increased duration of therapy, length of hospital stay, increasing severity of illness, and increasing baseline renal function.

VAN combined with PTZ was associated with twice the odds of AKI development compared to either agent as monotherapy. This demonstrates the need for judicious use of combination empiric therapy.

KEYWORDS: Antimicrobial stewardship, Vancomycin, Piperacillin-tazobactam, Acute Kidney Injury, Electronic health record

Wilbur Cliff Rutter

June 27th, 2016

ACUTE KIDNEY INJURY IN PATIENTS TREATED WITH VANCOMYCIN AND PIPERACILLIN-TAZOBACTAM: A RETROSPECTIVE COHORT ANALYSIS

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June 27th, 2016

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Chapter One: Introduction

The glycopeptide antibiotic vancomycin is commonly utilized in empiric coverage for methicillin-resistant *Staphylococcus aureus* (MRSA) in many types of infections. Literature from a variety of patient populations reports nephrotoxicity associated with vancomycin, targeting troughs greater than 15 µg/mL, to occur in 5 to 43% of patients.[1] In a study of critically ill patients, acute kidney injury (AKI) was found in 21% of patients receiving vancomycin, with increasing duration of vancomycin treatment, greater vancomycin levels, concomitant vasoactive medication administration, and intermittent infusion methods being associated with higher odds of AKI.[2] A recent report from adult internal medicine patients estimated the incidence of vancomycin-associated nephrotoxicity at 13.6% and implicated concomitant piperacillin-tazobactam therapy as a key factor in these patients.[3]

Further studies have explored the interaction between empiric beta-lactam and vancomycin therapy, showing mixed results. Reports of AKI associated with the combination of vancomycin and piperacillin-tazobactam range from 16.3 to 34.8% [4-8], while the cefepime-vancomycin combination is reported to range from 12.5 to 13.3%. [5,6] While vancomycin monotherapy groups were well represented, only one of these studies compared the piperacillin-tazobactam-vancomycin combination to a control group of piperacillin-tazobactam monotherapy.[7]

Chapter Two: Methods

This is a retrospective cohort study of adult patients conducted at the University of Kentucky Chandler Medical Center (UKMC) from September 1, 2010 through August 31, 2014. Patients were included if they: were at least 18 years of age on admission; remained hospitalized for at least 48 hours; received vancomycin combined with piperacillin-tazobactam (VAN/PTZ), vancomycin alone (VAN), or piperacillin-tazobactam alone (PTZ); and had at least 48 hours of therapy (and 48 hours of overlapping therapy in the VAN/PTZ group). Patients were excluded if they had underlying chronic kidney disease, were receiving renal replacement therapy prior to admission, had a diagnosis of cystic fibrosis, or were pregnant. Additionally, patients were excluded if: they presented with AKI, defined as baseline creatinine clearance less than 30 mL/min, or if baseline creatinine clearance was greater than four times the standard deviation from the mean; serum creatinine values were not obtained during admission; and if AKI occurred prior to therapy initiation, within 48 hours of initiation, or greater than 7 days after treatment was discontinued. Patients were followed throughout their stay until time of discharge.

Data Source

Patient data were collected from the University of Kentucky Center for Clinical and Translational Science Enterprise Data Trust (EDT). The EDT contains clinical data from the inpatient population of UKMC from 2006 to present. Data stored and updated nightly by the EDT includes: demographics, financial classification (Medicare, Medicaid, private insurance), provider-level detail (service line), medical diagnosis (International

Classification of Diseases 9 [ICD-9] codes), medical procedures (Current Procedural Terminology [CPT] codes), lab tests and results, medication administration details, visit details (age, length of stay, etc.), and vital signs. This study was approved by the UKMC Institutional Review Board.

Data collected for each patient included: demographic data, visit details (length of stay, admitting and primary diagnosis codes, etc.), severity of underlying illness as defined by the Charlson Comorbidity Index (CCI), all serum creatinine levels drawn per visit, medication administration information (dose, date, and time administered), all vancomycin trough levels, receipt of other nephrotoxic agents, blood pressures, and receipt of vasopressors.

Outcome Ascertainment

AKI was defined based on the RIFLE criteria (Risk, Injury, Failure, Loss, End-stage)[9] with risk defined as a 25 to 50% decrease in estimated glomerular filtration rate (GFR), injury as a 50 to 75% decrease in estimated GFR, and failure defined as a greater than 75% decrease in estimated GFR. Loss and end-stage classifications were not assessed due to the follow-up period of this study. The adjusted Cockcroft and Gault equation [10] was used to estimate GFR due to the inconsistency of weight availability in the dataset. Baseline creatinine clearance was calculated with the first serum creatinine obtained, and the minimum creatinine clearance was calculated using the maximum serum creatinine during each patient's visit; the percent decrease in creatinine clearance was calculated from these two values. AKI status was defined as meeting any of the RIFLE criteria. Mortality

was assessed for all patients and defined as the composite of in-hospital mortality and discharge or transfer to hospice care.

Exposure Ascertainment

Hypotension exposure was defined as experiencing one of the following: mean arterial blood pressure less than 60 mmHg, a diagnosis of hypotension by a physician, or receipt of vasopressors or inotropic agents. Days of therapy for each drug was obtained, and combination days of therapy was calculated by including only those days in which the patient received both medications. Total days of therapy was calculated by the sum of all days receiving at least one of the study agents. The average daily vancomycin dose was calculated for each patient by taking the sum of all vancomycin doses received and dividing by the days of vancomycin therapy. Exposure to other nephrotoxic agents (acyclovir, angiotensin converting enzyme inhibitors, angiotensin II receptor antagonists, aminoglycosides, amphotericin B, cyclosporine, foscarnet, loop diuretics, nonsteroidal anti-inflammatory drugs [NSAIDs], sulfonamides, tacrolimus, and tenofovir) was defined as receipt of at least one dose of the agent during hospitalization.

Statistical Analysis

Characteristics between groups were described with basic descriptive statistics. Continuous variables were compared with one-way ANOVA or the Kruskal-Wallis test. Categorical variables were compared with $\chi 2$ or Fisher's exact test. Yearly AKI trends were assessed with Pearson's correlation coefficient. Univariate models for all covariates were

created with probability of AKI as the outcome. Covariates significant after univariate were then incorporated into the multivariate model, which was subsequently adjusted to achieve the highest predictive accuracy by minimizing the Akaike information criterion (AIC). Model fit was assessed with a standardized Hosmer-Lemeshow goodness of fit test.[11] All statistical analyses were completed with RStudio v0.98 running R v3.1.2 (R Foundation for Statistical Computing, Vienna, Austria)[12]. All tests were two-tailed and significance was defined at an alpha of 0.05.

Role of Funding Source

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Chapter Three: Results

Baseline Patient Characteristics

Of 17,879 patients initially screened, 11,650 patients were evaluated, of which 5,497 received VAN and PTZ (VAN/PTZ), 3,055 received VAN alone, and 3,098 received PTZ alone (Figure 2). Table 1 contains basic demographic information. The average age of patients was 52.5 ± 16.8 years with 6,242 (53.6%) males. Patients receiving VAN/PTZ had higher CCIs than either monotherapy group and had significantly increased length of hospitalization. While patients in the combination therapy group were more likely to experience some level of hypotension, concomitant nephrotoxic agent exposure was more common in the VAN monotherapy group.

