



Antimicrobial Stewardship Outcomes Following Pharmacist-Directed Dose Optimization

Bekturov A^{1*}, Kaliyev B² and Amirkhanov A³

¹Department of Translational Medicine, Bishkek Institute of Pharmacology, Uzbekistan Scopus Author ID: 57185288004
Email: aizhan.bekturov@bishkek.edu

ORCID: <https://orcid.org/0081-6474-2311-337X>

²Department of Applied Sciences, Shymkent Institute of Applied Pharmacy, Tajikistan Scopus Author ID: 57183273746
Email: bekzat.kaliyev@shymkent.edu

ORCID: <https://orcid.org/8836-8524-3793-4541>

³Department of Biomedical Research, Bishkek Institute of Pharmacology, Kazakhstan Scopus Author ID: 57632821868
Email: aizhan.amirkhanov@bishkek.edu

ORCID: <https://orcid.org/3886-2738-1584-4985>

***Correspondence to:** Aizhan Bekturov, Department of Translational Medicine, Bishkek Institute of Pharmacology, Uzbekistan Scopus Author ID: 57185288004 Email: aizhan.bekturov@bishkek.edu

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Abstract

Dosing is often treated as a settled question once an appropriate antimicrobial has been selected, yet a substantial share of the measurable clinical and safety signal in antimicrobial therapy lives in the dose itself. This short communication synthesizes the outcomes literature on pharmacist-directed antimicrobial dose optimization, concentrating on the two areas with the most mature evidence base: vancomycin area-under-the-curve (AUC)-guided dosing and beta-lactam pharmacokinetic/pharmacodynamic (PK/PD) optimization. AUC-guided vancomycin dosing, now the consensus-recommended standard in place of trough-only monitoring, is associated with significantly lower nephrotoxicity in both a quasi-experimental cohort study and a subsequent pooled meta-analysis. For beta-lactams, prolonged or extended infusion improves target attainment relative to standard intermittent bolus dosing and is associated with a mortality reduction in sepsis, while therapeutic drug monitoring improves clinical cure and reduces nephrotoxicity-type adverse events relative to fixed dosing without monitoring. Both interventions sit within, and appear consistent with, the broader pattern of reduced antimicrobial consumption, cost, and length of stay reported for pharmacist-led antimicrobial stewardship programs generally. Realizing these gains depends on institutional investment in pharmacokinetic expertise, drug-level monitoring turnaround, and infusion workflow changes that remain unevenly available across hospitals. Pharmacist-directed dose optimization is best understood not as a single order-set adjustment but as an iterative, patient-specific clinical service with directly attributable safety and efficacy benefits.

Keywords: antimicrobial stewardship; pharmacist-directed dosing; vancomycin AUC-guided dosing; beta-lactam pharmacokinetics; nephrotoxicity

1. Introduction

Antimicrobial stewardship programs (ASPs) were built on a straightforward premise: antibiotics are a shared, depleting resource, and the choices made about which agent, dose, and duration to use in one patient shape the resistance risk faced by the next [1]. Much of the stewardship literature, and much of stewardship practice, has historically concentrated on the "front door" of that decision — de-escalation, agent selection, and duration — while treating dosing as a comparatively settled question once an appropriate drug has been chosen. That framing undersells how much of the measurable clinical and safety signal in antimicrobial therapy actually lives in the dose. Vancomycin and the beta-lactams, the two antibiotic classes with the deepest pharmacist-directed dosing literature, illustrate the point directly: get the exposure wrong in either direction and a "correctly selected" antibiotic can still under-treat an infection, over-expose a kidney, or both, depending on which side of a narrow target the patient's clearance happens to put them.

