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AUC-GUIDED VANCOMYCIN THERAPEUTIC DRUG MONITORING: CLINICAL EVIDENCE, PHARMACOKINETIC INNOVATIONS, IMPLEMENTATION CHALLENGES, AND FUTURE DIRECTIONS

Yazhini S.*, Visali K., Periya Karuppan A. R., Dr. P. Monika

Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Pharmaceutical Sciences, Technology and Advanced Studies (VISTAS), Chennai, India.

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Corresponding Author: Yazhini S.
Address: Department of Pharmacy Practice, School of Pharmaceutical Sciences, Vels Institute of Pharmaceutical Sciences, Technology and Advanced Studies (VISTAS), Chennai, India.
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ABSTRACT

Vancomycin is still the main antibiotic for treating serious methicillin-resistant Staphylococcus aureus (MRSA) infections. Traditionally, therapeutic drug monitoring (TDM) used trough serum concentrations as a marker for effectiveness and safety. However, recent evidence shows that monitoring trough levels can lead to higher kidney damage and often does not predict drug exposure accurately. As a result, the 2020 consensus guidelines recommended using area under the concentration-time curve to minimum inhibitory concentration (AUC/MIC)-guided dosing as the best approach for optimizing vancomycin therapy. AUC-guided monitoring allows for personalized dosing by combining pharmacokinetic and pharmacodynamic principles, improving effectiveness while reducing harmful kidney effects. Bayesian forecasting software and first-order pharmacokinetic methods have also made it easier to apply AUC-guided dosing in various clinical settings. This review summarizes the current evidence on AUC-guided vancomycin therapeutic drug monitoring, focusing on pharmacokinetic principles, clinical effectiveness, kidney damage outcomes, implementation strategies, and new innovations. We evaluated literature published from January 2020 to June 2026 using electronic databases such as PubMed, Scopus, Embase, Web of Science, and Google Scholar. We critically assessed recent systematic reviews, meta-analyses, randomized studies, observational research, and international clinical practice guidelines. Current evidence consistently shows that AUC-guided dosing achieves

similar or better clinical effectiveness while significantly decreasing vancomycin-related kidney injury compared to traditional trough-based monitoring. Nevertheless, broader implementation is limited by restricted access to Bayesian software, a lack of institutional resources, variability in lab support, and the need for specialized training for clinicians. New developments in artificial intelligence, machine learning, model-informed dosing, and electronic health record integration could further improve personalized vancomycin therapy. Ongoing collaboration among infectious disease doctors, clinical pharmacists, microbiologists, and pharmacometricians will be crucial to maximize the clinical benefits of AUC-guided therapeutic drug monitoring.

KEYWORDS: Vancomycin, Therapeutic Drug Monitoring (TDM), Area Under the Curve (AUC), Bayesian Dosing, Precision Dosing, Antimicrobial Stewardship.

INTRODUCTION

Vancomycin is a glycopeptide antibiotic that has been crucial in treating serious Gram-positive bacterial infections for over sixty years. Since it entered clinical use in 1958, vancomycin has been widely used to treat infections from methicillin-resistant Staphylococcus aureus (MRSA), methicillin-resistant coagulase-negative staphylococci, penicillin-resistant Streptococcus pneumoniae, and susceptible Enterococcus species. Even with newer anti-MRSA treatments like linezolid, daptomycin, ceftaroline, and tedizolid, vancomycin is still recommended as a first-line treatment for many severe infections. These include bacteremia, infective endocarditis, osteomyelitis, hospital-acquired pneumonia, central nervous system infections, and complicated skin and soft tissue infections due to its proven effectiveness, wide availability, and relatively low cost.

MRSA is one of the leading causes of healthcare-associated and community-acquired infections globally. It leads to significant illness, death, longer hospital stays, and rising healthcare costs. The ongoing rise of multidrug-resistant bacteria and the global issue of antibiotic resistance highlight the need to improve antimicrobial treatment to enhance patient outcomes while reducing toxicity and the risk of resistance. As a result, antimicrobial stewardship programs increasingly focus on optimizing vancomycin dosing to ensure effective treatment and maintain its long-term use.