FIGURE 1: Patient exclusion flowchart

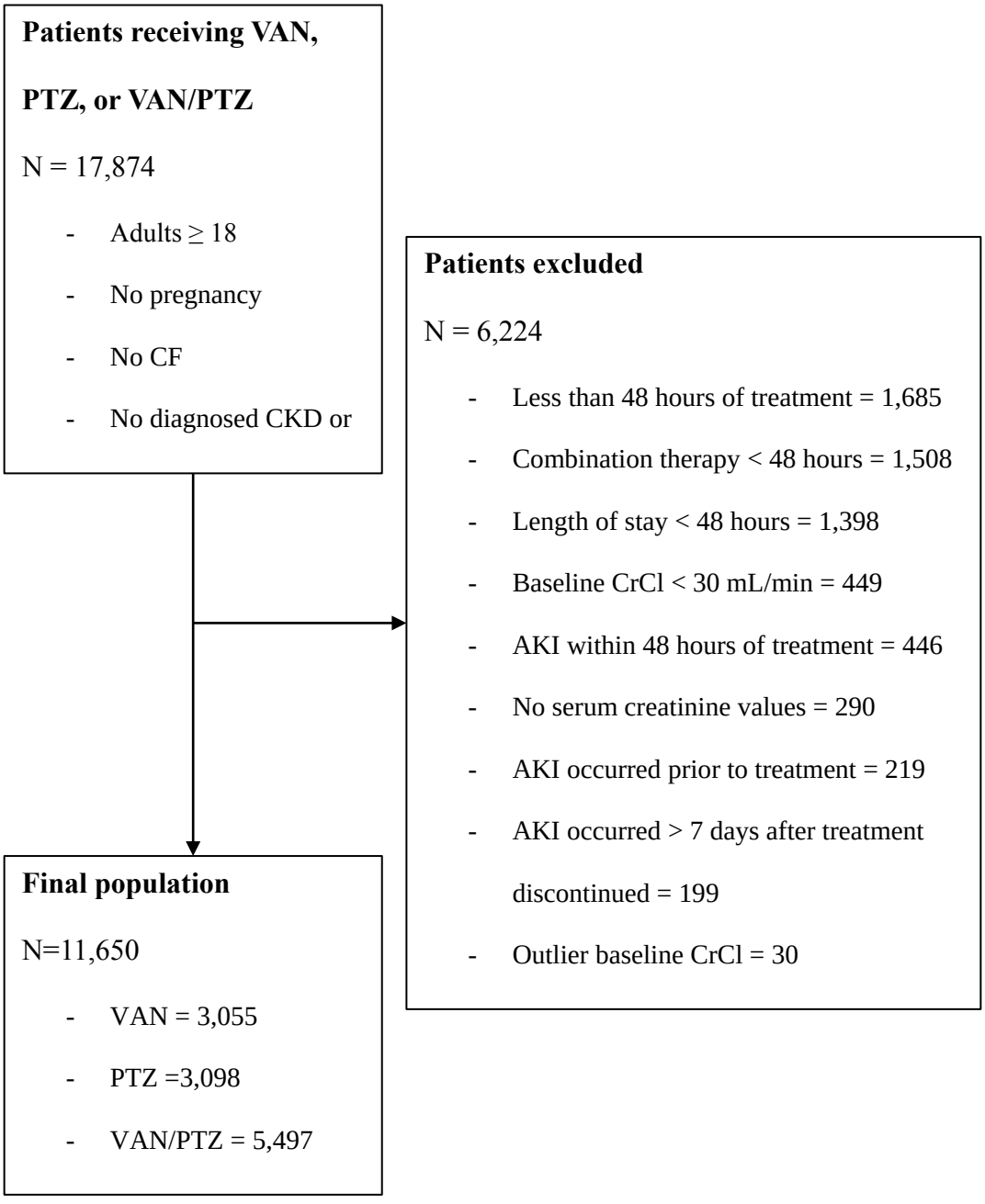


TABLE 1: Baseline patient characteristics

Outcome	**VAN (N=3,055)**	**PTZ (N=3,098)**	**VAN/PTZ (N=5,497)**
Age (years) [Mean (± SD)]	52.5 (16.9)	53.3 (17.5)	52.0 (16.3)
Age group (years)			
18-29	333 (10.9%)	379 (12.2%)	594 (10.8%)
30-49	940 (30.8%)	837 (27.0%)	1736 (31.6%)
50-64	984 (32.2%)	1034 (33.4%)	1904 (34.6%)
65-79	630 (20.6%)	632 (20.4%)	1019 (18.5%)
≥80	168 (5.5%)	216 (7.0%)	244 (4.4%)
Male gender	1462 (47.9%)	1523 (49.2%)	3257 (59.3%)
Charlson Comorbidity Index [Median (IQR)]	2 (0-4)	2 (0-5)	3 (1-5)
Baseline creatinine clearance (mL/min) [Mean (±SD)]*	100.9 (40.4)	100.1 (42.7)	101.9 (43.6)

Outcome	**VAN (N=3,055)**	**PTZ (N=3,098)**	**VAN/PTZ (N=5,497)**
CrCl group (mL/min)			
30-59	394 (12.9%)	528 (17.0%)	855 (15.6%)
60-89	984 (32.2%)	888 (28.7%)	1539 (28.0%)
≥90	1677 (54.9%)	1682 (54.3%)	3103 (56.4%)
Transfer from outside facility	646 (21.1%)	867 (28.0%)	1487 (27.1%)
Admission type			
Elective	904 (29.6%)	398 (12.8%)	644 (11.7%)
Emergency	1329 (43.5%)	1692 (54.6%)	2956 (53.8%)
Trauma	102 (3.3%)	137 (4.4%)	524 (9.5%)
Urgent	720 (23.6%)	871 (28.1%)	1373 (25.0%)
Hypotension exposure	447 (14.6%)	442 (14.3%)	1560 (28.4%)
Dehydration diagnosis	98 (3.2%)	225 (7.3%)	312 (5.7%)
Length of Stay (days) [Median (IQR)]	5 (3-9)	5 (3-9)	7 (4-14)
Total Days of Therapy (days) [Median (IQR)]	3 (2-5)	4 (3-6)	5 (4-8)

Outcome	**VAN (N=3,055)**	**PTZ (N=3,098)**	**VAN/PTZ (N=5,497)**
Length of Stay (days)			
≤7	2084 (68.2%)	2144 (69.2%)	2760 (50.2%)
8-14	596 (19.5%)	641 (20.7%)	1438 (26.2%)
15-21	182 (6.0%)	179 (5.8%)	637 (11.6%)
>21	193 (6.3%)	134 (4.3%)	662 (12.0%)
Nephrotoxic agent exposure	1970 (64.5%)	1434 (46.3%)	3343 (60.8%)
Acyclovir	202 (6.6%)	19 (0.6%)	109 (2.0%)
ACE-inhibitor	595 (19.5%)	545 (17.6%)	1142 (20.8%)
ARB	159 (5.2%)	133 (4.3%)	167 (3.0%)
Aminoglycoside	336 (11.0%)	126 (4.1%)	630 (11.5%)
Amphotericin B	30 (1.0%)	11 (0.4%)	78 (1.4%)
Cyclosporine*	8 (0.3%)	12 (0.4%)	13 (0.2%)
Foscarnet*	4 (0.1%)	1 (0.03%)	5 (0.1%)
Loop diuretic	594 (19.4%)	607 (19.6%)	1828 (33.3%)
NSAID	874 (28.6%)	309 (10.0%)	752 (13.7%)
Sulfonamide	19 (0.6%)	18 (0.6%)	95 (1.7%)
Tacrolimus	34 (1.1%)	75 (2.4%)	108 (2.0%)
Tenofovir*	27 (0.9%)	18 (0.6%)	29 (0.5%)

Footnote for Table 1:

Reported values are N (%) unless otherwise specified; All values are significantly different by standard tests unless denoted by * where $p>0.05$; SD: standard deviation; IQR: interquartile range; CrCl: creatinine clearance; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; NSAID: non-steroidal anti-inflammatory drug

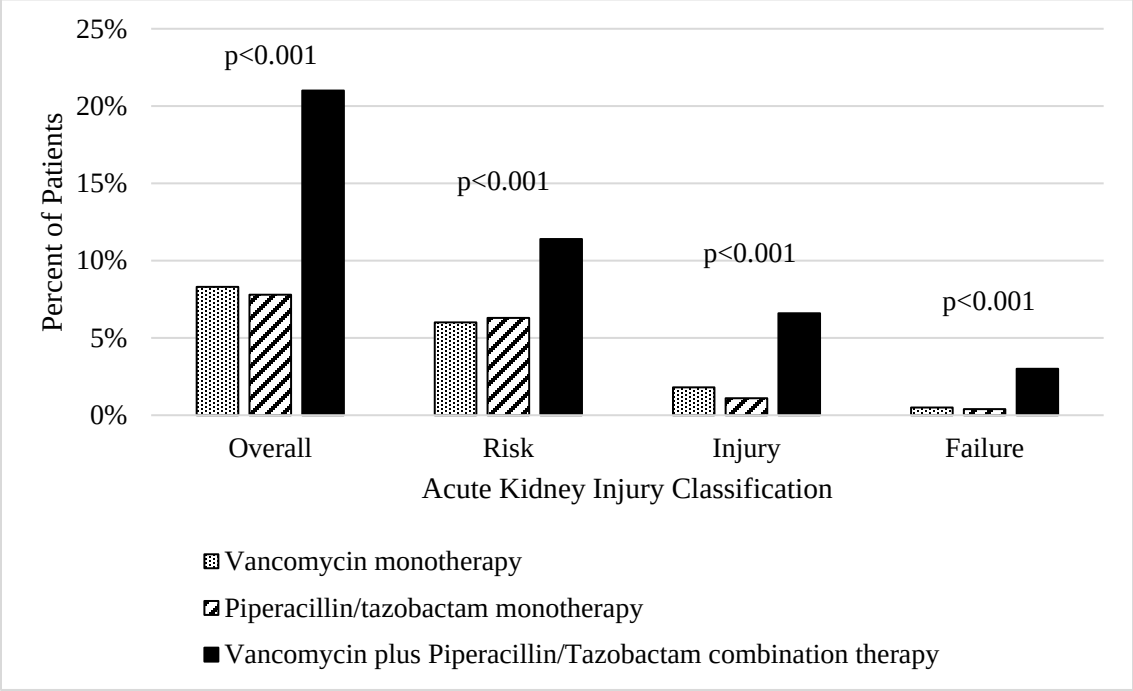
Unadjusted Acute Kidney Injury Incidence

RIFLE-defined AKI occurred in 1,647 (14.1%) across the entire cohort. AKI occurred in 21% of VAN/PTZ patients, 8.3% of VAN patients, and 7.8% of PTZ patients ($p<0.0001$). RIFLE-defined Risk, Injury, and Failure occurred more frequently in the VAN/PTZ cohort compared to the VAN and PTZ monotherapy groups (Figure 2). There were no differences in AKI rates between years studied ($r^2=0.4732$, $p=0.2$). Patients in the VAN/PTZ group experienced AKI on average of 8.0 days after treatment initiation, compared to 8.7 and 5.2 days for VAN and PTZ monotherapy groups, respectively. The composite of in-hospital mortality and transfer to hospice care was more common in VAN/PTZ patients (9.6%) compared to monotherapy groups (VAN 3.9%, PTZ 3.4%), most likely due to the increased severity of illness.

Factors associated with AKI in univariate analyses included treatment with VAN/PTZ, days of therapy, baseline creatinine clearance, transfer from outside hospitals, CCI, admission type, length of hospitalization, dehydration exposure, and hypotension exposure. Exposure to aminoglycosides, amphotericin B, ACE inhibitors, NSAIDs, tacrolimus, foscarnet, loop diuretics, sulfonamides, and tenofovir were all associated with increased odds of AKI in simple univariate logistic regression. Gender, age, year of

treatment, angiotensin II receptor antagonist exposure, and cyclosporine exposure were not significantly associated with AKI incidence.

FIGURE 2: Unadjusted incidence of AKI



Adjusted Acute Kidney Injury Incidence

After multivariate logistic regression, VAN/PTZ therapy was associated with increased odds of AKI compared to VAN and PTZ monotherapies (aOR_{VAN}=2.03; 95% CI_{VAN} 1.74-2.39; aOR_{PTZ}=2.31; 95% CI_{PTZ} 1.97-2.71). No difference in AKI incidence was observed between VAN and PTZ groups ($aOR_{PTZ\ compared\ to\ VAN}$=0.88; 95% CI 0.72-1.07). Table 2 describes the relationship between AKI and other covariates included in the model. Increased odds of AKI were seen with concomitant administration of amphotericin B, tacrolimus, loop diuretics, and tenofovir. Patients admitted urgently and emergently were at higher risk of AKI, while those admitted via the trauma center were less likely to

experience AKI compared to patients who were electively admitted. Increased length of stay and duration of therapy were both associated with increased likelihood of AKI, independent of treatment group; however, durations of therapy beyond 12 days was not associated with increased AKI. Hypotension, as previously defined, and diagnosed dehydration both independently increased AKI odds. Aside from those greater than 80 years old, increasing age was not associated with increased AKI risk. No evidence of overfitting was observed with the standardized Hosmer-Lemeshow p-value of 0.33, and the model provides good predictive accuracy with a c-statistic of 0.787.

