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The Role of Therapeutic Drug Monitoring (TDM) by Clinical Pharmacists in Patients Undergoing Antibiotic Therapy: A Narrative Review

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ABSTRACT: Therapeutic Drug Monitoring (TDM) is a vital clinical practice aimed at optimizing the effectiveness and safety of antibiotic therapy. This narrative review explores the impact of pharmacist led TDM on antibiotic use by evaluating its clinical, microbiological, and economic outcomes. A comprehensive literature search was conducted across Scopus, PubMed, and Google Scholar databases targeting peer reviewed studies published between 2015 and 2025. Studies were selected based on predefined inclusion criteria, and findings were thematically analysed. The review highlights that pharmacist led TDM significantly improves pharmacokinetic/pharmacodynamic (PK/PD) target attainment, reduces antibiotic related adverse events, shortens hospital stays, and enhances overall therapeutic outcomes. Furthermore, TDM contributes to antimicrobial resistance mitigation by ensuring precise antibiotic exposure and supporting rational use decisions such as de-escalation and oral conversion. In addition, economic evaluations demonstrate that TDM can reduce total healthcare costs, especially in patients with severe infections. Despite these advantages, barriers to widespread implementation include limited infrastructure, insufficient clinical training, lack of integrated information systems, and weak institutional policies. These findings underscore the need for stronger interdisciplinary collaboration, investment in clinical training and digital health tools, and the inclusion of TDM in antimicrobial stewardship frameworks. As a strategic intervention, pharmacist directed TDM offers substantial promise in optimizing antibiotic use and addressing the growing threat of antimicrobial resistance.

Keywords: Therapeutic Drug Monitoring, Clinical Pharmacist, Antibiotic Therapy, Pharmacokinetics, Antimicrobial Resistance, Patient Outcomes, Healthcare Cost.

INTRODUCTION

Therapeutic Drug Monitoring (TDM) has emerged as a cornerstone of precision pharmacotherapy, particularly in the management of infectious diseases where antibiotic stewardship is critical. By

measuring plasma drug concentrations and interpreting them against pharmacokinetic/pharmacodynamic (PK/PD) targets, clinicians aim to maximise therapeutic efficacy while minimising toxicity and the emergence of resistance (Rahmawati et al., 2023). International guidelines increasingly recommend TDM for antibiotics with narrow therapeutic indices such as vancomycin and aminoglycosides because even minor deviations from the optimal exposure range can translate into clinical failure or nephro ototoxicity (Ariyanto et al., 2023). Concurrently, the global rise of antimicrobial resistance (AMR) has intensified interest in individualised dosing strategies that both enhance patient outcomes and preserve antibiotic armamentaria for future generations (Tsalsabilla & Yulianti, 2022).

Recent systematic reviews highlight a robust body of evidence linking pharmacist led TDM interventions to reduced length of hospital stay, lower incidence of adverse drug reactions, and improved probability of target attainment in critically ill populations (Prasetya et al., 2023; Setiadi et al., 2020). Large scale cohort analyses conducted in high income settings demonstrate that integrating clinical pharmacists into multidisciplinary antimicrobial stewardship programmes (ASP) augments guideline adherence and facilitates timely dose optimisation (Nurfauzi et al., 2020). Parallel investigations in low and middle income countries (LMICs) show comparable trends, albeit tempered by infrastructural limitations and workforce shortages (Yulia et al., 2020). Collectively, these studies frame TDM not merely as a laboratory procedure but as an advanced clinical service that bridges pharmacology, infectious disease, and health systems science.

Despite its recognised value, the implementation of TDM encounters context specific hurdles. Hospitals in resource limited settings often lack rapid assay facilities, leading to delays that compromise dose adjustment cycles (Sadli et al., 2023). Moreover, data siloes within electronic health records impede real time sharing of concentration results among physicians, pharmacists, and nurses, thereby attenuating the potential benefits of iterative monitoring (Setiawan et al., 2017). Even in technologically equipped institutions, heterogeneity in analytical methods and PK/PD targets complicates comparison of outcomes across studies (Hidayat et al., 2019). These operational bottlenecks underscore the necessity of a harmonised framework that defines best practice standards for sampling schedules, assay validation, and interdisciplinary communications.

