Bridging the Gap from Vancomycin Trough to AUC Monitoring

Jena Foreman, PharmD, BCPS, BCIDP, Clinical Pharmacy Specialist,
HSHS St. Elizabeth's Hospital, O'Fallon, Illinois
Josh Schmees, PharmD, System Pharmacy Informaticist
HSHS St. Elizabeth's Hospital, O'Fallon, Illinois
Natalie Tucker, PharmD, BCPS, BCIDP, Clinical Pharmacy Specialist,
HSHS St. John's Hospital, Springfield, Illinois

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Conflicts of Interest

- Neither the speakers nor the planning staff have any relevant conflicts of interest to disclose.

Learning Objectives

1. Assess the benefit of precision dosing software as a best practice for vancomycin AUC monitoring.
2. Design a plan to implement precision dosing software in a healthcare system.
3. Predict the challenges of implementing precision dosing software for a variety of hospital types, including those with limited resources.

Hospital Sisters Health System (HSHS)

- HSHS hospitals are located in Illinois (9) and Wisconsin (6)
- Franciscan Catholic Healthcare Ministry
- Mix of critical access, community teaching, and tertiary care hospitals
- System antimicrobial stewardship and pharmacy & therapeutics committees
- 13 of the 15 hospitals on the same EMR platform and clinical decision support

https://line.17qq.com/articles/sueqrcrqx.html
https://www.sj-r.com/story/news/2021/03/30/hospital-sisters-st-francis-run-spiritual-retreat-closing/7058544002/

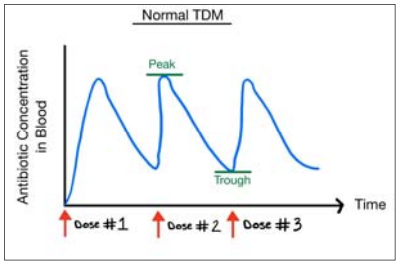
Benefits of AUC-Based Vancomycin Monitoring

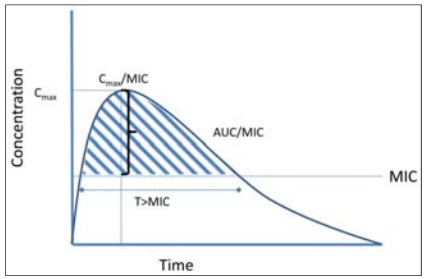
Integrative Activity – Use Handout

Why Implement Vancomycin AUC Monitoring?

- AUC monitoring by a pharmacist provides safer and more effective vancomycin therapy for patients, while decreasing vancomycin and lab utilization for a cost-benefit to healthcare facilities.

Trough vs. AUC





http://www.microbiologyoutsandbolts.co.uk/therapeutic-drug-monitoring.html
https://www.ncbi.nlm.nih.gov/books/NBK260259/figure/introduction-f1/

Clinical Background

What are the clinical benefits of transitioning from trough to AUC?

Efficacy

Safety

Efficacy Data

- In a simulation of 5000 patients on vancomycin 1g q8h, trough was poorly correlated with AUC
- High inter-patient variability with correlating trough to AUC

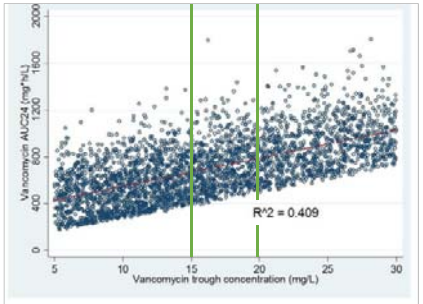
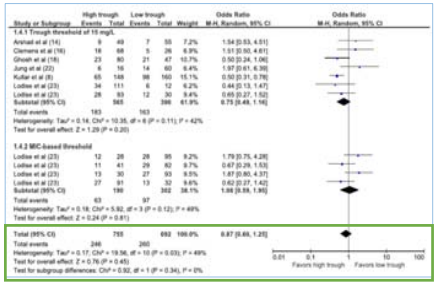


Fig. 2. Scatter and linear fit plot of vancomycin area under the curve over 24 h (AUC24) versus trough vancomycin concentration from 5000 subject Monte Carlo simulation.

Pai MP et al. Advan Drug Deliv Review. 2014;77:50-57.