TABLE 2: Univariate and multivariate association between combination VAN/PTZ therapy and AKI odds independent of other baseline covariates

Covariate	**Unadjusted**			**Adjusted**		
	OR	***95% CI***	***p***	***OR***	***95% CI***	***p***
Treatment group						
VAN/PTZ		(ref)			(ref)	
PTZ	0.34	0.29 - 0.39	**<0.001**	0.49	0.42 - 0.58	**<0.001**
VAN	0.32	0.27 - 0.37	**<0.001**	0.43	0.37 - 0.51	**<0.001**
Gender						
Female		(ref)				
Male	0.99	0.89 - 1.10	0.896			
Age (years)						
18-29		(ref)			(ref)	
30-49	1.09	0.91 - 1.32	0.361	0.98	0.80 - 1.21	0.862
50-64	1.23	1.02 - 1.48	**0.031**	1.04	0.84 - 1.30	0.697

Covariate	**Unadjusted**			**Adjusted**		
	OR	***95% CI***	***p***	***OR***	***95% CI***	***p***
Age (years)						
65-79	1.11	0.91 - 1.36	0.316	1.17	0.92 - 1.50	0.201
≥ 80	1.12	0.84 - 1.47	0.427	1.8	1.28 - 2.52	**0.001**
CCI (per point)	1.07	1.06 - 1.09	**<0.001**	1.05	1.03 - 1.07	**<0.001**
Baseline CrCl (mL/min)						
30-59		(ref)			(ref)	
60-89	1.02	0.85 - 1.23	0.816	1.4	1.14 - 1.72	**0.002**
≥ 90	1.7	1.45 - 2.01	**<0.001**	3.36	2.75 - 4.14	**<0.001**
Admission type						
Elective		(ref)			(ref)	
Emergency	1.19	1.02 - 1.39	**0.033**	1.21	1.01 - 1.45	**0.038**
Trauma	1.03	0.79 - 1.33	0.82	0.49	0.37 - 0.65	**<0.001**
Urgent	1.63	1.38 - 1.94	**<0.001**	1.39	1.14 - 1.71	**0.001**
Transfer from outside facility	1.56	1.39 - 1.74	**<0.001**	1.14	0.99 - 1.32	0.06
Hypotension exposure	2.81	2.52 - 3.15	**<0.001**	1.59	1.39 - 1.82	**<0.001**
Dehydration exposure	1.29	1.04 - 1.59	**0.018**	1.33	1.05 - 1.68	**0.017**

Covariate	**Unadjusted**			**Adjusted**		
	OR	***95% CI***	***p***	***OR***	***95% CI***	***p***
Nephrotoxic drug exposures						
Acyclovir	1.22	0.90 - 1.63	0.182	1.05	0.75 - 1.44	0.791
Aminoglycoside	1.89	1.62 - 2.20	**<0.001**	1.15	0.96 - 1.38	0.119
Amphotericin B	4.35	2.99 - 6.27	**<0.001**	2.22	1.45 - 3.37	**<0.001**
ACE inhibitor	1.34	1.18 - 1.51	**<0.001**	1.15	1.00 - 1.32	0.052
ARB	0.87	0.65 - 1.15	0.347	1.18	0.86 - 1.60	0.301
Cyclosporine	1.35	0.50 - 3.06	0.506	0.78	0.24 - 2.10	0.642
Foscarnet	6.09	1.69 - 21.92	**0.004**	1.98	0.41 - 9.46	0.387
Loop diuretic	3.51	3.15 - 3.91	**<0.001**	2.04	1.79 - 2.33	**<0.001**
NSAID	0.82	0.71 - 0.95	**0.009**	0.98	0.83 - 1.16	0.848
Sulfonamide	1.8	1.18 - 2.68	**0.005**	1.38	0.86 - 2.15	0.163
Tacrolimus	2.66	1.97 - 3.56	**<0.001**	2.08	1.45 - 2.96	**<0.001**
Tenofovir	1.96	1.12 - 3.28	**0.013**	1.85	1.00 - 3.29	**0.043**
Year of admission						
2010		(ref)				
2011	0.85	0.69 - 1.05	0.127			
2012	0.95	0.78 - 1.18	0.657			
2013	0.87	0.70 - 1.07	0.176			
2014	0.84	0.67 - 1.05	0.121			

Covariate	**Unadjusted**			**Adjusted**		
	OR	***95% CI***	***p***	***OR***	***95% CI***	***p***
Duration of therapy (days)						
2-3		(ref)			(ref)	
4-5	1.81	1.55 - 2.13	**<0.001**	1.32	1.12 - 1.56	**0.001**
6-7	3.23	2.74 - 3.81	**<0.001**	1.79	1.49 - 2.15	**<0.001**
8-9	5.09	4.22 - 6.13	**<0.001**	2	1.61 - 2.48	**<0.001**
10-11	5.94	4.71 - 7.46	**<0.001**	1.95	1.50 - 2.54	**<0.001**
12-13	5.25	3.84 - 7.12	**<0.001**	1.41	0.99 - 1.98	0.054
≥ 14	5.31	4.19 - 6.72	**<0.001**	1.27	0.95 - 1.70	0.107
Length of stay (days)						
≤ 7		(ref)			(ref)	
8-14	3.35	2.94 - 3.81	**<0.001**	2.03	1.74 - 2.36	**<0.001**
15-21	4.48	3.79 - 5.29	**<0.001**	2.28	1.86 - 2.81	**<0.001**
>21	5.88	5.01 - 6.91	**<0.001**	2.72	2.18 - 3.39	**<0.001**

Footnote for Table 2:

PTZ: piperacillin-tazobactam; VAN: vancomycin; VAN/PTZ: vancomycin plus piperacillin-tazobactam; CrCl: creatinine clearance; CCI: Charlson Comorbidity Index; ACE: angiotensin converting enzyme; ARB: angiotensin receptor blocker; NSAID: non-steroidal anti-inflammatory drug

Chapter Four: Conclusions

Summary of Findings

Acute kidney injury secondary to vancomycin therapy is a well characterized adverse effect, while AKI incidence secondary to piperacillin-tazobactam is less understood. Additionally, there appears to be an increased effect when these agents are used in combination. To date, this is the largest review of AKI in patients receiving vancomycin, piperacillin-tazobactam, or the combination of both agents.

There has been a recent surge in evidence suggesting increased nephrotoxicity in patients treated with the combination of vancomycin and anti-pseudomonal beta-lactams. The mechanism for the apparent increase in nephrotoxicity with the combination is not well-understood and needs further study in both animal models and humans.

Acute kidney injury rates related to vancomycin vary widely, with recent studies in critically ill and internal medicine patients estimating rates of 21% and 13.6%, respectively.[2,3] In our vancomycin monotherapy cohort, which includes critically ill patients, the AKI rate was 8.3%, with 2.3% of patients experiencing a greater than 50% decrease in creatinine clearance. Piperacillin-tazobactam-related AKI rates are not well-characterized; however, a small retrospective analysis estimated that 11.1% of piperacillin-tazobactam patients experienced acute renal failure (defined as either increase in serum creatinine $\geq$ 0.5 mg/dL or 50% increase from baseline).[13] In the present study, we found the piperacillin-tazobactam-related AKI rate to be 7.8%, which may be due to a more stringent definition of AKI. Additionally, Hellwig et al [13], found that piperacillin-tazobactam monotherapy was associated with higher AKI rates compared to vancomycin

monotherapy (11.1% vs. 4.9%; p=0.014). This was not replicated in our study, with vancomycin and piperacillin-tazobactam monotherapy having similar AKI rates (8.3% and 7.8%, respectively) and an adjusted odds ratio for AKI between piperacillin-tazobactam and vancomycin of 0.88 (95% CI 0.72-1.07). The estimated AKI incidence in the combination therapy group of 21% at our institution is consistent with prior literature which ranges from 16.3 to 34.8%.[4-8, 13]

Limitations

This study is not without limitations. As with all retrospective studies, it is difficult to determine a causal link between vancomycin and piperacillin-tazobactam combination therapy and increased AKI incidence due to confounding. We employed a rigorous study design that controlled for major confounders of AKI, such as concomitant nephrotoxic exposure, hypotension, and previous renal disease. Nephrotoxic potential of agents was assumed to be equal, which is not necessarily true. Additionally, the binary representation of nephrotoxic exposure does not describe the amount of the agent received; as such, our estimations of AKI odds may be artificially elevated. Approximately one quarter of the patients in this study were transferred from an outside hospital, for which no data regarding initial treatment is available. This may lead to exposure misclassification; however, we attempted to control for this factor in the regression model and found that, after controlling for other covariates, hospital transfer was not associated with odds of AKI. Finally, data was collected retrospectively from the electronic medical record and is subject to inaccuracies documented in the chart; however, any bias introduced should be nondifferential.

Application to Clinical Practice

In our large retrospective study of combination empiric therapy with vancomycin and piperacillin-tazobactam, we found that combination therapy was associated with over double the odds of AKI occurring compared to either monotherapy with vancomycin or piperacillin-tazobactam. Increasing duration of therapy was also associated with increases in AKI. These findings demonstrate the need for judicious use of combination therapy and strengthen the need for antimicrobial de-escalation when appropriate in order to avoid deleterious effects.

