

Personalized Antibiotic Therapy in Critically ill Patients: A Comprehensive Review of Pharmacokinetic/Pharmacodynamic Optimization in the Intensive Care Unit

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ABSTRACT

Infection-related morbidity and mortality remain disproportionately high in the intensive care unit (ICU), a challenge exacerbated by the global surge in multidrug-resistant organisms (MDROs) and a stagnating antimicrobial pipeline. Traditional "one-size-fits-all" antibiotic dosing regimens, largely derived from healthy volunteer data, routinely fail in critically ill patients. Sepsis and septic shock induce profound pathophysiological shifts including capillary leakage, massive fluid resuscitation, augmented renal clearance, and acute organ dysfunction that alter the volume of distribution (V_d) and clearance (CL) of hydrophilic and lipophilic antimicrobials alike. Suboptimal drug exposure drives clinical failure and accelerates the selection of resistant strains, while excessive exposure induces severe organ toxicities.

This review explores the mechanism-based rationale for personalized antibiotic therapy in the ICU. We evaluate key pharmacokinetic and pharmacodynamic (PK/PD) indices required for treatment optimization ($fT > MIC$, AUC_{24}/MIC , and C_{max}/MIC), outline the clinical integration of therapeutic drug monitoring (TDM), and discuss the utility of model-informed precision dosing (MIPD) using Bayesian forecasting software. Finally, we synthesize findings from recent landmark trials and outline future paradigms incorporating machine learning, point-of-care biosensors, and patient genomics to deliver true precision antimicrobial stewardship at the bedside.

Keywords- Personalized antibiotic therapy, ICU, pharmacokinetic, pharmacodynamic, Therapeutic drug monitoring, Sepsis.

I. INTRODUCTION

The intensive care unit (ICU) represents the epicenter of antimicrobial consumption within modern healthcare systems. Although critically ill patients account for fewer than 10% of total hospital admissions, the per-patient consumption of antimicrobials in the ICU is up to ten times higher than in general medical wards (Abdul-Aziz et al., 2020). Epidemiological data indicate that at any given time, approximately 50% of adult ICU patients are treated for a active, suspected, or proven infection, and up to 70% will receive at least one course of antibiotics during their critical care stay (Lonsdale & Lipman, 2021; Abdulla et al., 2020). Despite this

intensive utilization of broad-spectrum antimicrobials, infection-related mortality in the ICU remains unacceptably high, hovering around 30% globally, with significantly worse outcomes observed when infections are caused by multidrug-resistant organisms (MDROs) (Luyt et al., 2014; Wieringa et al., 2023).

The root cause of this therapeutic discordance lies in the historical paradigm of antimicrobial prescription. Traditional antibiotic dosing guidelines are fundamentally predicated on pharmacokinetic (PK) and pharmacodynamic (PD) data obtained from healthy volunteers or stable, ambulatory patients (Abdul-Aziz et al., 2020). These populations possess normal fluid status, intact endothelial barriers, predictable protein levels, and stable organ function.

In stark contrast, the physiology of a critically ill patient in the throes of sepsis or septic shock is highly dynamic, fluid, and profoundly altered (Monogue, 2026). The systemic inflammatory response syndrome (SIRS) triggers endothelial dysfunction, capillary leakage, and a subsequent massive shift of fluids from the intravascular to the extravascular compartments, which drastically increases the volume of distribution (V_d) of hydrophilic agents (Lonsdale & Lipman, 2021). Concurrently, fluctuating cardiac output and multi-organ failure lead to volatile drug clearance (CL), ranging from hyper-clearance states to severe acute kidney injury (AKI) (Monogue, 2026; Onita et al., 2025).

As a direct consequence of this extreme inter- and intra-individual PK variability, standardized dosing regimens lead to highly unpredictable plasma concentrations. Large-scale clinical audits have revealed that up to 45% of critically ill patients fail to achieve therapeutic target concentrations within the first 24 to 48 hours of treatment (Wieringa et al., 2023). This target non-attainment has grave implications: subtherapeutic levels promote clinical failure and accelerate the selective pressure for antimicrobial resistance (AMR), while supratherapeutic levels precipitate severe neurotoxicity, nephrotoxicity, and bone marrow suppression (Legg et al., 2023).