Efficacy Data

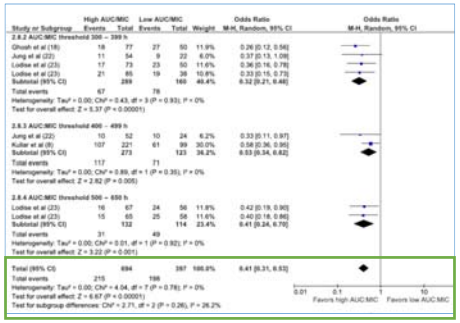
- Meta-analysis looking at association between vancomycin trough level and treatment outcomes
- Treatment failure = mortality or persistent bacteremia
- No difference in vancomycin treatment failure with high (≥ 15 mg/L) vs. low trough



Prybylski JP. Pharmacotherapy. 2015;35(19):889-898.

Efficacy Data

- Meta-analysis looking at association between vancomycin trough level and treatment outcomes
- Association between AUC:MIC and vancomycin treatment failure
- High AUC (≥ 400) associated with reduction in treatment failure



Prybylski JP. Pharmacotherapy. 2015;35(19):889-898.

Nephrotoxicity Data

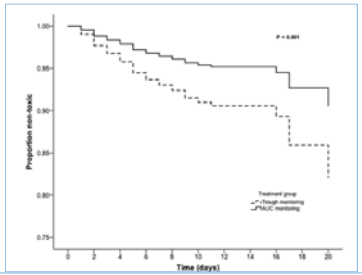


FIG 1 Time to nephrotoxicity by Cox proportional hazards regression. AUC-TD, AUC- and trough concentration-guided dosing.

- Quasi-experimental study of 1280 patients
- AUC monitoring demonstrated reduction in nephrotoxicity as well as decreased time to nephrotoxicity

Finch NA et al. Antimicrob Agents Chemother. 2017;61(2).

Nephrotoxicity Data

- Multivariable logistic regression found AUC monitoring associated with ~ 50% reduction in nephrotoxicity

TABLE 2 Multivariable logistic regression for 2009 vancomycin consensus guideline-defined nephrotoxicity

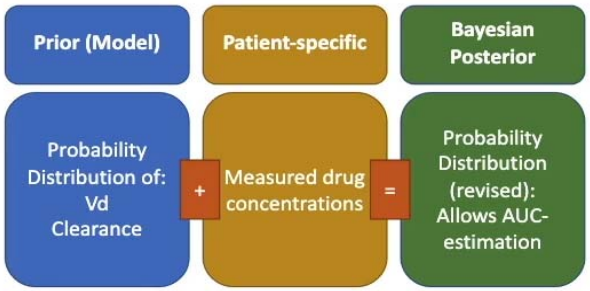
Variable	Unadjusted OR	95% CI for unadjusted OR	Adjusted OR	95% CI for adjusted OR	*P* value
AUC monitoring	0.724	0.488–1.074	0.514	0.332–0.794	0.003
Concomitant furosemide	3.226	2.136–4.873	1.771	1.127–2.784	0.013
Elixhauser comorbidity index	1.274	1.186–1.368	1.149	1.060–1.245	0.001
Duration of therapy	1.124	1.074–1.175	1.093	1.044–1.145	<0.001
APACHE II score	1.084	1.061–1.106	1.070	1.045–1.097	<0.001
Concomitant i.v. contrast dye	2.406	1.538–3.765			
Concomitant tobramycin	1.195	0.880–4.165			

Finch NA et al. Antimicrob Agents Chemother. 2017;61(2).

How Do I Calculate AUC?

- Two methods for calculating AUC
  - Two-sample AUC calculations by hand or using spreadsheet
    - Pros: Inexpensive technology, quick setup and implementation
    - Cons: More lab draws, levels must be at steady-state, more room for human error, time-consuming
  - One-sample AUC calculations using Bayesian software
    - Pros: Fewer lab draws, less room for human error, more efficient
    - Cons: Increased costs for technology, longer setup and implementation, downtime

Bayesian Method



Pai MP et al. Advan Drug Deliv Review. 2014;77:50-57.
Rybak MJ. Implementing the 2020 Vancomycin Guidelines [webinar]. Accessed September 8, 2020.