Appendix A: R codes

```
#### Acute Kidney injury in Vanc mono vs. PTZ mono vs. PTZ+VAN
meds<-read.csv('../Desktop/AKI         data         files/New_meds.csv',
colClasses='character')
##Cleaning up the medication dataset for better analysis.
meds$drug<-meds$Name                                    ##Using a separate
dataset so nothing is changed in the origninal unintentionally
meds$drug<-sub('Inj\\.','',meds$drug)
meds$drug<-sub('\\(Drip\\)','',meds$drug)
meds$drug<-sub('\\(PEDIATRIC\\)','',meds$drug)
meds$drug<-sub('\\(IntraMuscular\\)','',meds$drug)
meds$drug<-sub('-','',meds$drug)
meds$drug<-sub('Inj','',meds$drug)
library(stringr)                                        ##Load the stringr
package for access to the str_trim which eliminates whitespace
meds$drug<-str_trim(meds$drug)                          ##generated in the
steps above
meds$drug<-sub('zzz','',meds$drug)
meds$drug<-sub('Piperacillin / Tazobactam','PTZ',meds$drug)
library(dplyr)
meds2<-select(meds, Encounter.ID, MRN, drug)
meds2<-unique(meds2)
library(data.table)
meds2<-as.data.table(meds2)
meds3<-dcast.data.table(data = meds2, Encounter.ID+MRN~drug)


for(i in 1:nrow(meds3)){
  if(!is.na(meds3$Cefepime[i])       &       is.na(meds3$PTZ[i])       &
is.na(meds3$Vancomycin[i])){
    meds3$group[i]='CM'
  }
  if(is.na(meds3$Cefepime[i])       &       !is.na(meds3$PTZ[i])       &
is.na(meds3$Vancomycin[i])){
    meds3$group[i]='PM'
  }
  if(is.na(meds3$Cefepime[i])       &       is.na(meds3$PTZ[i])       &
!is.na(meds3$Vancomycin[i])){
    meds3$group[i]='VM'
  }
  if(is.na(meds3$Cefepime[i])       &       !is.na(meds3$PTZ[i])       &
!is.na(meds3$Vancomycin[i])){
    meds3$group[i]='PV'
  }
  if(!is.na(meds3$Cefepime[i])       &       is.na(meds3$PTZ[i])       &
!is.na(meds3$Vancomycin[i])){
    meds3$group[i]='CV'
  }
  if(!is.na(meds3$Cefepime[i])       &       !is.na(meds3$PTZ[i])       &
is.na(meds3$Vancomycin[i])){
    meds3$group[i]='CP'
  }
  if(!is.na(meds3$Cefepime[i])       &       !is.na(meds3$PTZ[i])       &
!is.na(meds3$Vancomycin[i])){
    meds3$group[i]='CVP'
  }
```

```
}

demo<-read.csv('../Desktop/AKI          data          files/demo.csv',
colClasses='character')    ##Imports RAW files
demo<-demo[demo$ENCNTR_ID %in% meds3$Encounter.ID,]
demo$EID<-demo$ENCNTR_ID
demo$ENCNTR_ID<-NULL
meds3$EID<-meds3$Encounter.ID
meds4<-select(meds3, EID, group)
demo2<-merge(demo, meds4, by='EID')
dat<-demo2[demo2$group %in% c('PM','PV','VM'),]
dat$AGE<-as.numeric(dat$AGE)
dat<-dat[dat$AGE>=18,]
dat$LENGTH_OF_STAY_NUM<-as.numeric(dat$LENGTH_OF_STAY_NUM)
dat<-dat[dat$LENGTH_OF_STAY_NUM>=2,]
meds<-meds[meds$Encounter.ID %in% demo2$EID,]

labs<-read.csv('../Desktop/AKI      data      files/New      Labs.csv',
colClasses='character')
labs<-labs[labs$ENCNTR_ID %in% dat$EID,]
scr<-labs[grepl('creatinine level', labs$ITEM_NAME, ignore.case = T),]
scr$date<-as.POSIXct(scr$ENTRD_DT_TM, format="%m/%d/%Y %I:%M:%S %p")
scr$VAL_NUM<-as.numeric(scr$VAL_NUM)
scr<-scr[!is.na(scr$VAL_NUM),]
scr$EID<-scr$ENCNTR_ID

dat<-dat[dat$EID %in% scr$EID,]

for(i in 1:nrow(dat)){
  x<-scr[scr$EID == dat$EID[i],]
  dat$baseline_scr_date[i]<-as.character(min(x$date))
  dat$baseline_scr[i]<-x$VAL_NUM[x$date==min(x$date)]
}

for(i in 1:nrow(dat)){
  x<-scr[scr$EID==dat$EID[i],]
  dat$max_scr_date[i]<-as.character(x$date[x$VAL_NUM==max(x$VAL_NUM,
na.rm=T)])
  dat$max_scr[i]<-max(x$VAL_NUM, na.rm=T)
}

class(meds$Performed.Date.Time)
meds$date<-sapply(strsplit(x  =  meds$Performed.Date.Time,  split  =  '
'),'[',1)
van<-meds[grepl('vancomycin', ignore.case = T, meds$drug),]
ptz<-meds[grepl('PTZ', meds$drug),]

for( i in 1:nrow(dat)){
  medx<-meds[meds$Encounter.ID == dat$EID[i],]
  dat$Total_DOT[i]<-length(unique(medx$date))
}

for(i in 1:nrow(dat)){
  if(dat$group[i]=='PV'){
    vanx<-van[van$Encounter.ID == dat$EID[i],]
    ptzx<-ptz[ptz$Encounter.ID == dat$EID[i],]
    dat$Van_DOT[i]<-length(unique(vanx$date))
```

```
    dat$PTZ_DOT[i]<-length(unique(ptzx$date))
  }
  if(dat$group[i]=='PM'){
    dat$Van_DOT[i]<-NA
    dat$PTZ_DOT[i]<-dat$Total_DOT[i]
  }
  if(dat$group[i]=='VM'){
    dat$PTZ_DOT[i]<-NA
    dat$Van_DOT[i]<-dat$Total_DOT[i]
  }
}

medstest<-meds[meds$Encounter.ID %in% dat$EID,]
dot(medstest)
library(plyr)
dot2<-ldply(DOT_list)
dot3<-select(dot2, V1,V5)
dot3$EID<-dot3$V1
dot3$Combo_DOT<-dot3$V5
dot3$V1<-NULL
dot3$V5<-NULL
dat<-merge(dat, dot3, by='EID')

dat<-dat[dat$Total_DOT>=2,]


for(i in 1:nrow(dat)){
  if(dat$GENDER[i]=='UNKNOWN'){
    dat$GENDER[i]<-'MALE'
  }
}
dat$baseline_scr<-as.numeric(dat$baseline_scr)
dat$max_scr<-as.numeric(dat$max_scr)

for(i in 1:nrow(dat)){
  dat$baseline_crcl[i]<-(140-dat$AGE[i])/dat$baseline_scr[i]
  dat$min_crcl[i]<-(140-dat$AGE[i])/dat$max_scr[i]
  if(dat$GENDER[i]=='FEMALE'){
    dat$baseline_crcl[i]<-dat$baseline_crcl[i]*0.85
    dat$min_crcl[i]<-dat$min_crcl[i]*0.85
  }
}

dat$percent_change<-(dat$min_crcl/dat$baseline_crcl-1)*100
for(i in 1:length(dat$EID)){                                    ##assign
RIFLE labels to appropriate degrees of renal impairment
  if (dat$percent_change[i]>=0){                                  ##if
percent_change is >=0, the max SCr is equal to baseline, suggesting GFR
improvement
    dat$RIFLE[i]<-"No injury"
  }
  else {
    if (abs(dat$percent_change[i])<25){
      dat$RIFLE[i]<-'No injury'
    }
    if (abs(dat$percent_change[i])>=25 & abs(dat$percent_change[i])<50){
      dat$RIFLE[i] <-'RISK'
```

```
    }
    if (abs(dat$percent_change[i])>=50 & abs(dat$percent_change[i])<75){
      dat$RIFLE[i] <-'INJURY'
    }
    if (abs(dat$percent_change[i])>=75){
      dat$RIFLE[i] <- 'Failure'
    }
  }
}

for(i in 1:length(dat$EID)){                                          ##Assigns
binary outcome for AKI (Risk, Injury, Failure) vs No AKI
  if(dat$RIFLE[i] =='No injury'){                                        ##Can
convert to a 0/1 answer for modeling.
    dat$AKI[i]<-"No AKI"
  }
  else{
    dat$AKI[i]<-'AKI'
  }
}

dat$van_start<-NA
dat$ptz_start<-NA
ptz$date<-as.Date(ptz$date, format='%m/%d/%Y')
van$date<-as.Date(van$date, format='%m/%d/%Y')


for(i in 1:nrow(dat)){
  if(dat$group[i]=='PM'){
    #x<-van[van$Encounter.ID==dat$EID[i],]
    #x<-x[!is.na(x$date),]
    #dat$van_start[i]<-as.character(min(x$date))
    y<-ptz[ptz$Encounter.ID==dat$EID[i],]
    y<-y[!is.na(y$date),]
    dat$ptz_start[i]<-as.character(min(y$date))
    dat$van_start[i]<-NA
  }
  if(dat$group[i]=='VM'){
    x<-van[van$Encounter.ID==dat$EID[i],]
    x<-x[!is.na(x$date),]
    dat$van_start[i]<-as.character(min(x$date))
    dat$ptz_start[i]<-NA
    #y<-ptz[ptz$Encounter.ID==dat$EID[i],]
    #y<-y[!is.na(y$date),]
    #dat$ptz_start[i]<-as.character(min(y$date))
  }
  if(dat$group[i]=='PV'){
    x<-van[van$Encounter.ID==dat$EID[i],]
    x<-x[!is.na(x$date),]
    dat$van_start[i]<-as.character(min(x$date))
    y<-ptz[ptz$Encounter.ID==dat$EID[i],]
    y<-y[!is.na(y$date),]
    dat$ptz_start[i]<-as.character(min(y$date))
  }
}

dat$ptz_start<-as.Date(dat$ptz_start)
```

```
dat$van_start<-as.Date(dat$van_start)

for(i in 1:nrow(dat)){
  dat$tx_index[i]<-as.character(min(dat$van_start[i],  dat$ptz_start[i],
na.rm = T))
}
dat$tx_index<-as.Date(dat$tx_index)

for(i in 1:nrow(dat)){
  if(dat$group[i]=='PM' | dat$group[i]=='VM'){
    dat$Combo_DOT[i]<-NA
  }
}

dat<-dat[dat$Combo_DOT>=2 | is.na(dat$Combo_DOT),]
crclcut<-mean(dat$baseline_crcl)+4*sd(dat$baseline_crcl)
dat<-dat[dat$baseline_crcl<=crclcut,]
dat<-dat[dat$baseline_crcl>=30,]

dat$max_scr_date2<-sapply(strsplit(dat$max_scr_date, ' '),'[',1)
dat$max_scr_date2<-as.Date(dat$max_scr_date2)


for(i in 1:nrow(dat)){
  if(dat$max_scr_date2[i] < dat$tx_index[i]){
    dat$aki_before_tx[i]<-'Y'
  }
  else{
    dat$aki_before_tx[i]<-'N'
  }
}

dat<-dat[!(dat$aki_before_tx=='Y' & dat$AKI=='AKI'),]

for(i in 1:nrow(dat)){
  if(dat$AKI[i]=='No AKI'){
    dat$time_to_aki[i]<-NA
  }
  else{
    dat$time_to_aki[i]<-as.numeric(dat$max_scr_date2[i]-
dat$tx_index[i])
  }
}

dat_b<-dat
dat<-dat[dat$time_to_aki>=2 | is.na(dat$time_to_aki),]


dat$van_end<-NA
dat$ptz_end<-NA

for(i in 1:nrow(dat)){
  if(dat$group[i]=='VM'){
    x<-van[van$Encounter.ID==dat$EID[i],]
    x<-x[!is.na(x$date),]
    dat$van_end[i]<-as.character(max(x$date))
    dat$ptz_end[i]<-NA
```

```
  }
  if(dat$group[i]=='PM'){
    dat$van_end[i]<-NA
    y<-ptz[ptz$Encounter.ID==dat$EID[i],]
    y<-y[!is.na(y$date),]
    dat$ptz_end[i]<-as.character(max(y$date))
  }
  if(dat$group[i]=='PV'){
    x<-van[van$Encounter.ID==dat$EID[i],]
    x<-x[!is.na(x$date),]
    dat$van_end[i]<-as.character(max(x$date))
    y<-ptz[ptz$Encounter.ID==dat$EID[i],]