Compounding these logistical concerns is the accelerating trajectory of AMR, which threatens to render common infections untreatable and imposes a substantial economic burden on health systems. The misuse and overuse of antibiotics frequently in suboptimal doses have been identified as chief drivers of resistance (Lisni et al., 2021). TDM, when executed within an ASP, provides a mechanism for dose individualisation that aligns drug exposure with bacterial susceptibility profiles, thereby reducing selection pressure for resistant strains (Sidabalok & Widayati, 2022). Nevertheless, a disjunction persists between the theoretical promise of TDM and its routine uptake in daily practice, particularly outside critical care environments.

An equally pressing challenge involves the dynamic physiology of special populations. Critically ill patients exhibit augmented renal clearance, hypoalbuminaemia, and capillary leak, all of which distort

conventional dosing algorithms (Sugiyono & Padmasari, 2019). Paediatric and geriatric cohorts further complicate dosing due to maturational or degenerative changes in drug metabolism. TDM offers a pragmatic solution to these physiological variabilities, yet evidence regarding its impact on hard clinical endpoints such as mortality or resolution of infection remains inconclusive because many studies employ surrogate PK/PD markers as primary outcomes (Munarsih et al., 2018). Consequently, clinicians and policy makers lack consensus on which antibiotics, patient groups, and clinical scenarios warrant mandatory monitoring.

Literature appraisals also reveal methodological gaps that restrict the generalisability of findings. The majority of investigations are observational, single centre, and lack standardised comparator groups (Elizabeth & Rusdiana, 2023). Variation in inclusion criteria spanning from surgical wards to neonatal intensive care units further obscures the interpretation of pooled data (Febriana et al., 2024). Additionally, outcome measures differ widely, ranging from pharmacokinetic indices (e.g., trough concentration) to composite clinical endpoints, impeding meta analytic synthesis ((Prasetyo & Kusumaratni, 2024)). Such heterogeneity underscores the need for rigorously designed randomised controlled trials (RCTs) and unified reporting frameworks that can delineate the true incremental benefit of pharmacist driven TDM.

Against this backdrop, the present narrative review seeks to consolidate contemporary evidence on the clinical, microbiological, and economic outcomes associated with pharmacist managed TDM in antibiotic therapy. By critically evaluating data from both high resource and low resource health systems, the review aims to clarify the circumstances under which TDM delivers tangible clinical value, elucidate barriers to effective implementation, and identify leverage points for policy intervention. Specifically, it will appraise outcome domains such as PK/PD target attainment, incidence of nephro or ototoxicity, length of hospitalisation, emergence of resistance, and cost effectiveness.

The scope of this review encompasses peer reviewed primary studies, systematic reviews, and practice guidelines published from 2015 onwards, capturing the period during which digital health innovations and stewardship mandates have markedly transformed pharmacy practice. Although global in outlook, the analysis pays particular attention to data originating from Southeast Asia and other LMIC regions, where the dual burdens of infectious disease and constrained resources make efficient antibiotic management paramount (Rizki et al., 2025). By juxtaposing these findings with data from North America, Europe, and Australia, the review aspires to generate context sensitive insights that inform scalable models of TDM service delivery.

In summary, while the theoretical merits of TDM in antibiotic stewardship are well articulated, empirical evidence remains fragmented, and practical integration within diverse health systems is uneven. This review intends to bridge these knowledge gaps by offering a comprehensive synthesis of current research, highlighting operative challenges, and proposing avenues for future investigation aimed at standardising and expanding pharmacist led TDM services worldwide.

METHOD

This narrative review explored the impact of pharmacist managed Therapeutic Drug Monitoring (TDM) on antibiotic therapy. A comprehensive literature search was undertaken across PubMed, Scopus, Google Scholar and ScienceDirect for studies published between January 2015 and April 2025. Pre-defined Boolean search strings combined core terms "Therapeutic Drug Monitoring", "Clinical Pharmacist", "Antibiotic Therapy", "Pharmacokinetics", "Pharmacodynamics" and "Clinical Outcomes" to maximise both sensitivity and specificity. Only peer reviewed primary investigations, systematic reviews or meta analyses that empirically or theoretically examined pharmacist involvement in TDM and reported clinical, microbiological or economic outcomes were eligible. Records not written in English, lacking direct empirical evidence, or published outside recognised scholarly venues were excluded.