Vancomycin works by killing bacteria in a time-dependent manner, and its effectiveness is best understood through pharmacokinetic and pharmacodynamic (PK/PD) principles. Among

various PK/PD measurements, the ratio of the 24-hour area under the plasma concentration-time curve to the minimum inhibitory concentration ($AUC_{0–24}$/MIC) consistently shows the strongest link to bacterial eradication and treatment success. Research indicates that maintaining an AUC/MIC ratio between 400 and 600 mg·h/L (assuming an MIC of 1 mg/L from broth microdilution) offers the best antibacterial activity while lowering the risk of kidney damage. These insights have changed how we monitor vancomycin treatment.

For many years, therapeutic drug monitoring relied on trough serum concentrations as a substitute for measuring overall drug exposure. Clinical guidelines released in 2009 advised keeping trough levels between 15 and 20 mg/L in patients with serious MRSA infections to reach the desired AUC/MIC goal. However, later studies showed that trough levels do not correlate well with actual AUC values and often overestimate drug exposure. High trough concentrations have also been linked to an increased rate of vancomycin-related acute kidney injury without consistently improving outcomes. These issues highlight the need for a more accurate and personalized approach to vancomycin dosing.

Recent developments in pharmacometric modeling, Bayesian forecasting, and population pharmacokinetics have changed therapeutic drug monitoring. These methods allow healthcare providers to estimate AUC directly from limited serum concentrations. Bayesian software combines patient-specific factors with established population PK models to provide precise drug exposure estimates, often needing just one serum concentration. Alternatively, using first-order PK equations with two post-distribution serum concentrations remains a practical option when Bayesian software is not available. These strategies help optimize dosing early, improve target achievement, and minimize unnecessary drug exposure, especially for critically ill patients with variable drug processing.

With the increasing evidence supporting exposure-guided dosing, the joint consensus guidelines published in 2020 by the American Society of Health-System Pharmacists (ASHP), the Infectious Diseases Society of America (IDSA), the Pediatric Infectious Diseases Society (PIDS), and the Society of Infectious Diseases Pharmacists (SIDP) recommended AUC-guided therapeutic drug monitoring as the best method for patients with serious MRSA infections. The guidelines suggest maintaining an $AUC_{0–24}$/MIC target of 400–600 mg·h/L to optimize effectiveness while decreasing the risk of kidney damage. Since these recommendations were published, various observational studies and reviews have

shown that AUC-guided monitoring lowers vancomycin-related kidney injuries without affecting microbiological or clinical results.

Despite the recognized benefits of AUC-guided monitoring, its broad application remains difficult. Many healthcare facilities still depend on traditional trough-based monitoring due to limited access to Bayesian software, inadequate laboratory resources, budget limits, lack of trained staff, and varied institutional guidelines. Other challenges include uncertainty surrounding the best sampling strategies, differences between pharmacokinetic software, managing patients with rapidly changing kidney function, and applying AUC-guided dosing to special groups like critically ill patients, children, obese individuals, and those on renal replacement therapy. Overcoming these challenges is crucial for successfully integrating precision dosing into everyday clinical practice.

Recent advancements in digital health tools have expanded the potential for AUC-guided therapeutic drug monitoring. Investigations into artificial intelligence, machine learning algorithms, model-informed precision dosing, clinical decision support systems, and connections to electronic health records aim to automate dose adjustments and improve the efficiency of therapeutic drug monitoring. These innovations may enable real-time predictions of drug behavior, lessen the clinical workload, enhance dosing precision, and support efforts in antimicrobial stewardship across various healthcare environments.

Given the rapid development of pharmacokinetic modeling methods, new clinical evidence, and the growth of precision medicine, a fresh overview of the available information is needed. Current reviews have mainly centered on guideline recommendations or comparisons between trough-based and AUC-guided monitoring, with few comprehensively analyzing recent advances in Bayesian pharmacokinetic modeling, strategies for implementation, emerging technologies, and future research areas.

This review seeks to provide a thorough, evidence-based overview of AUC-guided vancomycin monitoring by critically assessing current clinical data, innovations in pharmacokinetics, challenges in implementation, and future directions. It also emphasizes the evolving role of clinical pharmacists in fine-tuning individualized vancomycin therapy and discusses how precision dosing technologies may improve patient outcomes and support better stewardship of antibiotics in modern healthcare.