Pharmacist-directed dose optimization — clinical pharmacists calculating, monitoring, and iteratively adjusting antimicrobial doses using pharmacokinetic principles, renal function trending, and, where available, measured drug concentrations — sits squarely inside the "optimize dosing" domain the Infectious Diseases Society of America and Society for Healthcare Epidemiology of America's stewardship guideline lists as a core, evidence-supported ASP action alongside prospective audit-and-feedback and formulary restriction [1]. Unlike agent selection, dose optimization is not a discrete decision made once at admission; it is a longitudinal process that has to track a moving target, since renal function, volume status, and body composition all shift over the course of a hospitalization, and the pharmacokinetic literature underlying vancomycin and beta-lactam dosing has itself moved substantially over the past decade, from trough-only targets toward area-under-the-curve (AUC) and continuous-infusion pharmacodynamic targets that are harder to hit without dedicated, iterative pharmacist involvement [2,3].

The stakes for getting this right are not abstract. Bacterial antimicrobial resistance was associated with an estimated 4.95 million deaths globally in 2019, with 1.27 million deaths directly attributable to resistant

infections — a burden the same analysis ranks above HIV/AIDS and malaria for that year [4]. Underdosing that fails to achieve a pharmacodynamic target is one of the more direct, mechanistically plausible drivers of that burden at the bedside, since subtherapeutic exposure selects for resistant subpopulations even when the "right" drug was chosen. Overdosing carries its own, more immediate cost in nephrotoxicity, particularly with vancomycin, where the relationship between drug exposure and acute kidney injury (AKI) is one of the best-quantified dose-toxicity relationships in the antimicrobial literature [5,6].

This short communication synthesizes the outcomes literature on pharmacist-directed antimicrobial dose optimization, focusing on the two areas — vancomycin AUC-guided dosing and beta-lactam pharmacokinetic/pharmacodynamic (PK/PD) optimization — where pharmacist-led dosing services have the most mature evidence base, before summarizing the broader stewardship-outcomes literature that situates dose optimization within pharmacist-led ASPs as a whole.

2. Rationale for Pharmacist-Directed Dose Optimization

Dose optimization asks pharmacists to do something most other stewardship interventions do not: apply quantitative pharmacokinetic reasoning to an individual patient's changing physiology, repeatedly, over the course of a single antibiotic course. A patient's creatinine clearance on hospital day one may differ substantially from clearance on day four after volume resuscitation, an episode of acute kidney injury, or the start of renal replacement therapy, and each of these shifts changes the dose required to hit the same pharmacodynamic target. Hou et al.'s single-center evaluation of clinical pharmacist intervention in ICU patients with antimicrobial-induced AKI found that pharmacist-directed renal function monitoring and dose adjustment was associated with measurably better recovery of renal function during the ICU stay relative to a historical comparison group, underscoring that the dosing decision is not a one-time calculation but an ongoing clinical task that benefits from dedicated pharmacist attention [7].

Body composition adds a second axis of complexity that generic weight-based dosing formulas handle poorly. Updated consensus dosing recommendations for obese

patients highlight that volume of distribution and clearance for many antimicrobials, vancomycin included, scale non-linearly with total body weight, such that dosing regimens validated in patients of average body habitus can systematically under- or over-dose patients at the extremes of body weight unless a pharmacist applies an obesity-specific dosing strategy [8]. Neither the renal-trajectory problem nor the body-composition problem is solved by a fixed order-set dose; both require the kind of iterative, patient-specific recalculation that pharmacist-directed dosing services were built to provide.

3. Vancomycin AUC-Guided Dosing

Vancomycin dosing has undergone the most consequential practice shift of any antimicrobial in the past decade. The 2020 revised ASHP/PIDS/SIDP/IDSA consensus guideline formally recommends AUC-guided dosing, targeting an AUC-to-minimum-inhibitory-concentration ratio of 400–600, in place of the trough-only monitoring (typically targeting troughs of 15–20 mg/L) that had been standard practice for the preceding decade, citing accumulating evidence that trough-only targeting drives unnecessarily high exposure and nephrotoxicity risk without a compensating gain in efficacy [2]. Translating that guideline into practice is, in most institutions, a pharmacist-driven exercise: Bayesian or first-order pharmacokinetic AUC calculation, and the dose adjustments that follow from it, require either dedicated software or the kind of pharmacokinetic training that sits within clinical pharmacy practice rather than routine physician workflow.