The selection process followed a multi stage protocol. Titles and abstracts retrieved from each database were screened independently by four reviewers to remove duplicates and clearly irrelevant citations. Full text articles of potentially eligible studies were then assessed against the inclusion criteria and appraised for methodological rigour. Discrepancies were resolved through consensus meetings, ensuring consistent application of eligibility standards and enhancing the reliability of study selection.

Data were extracted on study design, patient population, antibiotic class, TDM implementation strategy, and reported outcomes. Using an inductive thematic approach, key findings were synthesised to identify recurrent patterns in how pharmacist led TDM influences dose individualisation, target PK/PD attainment, adverse event mitigation, antimicrobial resistance trends, and cost effectiveness. This synthesis provides an integrated perspective on the mechanisms and contexts through which clinical pharmacists add value to antibiotic management via TDM.

RESULTS AND DISCUSSION

The analysis of available literature highlights the substantial clinical, microbiological, and economic advantages of Therapeutic Drug Monitoring (TDM) when managed by clinical pharmacists, particularly in antibiotic therapy. Several key themes emerged across the reviewed studies, underscoring the impact of pharmacist led TDM on improving PK/PD target attainment, clinical outcomes, antimicrobial resistance control, antibiotic rationalisation, and cost effectiveness in diverse healthcare settings.

Pharmacist led TDM has demonstrated measurable improvements in achieving pharmacokinetic and pharmacodynamic targets in antibiotic therapy. Studies consistently report that clinical pharmacists facilitate optimal dosing through continuous serum concentration monitoring, particularly for antibiotics with narrow therapeutic indices such as vancomycin and aminoglycosides (2,8). Through regular dose adjustments based on renal function and infection severity, pharmacists ensure that antibiotic concentrations remain within therapeutic ranges, improving efficacy and reducing toxicity.

Evidence from (Mulyawantie et al., 2023) supports that structured TDM protocols involving pharmacists result in higher rates of target PK/PD attainment. Collaborative practice among pharmacists and physicians further enhances communication and responsiveness, enabling timely interventions that are adapted to patient specific factors such as renal clearance and comorbidities (Lukitasari et al., 2019).

Improved clinical outcomes are also strongly associated with TDM implementation. Patients receiving pharmacist monitored TDM tend to have shorter hospital stays and lower incidence of adverse events. Fatin et al. (2019) and Salim et al. (2023) noted that TDM allows faster optimisation of antibiotic regimens, thereby reducing the duration of ineffective therapy and associated complications. A study by (Hidayat et al., 2019) indicated that TDM contributes to shorter hospitalisations by preventing underdosing or overdosing events. Additionally, Salim et al. found a lower frequency of antibiotic related adverse drug reactions in patients managed with TDM, which subsequently reduced the need for further interventions and enhanced overall therapeutic outcomes. (Wijaya et al., 2021) also emphasized that individualized dosing guided by renal function and infection status maximised therapeutic success while mitigating complication.

The involvement of pharmacists in antimicrobial stewardship programs (ASPs) through TDM practices has further been linked with enhanced interprofessional collaboration, which optimizes clinical decision making. According to Maharani et al. (2019) the presence of pharmacists in care teams contributed significantly to better therapeutic monitoring, dose recommendations, and education of both healthcare providers and patients, leading to improved adherence and health outcomes (23). These outcomes affirm the role of TDM in not only improving drug efficacy but also reducing preventable drug related harm.

