

Vancomycin area under the curve/minimum inhibitory concentration (AUC/MIC) and trough level concordance – Evaluation on an Urban Health unit (VACatE)



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Background

- A vancomycin AUC/MIC between 400-600 mg·hr/L is associated with improved clinical outcomes for treatment of MRSA bacteremia
- Previous studies suggest that targeting vancomycin trough concentrations of 15-20 mg/L may achieve suprathreshold AUC/MIC and an increased risk of acute kidney injury
- In 2020, St. Paul's Hospital (SPH) started AUC/MIC monitoring in patients admitted to the Urban Health unit
- Logistical considerations and patient preferences pose a clinical challenge to AUC/MIC monitoring where 2 time-sensitive levels are required
- Identifying patients with AUC/MIC and trough discordance may reduce unnecessary dose escalations and reduce risk of toxicity

Objectives

- Primary:**
 - Proportion of AUC/MIC values within target that prompt no dose change despite subtherapeutic troughs
 - Proportion of AUC/MIC values that prompt a dose decrease due to suprathreshold AUC/MIC when trough level is within target
- Secondary:**
 - Compare vancomycin total daily dose using AUC/MIC monitoring and trough-guided monitoring
 - Identify factors associated with discordant AUC/MIC and trough
 - Determine the frequency of vancomycin-associated nephrotoxicity

Methods

- Design:** Retrospective chart review
- Population:** Convenience sample size of patients under the Urban Health service at SPH between November 16, 2019 to January 17, 2021
- Inclusion:**
 - ≥ 18 years of age
 - Received at least 3 doses of IV vancomycin
 - At least 1 set of peak and trough drawn at steady state
- Exclusion:**
 - Require renal replacement therapy
 - Pregnancy
 - MRSA with MIC ≥ 2 mg/L
- Formulas Used:** Sawchuk-Zaske method for patient-specific pharmacokinetic parameters and linear trapezoidal method for AUC/MIC
- Nephrotoxicity:** ↑ serum creatinine (SCr) by 50% or ≥ 26.4 μmol/L from baseline during vancomycin treatment
- Statistics:** Descriptive statistics, linear and multivariate regression

Figure 1. Patient Screening

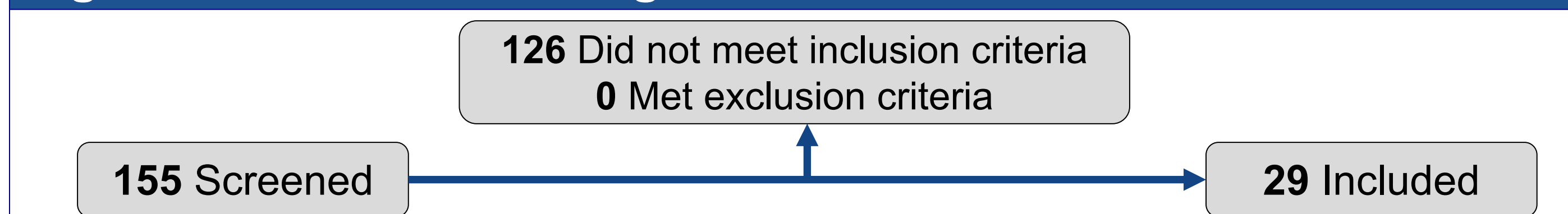


Table 1. Patient Characteristics (N=29)

