

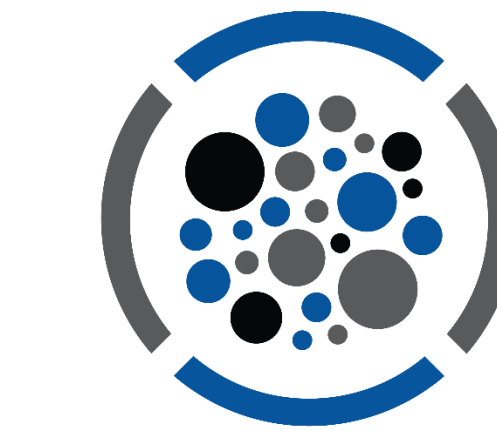
Vancomycin AUC Dosing: Is One Concentration in the Hand Worth Two in the Bush?



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Background

- A pre-specified trough range of 15 to 20 mcg/mL is a poor surrogate for targeting a 24-hour area-under-the-curve to minimum inhibitory concentration (AUC/MIC) ratio of 400 to 600 mg*h/L and has been associated with an increased risk of nephrotoxicity¹⁻⁵
- Revised guidelines recommend a transition to AUC/MIC therapeutic drug monitoring (TDM) to optimize vancomycin exposure for serious invasive methicillin-resistant *Staphylococcus aureus* (MRSA) infections while minimizing toxicity based on limited data without high quality evidence and limitations in strength⁶
- AUC/MIC TDM requires substantial clinical and operational resources when the majority of prescribed vancomycin is empiric and not required beyond a few days with implementation of rapid diagnostics and antimicrobial stewardship initiatives
- There is sparse published data comparing the accuracy of single-level to two-level AUC/MIC estimations with a suggested ~8% (AUC peak-trough/AUC full ratio: 0.86 vs AUC trough/AUC full: 0.78) difference in accuracy as described by Neely, et al⁵

Objectives

Primary Objective

Compare the accuracy of AUC TDM calculated from two points using trapezoidal calculations to a single steady-state trough combined with population assumptions

Secondary Objective

Evaluate clinical application (e.g., subsequent dose adjustment) of AUC TDM calculated from two points using trapezoidal calculations to a single steady-state trough combined with population assumptions

Methods

- Prospective cohort analysis of hospitalized adult patients with stable renal function prescribed vancomycin who required TDM from 10/2020 to 12/2020
- Two appropriate vancomycin concentrations defined as a peak at least two hours after the end of the infusion and a trough within one hour of the next dose were obtained at steady-state during a single dosing interval for each patient
- AUC was calculated by two methods:

Trapezoidal equations
utilizing peak and
trough concentrations (P/T)

Trough (T)-only
concentration combined
with a population volume of
distribution

- Estimation of population volume of distribution (Vd):
 - Body mass index (BMI) ≤ 25: total body weight (kg) multiplied by 0.7
 - BMI > 25: total body weight (kg) multiplied by 0.5
- Trapezoidal method equations per Pai MP, et al¹
- Accuracy of the AUC TDM estimation method was analyzed by comparing the percent and actual AUC difference calculated between the P/T and T-only AUC for each patient
- Clinical application patient level review was independently conducted by two clinical pharmacists to evaluate if a change in dosing would have been made according to AUC estimation methodology

Results

- Appropriate steady-state P/T concentrations were attained in thirty-one patients (Table 1)
- The mean calculated AUC for both groups was similar (P/T 544.8 mg*h/L vs T-only 549.8 mg*h/L) with median AUC absolute difference of 25.82 mg*h/L (Table 2)

Results

- Greatest variance between calculated T-only and P/T AUC was seen in a 158 kg patient (17% difference) and patients with CrCL >150 mL/min (> 10% difference)
- Both methods resulted in the same modification to the vancomycin regimen based on patient level chart review

Table 1. Baseline Characteristics

Characteristic (N=31)	Value
Age, median	59 years
Sex, male (%)	23 (69.7%)
Weight (kg), median (IQR)	85.5 (75.3-109.9)
BMI kg/m ² , median (IQR)	28.2 (25.3 to 34.5)
Serum creatinine mg/dL, median (IQR)	1 (0.75 to 1.07)

Table 2. Comparison of Calculated AUC

Parameter (N=31)	T-only vs P/T
Mean % difference in AUC (SD)	1.85% (7.3)
Median % difference in AUC (IQR)	0.65% (-3.8 to 8.2)
Mean absolute difference in AUC (SD)	30.85 mg*h/L (24.4)
Median absolute difference in AUC (IQR)	25.82 mg*h/L (16.7 to 42.2)
Trough values, mean (SD)	14.3 mg/L (5.9)