TDM also plays a critical role in addressing antimicrobial resistance in hospital settings. By ensuring appropriate antibiotic exposure, TDM mitigates subtherapeutic dosing, a major contributor to bacterial resistance. Studies by Lechtig et al. (2021) and Koch et al. (2022) revealed that hospitals applying TDM protocols demonstrated better control over multi drug resistant organisms. Abouelhassan & Nicolau (2022) emphasized that maintaining therapeutic drug levels reduces selective pressure, thereby decreasing the risk of resistance emergence. Data from intensive care units suggest that TDM minimizes therapeutic failures by ensuring consistent antimicrobial exposure, even in physiologically unstable patients Jang et al. (2020).

Moreover, TDM contributes to more precise antibiotic selection by integrating serum drug level data with local resistance profiles. This enhances the rationalisation of antibiotic use in clinical practice, as evidenced by Osorio et al. (2021) and Avila et al. (2020), who reported that targeted dosing based on TDM was associated with lower resistance rates in hospitalised populations. Despite some variability in outcomes due to differing implementation models, these findings reinforce the value of TDM in resistance prevention.

Rational antibiotic use is further promoted through TDM supported decisions for de-escalation and oral conversion. Studies by Shahrami et al. (2021) and Stašek et al. (2023) demonstrate that TDM facilitates timely de-escalation from broad spectrum to narrow spectrum antibiotics based on microbial sensitivity and patient response. Similarly, Yow et al. (2022) and Kilianova et al. (2024) observed that TDM guided interventions accelerated intravenous to oral conversion, reducing hospitalization length and treatment cost. Koch et al. (2022) reported that pharmacists' recommendations based on TDM minimized toxicity risks, enhanced safety, and supported better adherence.

The role of TDM is particularly valuable in patients with altered pharmacokinetics, such as those in intensive care or undergoing renal replacement therapy. Abdul–Aziz et al. (2022) and Kumta et al. (2020) highlighted how TDM data inform dose modifications in critically ill populations, enabling effective therapy despite dynamic changes in drug metabolism. These adaptations are essential for maintaining therapeutic efficacy and preventing drug accumulation or ineffectiveness.

From an economic perspective, multiple studies affirm that TDM enhances healthcare cost efficiency. Vithanachchi et al. (2020) found that TDM in oncology reduced adverse drug events and total care costs while improving drug utilisation. Fekete et al. (2022) similarly reported cost savings in psychiatric care due to reduced adverse reactions and shorter hospital stays. Kim et al. (2019) found TDM particularly cost effective among non-adherent patients with chronic myeloid leukaemia, highlighting its role in promoting adherence and improving outcomes.

Liu et al. (2022) demonstrated that although TDM incurs upfront monitoring costs, total medical expenses are lower among patients undergoing TDM due to fewer complications and shorter treatment durations. These savings outweigh the initial investment, especially in resource constrained settings where treatment failure bears higher downstream costs. TDM thus contributes to healthcare system sustainability by optimising antibiotic use and reducing waste.

In the context of severe infections, TDM shows economic viability as well. Studies on vancomycin TDM by Kim et al. (2019) and Breslin et al. (2023) noted significantly lower overall treatment costs among patients enrolled in TDM programs. Kim et al. found an average savings of over USD 800 in total costs per patient, attributed to more effective dosing, fewer complications, and shorter hospital stays. Gatti et al. (2022) further observed that early oral switch, enabled by TDM guided optimisation, substantially decreased resource consumption and hospital bed occupancy.

These findings reinforce the argument for embedding TDM in routine antibiotic management protocols. Despite variations in implementation depending on regional infrastructure and policy support, the overarching trends suggest that TDM improves both health and economic outcomes. The evidence affirms the essential role of clinical pharmacists in leading TDM efforts, ensuring that antibiotics are used judiciously, safely, and effectively. The next phase in antibiotic stewardship should focus on scaling TDM services through workforce training, digital infrastructure, and collaborative care models that sustain long term gains in patient care and resistance mitigation.