Cost-Benefit

- Lee BV, et al. published a detailed cost analysis comparing 3 groups: trough-only, non-Bayesian AUC monitoring, and Bayesian AUC monitoring
- Trough group – Standard of care set by 2009 IDSA guidelines
- Non-Bayesian: Two-sample AUC monitoring using spreadsheet
- Bayesian: One-sample monitoring using precision dosing software
- Drug levels completed within first 48 hours of treatment
- Outcomes monitored from 48 hours to end of therapy

Lee BV, et al. Cost-benefit analysis comparing trough, two-level AUC and Bayesian AUC dosing for vancomycin. *Clin Micro Infect*. 19 November 2020. https://doi.org/10.1016/j.cmi.2020.11.008

Cost-Benefit

Specific costs that were included:

- Vancomycin drug concentrations
- Bayesian software costs
- Hospitalizations for Acute Kidney Injury (AKI)

Cost-Benefit

Dosing Method	Trough (US $)	Two-sample AUC (US $)	Bayesian AUC (US $)
Additional AKI treatment cost per patient	2,982	2,136	917
Incremental Cost Benefit per Patient vs Trough	-	846	2065
Incremental Cost Benefit for 1000 Vancomycin Patients/Year vs Trough	-	846,810	2,065,720

DE Wit JZ et al. Cost-benefit analysis comparing trough, two-level AUC and Bayesian AUC dosing for vancomycin. *Clin Micro Infect*. 19 November 2020. https://doi.org/10.1016/j.cmi.2020.11.008

Cost-Benefit

Other potential cost and time savings:

- Decreased drug costs
- Decreased nursing and laboratory time for lab draws
- Increased pharmacist productivity due to time efficiency

DE Wit JZ et al. Cost-benefit analysis comparing trough, two-level AUC and Bayesian AUC dosing for vancomycin. *Clin Micro Infect*. 19 November 2020. https://doi.org/10.1016/j.cmi.2020.11.008

Integrative Activity – Use Handout

Crunch the Numbers!

- Cost avoidance:
- 2,065,720 dollars/year per 1000 vancomycin patients

= $2,065.72 saved per patient!

Integrative Activity – Use Handout

Break-even analysis for Bayesian Precision Dosing Software

- Cost of Software:
- $100,000 annual cost/$2,065.72 cost avoidance per patient

= 41 vancomycin patients per year

Implementation

"You do not rise to the level of your goals.
You fall to the level of your systems."

- James Clear, "Atomic Habits"

Make a Detailed To-Do List

Integrative Activity – Use Handout

How do I get started?

1. Find your experts and build your team

Key Players

- Infectious Diseases Pharmacist
- Infectious Diseases Physician
- Director of Pharmacy / Pharmacy Manager
- Pharmacy Informatics
- Financial Analyst
- Hospital Leadership

Hospital / System Committees

- Antimicrobial Stewardship
- Pharmacy & Therapeutics
- Fiscal Stewardship
- Informatics

Integrative Activity – Use Handout

Leadership Buy-In

1. Present clinical data and break-even analysis for your specific institution or institutions.
2. Assess whether implementation makes sense on a local or system level.
3. Decide which Bayesian precision dosing software platform is the best fit.
   - Turner RB. Pharmacotherapy. 2018;38(12):1174-1183.

Integrative Activity – Use Handout

Build Your Systems

- Calculation decisions
- Bayesian Software Data Validation
- Vancomycin Monitoring Protocol
- Work-aids
- Educational Materials
  - Pharmacists
  - Nurses
  - Physicians/Mid-level providers

Integrative Activity – Use Handout

Education & Training

Pharmacists

- Clinical Education – continuing education programs, IDSA guidelines
- Software Training – live classes, videos, practice
- Proof of Competency – CE certificates, competencies, patient case studies
- Question/Answer sessions

Integrative Activity – Use Handout

Education & Training

Physicians, Mid-level Providers, Nurses

- Memos
- Committee meetings
- Department huddles
- Email
- Onboarding

Integrative Activity – Use Handout

After Go-Live

- Troubleshooting
- Evaluation – revise protocol, patient case studies, communication of common errors

Excellent Implementation Resources

- https://mad-id.org/vancomycin/
- https://www.sidp.org/Vancomycin-AUC-Implementation-Toolkit-Guide
- https://www.proce.com/activities/activity_detail?id=869
- Heil EL, Claeys KC, Mynatt RP, et al. Making the change to area under the curve-based vancomycin dosing. *Am J Health-Syst Pharm*. 2018;75:1986-1995.