MATERIALS AND METHODS

Study Design

This review was conducted as a comprehensive narrative review using a structured literature search strategy to summarize current evidence regarding AUC-guided vancomycin therapeutic drug monitoring (TDM). The review focused on evaluating recent advances in pharmacokinetic principles, clinical efficacy, nephrotoxicity, Bayesian pharmacokinetic modeling, implementation challenges, and emerging technologies associated with AUC-guided vancomycin dosing

Literature Search Strategy

A comprehensive electronic literature search was performed using the PubMed/MEDLINE, Scopus, Embase, Web of Science, and Google Scholar databases to identify relevant studies published between January 2020 and June 2026. Additional articles were identified by manually reviewing the reference lists of eligible publications and relevant clinical practice guidelines.

The search strategy incorporated Medical Subject Headings (MeSH) and free-text terms using Boolean operators. The principal search terms included:

- Vancomycin
- Therapeutic Drug Monitoring
- AUC-guided dosing
- Area Under the Curve
- AUC/MIC
- Bayesian dosing
- Population pharmacokinetics
- Vancomycin nephrotoxicity
- Precision dosing
- Model-informed precision dosing
- Antimicrobial stewardship
- Methicillin-resistant *Staphylococcus aureus* (MRSA)

Search terms were combined using the Boolean operators AND and OR to maximize the retrieval of relevant literature.

Inclusion Criteria

Studies were included if they met one or more of the following criteria:

- Published in peer-reviewed journals.
- Published between January 2020 and June 2026.
- Written in English.
- Evaluated AUC-guided vancomycin dosing or therapeutic drug monitoring.
- Investigated clinical efficacy, pharmacokinetic/pharmacodynamic relationships, nephrotoxicity, Bayesian dosing methods, odelling trics odelling, or implementation strategies.
- Included systematic reviews, meta-analyses, randomized controlled trials, prospective studies, retrospective cohort studies, observational studies, consensus guidelines, and expert recommendations.

Exclusion Criteria

The following publications were excluded:

- Conference abstracts without full-text availability.
- Editorials, commentaries, letters to the editor, and opinion articles lacking original clinical evidence.
- Animal or in vitro studies without direct clinical applicability.
- Duplicate publications.
- Studies published in languages other than English.
- Studies primarily evaluating antibiotics other than vancomycin unless directly relevant to comparative therapeutic drug monitoring strategies.

Study Selection

All retrieved records were screened based on their titles and abstracts for relevance to the review objectives. Potentially eligible studies underwent full-text assessment before inclusion. Particular emphasis was placed on high-quality evidence, including international consensus guidelines, systematic reviews, meta-analyses, randomized controlled trials, and large multicenter observational studies. Additional landmark publications published before 2020 were included where necessary to provide historical context regarding the evolution of vancomycin therapeutic drug monitoring.

Data Extraction

Relevant information from each eligible study was extracted using a standardized approach. Extracted variables included:

- Study characteristics (author, publication year, country, study design)
- Patient population
- Clinical setting
- Vancomycin dosing strategy
- Therapeutic drug monitoring methodology
- Target AUC/MIC values
- Pharmacokinetic modeling approach
- Bayesian software utilization (where applicable)
- Clinical efficacy outcomes
- Nephrotoxicity outcomes
- Microbiological response
- Mortality
- Length of hospital stay
- Major conclusions and clinical implications

Data Synthesis

The findings were synthesized qualitatively and organized into thematic sections. Evidence was categorized according to major domains, including vancomycin pharmacokinetics and pharmacodynamics, evolution of AUC-guided monitoring, Bayesian pharmacokinetic modeling, clinical efficacy, nephrotoxicity, implementation challenges, special patient populations, antimicrobial stewardship, and emerging innovations such as artificial intelligence and model-informed precision dosing. Where appropriate, findings from systematic reviews, meta-analyses, and major clinical studies were compared to identify areas of agreement, controversy, and future research priorities.