    y<-y[!is.na(y$date),]
    dat$ptz_end[i]<-as.character(max(y$date))
  }
}

dat$van_end<-as.Date(dat$van_end)
dat$ptz_end<-as.Date(dat$ptz_end)
for(i in 1:nrow(dat)){
  dat$tx_end[i]<-as.character(max(dat$van_end[i], dat$ptz_end[i], na.rm
= T))
}
dat$tx_end<-as.Date(dat$tx_end)
for( i in 1:nrow(dat)){
  if(as.numeric(dat$tx_end[i] - dat$max_scr_date2[i])> 7){
    dat$aki_out_range[i]<-'Y'
  }
  else{
    dat$aki_out_range[i]<-'N'
  }
}

dat<-dat[!(dat$aki_out_range=='Y' & dat$AKI=='AKI'),]


for(i                          in                          1:length(dat$EID)){
##gives a single Y/N variable for occurence of hypotension

ifelse(dat$MEAN_ARTERIAL_UNDER_60_FLG[i]=='Y'|dat$HYPOTENSION_FLG[i]=='
Y'|   ##this excludes SBP < 100 mmHg flag as this really isn't defensible
          dat$VASOPRESSORS_FLG[i]=='Y'|dat$INOTROPES_FLG[i]=='Y',
        dat$hypotension[i]<-'Y',dat$hypotension[i]<-'N')
}

for(i in 1:length(dat$EID)){                                          ##Y/N
for nephrotoxic drug exposure. Does not give a count.
  ifelse(dat$ACYCLOVIR_FLG[i]=='Y'|
dat$AMINOGLYCOSIDES_FLG[i]=='Y'|dat$AMPHOTERICIN_B_FLG[i]=='Y'|
          dat$ANGIOTENSIN_FLG[i]=='Y'|
dat$ANGIOTENSION_FLG[i]=='Y'|dat$COLISTIN_FLG[i]=='Y' |
          dat$CYCLOSPORINE_FLG[i]=='Y'|      dat$FOSCARNET_FLG[i]=='Y'|
dat$LOOP_DIURETICS_FLG[i]=='Y'|
          dat$NON_STEROIDAL_ANTI_FLG[i]=='Y'|
dat$SULFONAMIDES_FLG[i]=='Y'| dat$TACROLIMUS_FLG[i]=='Y'|
          dat$TENOFOVIR_FLG[i]=='Y',dat$nephrotoxic_drug[i]<-
"Y",dat$nephrotoxic_drug[i]<-"N")
```

```
}

labs<-labs[labs$ENCNTR_ID %in% dat$EID,]
meds<-meds[meds$Encounter.ID %in% dat$EID,]
ptz<-meds[meds$drug=='PTZ',]
van<-meds[meds$drug=='Vancomycin',]

dat$year<-sapply(strsplit(as.character(dat$tx_index), '-',),'[',1)

van$Dose<-as.numeric(van$Dose)
for(i in 1:nrow(van)){
  if(van$UOM[i]=='gram'){
    van$Dose[i]<-van$Dose[i]*1000
    van$UOM[i]<-'MG'
  }
}

for(i in 1:nrow(van)){
  if(van$Dose[i]==1){
    van$Dose[i]<-1000
  }
  if(van$Dose[i]==100){
    van$Dose[i]<-1500
  }
}

van$date<-sapply(strsplit(van$Performed.Date.Time, ' '),'[',1)
van$date<-as.Date(van$date, format='%m/%d/%Y')

for(i in 1:nrow(dat)){
  if(dat$group[i]=='PM'){
    dat$avg_daily_van_dose[i]<-NA
  }
  if(dat$group[i] %in% c('PV','VM')){
    x<-van[van$Encounter.ID==dat$EID[i],]
    dat$avg_daily_van_dose[i]<-mean(by(x$Dose, x$date, sum))
  }
}

labs<-labs[labs$ENCNTR_ID %in% dat$EID,]
vtr<-labs[grepl('trough', labs$ITEM_NAME, ignore.case = T),]
vtr$VAL_NUM<-as.numeric(vtr$VAL_NUM)
vtr$date<-sapply(strsplit(vtr$ENTRD_DT_TM, ' '), '[',1)
vtr$date<-as.Date(vtr$date, format='%m/%d/%Y')
vtr<-vtr[!is.na(vtr$VAL_NUM),]

for(i in 1:nrow(dat)){
  if(!(dat$EID[i] %in% vtr$ENCNTR_ID)){
    dat$first_van_tr[i]<-NA
    dat$first_van_tr_date[i]<-NA
    dat$max_van_tr[i]<-NA
    dat$max_van_tr_date[i]<-NA
  }
  if(dat$EID[i] %in% vtr$ENCNTR_ID){
    x<-vtr[vtr$ENCNTR_ID==dat$EID[i],]
    dat$first_van_tr[i]<-x$VAL_NUM[x$date==min(x$date)]
    dat$first_van_tr_date[i]<-as.character(min(x$date))
```

```
    dat$max_van_tr[i]<-max(x$VAL_NUM)
    dat$max_van_tr_date[i]<-
as.character(x$date[x$VAL_NUM==max(x$VAL_NUM)])
  }
}
dat$max_van_tr<-as.numeric(dat$max_van_tr)
dat$first_van_tr<-as.numeric(dat$first_van_tr)

for(i in 1:nrow(dat)){
  if(!is.na(dat$first_van_tr[i])){
    if(dat$first_van_tr[i]<10){
      dat$first_van_tr_class[i]<-'subtherapeutic'
    }
    if(dat$first_van_tr[i]<15 & dat$first_van_tr[i]>=10){
      dat$first_van_tr_class[i]<-'therapeutic_low'
    }
    if(dat$first_van_tr[i]<=20 & dat$first_van_tr[i]>=15){
      dat$first_van_tr_class[i]<-'therapeutic_high'
    }
    if(dat$first_van_tr[i]>20){
      dat$first_van_tr_class[i]<-'supratherapeutic'
    }
  }
  if(!is.na(dat$max_van_tr[i])){
    if(dat$max_van_tr[i]<10){
      dat$max_van_tr_class[i]<-'subtherapeutic'
    }
    if(dat$max_van_tr[i]<15 & dat$max_van_tr[i]>=10){
      dat$max_van_tr_class[i]<-'therapeutic_low'
    }
    if(dat$max_van_tr[i]<=20 & dat$max_van_tr[i]>=15){
      dat$max_van_tr_class[i]<-'therapeutic_high'
    }
    if(dat$max_van_tr[i]>20){
      dat$max_van_tr_class[i]<-'supratherapeutic'
    }
  }
}

for(i in 1:nrow(dat)){
  if(is.na(dat$max_van_tr[i])){
    dat$max_van_tr_class[i]<-NA
    dat$first_van_tr_class[i]<-NA
  }
}

for(i in 1:nrow(dat)){
  if(dat$baseline_crcl[i]>=90){
    dat$baseline_crcl_group[i]<-'>=90'
    dat$baseline_crcl_group_num[i]<-'1'
  }
  if(dat$baseline_crcl[i]<90 & dat$baseline_crcl[i]>=60){
    dat$baseline_crcl_group[i]<-'>=60 to <90'
    dat$baseline_crcl_group_num[i]<-'2'
  }
  if(dat$baseline_crcl[i]<60 & dat$baseline_crcl[i]>=30){
    dat$baseline_crcl_group[i]<-'>=30 to <60'
```

```
    dat$baseline_crcl_group_num[i]<-'3'
  }
}

for(i in 1:nrow(dat)){
  if(dat$AKI[i] =='AKI'){
    dat$aki_num[i]<-1
  }
  else{
    dat$aki_num[i]<-0
  }
}

for(i in 1:nrow(dat)){
  if(grepl('TRANS', dat$ADMT_SRC_CD_DES[i])){
    dat$transfer[i]<-1
  }
  else{
    dat$transfer[i]<-0
  }
}

for(i in 1:nrow(dat)){
  if(grepl('HOSPICE',         dat$DISCHRG_DES[i])|         grepl('DEATH',
dat$DISCHRG_DES[i])){
    dat$mortality[i]<-1
  }
  else{
    dat$mortality[i]<-0
  }
}
dat$TOTAL_CHARLSON_SCORE<-as.numeric(dat$TOTAL_CHARLSON_SCORE)

for(i in 1:nrow(dat)){
  if(dat$AGE[i]>=65){
    dat$age_65[i]<-'Y'
  }
  else{
    dat$age_65[i]<-'N'
  }
}

for(i in 1:nrow(dat)){
  if(dat$AGE[i]<30){
    dat$age_group[i]<-'<30'
  }
  if(dat$AGE[i]>=30 & dat$AGE[i]<50){
    dat$age_group[i]<-'30 to <50'
  }
  if(dat$AGE[i]>=50 & dat$AGE[i]<65){
    dat$age_group[i]<-'50 to <65'
  }
  if(dat$AGE[i]>=65 & dat$AGE[i]<80){
    dat$age_group[i]<-'65 to <80'
  }
  if(dat$AGE[i]>=80){
    dat$age_group[i]<-'>=80'
```

```
  }
}
for(i in 1:nrow(dat)){
  if(dat$LENGTH_OF_STAY_NUM[i]>7){
    dat$los_7[i]<-'Y'
  }
  else{
    dat$los_7[i]<-'N'
  }
}
dat$los_weeks<-dat$LENGTH_OF_STAY_NUM/7

for(i in 1:nrow(dat)){
  if(dat$LENGTH_OF_STAY_NUM[i]<=7){
    dat$los_group[i]<-'<=7'
  }
  if(dat$LENGTH_OF_STAY_NUM[i]>7 & dat$LENGTH_OF_STAY_NUM[i]<=14){
    dat$los_group[i]<-'8-14'
  }
  if(dat$LENGTH_OF_STAY_NUM[i]>14 & dat$LENGTH_OF_STAY_NUM[i]<=21){
    dat$los_group[i]<-'15-21'
  }
  if(dat$LENGTH_OF_STAY_NUM[i]>21){
    dat$los_group[i]<-'>21'
  }
}

for(i in 1:nrow(dat)){
  if(dat$ANGIOTENSIN_FLG[i] =='Y' | dat$ANGIOTENSION_FLG[i]=='Y'){
    dat$ace.arb[i]<-'Y'
  }
  else{
    dat$ace.arb[i]<-'N'
  }
}

for(i in 1:nrow(dat)){
  if(dat$TACROLIMUS_FLG[i] =='Y' | dat$CYCLOSPORINE_FLG[i]=='Y'){
    dat$tac.cyc[i]<-'Y'
  }
  else{
    dat$tac.cyc[i]<-'N'
  }
}

#begin simple models
x<-'binomial'
age<-glm(aki_num~AGE, family='binomial') #AGE as continuous variable
age65<-glm(aki_num~age_65, family='binomial', data=dat) # age as binary
>=65 variable
agegroup<-glm(aki_num~age_group, family='binomial', data=dat)
gender<-glm(aki_num~GENDER, family='binomial', data=dat)
cci<-glm(aki_num~TOTAL_CHARLSON_SCORE, family = 'binomial', data=dat)
adsrc<-glm(aki_num~ADMT_SRC_CD_DES,  family='binomial',  data=dat)  #ugly
regression use adtype
adtype<-glm(aki_num~ADMT_TYP_CD_DES, family=x, data=dat)
los<-glm(aki_num~LENGTH_OF_STAY_NUM, family=x, data=dat)
```

```
los7<-glm(aki_num~los_7, family=x, data=dat)
losw<-glm(aki_num~los_weeks, family=x, data=dat)
losg<-glm(aki_num~los_group, family=x, data=dat)
map<-glm(aki_num~MEAN_ARTERIAL_UNDER_60_FLG, family=x, data=dat)
dehy<-glm(aki_num~DEHYDRATION_FLG, family=x, data=dat)
hypof<-glm(aki_num~HYPOTENSION_FLG, family=x, data=dat)
acy<-glm(aki_num~ACYCLOVIR_FLG, family=x, data=dat)
ag<-glm(aki_num~AMINOGLYCOSIDES_FLG, family=x, data=dat)
ab<-glm(aki_num~AMPHOTERICIN_B_FLG, family=x, data=dat)
ace<-glm(aki_num~ANGIOTENSIN_FLG,family=x, data=dat)
arb<-glm(aki_num~ANGIOTENSION_FLG, family=x, data=dat)
acearb<-glm(aki_num~ace.arb, family=x, data=dat)
cyc<-glm(aki_num~CYCLOSPORINE_FLG, family=x, data=dat)
tac<-glm(aki_num~TACROLIMUS_FLG, family=x, data=dat)
taccyc<-glm(aki_num~tac.cyc, family=x, data=dat)
fos<-glm(aki_num~FOSCARNET_FLG, family=x, data=dat)
loop<-glm(aki_num~LOOP_DIURETICS_FLG, family=x, data=dat)
nsaids<-glm(aki_num~NON_STEROIDAL_ANTI_FLG, family=x, data=dat)
sulf<-glm(aki_num~SULFONAMIDES_FLG, family=x, data=dat)
ten<-glm(aki_num~TENOFOVIR_FLG, family=x, data=dat)
vas<-glm(aki_num~VASOPRESSORS_FLG, family=x, data=dat)
ino<-glm(aki_num~INOTROPES_FLG, family=x, data=dat)
txgroup<-glm(aki_num~group, family=x, data=dat)
tdot<-glm(aki_num~Total_DOT, family=x, data=dat)
vdot<-glm(aki_num~Van_DOT, x, dat)
pdot<-glm(aki_num~PTZ_DOT, x, dat)
crcl<-glm(aki_num~baseline_crcl, x, dat)
crclg<-glm(aki_num~factor(baseline_crcl_group),x,dat)
hypoc<-glm(aki_num~hypotension, x, dat)
