Subgroup Analysis of Bayesian-Derived Vancomycin AUC_{24h} and AUC_{24h}/MIC for MRSA-Associated Infections and Special Populations

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2020 Revised Consensus Guideline for Vancomycin Monitoring

- High degree of inter-individual variability between trough concentrations and AUCs
- Recommends new optimal vancomycin PK/PD target of Bayesian-derived AUC/MIC of 400-600 and an AUC of 400-600 mg*h/L assuming MRSA MIC is 1.
- No longer recommends trough concentrations of 15-20 mg/L for severe MRSA infections.

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Study Objective

- To investigate vancomycin's optimal AUC/MIC ratio to maximize efficacy and maximum AUC to minimize nephrotoxicity in different MRSA-associated infections and vancomycin special populations.
  - MRSA-Associated Infections: pneumonia, bacteremia, sepsis, endocarditis, septic joints, SSTIs, infected hardware, osteomyelitis
  - Special Populations: critically ill/ICU patients, patients on concomitant nephrotoxins or immunosuppressants, amputees, meth users, IVDUs, HIV patients

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Methodology

- Retrospective research consisting of patients at San Joaquin General Hospital from June 2019 to June 2020
- Data collection is still in progress
- Interim analysis focuses on the AUC threshold for nephrotoxicity for critically ill/ICU patients and patients on concomitant nephrotoxins

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FIGURE 1:
AUC_{24h} >638 mg*h/L is associated with an increased likelihood of nephrotoxicity

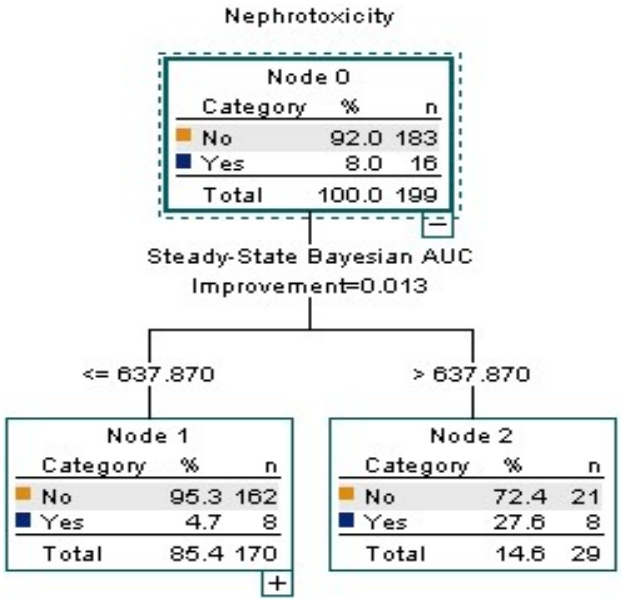

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FIGURE 2:
AUC_{24h} >461 is associated with an increased likelihood of nephrotoxicity in critically ill or ICU patients

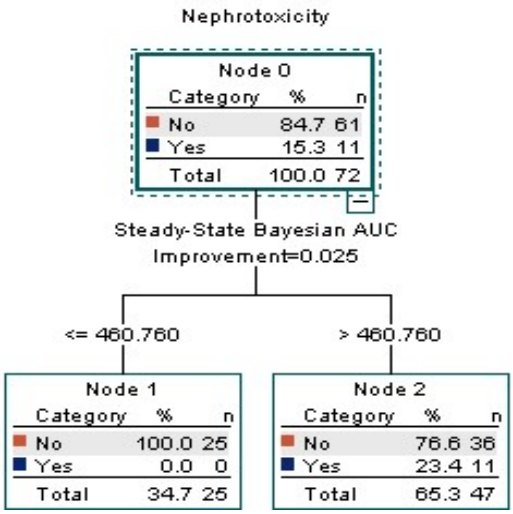

FIGURE 3:
AUC_{24h} >546 is associated with higher nephrotoxicity risk in patients on concomitant nephrotoxins

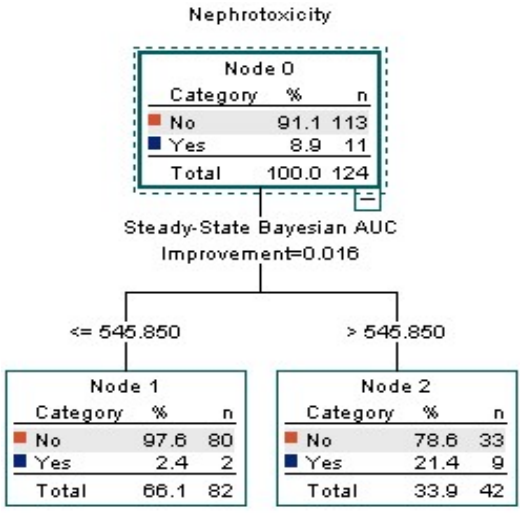

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Table 2: Nephrotoxic vs. Non-Nephrotoxic Critically Ill or ICU Patients

	Non-Nephrotoxic (n=61)	Nephrotoxic (n=11)	P-value
Steady-State Bayesian AUC_{24h}, median (IQR)	500 (405-568)	561 (495-659)	0.023

Table 3: Nephrotoxic vs. Non-Nephrotoxic Patients on Concomitant Nephrotoxins

	Non-Nephrotoxic (n=113)	Nephrotoxic (n=11)	P-value
Steady-State Bayesian AUC_{24h}, median (IQR)	479 (399-575)	583 (546-661)	0.018

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Conclusion

- Interim analysis suggests a lower maximum AUC for vancomycin may be considered to minimize nephrotoxicity risk for certain vancomycin special populations such as patients who are critically ill or are ICU patients and patients on concomitant nephrotoxins
- Completion of data collection may increase the reliability and precision of AUC threshold estimates
- Predictive performance of the AUC thresholds will be evaluated
  - Negative predictive value
  - Predictive value
  - Receive operating characteristic (ROC) curves analysis

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Thank you!

For questions or comments, please contact me at dho1@pacific.edu.

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References

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3. Holmes NE, Turnidge JD, Munckhof WJ, et al. Vancomycin AUC/MIC ratio and 30-day mortality in patients with staphylococcus aureus bacteremia. *Antimicrob Agents Chemother*. 2013;57(4):1654-1663. https://www.ncbi.nlm.nih.gov/pubmed/23335735. Accessed Mar 9, 2020. doi: 10.1128/AAC.01485-12.

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