The present synthesis confirms that pharmacist directed Therapeutic Drug Monitoring (TDM) consistently improves pharmacokinetic pharmacodynamic (PK/PD) target attainment, clinical outcomes, and cost efficiency across diverse care settings while simultaneously supporting antimicrobial stewardship initiatives (Ariyanto et al., 2023; Sadli et al., 2023). Yet, when these findings are juxtaposed with prevailing institutional policies, a conspicuous implementation gap becomes evident. Although many tertiary hospitals endorse TDM in principle, actual bedside adoption remains fragmented because policies often lack operational detail, funding commitments, or mechanisms for inter professional accountability (Adiana & Maulina, 2022). Consequently, the clinical benefits documented in controlled investigations are only partially realised in routine practice, particularly in low and middle income countries (LMICs) where infrastructure is rudimentary and laboratory turnaround times are protracted Fuentes et al. (2021).

A central theme emerging from the literature is the decisive contribution of clinical pharmacists to closing this gap. Their advanced competence in PK/PD interpretation and dose individualisation allows them to act as therapeutic liaisons between laboratory data and prescribing decisions, thereby accelerating dose adjustment cycles and mitigating the risks of both sub therapeutic exposure and toxicity (Lukitasari et al., 2019). Hospitals that formalise pharmacist authority through collaborative practice agreements report stronger adherence to TDM protocols and earlier achievement of therapeutic targets than institutions where pharmacists retain a primarily dispensary oriented remit (Mulyawantie et al., 2023). Nevertheless, the scope of such agreements varies widely across jurisdictions, reflecting divergent regulatory landscapes and professional cultures. Where legislation restricts pharmacists' prescribing autonomy, TDM interventions may be confined to informal recommendations that can be overlooked or delayed by the medical team, thereby diluting their impact (Karuniawati, 2023).

System level determinants further shape the trajectory of TDM implementation. Adequate laboratory capacity, including liquid chromatography or immunoassay platforms capable of timely serum antibiotic quantification, is essential for actionable monitoring. Studies from Southeast Asia illustrate that hospitals equipped with on-site assays achieve median turnaround times under six hours, facilitating same day dose optimisation, whereas facilities relying on external laboratories experience delays exceeding 24 hours, rendering TDM reactive rather than proactive (Setiadi et al., 2020). Information technology infrastructure plays an equally critical role. Integrated electronic health record (EHR) modules that aggregate drug levels, renal function trends, and microbiological data allow pharmacists to generate real time dosing recommendations that are automatically flagged in physicians' order entry screens (Maarif, 2024). In settings where such interoperability is absent, pharmacists must reconcile heterogeneous data sources manually, a process vulnerable to transcription errors and workflow bottlenecks (Fuentes et al., 2021).

Financial considerations intersect with these infrastructural factors. While individual assays incur direct costs, health economic analyses consistently demonstrate net savings once reductions in adverse drug reactions, hospital length of stay, and readmissions are considered (Breslin et al., 2023). However,

budget lines for laboratory reagents and pharmacist staffing are often siloed from inpatient cost avoidance metrics, obscuring the broader fiscal value proposition. Institutions that have overcome this misalignment typically employ bundled funding models, wherein stewardship related savings are reinvested into analytical capacity and workforce development, creating a virtuous feedback loop that sustains TDM services (Vithanachchi et al., 2020).

Beyond infrastructure and economics, professional education emerges as a pivotal modulator of TDM quality. Evidence indicates that pharmacists who complete postgraduate residencies or certificate programmes in infectious diseases and PK/PD achieve higher dosing accuracy and stronger interdisciplinary collaboration than peers without formal training (Ratnawati & Lestari, 2025). Parallel educational interventions for physicians and nurses bolster acceptance of pharmacist led dose adjustments, reducing therapeutic inertia. Nevertheless, curricular exposure to TDM remains inconsistent across pharmacy schools, and continuing professional development opportunities are scarce in LMICs (Karuniawati, 2023). Strategic partnerships with academic institutions and professional societies could harmonise competency standards and facilitate knowledge transfer through blended learning modalities.