Transitioning from empirical, weight-standardized dosing regimens to personalized antibiotic therapy is no longer an intellectual luxury; it is a clinical necessity (Lonsdale & Lipman, 2021). This comprehensive review delineates the pathophysiological drivers of altered antibiotic PK in critical illness, defines modern PK/PD targets, evaluates the implementation of therapeutic drug monitoring (TDM) and computerized precision dosing models, and reviews the current clinical evidence supporting personalized antimicrobial strategies.

II. PATHOPHYSIOLOGICAL ALTERATIONS DRIVING PHARMACOKINETIC UNPREDICTABILITY

To successfully personalize antibiotic therapy, clinicians must understand the physical and biochemical mechanisms that destabilize drug handling in the critically ill. Pharmacokinetics describes the mathematical relationship between drug administration and plasma/tissue concentrations over time, structurally defined by absorption, distribution, metabolism, and elimination. In the ICU, every single phase of this lifecycle is disrupted.

2.1. Capillary Leakage, Fluid Resuscitation, and Volume of Distribution

The volume of distribution (V_d) is a theoretical construct relating the total amount of drug in the body to its plasma concentration (C_0), expressed as:

$$V_d = \text{Dose}/C_0$$

Antimicrobials are generally categorized into two major physiochemical groups: hydrophilic (e.g., β -lactams, aminoglycosides, glycopeptides) and lipophilic (e.g., fluoroquinolones, macrolides, linezolid, tigecycline) (Monogue, 2026). Hydrophilic drugs are water-soluble, possess low intracellular penetration, and are primarily confined to the intravascular and extracellular fluid spaces.

In severe sepsis, the release of vasodilatory mediators and pro inflammatory cytokines damages the endothelial glycocalyx, disrupting tight junctions and inducing severe capillary leakage (Schrader et al., 2021). This phenomenon, coupled with the aggressive intravenous fluid resuscitation required to maintain mean arterial pressure, drastically expands the extracellular fluid volume. Consequently, the V_d of hydrophilic antibiotics increases exponentially (Monogue, 2026). For instance, the V_d of aminoglycosides or piperacillin can double during septic shock. According to the equation above, an expanded V_d causes a proportional reduction in the initial peak serum concentration (C_0), frequently plunging the patient into subtherapeutic ranges during the critical early hours of an infection (Lonsdale & Lipman, 2021).

Conversely, lipophilic antibiotics readily cross cell membranes and distribute into adipose and intracellular tissue. Their V_d is intrinsically large and is less affected by acute fluid shifts, though it can be substantially altered by body composition changes, such as severe obesity or severe muscle wasting common in long-term ICU stays (Monogue, 2026).

2.2. Volatile Elimination: Augmented Renal Clearance vs. Renal Dysfunction

The elimination of water-soluble antibiotics depends directly on renal function. ICU patients exhibit extreme polarization in renal clearance, often shifting rapidly between hyper-filtration and severe failure.

Augmented Renal Clearance (ARC) is a frequently under-recognized phenomenon in the ICU, defined as a measured creatinine clearance (CrCl) exceeding 130 mL/min/1.73m² (Monogue, 2026). Driven by a high cardiac output during the hyperdynamic phase of sepsis, major burns, or traumatic brain injury, ARC leads to the rapid filtration and excretion of hydrophilic drugs (Onita et al., 2025). When a patient exhibits ARC, the elimination half-life ($t_{1/2}$) of an antibiotic is drastically truncated, as described by the fundamental relationship:

$$t_{1/2} = \ln(2) \cdot V_d / CL$$

As a result, plasma concentrations drop rapidly, rendering conventional intermittent dosing intervals completely inadequate to maintain therapeutic thresholds (Monogue, 2026).