Quality Considerations

Priority was given to high-quality evidence, including international consensus guidelines, systematic reviews, meta-analyses, and multicenter clinical studies. The review emphasizes evidence published after the release of the 2020 consensus guidelines recommending AUC-guided therapeutic drug monitoring while incorporating seminal studies that established the pharmacokinetic and pharmacodynamic rationale for exposure-guided vancomycin dosing.

Every effort was made to ensure that the information presented reflects current clinical practice and advances in precision dosing.

RESULT AND DISCUSSIONS

Vancomycin has been a crucial antimicrobial for treating serious infections caused by methicillin-resistant Staphylococcus aureus (MRSA) and other resistant Gram-positive organisms. Since it was first used in clinical practice in 1958, vancomycin dosing strategies have changed significantly due to improved understanding of its pharmacokinetics and pharmacodynamics. In the beginning, dosing decisions mainly relied on body weight, kidney function, and the patient's clinical response. However, the wide variability in how different patients respond to vancomycin showed the need for tailored dosing strategies to ensure effective treatment while minimizing toxicity.

Therapeutic drug monitoring (TDM) has become an important tool for optimizing vancomycin therapy. Early monitoring methods included measuring both peak and trough serum concentrations. Initially, peak concentrations were thought to be crucial for evaluating how well the drug worked, while trough concentrations were tracked to prevent drug buildup and toxicity. However, later pharmacodynamic studies showed that peak concentrations did not significantly relate to clinical outcomes, which led doctors to stop routinely monitoring them. Trough concentrations then became the main focus for dose adjustments, as they were easier to measure routinely and were thought to relate to overall drug exposure. The release of the 2009 consensus guidelines was a significant milestone in vancomycin monitoring. These guidelines suggested keeping steady-state trough concentrations between 15 and 20 mg/L for patients with serious MRSA infections to maintain an AUC/MIC ratio of at least 400. For many years, this recommendation was widely adopted in hospitals worldwide due to its simplicity and practicality. However, growing clinical evidence gradually exposed critical limitations of relying solely on trough measurements. Several pharmacokinetic studies found that trough concentrations only weakly correlated with total systemic drug exposure and often failed to predict the actual AUC in individual patients. As a result, patients with seemingly therapeutic trough levels sometimes received excessive vancomycin, increasing the risk of kidney damage without any additional clinical benefit.

Improvements in pharmacokinetic modeling significantly shifted the understanding of vancomycin exposure. Multiple studies identified the 24-hour area under the concentration–time curve to minimum inhibitory concentration ratio ($AUC_{0–24}$/MIC) as the

pharmacodynamic metric most closely linked to bacterial elimination and favorable clinical results. Unlike trough concentrations, which only reflect a single value during a dosing interval, the AUC captures the total drug exposure over 24 hours, offering a clearer view of treatment effectiveness. Clinical studies consistently showed that maintaining an $AUC_{0–24}$/MIC ratio between 400 and 600 mg·h/L optimizes bacterial killing and significantly reduces the risk of vancomycin-related acute kidney injury.

The introduction of Bayesian pharmacokinetic software further sped up the shift to AUC-guided monitoring. Bayesian forecasting uses patient-specific details, such as age, weight, kidney function, dosing history, and measured serum concentrations, along with validated population pharmacokinetic models to accurately estimate individual AUC values. Compared to traditional pharmacokinetic calculations, Bayesian methods typically require fewer blood samples, allow for quicker dose adjustments, and enhance the precision of therapeutic drug monitoring. These benefits have made Bayesian-guided dosing more appealing in both adult and pediatric care.

A landmark development in 2020 occurred when the American Society of Health-System Pharmacists (ASHP), the Infectious Diseases Society of America (IDSA), the Pediatric Infectious Diseases Society (PIDS), and the Society of Infectious Diseases Pharmacists (SIDP) jointly recommended AUC-guided therapeutic drug monitoring as the best dosing strategy for serious MRSA infections. The updated consensus guidelines suggested targeting an $AUC_{0–24}$/MIC ratio of 400–600 mg·h/L, assuming a vancomycin MIC of 1 mg/L measured by broth microdilution. These recommendations were backed by growing evidence that AUC-guided dosing maintains the drug's effectiveness while greatly reducing the risk of kidney damage compared to trough-based monitoring.