The integration of TDM into antimicrobial stewardship (AMS) frameworks offers a mechanism to institutionalise these educational and infrastructural investments. Stewardship programmes already emphasise prospective audit and feedback, formulary restriction, and guideline adherence; TDM adds a quantitative dimension by ensuring that selected antibiotics are delivered at exposures that suppress resistance and maximise efficacy (Abouelhassan & Nicolau, 2022). Empirical data from intensive care units show that pairing pharmacist led TDM with AMS rounds reduces the incidence of cefepime and piperacillin + tazobactam resistant Pseudomonas aeruginosa, highlighting the synergies between pharmacological and microbiological surveillance (Koch et al., 2022). Furthermore, TDM informs timely de-escalation and intravenous to oral switch decisions, aligning with AMS goals of spectrum minimisation and resource stewardship (Yow et al., 2022; Kilianova et al., 2024).

Cultural and behavioural dimensions also influence TDM uptake. Hierarchical team dynamics may discourage junior physicians from endorsing pharmacist recommendations, especially in environments where prescriptive authority is viewed as an exclusive medical prerogative (Adiana & Maulina, 2022). Conversely, institutions cultivating flattened hierarchies and shared accountability report smoother implementation. Leadership endorsement, exemplified by appointing pharmacists as AMS co-chairs, legitimises their contribution and normalises interdisciplinary decision making. Quality improvement initiatives that publicise TDM outcome dashboards highlighting reduced nephrotoxicity or shorter hospital stay further reinforce collective buy in and sustain practice change.

Global comparisons reveal that high income countries (HICs) leverage advanced diagnostics and robust policy frameworks to embed TDM in routine care, whereas LMICs must navigate fragmented supply chains and variable staffing ratios. Despite these disparities, successful LMIC exemplars demonstrate that staged implementation beginning with high risk antibiotics and establishing referral partnerships for analytical services can yield incremental benefits while building a business case for

local assay capacity (Fuentes et al., 2021). This underscores the importance of context specific strategies rather than transplanting HIC models wholesale. Donor funded laboratory networks and telepharmacy consultations may bridge resource gaps, but long term sustainability hinges on national regulatory support and workforce retention.

This review relied on heterogeneous primary studies that varied in design quality, patient population, antibiotic class, and outcome metrics, which may limit the comparability of findings and introduce publication bias. The narrative approach precluded quantitative synthesis, and grey literature was not systematically explored, potentially omitting data from under resourced settings where TDM faces unique challenges.

Future research should prioritise multicentre randomised controlled trials that standardise PK/PD endpoints and incorporate antibiotic resistance surveillance as a core outcome. Implementation science frameworks are needed to elucidate how organisational culture, funding mechanisms, and digital infrastructure mediate TDM effectiveness. Developing scalable educational programmes and decision support algorithms tailored to resource limited environments will be essential for equitable global uptake. Continuous monitoring of cost savings and patient outcomes should inform adaptive policy cycles that sustain pharmacist led TDM as a cornerstone of antimicrobial stewardship.

CONCLUSION

This narrative review affirms the critical role of pharmacist led Therapeutic Drug Monitoring (TDM) in enhancing the safety, efficacy, and cost effectiveness of antibiotic therapy. Key findings reveal that pharmacist involvement significantly improves pharmacokinetic/pharmacodynamic target attainment, reduces adverse drug reactions, shortens hospital stays, and contributes to antimicrobial resistance control. Despite these benefits, implementation remains inconsistent across healthcare settings due to barriers such as limited infrastructure, insufficient interdisciplinary collaboration, inadequate education, and weak policy frameworks. These systemic challenges hinder the routine integration of TDM into clinical practice, especially in low resource environments.

There is an urgent need for policy driven strategies that support standardized TDM protocols, investment in diagnostic infrastructure, and the expansion of pharmacists' clinical authority. Educational initiatives, both pre service and in service, must also be scaled to enhance competencies in pharmacokinetics and antimicrobial stewardship. Integrating TDM into national antimicrobial stewardship programs, supported by interoperable health information systems, could further improve care delivery and resistance mitigation.

Future research should prioritise multicenter trials that measure the clinical and economic impact of TDM across diverse populations and healthcare systems. Additionally, implementation science approaches are needed to explore how organisational culture, policy support, and digital tools influence TDM outcomes. As shown in this review, TDM, particularly when directed by clinical

pharmacists, should be recognised as a strategic intervention to optimise antibiotic use, reduce healthcare costs, and combat the global threat of antimicrobial resistance.

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