neph<-glm(aki_num~nephrotoxic_drug, x, dat)
yr<-glm(aki_num~factor(year), x, dat)
vd<-glm(aki_num~avg_daily_van_dose, x, dat)
dat$avd_grams<-dat$avg_daily_van_dose/1000
vdg<-glm(aki_num~avd_grams, x, dat)
trans<-glm(aki_num~transfer, x, dat)

dat$group<-relevel(dat$group, ref = 'PV')

model1lrm<-
lrm(aki_num~group+age_65+TOTAL_CHARLSON_SCORE+transfer+DEHYDRATION_FLG+
ACYCLOVIR_FLG+AMINOGLYCOSIDES_FLG+AMPHOTERICIN_B_FLG+ANGIOTENSIN_FLG
              +
LOOP_DIURETICS_FLG+TACROLIMUS_FLG+Total_DOT+baseline_crcl_group+hypoten
sion, data=dat)
model1glm<-
glm(aki_num~group+age_65+TOTAL_CHARLSON_SCORE+transfer+DEHYDRATION_FLG+
ACYCLOVIR_FLG+AMINOGLYCOSIDES_FLG+AMPHOTERICIN_B_FLG+ANGIOTENSIN_FLG
              +
LOOP_DIURETICS_FLG+TACROLIMUS_FLG+Total_DOT+baseline_crcl_group+hypoten
sion, data=dat, x)

compmodelglm<-glm(aki_num~group       +       factor(age_group)       +
TOTAL_CHARLSON_SCORE+ factor(baseline_crcl_group)+ transfer+hypotension+
GENDER+

year+factor(los_group)+DEHYDRATION_FLG+ACYCLOVIR_FLG+AMINOGLYCOSIDES_FL
G+ AMPHOTERICIN_B_FLG+
```

```
ace.arb+tac.cyc+FOSCARNET_FLG+LOOP_DIURETICS_FLG+NON_STEROIDAL_ANTI_FLG
+SULFONAMIDES_FLG+
                    TENOFOVIR_FLG+Total_DOT+nephrotoxic_drug, x, dat)
compmodellrm<-lrm(aki_num~group       +       factor(age_group)       +
TOTAL_CHARLSON_SCORE+ factor(baseline_crcl_group)+ transfer+hypotension+
GENDER+

year+factor(los_group)+DEHYDRATION_FLG+ACYCLOVIR_FLG+AMINOGLYCOSIDES_FL
G+ AMPHOTERICIN_B_FLG+

ace.arb+tac.cyc+FOSCARNET_FLG+LOOP_DIURETICS_FLG+NON_STEROIDAL_ANTI_FLG
+SULFONAMIDES_FLG+
                    TENOFOVIR_FLG+Total_DOT+nephrotoxic_drug, dat)

compsteplrm<-lrm(aki_num     ~     group     +     factor(age_group)     +
TOTAL_CHARLSON_SCORE +
                   factor(baseline_crcl_group) + transfer + hypotension
+ GENDER +
                   year   +   factor(los_group)   +   DEHYDRATION_FLG   +
AMPHOTERICIN_B_FLG +
                   tac.cyc + LOOP_DIURETICS_FLG + NON_STEROIDAL_ANTI_FLG
+ TENOFOVIR_FLG +
                   Total_DOT + nephrotoxic_drug, dat)

finmodel1glm<-glm(aki_num     ~     group     +     factor(age_group)     +
TOTAL_CHARLSON_SCORE +
                    factor(baseline_crcl_group) + transfer + hypotension
+ GENDER +
                    factor(year) + factor(los_group) + DEHYDRATION_FLG +
AMPHOTERICIN_B_FLG +
                    tac.cyc        +        LOOP_DIURETICS_FLG        +
NON_STEROIDAL_ANTI_FLG + TENOFOVIR_FLG +
                    Total_DOT,x, dat)
finmodel2lglm<-glm(aki_num~group       +       factor(age_group)       +
TOTAL_CHARLSON_SCORE+ factor(baseline_crcl_group)+ transfer+hypotension+
GENDER+

factor(year)+factor(los_group)+DEHYDRATION_FLG+ACYCLOVIR_FLG+AMINOGLYCO
SIDES_FLG+ AMPHOTERICIN_B_FLG+

ace.arb+tac.cyc+FOSCARNET_FLG+LOOP_DIURETICS_FLG+NON_STEROIDAL_ANTI_FLG
+SULFONAMIDES_FLG+
                     TENOFOVIR_FLG+Total_DOT, x, dat)
finmodel2lglm2<-glm(aki_num~group       +       factor(age_group)       +
TOTAL_CHARLSON_SCORE+ factor(baseline_crcl_group)+ transfer+hypotension+
GENDER+

factor(year)+factor(los_group)+DEHYDRATION_FLG+Total_DOT+nephrotoxic_dr
ug, x, dat)

finmodel2lrm<-lrm(aki_num~group       +       factor(age_group)       +
TOTAL_CHARLSON_SCORE+ factor(baseline_crcl_group)+ transfer+hypotension+
GENDER+

factor(year)+factor(los_group)+DEHYDRATION_FLG+ACYCLOVIR_FLG+AMINOGLYCO
SIDES_FLG+ AMPHOTERICIN_B_FLG+
```

```
ace.arb+tac.cyc+FOSCARNET_FLG+LOOP_DIURETICS_FLG+NON_STEROIDAL_ANTI_FLG
+SULFONAMIDES_FLG+
                    TENOFOVIR_FLG+Total_DOT, dat)
finmodel2lrm2<-lrm(aki_num~group       +       factor(age_group)       +
TOTAL_CHARLSON_SCORE+ factor(baseline_crcl_group)+ transfer+hypotension+
GENDER+

factor(year)+factor(los_group)+DEHYDRATION_FLG+Total_DOT+nephrotoxic_dr
ug, dat)


dat$dc_date<-sapply(strsplit(dat$DISCHRG_DT, ' '),'[',1)
dat$dc_date<-as.Date(dat$dc_date, format='%m/%d/%Y')
dat$starttime<-0
for(i in 1:nrow(dat)){
  if(dat$AKI[i]=='No AKI'){
    dat$stoptime[i]<-as.numeric(dat$dc_date[i]-dat$tx_index[i])
  }
  if(dat$AKI[i]=='AKI'){
    dat$stoptime[i]<-as.numeric(dat$time_to_aki[i])
  }
}

for(i in 1:nrow(dat)){
  if(dat$AKI[i]=='No AKI'){
    dat$stoptime2[i]<-min(as.numeric(dat$tx_end[i]-dat$tx_index[i])+7,
as.numeric(dat$dc_date[i]-dat$tx_index[i]) )
  }
  if(dat$AKI[i]=='AKI'){
    dat$stoptime2[i]<-as.numeric(dat$time_to_aki[i])
  }
}

cxmod<-
coxph(S~group+factor(age_group)+nephrotoxic_drug+hypotension+DEHYDRATIO
N_FLG+

TOTAL_CHARLSON_SCORE+factor(baseline_crcl_group)+GENDER+factor(year),
data=dat)

dat_b<-dat
dat$age_group<-as.factor(dat$age_group)
treat<-with(dat, data.frame(group=levels(group),
                            age_group=rep(levels(age_group)[1],3),

nephrotoxic_drug=rep('N',3),#rep(levels(nephrotoxic_drug)[1],3),
                            hypotension=rep('N',3),
                            DEHYDRATION_FLG=rep('N',3),

TOTAL_CHARLSON_SCORE=rep(mean(TOTAL_CHARLSON_SCORE),3),

baseline_crcl_group=rep(levels(baseline_crcl_group)[1],3),
                            GENDER=rep("MALE",3),
                            year=rep(levels(year)[1],3)
                            #los_group=rep(levels(los_group)[1],3),
                            #Total_DOT=rep(mean(Total_DOT),3)
```

```
))
plot(survfit(cxmod, newdata = treat),
     col=c('red','blue', 'green'),
     xlab='Days after treatment initiation',
     ylab='Proportion without AKI',
     conf.int=F)
legend('bottomright',   c('PTZ/VAN',   'PTZ',   'VM'),lty=1,col=c('red',
'blue','green'))


finmodel2glm<-glm(aki_num~group       +       factor(age_group)       +
TOTAL_CHARLSON_SCORE+ factor(baseline_crcl_group)+ transfer+hypotension+
GENDER+

factor(los_group)+DEHYDRATION_FLG+ACYCLOVIR_FLG+AMINOGLYCOSIDES_FLG+
AMPHOTERICIN_B_FLG+

ace.arb+tac.cyc+FOSCARNET_FLG+LOOP_DIURETICS_FLG+NON_STEROIDAL_ANTI_FLG
+SULFONAMIDES_FLG+
                     TENOFOVIR_FLG+Total_DOT, x, dat)

finmodel2lrm<-lrm(aki_num~group       +       factor(age_group)       +
TOTAL_CHARLSON_SCORE+ factor(baseline_crcl_group)+ transfer+hypotension+
GENDER+

factor(los_group)+DEHYDRATION_FLG+ACYCLOVIR_FLG+AMINOGLYCOSIDES_FLG+
AMPHOTERICIN_B_FLG+

ace.arb+tac.cyc+FOSCARNET_FLG+LOOP_DIURETICS_FLG+NON_STEROIDAL_ANTI_FLG
+SULFONAMIDES_FLG+
                    TENOFOVIR_FLG+Total_DOT, dat)

for(i in 1:nrow(dat)){
  if(dat$Total_DOT[i]<=3){
    dat$tdot_group[i]<-'2-3'
  }
  if(dat$Total_DOT[i]>=4 & dat$Total_DOT[i]<6){
    dat$tdot_group[i]<-'4-5'
  }
  if(dat$Total_DOT[i]>=6 & dat$Total_DOT[i]<8){
    dat$tdot_group[i]<-'6-7'
  }
  if(dat$Total_DOT[i]>=8 & dat$Total_DOT[i]<10){
    dat$tdot_group[i]<-'8-9'
  }
  if(dat$Total_DOT[i]>=10 & dat$Total_DOT[i]<12){
    dat$tdot_group[i]<-'10-11'
  }
  if(dat$Total_DOT[i]>=12 & dat$Total_DOT[i]<14){
    dat$tdot_group[i]<-'12-13'
  }
  if(dat$Total_DOT[i]>=14)
    dat$tdot_group[i]<-'>=14'
  }
}
dat$tdot_week<-dat$Total_DOT/7
dat$tdot_group<-as.factor(dat$tdot_group)
```

```
dat$tdot_group<-relevel(dat$tdot_group, ref = '2-3')
finmodel2glma<-glm(aki_num~group       +       factor(age_group)       +
TOTAL_CHARLSON_SCORE+ factor(baseline_crcl_group)+ transfer+hypotension+
GENDER+

factor(los_group)+DEHYDRATION_FLG+ACYCLOVIR_FLG+AMINOGLYCOSIDES_FLG+
AMPHOTERICIN_B_FLG+

ace.arb+tac.cyc+FOSCARNET_FLG+LOOP_DIURETICS_FLG+NON_STEROIDAL_ANTI_FLG
+SULFONAMIDES_FLG+
                    TENOFOVIR_FLG+ tdot_group, x, dat)
finmodel2lrma<-lrm(aki_num~group       +       factor(age_group)       +
TOTAL_CHARLSON_SCORE+ factor(baseline_crcl_group)+ transfer+hypotension+
GENDER+

factor(los_group)+DEHYDRATION_FLG+ACYCLOVIR_FLG+AMINOGLYCOSIDES_FLG+
AMPHOTERICIN_B_FLG+

ace.arb+tac.cyc+FOSCARNET_FLG+LOOP_DIURETICS_FLG+NON_STEROIDAL_ANTI_FLG
+SULFONAMIDES_FLG+
                     TENOFOVIR_FLG+tdot_group, dat)


MODEL<-
glm(aki_num~group+factor(age_group)+TOTAL_CHARLSON_SCORE+factor(baselin
e_crcl_group)+transfer+hypotension+GENDER+

factor(los_group)+DEHYDRATION_FLG+ACYCLOVIR_FLG+AMINOGLYCOSIDES_FLG+AMP
HOTERICIN_B_FLG+ANGIOTENSIN_FLG+ANGIOTENSION_FLG+
             TACROLIMUS_FLG+FOSCARNET_FLG+CYCLOSPORINE_FLG+
LOOP_DIURETICS_FLG+NON_STEROIDAL_ANTI_FLG+SULFONAMIDES_FLG+TENOFOVIR_FL
G+
             factor(tdot_group), x, dat)
MODELlrm<-
lrm(aki_num~group+factor(age_group)+TOTAL_CHARLSON_SCORE+factor(baselin
e_crcl_group)+transfer+hypotension+GENDER+

factor(los_group)+DEHYDRATION_FLG+ACYCLOVIR_FLG+AMINOGLYCOSIDES_FLG+AMP
HOTERICIN_B_FLG+ANGIOTENSIN_FLG+ANGIOTENSION_FLG+
             TACROLIMUS_FLG+FOSCARNET_FLG+CYCLOSPORINE_FLG+
LOOP_DIURETICS_FLG+NON_STEROIDAL_ANTI_FLG+SULFONAMIDES_FLG+TENOFOVIR_FL
G+
             factor(tdot_group), dat)
```