Male – no. (%)	22 (75.9)
Age (years) – mean (SD)	42.2 (13.0)
Height (cm) – mean (SD)	174.2 (6.7)
Weight (kg) – mean (SD)	
Actual Weight	65.4 (10.6)
Ideal Body Weight	68.6 (7.4)
Baseline SCr (μmol/L) – mean (SD)	59.5 (20.6)
Comorbidities – no. (%)	
Polysubstance/opioid use disorder	25 (86.2)
HIV	19 (65.5)
Hepatitis C (untreated)	16 (55.2)
Iron deficiency anemia	15 (51.7)
Asthma/COPD	5 (17.2)
Patients on concurrent nephrotoxins – no. (%)	12 (41.4)
Concurrent nephrotoxins – no. (%)	
Furosemide	3 (10.3)
Cobicistat	3 (10.3)
Tenofovir disoproxil fumarate	3 (10.3)
Dolutegravir	3 (10.3)
Other	5 (17.2)
Sources of Infection – no. (%)	
Bacteremia	15 (51.7)
Skin & Soft Tissue Infection	6 (20.7)
Septic Arthritis	5 (17.2)
Infective Endocarditis	4 (13.8)
Osteomyelitis	4 (13.8)
Pneumonia	1 (3.4)
Culture Results – no. (%)	
MRSA	15 (51.7)
MSSA	5 (17.2)
Streptococcus spp.	5 (17.2)
Coagulase negative Staphylococcus	4 (13.8)
Negative	4 (13.8)
Mixed/Other	2 (6.9)
Duration of vancomycin (d) – mean (SD)	28.2 (23.0)
Vancomycin Trough (mg/L) – median (range)	13.5 (7.6 – 26.8)
Vancomycin AUC ₂₄ (mg·hr/L) – median (range)	572 (339 – 863)

Table 2. Comparison of AUC₂₄/MIC and Trough Concentration

Steady state peak and trough sets (N=57)			
Concordant AUC/MIC* – no. (%)			
Discordant AUC/MIC – no. (%)			
Trough (mg/L)	AUC < 400 no. (%)	AUC 400-600 no. (%)	AUC > 600 no. (%)
< 10 (n=5)	1 (20.0)	4 (80.0)	0 (0.0)
10-15 (n=31)	2 (6.5)	21 (67.7)	8 (25.8)
15-20 (n=13)	0 (0.0)	4 (30.8)	9 (69.2)
> 20 (n=8)	0 (0.0)	1 (12.5)	7 (87.5)

* Concordant if trough < 15 and AUC < 400, trough 15-20 and AUC 400-600, trough > 20 and AUC > 600