After the updated guidelines were published, healthcare institutions in many countries began to adopt AUC-guided dosing protocols. Numerous observational studies, systematic reviews, and meta-analyses released in recent years consistently show reduced rates of vancomycin-related acute kidney injury, improved target attainment, and similar or better clinical outcomes for patients managed with AUC-guided therapeutic drug monitoring. The integration of Bayesian software into hospital electronic prescription systems and antimicrobial stewardship programs has further facilitated the regular use of individualized dosing strategies.

DISCUSSION

The evolution of vancomycin therapeutic drug monitoring marks a broader shift from standard antimicrobial dosing to more precise pharmacotherapy. While trough concentration monitoring was a significant improvement over empirical dosing, it has become clear that trough levels alone cannot reliably define systemic vancomycin exposure. A single serum measurement offers limited pharmacokinetic insights and does not fully consider patient-specific differences in drug clearance, distribution, or changing kidney function. Consequently, sticking only to trough concentrations may lead to excessively high drug levels or fail to ensure sufficient antibacterial exposure in critically ill patients.

Switching to AUC-guided monitoring is a scientifically grounded strategy that incorporates pharmacokinetic and pharmacodynamic principles into everyday clinical practice. By measuring total daily drug exposure, clinicians can customize vancomycin dosing to fit the patient's physiological traits and treatment needs. This personalized approach is particularly significant for critically ill patients, children, obese individuals, and patients with quickly changing kidney function, where variability in pharmacokinetics is most pronounced.

Recent systematic reviews and meta-analyses have consistently shown that AUC-guided dosing significantly lowers the incidence of vancomycin-related acute kidney injury without compromising the effectiveness of microbiological eradication, treatment success, or overall survival. These results strongly back the 2020 international consensus guidelines and emphasize the growing importance of exposure-guided dosing as the preferred standard of care. Additionally, the rising availability of Bayesian pharmacokinetic software, electronic clinical decision support systems, and pharmacist-led antimicrobial stewardship programs has made it easier to implement AUC-guided monitoring in hospitals.

Despite these advancements, several challenges still hinder widespread adoption. Implementing Bayesian software requires financial investment, staff training, and compatibility with existing hospital information systems. Many healthcare facilities, especially in resource-limited areas, continue to rely on traditional trough-based monitoring due to infrastructure limitations and a lack of pharmacokinetic expertise. However, ongoing technological innovations, including cloud-based Bayesian platforms, machine learning algorithms, and model-informed precision dosing systems, are expected to simplify AUC estimation and encourage broader use globally.

Overall, the shift from trough-guided monitoring to AUC-guided therapeutic drug monitoring represents one of the most important advancements in modern antimicrobial pharmacotherapy. By enhancing treatment precision and lessening drug-related toxicity, AUC-guided dosing has set a new standard for personalized vancomycin therapy and continues to bolster antimicrobial stewardship initiatives aimed at improving patient outcomes while maintaining the long-term effectiveness of this vital antibiotic.

Table 1

Comparison of Trough-Guided and AUC-Guided Vancomycin Therapeutic Drug Monitoring

Parameter	Trough-Guided Monitoring	AUC-Guided Monitoring
Therapeutic target	15–20 mg/L	$AUC_{0–24}$/MIC 400–600 mg·h/L
PK/PD parameter	Single trough concentration	Total drug exposure (AUC)
Clinical efficacy	Variable	More consistent
Risk of nephrotoxicity	Higher	Lower
Dose individualization	Limited	High
Bayesian software	Not required	Preferred
Current guideline status	Historical approach	Recommended by 2020 consensus guidelines

Table 2

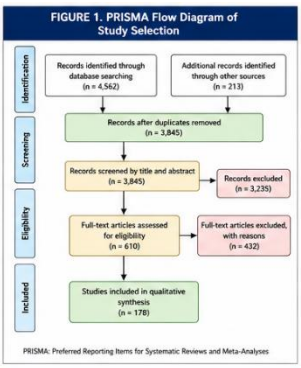
Evolution of Vancomycin Therapeutic Drug Monitoring