The outcomes evidence for this shift is reasonably direct. Finch et al.'s quasi-experimental before-after study compared trough-only monitoring against AUC-guided dosing and found AUC-guided dosing independently associated with lower nephrotoxicity (adjusted odds ratio 0.52, 95% CI 0.34–0.80) after adjusting for relevant confounders [5]. Abdelmessih et al.'s subsequent systematic review and meta-analysis pooled data across multiple comparative studies and confirmed the same direction of effect: AUC-guided dosing was associated with a significantly lower risk of acute kidney injury than trough-only dosing, without evidence of a corresponding loss of clinical efficacy [6]. Because AUC calculation and the resulting dose titration is, in most reported implementations, executed by pharmacists

rather than prescribers, this nephrotoxicity reduction functions in practice as a direct outcome of pharmacist-directed dose optimization rather than of the guideline change alone — the guideline set the target, but pharmacist-run dosing services are what actually hit it consistently across a hospitalized population.

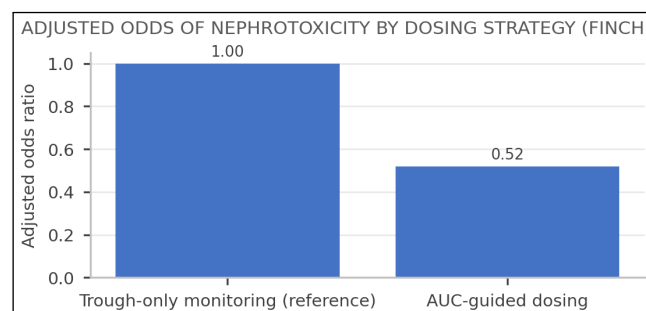


Figure 1: Adjusted odds of nephrotoxicity with AUC-guided vancomycin dosing relative to trough-only monitoring (reference = 1.0), as reported by Finch et al.'s quasi-experimental cohort study [5].

4. Beta-Lactam Pharmacokinetic/Pharmacodynamic Optimization

Beta-lactam dosing raises a related but distinct problem: rather than a single trough or AUC target, beta-lactam efficacy is driven by the proportion of the dosing interval during which free drug concentration exceeds the pathogen's minimum inhibitory concentration (%fT>MIC), a target that standard intermittent bolus dosing regimens frequently fail to achieve in critically ill patients with altered, typically increased, drug clearance. The multinational DALI point-prevalence study measured beta-lactam concentrations in a large cohort of critically ill patients receiving standard dosing and found that a substantial proportion of measured concentrations, particularly among patients with augmented renal clearance, failed to reach even conservative PK/PD targets, despite patients receiving doses considered standard-of-care at the time [3]. That finding reframed beta-lactam underdosing in the ICU as a common, largely invisible failure mode rather than an occasional edge case.

Two complementary interventions address this gap, both of which depend heavily on pharmacist involvement to implement correctly. First, prolonged or continuous infusion, rather than traditional 30-minute intermittent bolus dosing, extends the fraction of the dosing interval above MIC for a given total daily dose. A systematic review and meta-analysis of randomized

trials comparing prolonged/extended versus intermittent beta-lactam infusion in patients with sepsis found that prolonged infusion was associated with a significant reduction in mortality relative to intermittent infusion, a finding that held up under trial sequential analysis intended to guard against a false-positive pooled result from cumulative underpowered trials [9]. Second, therapeutic drug monitoring (TDM) closes the loop by measuring actual free-drug concentrations and allowing iterative dose adjustment rather than relying on population pharmacokinetic assumptions alone; a systematic review and meta-analysis of beta-lactam TDM in critically ill patients reported that TDM-guided dosing was associated with improved clinical cure and a reduced risk of nephrotoxicity-type adverse events relative to fixed dosing without monitoring, though the authors were candid that the certainty of evidence for individual outcomes varied across the included studies [10]. Both interventions — selecting a prolonged-infusion regimen and interpreting a TDM result to adjust the next dose — are, in most institutions that have implemented them, pharmacist-driven decisions embedded in a stewardship-adjacent dosing service rather than routine prescriber tasks.

Table 1: Pharmacist-directed dosing interventions for vancomycin and beta-lactams, the comparator each cited study evaluated them against, and the reported outcome effect. [5,6,2,3,9,10].