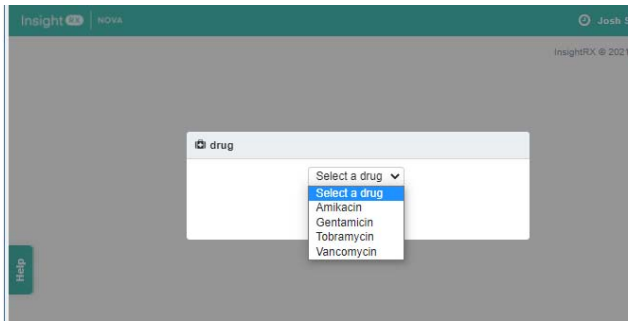
Workflow Considerations

Workflow Overview

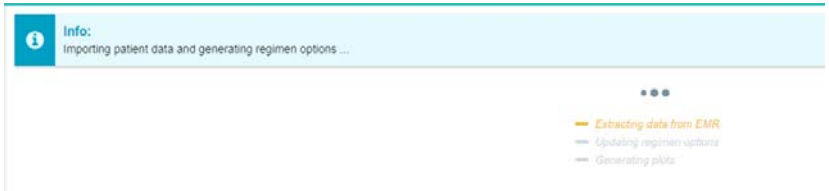
- Pick your patient
- Pick your medication
- Review data
- Perform analysis
- Copy decision into progress note

Launch Tool

Select Drug

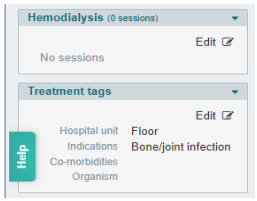


Data Extraction



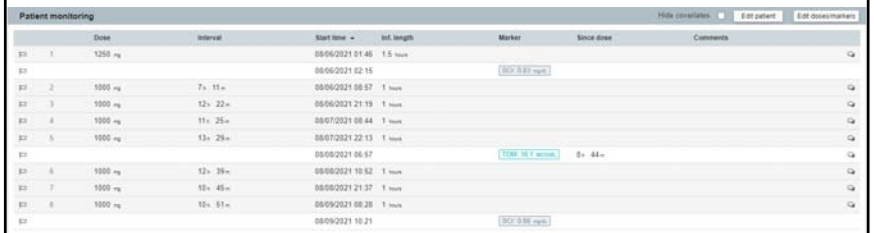
Review Pertinent Data

- Interfaced lab data and calculations
- Non-interfaced data (e.g. hemodialysis)



Historical Timing

- Past doses, levels, labs
- Calculated interval, infusion length

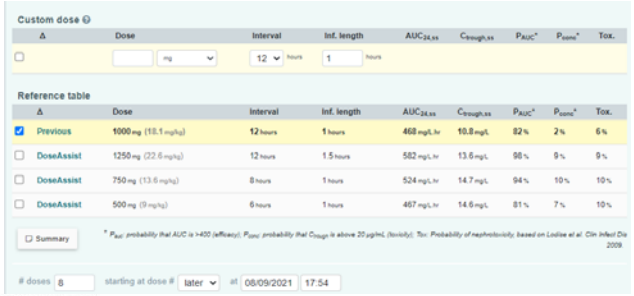


Timing Interactions

- Flag or remove data inaccuracies
- Tag comments to data
- Edit to add missing troughs or doses
  - How do you handle an outage with an integrated solution?