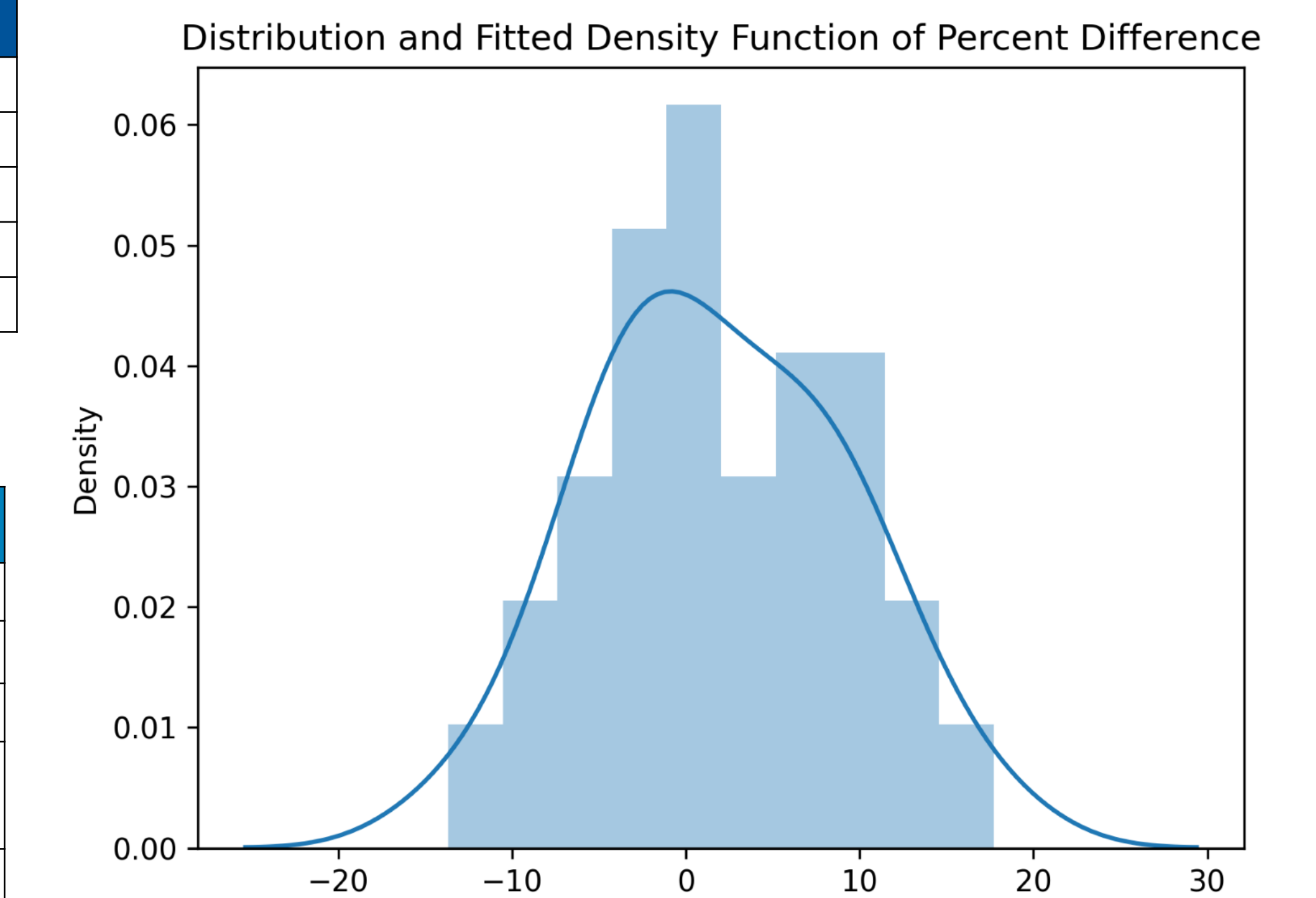


Figure 1. Percent Difference between PT and T-only Methods with apparent normal distribution, p=0.94 by Shapiro's test

Conclusions

- T-only AUC method performed similarly to the more laborious trapezoidal P/T AUC method resulting in no dose adjustment differences between groups
- Trapezoidal P/T method should be considered for patients with body weight >150kg, significant volume changes, or augmented renal function to increase accuracy of AUC estimation
- T-only AUC method may represent a resource and workflow conscious AUC estimation method for patients meeting population assumptions