Intervention	Source	Comparator	Reported Effect
Vancomycin AUC-guided dosing	Finch et al. [5]	Trough-only monitoring	Adjusted OR 0.52 (95% CI 0.34-0.80) for nephrotoxicity
Vancomycin AUC-guided dosing (pooled)	Abdelmessih et al. [6]	Trough-only monitoring	Significantly lower pooled risk of acute kidney injury
AUC 400-600 mg-h/L target	Rybak et al. consensus guideline [2]	Trough 15-20 mg/L target	Recommended as revised standard of care
Standard intermittent beta-lactam dosing	Roberts et al., DALI study [3]	Conservative PK/PD target (50% fT>MIC)	Target not reached in a substantial proportion of ICU patients, especially with augmented renal clearance
Prolonged/extended beta-lactam infusion	Li et al. meta-analysis [9]	Intermittent bolus infusion	Significant mortality reduction in sepsis, robust to trial sequential analysis
Beta-lactam therapeutic drug monitoring	Mangalore et al. meta-analysis [10]	Fixed dosing without monitoring	Improved clinical cure; reduced nephrotoxicity-type adverse events

5. Outcomes of Pharmacist-Directed Dosing Within Broader Stewardship

Placing dose optimization within the wider pharmacist-led stewardship literature helps calibrate how much of the aggregate ASP outcomes signal plausibly traces back to dosing specifically. Karanika et al.'s systematic review and meta-analysis of hospital-based antimicrobial stewardship programs, most of which are pharmacist-driven or pharmacist-co-led, found significant reductions in antimicrobial consumption and in overall hospital cost associated with ASP implementation across the pooled studies [11]. Mahmood et al.'s more recent meta-analysis focusing specifically on pharmacist-led stewardship services similarly reported improved clinical outcomes, including reduced length of stay, associated with pharmacist involvement relative to usual prescriber-driven care [12]. A 2026 randomized controlled trial of clinical pharmacist-led stewardship in hospital-acquired and ventilator-associated pneumonia reported improvements in antibiotic appropriateness and reductions in antimicrobial consumption in the pharmacist-led arm relative to standard care, adding a randomized data point to a literature that has historically leaned on before-after and quasi-experimental designs [13]. The same pattern extends beyond the medical ICU: Naseralallah et al.'s systematic review and meta-analysis of pharmacist-led stewardship in perioperative settings, where dosing decisions for surgical prophylaxis are similarly time-sensitive and pharmacist-driven, found consistent reductions in inappropriate antibiotic use and improved compliance with dosing and redosing protocols across the pooled studies [14].

Dosing-specific outcomes are, within these broader stewardship evaluations, usually reported as one contributing element among several (alongside de-escalation rates, time-to-appropriate-therapy, and duration) rather than isolated as an independent variable, which makes it difficult to attribute a precise fraction of the pooled length-of-stay or cost effect to dose optimization specifically. What the vancomycin and beta-lactam literatures add, by contrast, is exactly that isolation: because AUC-guided dosing and PK/PD-optimized beta-lactam regimens can be evaluated against a clearly defined comparator (trough-only monitoring; intermittent bolus dosing) on a narrowly defined outcome (nephrotoxicity; mortality; clinical cure), they offer some of the cleanest attributable-effect estimates available anywhere in the

stewardship-outcomes literature, even though they represent only two of the many activities a pharmacist-led ASP performs.

6. Implementation Challenges

None of the dosing interventions summarized above are self-executing. AUC-guided vancomycin dosing requires either Bayesian dosing software or trained staff comfortable with first-order pharmacokinetic calculations, and institutions without either resource default back toward trough-only monitoring by necessity rather than choice. Beta-lactam TDM requires an assay turnaround time fast enough to inform a dosing decision before the next scheduled dose, a capability that remains limited to a minority of hospitals even in health systems that have otherwise invested heavily in stewardship infrastructure [10]. Prolonged-infusion beta-lactam regimens require compatible infusion pump programming and nursing workflow changes that are logistically nontrivial to roll out across an entire hospital rather than a single unit.