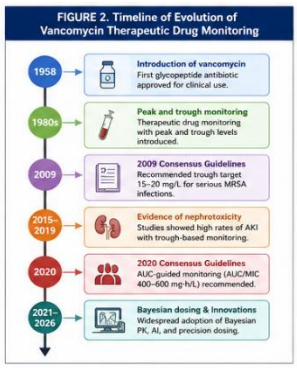
Year	Milestone	Clinical Significance
1958	Vancomycin introduced	First glycopeptide antibiotic
1980s	Peak/trough monitoring	Beginning of TDM
2009	Consensus guideline	Trough target 15–20 mg/L
2020	Revised guideline	AUC-guided monitoring recommended
2021–2026	Bayesian dosing	Precision dosing expansion

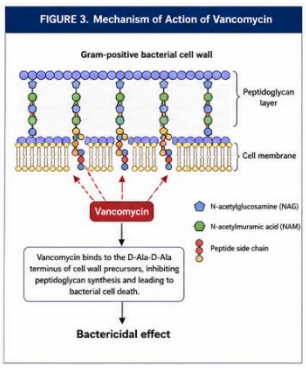
Table 3

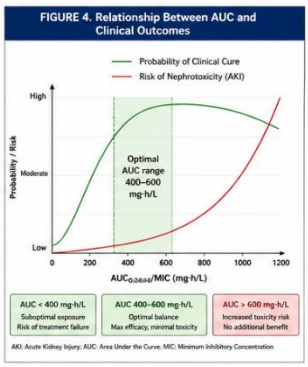
Pharmacokinetic Properties of Vancomycin

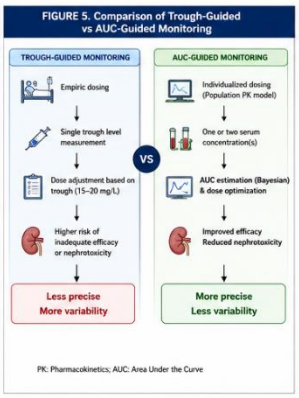
Parameter	Characteristics
Bioavailability	Poor oral absorption
Route	Intravenous for systemic infection
Protein binding	30–55%
Volume of distribution	0.4–1 L/kg
Half-life	4–8 h
Elimination	Renal
PK/PD index	AUC/MIC

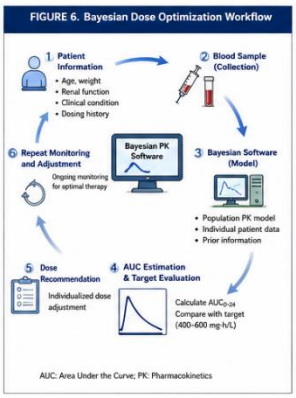


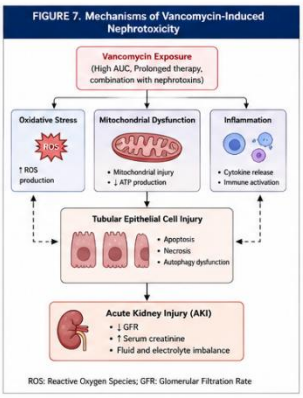


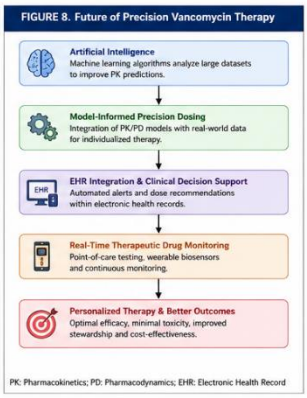












The transition from trough-based monitoring to AUC-guided dosing represents one of the most important advances in clinical pharmacokinetics over the past decade. While trough concentrations provide only a single snapshot of drug exposure, AUC incorporates the entire concentration–time profile and therefore offers a more comprehensive assessment of antimicrobial therapy. This distinction is clinically significant because both inadequate and excessive vancomycin exposure can adversely affect patient outcomes. Insufficient exposure may lead to treatment failure, persistent bacteremia, and the emergence of bacterial resistance, whereas excessive exposure substantially increases the risk of nephrotoxicity.