On the opposite end of the spectrum, sepsis-associated acute kidney injury (AKI) or chronic kidney disease (CKD) dramatically decreases drug clearance (CL), leading to progressive accumulation and toxicity (Monogue, 2026). The clinical challenge is compounded by the fact that serum creatinine is a delayed, highly unreliable biomarker of glomerular filtration rate (GFR) in the critically ill, due to muscle wasting, fluid dilution, and delayed equilibration. Consequently, standard GFR estimation formulas (such as Cockcroft-Gault or CKD-EPI) regularly miscalculate renal function, leading to erroneous antibiotic dosing (Onita et al., 2025).

2.3. Hypoalbuminemia and Altered Protein Binding

Many antibiotics bind extensively to circulating plasma proteins, primarily albumin. Crucially, only the unbound, free fraction of the drug (f) is pharmacologically active, capable of diffusing into interstitial tissues, binding to bacterial targets, and undergoing hepatic or renal clearance (Abdul-Aziz et al., 2020; Legg et al., 2023).

Hypoalbuminemia (serum albumin < 25 g/L) occurs in up to 40% to 50% of ICU patients, driven by decreased hepatic synthesis, increased capillary escape, and accelerated catabolism during critical illness (Monogue, 2026). For highly protein-bound antibiotics (e.g., ceftriaxone, ertapenem, teicoplanin, daptomycin), a drop in serum albumin increases the free fraction of the drug. While this initially elevates the concentration of active drug available for bacterial killing, it also exponentially increases the amount of drug available for renal filtration and hepatic clearance (Monogue, 2026). The net result is an accelerated total clearance and a rapid decline in overall drug exposure, causing a high rate of target non-attainment if total (bound + unbound) serum concentrations are monitored instead of directly measuring free drug levels (Abdul-Aziz et al., 2020).

2.4. Extracorporeal Support Systems (ECMO and CRRT)

The integration of advanced life-support modalities introduces artificial compartments that further

convolute antibiotic pharmacokinetics. Extracorporeal membrane oxygenation (ECMO) circuits can profoundly affect drug disposition via two main mechanisms: the expansion of the circuit volume (V_d expansion) and the physical adsorption of drug molecules onto the plastic tubing and polyurethane/polypropylene oxygenator membranes (Monogue, 2026). Lipophilic and highly protein-bound drugs (e.g., voriconazole, daptomycin, teicoplanin) are highly susceptible to significant sequestration within ECMO circuits, requiring escalated dosing strategies.

Similarly, Continuous Renal Replacement Therapy (CRRT) introduces a highly efficient, non-biological clearance pathway. The clearance of an antibiotic via CRRT is governed by the operational parameters of the machine including the ultrafiltration rate (in continuous venovenous hemofiltration [CVVH]), the dialysate flow rate (in continuous venovenous hemodialysis [CVVHD]), the membrane surface area, and the drug's sieving coefficient (S_c) or saturation coefficient (Onita et al., 2025). Standard drug references fail to account for these specific mechanical settings, frequently causing clinicians to underdose patients on high-effluent CRRT, which results in subtherapeutic levels.

III. PHARMACODYNAMIC INDICES AND TARGETS FOR PRECISION DOSING

Pharmacodynamics integrates the exposure profiles of an antimicrobial with its microbiological activity, quantified by the Minimum Inhibitory Concentration (MIC) of the infecting pathogen. Personalizing therapy requires selecting the correct PK/PD index and aiming for optimized clinical targets tailored to the severity of critical illness.

Table 1-Pharmacokinetic/Pharmacodynamic (PK/PD) Indices and Dosing Targets for Major Antibiotic Classes in Conventional vs. Critically Ill Patients

Antibiotic Class	Primary PK/PD Index	Conventional Clinical Target	Optimized ICU Target	Rationale for ICU Targets
Penicillins, Cephalosporins, Carbapenems	$fT > MIC$	40%–70% $fT > 1 \times MIC$	100% $fT > 1-4 \times MIC$	Combats altered tissue penetration; prevents emergence of resistance in hyper-mutable strains.
Aminoglycosides	C_{max}/MIC	$8-10 \times MIC$	$10-12 \times MIC$	Maximizes concentration-dependent bactericidal activity and optimizes the post-antibiotic effect (PAE).
Glycopeptides, Fluoroquinolones, Linezolid	AUC_{24}/MIC	$AUC_{24}/MIC > 400$ (Vancomycin)	$AUC_{24}/MIC = 400-600$	Balances maximal efficacy against <i>S. aureus</i> with a strict upper limit to prevent acute kidney injury (AKI).