There is also a workforce constraint that the outcomes literature rarely quantifies directly: iterative, patient-specific dose optimization is time-intensive pharmacist work, and scaling it across an entire hospitalized population, rather than a curated high-risk subset, requires a staffing model that not every institution can support. The studies synthesized here were, almost without exception, conducted at academic or large tertiary centers with dedicated pharmacokinetics services already in place, which leaves open how much of the reported benefit is attributable to the dosing strategy itself versus the concentrated pharmacist expertise available to execute it — a distinction that matters for institutions considering whether to invest in the service model rather than simply the dosing target.

7. Conclusion

The literature on pharmacist-directed antimicrobial dose optimization supports a fairly specific, evidence-grounded claim rather than a general endorsement of stewardship: vancomycin AUC-guided dosing measurably reduces nephrotoxicity relative to trough-only monitoring [5,6,2], and beta-lactam PK/PD optimization, through prolonged infusion and therapeutic drug monitoring, measurably improves target attainment and, in the case of prolonged infusion

in sepsis, mortality [3,9,10]. Both interventions sit inside the broader pattern of favorable outcomes reported for pharmacist-led antimicrobial stewardship generally [11,12,13,1], but they are distinguished from most other stewardship activities by having a comparator and outcome specific enough to isolate their individual contribution. Realizing these gains at scale depends on institutional investment in the pharmacokinetic expertise, monitoring infrastructure, and workflow changes that pharmacist-directed dosing services require [8,7] — an implementation cost that the outcomes literature demonstrates is worth paying, but that remains unevenly distributed across the hospitals that would benefit from it.

8. References

1. Barlam, T.F., Cosgrove, S.E., Abbo, L.M., MacDougall, C., Schuetz, A.N., Septimus, E.J., et al. (2016) Implementing an Antibiotic Stewardship Program: Guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clinical Infectious Diseases*, 62(10): e51-e77. DOI: [10.1093/cid/ciw118](https://doi.org/10.1093/cid/ciw118)
2. Rybak, M.J., Le, J., Lodise, T.P., Levine, D.P., Bradley, J.S., Liu, C., et al. (2020) Therapeutic monitoring of vancomycin for serious methicillin-resistant *Staphylococcus aureus* infections: A revised consensus guideline by the American Society of Health-System Pharmacists, IDSA, PIDS, and SIDP. *American Journal of Health-System Pharmacy*, 77(11): 835-864. DOI: [10.1093/ajhp/zxaa036](https://doi.org/10.1093/ajhp/zxaa036)
3. Roberts, J.A., Paul, S.K., Akova, M., Bassetti, M., De Waele, J.J., Dimopoulos, G., et al. (2014) DALI: Defining Antibiotic Levels in Intensive Care Unit Patients: Are Current beta-Lactam Antibiotic Doses Sufficient for Critically Ill Patients? *Clinical Infectious Diseases*, 58(8): 1072-1083. DOI: [10.1093/cid/ciu027](https://doi.org/10.1093/cid/ciu027)
4. Antimicrobial Resistance Collaborators (2022) Global burden of bacterial antimicrobial resistance in 2019: a systematic analysis. *The Lancet*, 399(10325): 629-655. DOI: [10.1016/S0140-6736\(21\)02724-0](https://doi.org/10.1016/S0140-6736(21)02724-0)
5. Finch, N.A., Zasowski, E.J., Murray, K.P., Mynatt, R.P., Zhao, J.J., Yost, R., Pogue, J.M., Rybak, M.J. (2017) A Quasi-Experiment To Study the Impact of Vancomycin Area under the Concentration-Time Curve-Guided Dosing on Vancomycin-Associated Nephrotoxicity. *Antimicrobial Agents and Chemotherapy*, 61(12): e01293-17. DOI: [10.1128/aac.01293-17](https://doi.org/10.1128/aac.01293-17)
6. Abdelmessih, E., Patel, N., Vekaria, J., Crovetto, B., SanFilippo, S., Adams, C., Brunetti, L. (2022) Vancomycin area under the curve versus trough only guided dosing and the risk of

acute kidney injury: Systematic review and meta-analysis. *Pharmacotherapy*, 42(9): 741-753. DOI: [10.1002/phar.2722](https://doi.org/10.1002/phar.2722)