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WILBUR CLIFF RUTTER

EDUCATION

08/2009 – 05/2013	**Doctor of Pharmacy** The University of Texas at Austin College of Pharmacy The University of Texas Health Science Center at San Antonio Graduate School
08/2007 – 05/2009	**Undergraduate/Chemistry** The University of Texas at Austin College of Natural Sciences
08/2006 – 08/2007	**Undergraduate/Chemistry** The University of Texas at San Antonio College of Sciences

PROFESSIONAL TRAINING

07/2014 – 06/2016	**Pharmacy Fellowship in Infectious Disease** The University of Kentucky College of Pharmacy, Lexington, KY Director: David S. Burgess, PharmD, FCCP
07/2013 – 06/2014	**ASHP Accredited Pharmacy Practice Residency** St. Claire Regional Medical Center, Morehead, KY Directors: Catherine L. Shely, PharmD, BCPS Samuel H. Wornall, PharmD, BCPS

PROFESSIONAL POSITIONS

12/2014 – Present	**On-Call Pharmacist – Internal Medicine** University of Kentucky Medical Center, Lexington, KY
10/2007 – 08/2011	**Certified Pharmacy Technician** Seton Medical Center, Austin, TX

PUBLICATIONS

Rutter WC, Burgess DR, Talbert JC, Burgess DS. Acute kidney injury in patients treated with vancomycin and piperacillin-tazobactam alone and in combination: a retrospective cohort analysis. *Journal of Hospital Medicine.* [Under Review]

Rutter WC, Burgess DR, Burgess DS. Increasing Incidence of Multidrug Resistance among Cystic Fibrosis Respiratory Bacterial Isolates. *Microbial Drug Resistance*. [In Press]

Thompson RZ, Martin CA, Burgess DR, **Rutter WC,** Burgess DS. Optimizing beta-lactam pharmacodynamics against *Pseudomonas aeruginosa* in adult cystic fibrosis patients. *Journal of Cystic Fibrosis*. 2016 Apr 27. pii: S1569-1993(16)30019-4. doi: 10.1016/j.jcf.2016.04.002.