Recent systematic reviews and meta-analyses consistently demonstrate that AUC-guided monitoring improves target attainment and significantly reduces vancomycin-associated acute kidney injury without compromising clinical efficacy. These findings have prompted international guideline committees to endorse AUC-guided dosing as the preferred therapeutic monitoring strategy for serious MRSA infections. Furthermore, advances in Bayesian pharmacokinetic software have greatly improved the feasibility of implementing exposure-guided dosing in routine clinical practice, allowing clinicians to obtain accurate AUC estimates with fewer serum samples and less computational complexity.

Despite these advances, several practical challenges remain. Accurate AUC estimation requires reliable laboratory support, validated pharmacokinetic models, and appropriate clinician training. Variability in Bayesian software platforms, institutional protocols, and laboratory turnaround times may influence the consistency of dose recommendations. In addition, patients with rapidly changing renal function or complex critical illness continue to present challenges for pharmacokinetic prediction. Continued refinement of model-informed precision dosing algorithms, together with integration into electronic health records and clinical decision support systems, is expected to further improve the accuracy and accessibility of AUC-guided therapeutic drug monitoring in the coming years.

CONCLUSION

Vancomycin continues to play a pivotal role in the management of serious infections caused by methicillin-resistant *Staphylococcus aureus* (MRSA) and other resistant Gram-positive pathogens. The evolution of therapeutic drug monitoring from conventional trough-based monitoring to area under the concentration–time curve (AUC)-guided dosing represents a major advancement in precision antimicrobial therapy. A growing body of evidence consistently demonstrates that AUC-guided therapeutic drug monitoring provides a more accurate assessment of vancomycin exposure than trough concentrations alone, enabling clinicians to optimize antimicrobial efficacy while substantially reducing the risk of vancomycin-associated nephrotoxicity.

The 2020 international consensus guidelines have established an $AUC_{0–24}$/MIC target of **400–600 mg·h/L** as the preferred therapeutic range for patients with serious MRSA infections. Subsequent observational studies, systematic reviews, and meta-analyses have reinforced these recommendations by showing that AUC-guided dosing achieves improved target attainment and a lower incidence of acute kidney injury without compromising microbiological eradication, clinical cure, or patient survival. These findings support the transition toward exposure-based monitoring as the contemporary standard of care for vancomycin therapy.

The successful implementation of AUC-guided therapeutic drug monitoring depends on the integration of pharmacokinetic principles into routine clinical practice. Bayesian pharmacokinetic software and model-informed precision dosing have simplified individualized dose optimization and enhanced the feasibility of AUC estimation in diverse healthcare settings. Nevertheless, important implementation barriers remain, including

limited access to validated software, infrastructure constraints, variability in institutional protocols, laboratory resource limitations, and the need for clinician education and interdisciplinary collaboration. Overcoming these challenges will be essential to ensure equitable adoption of AUC-guided monitoring across both resource-rich and resource-limited healthcare systems.

Clinical pharmacists have an increasingly important role in facilitating AUC-guided vancomycin monitoring through dose optimization, interpretation of pharmacokinetic data, therapeutic drug monitoring, multidisciplinary collaboration, and antimicrobial stewardship initiatives. Their involvement contributes to improved medication safety, individualized patient care, and rational antimicrobial use.

Looking ahead, advances in artificial intelligence, machine learning, electronic health record integration, and model-informed precision dosing are expected to further transform vancomycin therapeutic drug monitoring. These technologies have the potential to automate dose individualization, improve prediction accuracy, support real-time clinical decision-making, and expand access to precision dosing strategies. Future multicenter prospective studies should evaluate the long-term clinical, economic, and implementation outcomes of these emerging technologies across diverse patient populations, including critically ill patients, pediatric patients, individuals with obesity, and those receiving renal replacement therapy.

In conclusion, AUC-guided vancomycin therapeutic drug monitoring represents a paradigm shift from empirical dosing toward evidence-based precision pharmacotherapy. By integrating pharmacokinetic principles with individualized patient care, this approach improves therapeutic precision, enhances patient safety, and strengthens antimicrobial stewardship efforts. Continued research, technological innovation, and interdisciplinary collaboration will be critical to maximizing the clinical benefits of AUC-guided monitoring and ensuring its sustainable implementation as the global standard for optimizing vancomycin therapy.

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