7. Hou, J., Li, J.F., Yan, X.J., Zhang, Y.L., Zhang, M.Y., Zhang, Y. (2023) The Effect of Clinical Pharmacist Intervention on Renal Function Impairment in Patients with Antimicrobial-Induced Acute Kidney Injury in ICU. Patient Preference and Adherence, 17: 711-718. DOI: [10.2147/PPA.S397873](https://doi.org/10.2147/PPA.S397873)
8. Castro-Balado, A., Varela-Rey, I., Mejuto, B., Mondelo-Garcia, C., Zarra-Ferro, I., Rodriguez-Jato, T., Fernandez-Ferreiro, A. (2024) Updated antimicrobial dosing recommendations for obese patients. *Antimicrobial Agents and Chemotherapy*, 68(5): e01719-23. DOI: [10.1128/aac.01719-23](https://doi.org/10.1128/aac.01719-23)
9. Li, X., Long, Y., Wu, G., Li, R., Zhou, M., He, A., Jiang, Z. (2023) Prolonged vs intermittent intravenous infusion of beta-lactam antibiotics for patients with sepsis: a systematic review of randomized clinical trials with meta-analysis and trial sequential analysis. *Annals of Intensive Care*, 13: 121. DOI: [10.1186/s13613-023-01222-w](https://doi.org/10.1186/s13613-023-01222-w)
10. Mangalore, R.P., Ashok, A., Lee, S.J., Romero, L., Peel, T.N., Udy, A.A., Peleg, A.Y. (2022) Beta-Lactam Antibiotic Therapeutic Drug Monitoring in Critically Ill Patients: A Systematic Review and Meta-Analysis. *Clinical Infectious Diseases*, 75(10): 1848-1860. DOI: [10.1093/cid/ciac506](https://doi.org/10.1093/cid/ciac506)
11. Karanika, S., Paudel, S., Grigoras, C., Kalbasi, A., Mylonakis, E. (2016) Systematic Review and Meta-analysis of Clinical and Economic Outcomes from the Implementation of Hospital-Based Antimicrobial Stewardship Programs. *Antimicrobial Agents and Chemotherapy*, 60(8): 4840-4849. DOI: [10.1128/aac.00825-16](https://doi.org/10.1128/aac.00825-16)
12. Mahmood, R.K., Gillani, S.W., Saeed, M.W., Vippadapu, P., Alzaabi, M.J.M.A. (2021) Impact of pharmacist-led services on antimicrobial stewardship programs: a meta-analysis on clinical outcomes. *Journal of Pharmaceutical Health Services Research*, 12(4): 615-625. DOI: [10.1093/jphsr/rmab036](https://doi.org/10.1093/jphsr/rmab036)
13. Alsubaie, N., Ilyas, M., Shah, Z.A., Habib, I., Binsaleh, A.Y., Alrossies, A.S. (2026) Impact of clinical pharmacist-led antimicrobial stewardship on antibiotic appropriateness, clinical outcomes, and antimicrobial consumption in hospital-acquired and ventilator-associated pneumonia: a randomized controlled trial. *Frontiers in Public Health*, 14: 1700328. DOI: [10.3389/fpubh.2026.1700328](https://doi.org/10.3389/fpubh.2026.1700328)
14. Naseralallah, L., Koraysh, S., Aboujabal, B., Alasmar, M. (2024) Effectiveness of pharmacist-led antimicrobial stewardship programs in perioperative settings: A systematic review and meta-analysis. *Research in Social and Administrative Pharmacy*, 20(11): 1023-1037. DOI: [10.1016/j.sapharm.2024.08.006](https://doi.org/10.1016/j.sapharm.2024.08.006)

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Conflict of Interest

The authors declare that they have no competing interests relevant to this work.

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Ethical Approval

Not applicable. This article synthesizes previously published literature and did not involve human participants, animal subjects, or the collection of primary clinical data by the authors.

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