Results

Figure 2. Vancomycin Trough Concentration vs AUC₂₄

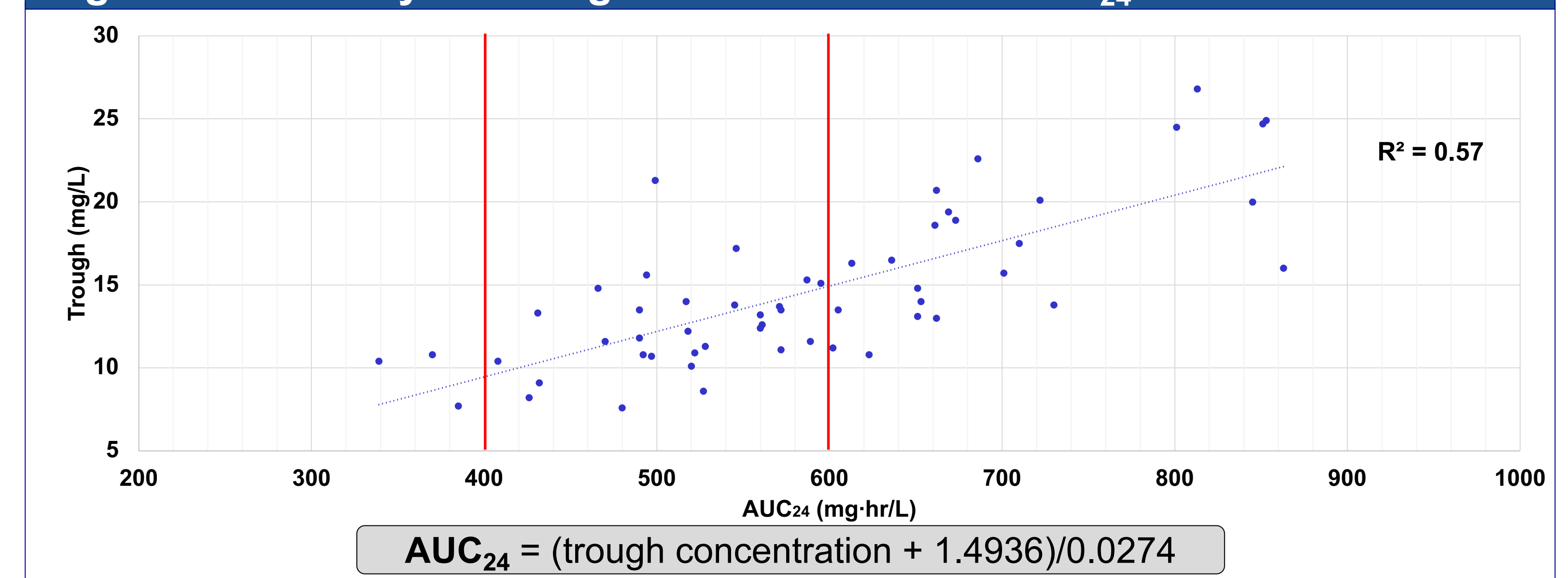
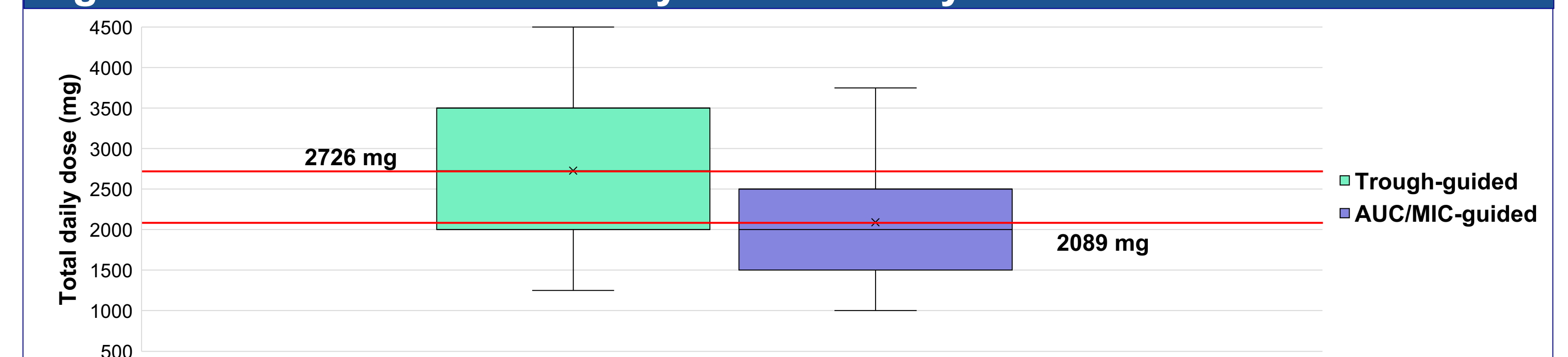


Table 3. Predictors of AUC: Multivariate Model

	Coefficient	95% CI	P-value
Age (years)	-0.01	-2.41 – 2.43	0.99
Actual Weight (kg)	4.78	-4.05 – 13.61	0.61
Baseline SCr (μmol/L)	1.04	-0.85 – 2.93	0.26
Trough (mg/L)	21.69	15.46 – 27.92	< 0.001

Figure 3. Difference in Vancomycin Total Daily Dose



Nephrotoxicity Outcome

- Incidence of nephrotoxicity was 5 cases (17.2%), with 3 documented as vancomycin-associated. Other documented causes: septic shock, dehydration

Limitations

- Retrospective chart review design and small sample size
- Extrapolation of steady state concentrations
- Vancomycin dose adjustments can vary based on clinical judgement
- Lack of assessment of clinical effectiveness

Conclusions

- Target trough range of 15-20 mg/L often results in AUC greater than target range
- AUC > 400 was achieved in majority of patients with trough levels of 10-15 mg/L
- AUC/MIC monitoring can result in targeting lower average trough concentrations and reduced daily exposure of vancomycin
- Further studies with larger sample size to strengthen predictive model, assess clinical effectiveness and safety