Cox JN, **Rutter WC,** Martin CA, Burgess DR, Zephyr D, Burgess DS. Acute Kidney Injury during therapy with vancomycin in combination with beta-lactams: a matched-cohort study. *American Journal of Medicine*. [In preparation]

Rutter WC, Talbert JC, Burgess DS. Factors associated with supratherapeutic vancomycin levels in adult patients. *Pharmacotherapy.* [In Preparation]

Rutter WC, Burgess DR, Burgess DS. Unit-specific Pharmacodynamic Modelling to Aid in Empiric Therapy Selection. [In Preparation]

Rutter WC, Seltzer JK. West Nile virus. *Texas Society of Health-system Pharmacists drug information alerts*. Available at: http://tshp.org/drug-information-alerts.html. Accessed August 4, 2012.

POSTER PRESENTATIONS/ABSTRACTS

Rutter WC, Burgess DS. *Acute Kidney Injury in Patients Treated with Beta-lactam/Beta-lactamase Inhibitor Combinations.* Presented at ID Week 2016; 26-30 Oct 2016; New Orleans, LA. [submitted]

Rutter WC, Burgess DS. *Trends in Acute Injury Incidence in Patients Treated with Vancomycin plus Piperacillin-Tazobactam or Cefepime.* Presented at ID Week 2016; 26-30 Oct 2016; New Orleans, LA. [submitted]

Rutter WC, Burgess DS. *Nephrotoxicity and Clinical Outcomes in Patients Treated with Nafcillin or Cefazolin.* Presented at ID Week 2016; 26-30 Oct 2016; New Orleans, LA. [submitted]

Rutter WC, Burgess DS. *Comparative Rates of Nephrotoxicity in Patients Treated with Piperacillin-tazobactam and Meropenem: a Retrospective Cohort Study.* Presented at ID Week 2016; 26-30 Oct 2016; New Orleans, LA. [submitted]

Crass RL, **Rutter WC,** Burgess DR, Martin CA, Burgess DS. *Development of Acute Kidney Injury in Patients treated with Polymyxin B Compared to Colistimethate Sodium*. Presented at ID Week 2016; 26-30 Oct 2016; New Orleans, LA. [submitted]

Rutter WC, Burgess DS. *Is there a Difference in Acute Kidney Injury Incidence Among Patients Treated with Piperacillin-tazobactam or Levofloxacin?* Presented at ID Week 2016; 26-30 Oct 2016; New Orleans, LA. [submitted]

Cotner S, **Rutter WC,** Burgess DR, Martin CA, Burgess DS. *Influence of Beta-lactam Infusion Strategy on Acute Kidney Injury*. Presented at ID Week 2016; 26-30 Oct 2016; New Orleans, LA. [submitted]

Patel SK, **Rutter WC,** Moga DC, Martin CA. *Difference in Nephrotoxicity between Nafcillin and Piperacillin-Tazobactam*. Presented at ID Week 2016; 26-30 Oct 2016; New Orleans, LA. [submitted]

Crass RL, **Rutter WC,** Burgess DR, Martin CA, Burgess DS. *Comparative Nephrotoxicity of Polymyxin B and Colistimethate Sodium in Patients with Cystic Fibrosis*. Presented at ID Week 2016; 26-30 Oct 2016; New Orleans, LA. [submitted]

Cady E, **Rutter WC,** Burgess DR, Kincaid SE, Martin CA, Burgess DS. *Utilizing Nanosphere's Verigene® Technology to Assist with Possible Rapid Pharmacologic De-escalation of Antimicrobial Therapy In A University Hospital Setting.* Presented at ID Week 2016; 26-30 Oct 2016; New Orleans, LA. [submitted]

Rutter WC, Talbert JC, Burgess DS. *Characteristics of Multidrug Resistant Cultures at an Academic Medical Center.* Presented at ID Week 2016; 26-30 Oct 2016; New Orleans, LA. [submitted]

Olsufka RA, **Rutter WC,** Burgess DS. *Probability of Pharmacodynamic Target Attainment with Elevated Ceftolozane-tazobactam Doses Against a Fixed and an Institution-specific MIC Distribution.* Presented at ID Week 2016; 26-30 Oct 2016; New Orleans, LA. [submitted]

Rutter WC, Lee GC, Burgess DS. *Antimicrobial Susceptibility and Resistomes of Carbapenem Resistant Enterobacteriaceae*. Presented at ASM Microbe 2016; 16-20 June 2016; Boston, MA.

Rutter WC, Burgess DS. *In-Vitro Characterization of Amikacin and Polymyxin B Therapy in Combination with Meropenem for Carbapenem-resistant Enterobacter cloacae*. Presented at ASM Microbe 2016; 16-20 June 2016; Boston, MA.

Rutter WC, Talbert JC, Burgess DS. *Incidence of Acute Kidney Injury in Patients Treated with Vancomycin and Piperacillin/Tazobactam.* Presented at ID Week 2015; 7-11 Oct 2015; San Diego, CA.

Rutter WC, Burgess DS. *Development of an Automated Process for Antibiogram Generation.* Presented at ID Week 2015; 7-11 Oct 2015; San Diego, CA.

Rutter WC, Burgess DR, Burgess DS. *Increasing Incidence of Multidrug Resistance Among Cystic Fibrosis Respiratory Isolates.* Presented at ID Week 2015; 7-11 Oct 2015; San Diego, CA.

Rutter WC, Burgess DR, Burgess DS. *Unit-specific Pharmacodynamic Modelling to Aid in Empiric Therapy Selection.* Presented at ID Week 2015; 7-11 Oct 2015; San Diego, CA.

Rutter WC, Talbert JC, Burgess DS. *Factors Associated with Supratherapeutic Vancomycin Trough Concentrations in a Referral Center.* Presented at ID Week 2015; 7-11 Oct 2015; San Diego, CA.

Burgess DR, **Rutter WC,** Tennant SJ, Ribes J, Burgess DS. *Antimicrobial Stewardship and the Use of Verigene ® Gram-Positive and Gram-Negative Rapid Identification System.* Presented at ID Week 2015; 7-11 Oct 2015; San Diego, CA.

Thompson RZ, Martin CA, Burgess DR, **Rutter WC**, Burgess DS. *Optimizing Beta-Lactam Pharmacodynamics Against Pseudomonas aeruginosa in Adult Cystic Fibrosis Patients.* Presented at ID Week 2015; 7-11 Oct 2015; San Diego, CA.

Cox JN, **Rutter WC**, Martin CA, Burgess DR, Zephyr D, Burgess DS. *Incidence of Acute Kidney Injury During Therapy with Vancomycin in Combination with Beta-Lactam Antibiotics*. Presented at ID Week 2015; 7-11 Oct 2015; San Diego, CA.

Rutter WC, Burgess DS. *Multiple methods of describing antimicrobial susceptibility: What do they tell us?* Presented at Rho Chi Research Day, University of Kentucky; 17 Apr 2015; Lexington, KY.

Rutter WC, Burgess DS. *In vitro characterization of amikacin and polymyxin b therapy in combination with meropenem for carbapenem-resistant Enterobacter cloacae*. Presented at Rho Chi Research Day, University of Kentucky; 17 Apr 2015; Lexington, KY.

Cox JN, **Rutter WC**, Martin CA, Burgess DR, Zephyr D, Burgess DS. *Incidence of Acute Kidney Injury During Therapy with Vancomycin in Combination with Beta-Lactam Antibiotics*. Presented at Rho Chi Research Day, University of Kentucky; 17 Apr 2015; Lexington, KY.

Rutter WC, Wornall SH, Shely CL. *Evaluation of MRSA treatment failures associated with elevated vancomycin minimum inhibitory concentrations in a rural, nonacademic hospital*. Poster presented at: ASHP Midyear clinical meeting 2013; 11 Dec 2013; Orlando, FL.

Rutter WC, Lee G, Burgess D, Winkler K, Burgess DS. *Surveillance of resistance trends of community-acquired versus hospital-acquired urinary tract infections*. Poster presented at: ASHP Midyear clinical meeting 2012; 3 Dec 2012; Las Vegas, NV.

Rutter WC, Burgess D, Winkler K, Lee G, Burgess DS. *Evaluation of epidemiology and susceptibility trends in urinary tract infections over 5 years in a community hospital*. Poster presented at: IDWeek 2012. The 1st joint meeting of the Infectious Disease Society of America, the Society of Healthcare Epidemiology of America, the HIV Medicine Association, and the Pediatric Infectious Disease Society; 17-21 Oct 2012; San Diego, CA.

Rutter WC, Lee G, Burgess D, Winkler K, Burgess DS. *Surveillance of resistance trends of community-acquired versus hospital-acquired urinary tract infections.* Poster presented at: IDWeek 2012. The 1st joint meeting of the Infectious Disease Society of America, the Society of Healthcare Epidemiology of America, the HIV Medicine

Association, and the Pediatric Infectious Disease Society; 17-21 Oct 2012; San Diego, CA.

Rutter WC, Burgess D, Winkler K, Dasher T, Burgess DS. *Evaluation of urinary tract infection antimicrobial susceptibility in a community hospital*. Poster presented at: Eighth Annual Louis C. Littlefield Celebrating Pharmacy Research Excellence Day; 17 Apr 2012; Austin, TX.

SCHOLASTIC AND PROFESSIONAL HONORS

11/2015 – Present	The Medicines Company Infectious Disease Pharmacotherapy Research Award Society of Infectious Disease Pharmacists
04/2013	Student Research/Scholarship Award Graduate School of Biomedical Sciences – College of Pharmacy
05/2008 – 05/2013	The University of Texas at Austin – University Honors
08/2010 – 08/2012	Pharmacy Alumni Association Endowed Scholarship
08/2007 – 01/2008	The National Science & Mathematics Access to Retain Talent (SMART) Grant Recipient
12/2006	The University of Texas at San Antonio – Dean's List

PROFESSIONAL SERVICE

07/2013 – 06/2014	**Pharmacy and Therapeutics committee** St. Claire Regional Medical Center
10/2013	**Medication administration Kaizen event team member** St. Claire Regional Medical Center