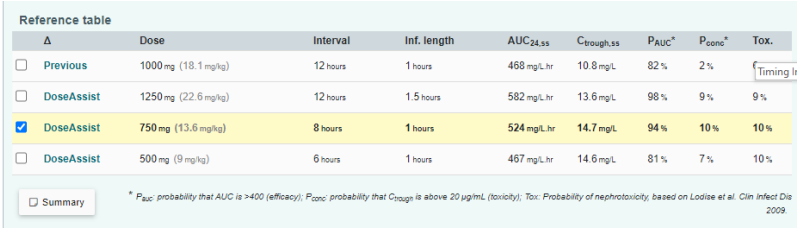
Dose Analysis

- Review guidance on different dosing regimens



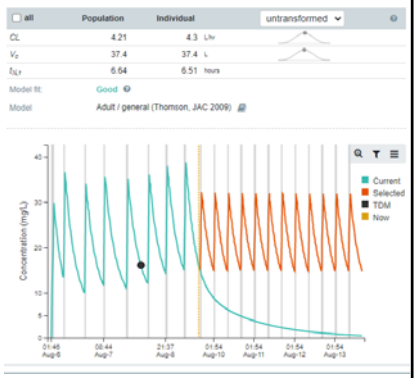
Select New Dose

- Alter dosing to see the impact over time



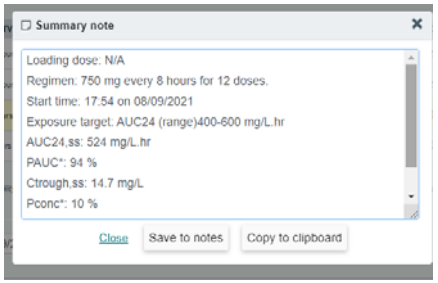
Model Analysis

- Visual changes overtime
  - Based on the closest selected model



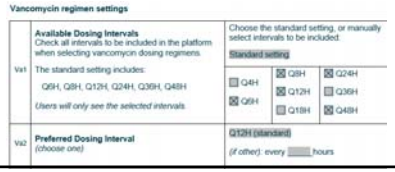
Documentation

- Adjust and copy calculations into your progress note



Technical Considerations

- HIPAA
  - Contains patient data so platform needs to secure
- Relies on medication administration interface for key data
  - HL7 vs Flatfile setup
  - How often is data exchanged (real-time vs daily)
- Understand settings that impact recommendations made
  - E.g. dose rounding



Implementation Challenges

Implementation Challenges

- COVID-19-related
  - Furloughs
  - Increased patient census
  - Vaccine rollout
- Hospital resource-related
  - EMR continuity
  - After-hours coverage
  - Data validation for software
  - Limited clinical staff

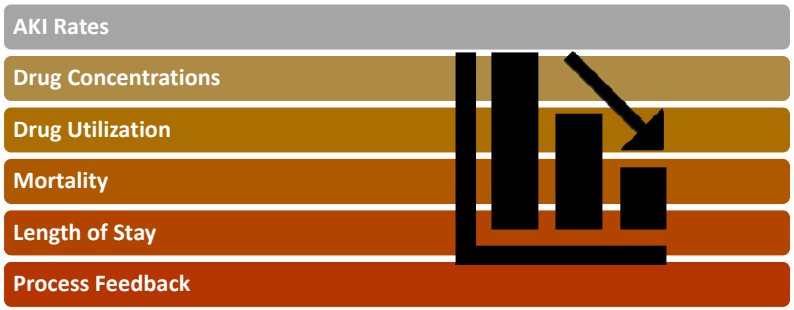
Implementation Challenges

- Education-related
  - Pharmacists with different levels of training and experience
  - Pharmacy to dose vancomycin in ALL patients
  - Hospitals with and without ID services

Implementation Challenges

- Informatics-related
  - Use integrated data when possible
    - Adjusted infusion length to come from interfaced order
    - Using calculated interval vs ordered interval
  - Ensure outage training for rare interface downtimes
  - Have system pharmacy operational leads engaged in build and training design

Outcomes Evaluation In Progress



Case Study

Happy Days Hospital is a 35-bed critical access hospital which is part of a 12-hospital health-system. They have no clinical pharmacist or infectious diseases experts, but they do have a system antimicrobial stewardship committee. They have an integrated EMR/clinical decision support since they are part of the health-system. The inpatient pharmacy is open daily from 0700 – 1900 with after hours coverage by a sister hospital.

What are the barriers for implementing vancomycin AUC monitoring with Bayesian software?

Summary

- Implementation of AUC monitoring is possible…even during a pandemic
- Create an implementation plan
- Buy-in from leadership, stewardship, and informatics teams is required
- Bayesian software is a crucial tool for AUC monitoring
- Completing a break-even analysis, securing buy-in, and thorough staff training and education are critical steps for success

Self Assessment #1
Before proposing the purchase of Bayesian software to hospital leadership, what is the best way to prepare?

A. Develop educational material for pharmacy staff
B. Conduct a break-even analysis
C. Draft AUC monitoring guidelines
D. Pray or Meditate

Self Assessment #2
Which step is necessary after implementation of Bayesian software and vancomycin AUC monitoring?

A. Nursing education
B. Pharmacist education
C. Process evaluation
D. Software data validation

Self Assessment #3.
Which of the following is a common limitation to implementing vancomycin AUC monitoring in small, independent, rural hospitals?

A. Lack of buy-in from hospital leadership
B. Lack of internet access
C. Presence of rodents in the hospital
D. Lack of infectious disease expertise

Self Assessment #4
The most efficient vancomycin dosing software setup will:

A. Avoid using population modeling
B. Use data daily
C. Integrate patient data directly from the electronic health record
D. Exclude patient data for security reasons

Questions