3.1. gTime-Dependent Killers (β -lactams)

For β -lactam antibiotics, the primary determinant of efficacy is the percentage of time that the

unbound plasma concentration remains above the MIC during a given dosing interval ($fT > MIC\%$) (Fratoni et al., 2021). While historical data in non-critically ill

cohorts suggest that a target of 40% to 50% $fT > 1$ times MIC for penicillins and 60% to 70% for cephalosporins is sufficient for bacteriostasis, the clinical reality of the ICU demands far more aggressive targets (Pai Mangalore et al., 2024).

Critically ill patients often present with impaired immune function, high bacterial inoculums, and deep-seated tissue infections (such as ventilator-associated pneumonia) where drug penetration is severely compromised (Legg et al., 2023). Consequently, international consensus guidelines now strongly advocate for an optimized ICU target of **100% $fT > 1$ times MIC**, with growing evidence supporting **100% $fT > 4$ times MIC** to maximize bactericidal eradication and suppress the development of resistant mutant subpopulations (Abdul-Aziz et al., 2020; Fratoni et al., 2021).

3.2. Concentration-Dependent (Aminoglycosides)

Killers

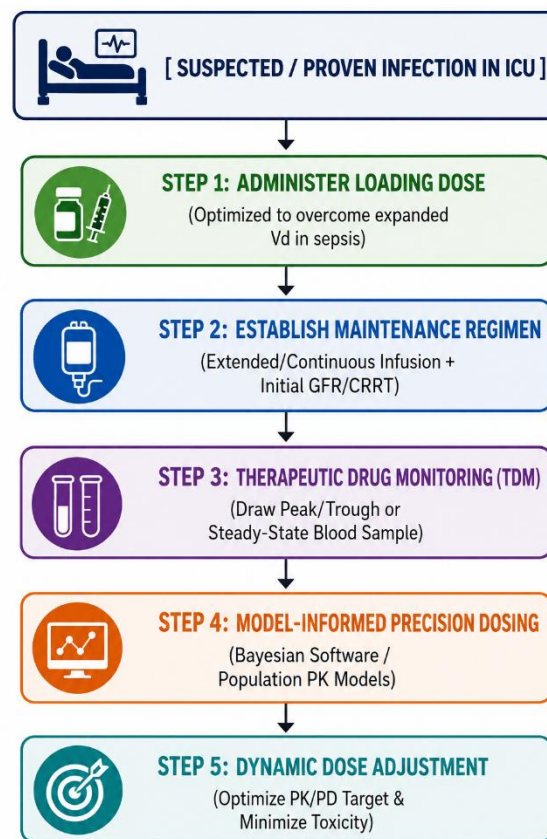
Aminoglycosides (e.g., amikacin, gentamicin) exhibit concentration-dependent killing, where the rate and extent of bacterial eradication are directly correlated with the ratio of the maximal free drug concentration to the MIC (C_{max}/MIC) (Abdul-Aziz et al., 2020). Achieving a high peak concentration (C_{max}) is critical not only to maximize the initial bacterial kill rate but also to optimize the post-antibiotic effect (PAE), which suppresses bacterial regrowth even after serum levels fall below the MIC. In the ICU, given the expanded V_d , standard doses often fail to reach the necessary peak. Clinicians must utilize high-dose, extended-interval dosing regimens (e.g., amikacin 25–30 mg/kg) to confidently achieve an optimized target of $C_{max}/MIC > 10–12$, while allowing a prolonged dosing interval for concentrations to drop, minimizing accumulation-driven nephrotoxicity and ototoxicity (Abdul-Aziz et al., 2020).

3.3. Exposure-Dependent Killers (Glycopeptides and Fluoroquinolones)

For agents like vancomycin, fluoroquinolones, and linezolid, efficacy is driven by the total 24-hour exposure relative to the pathogen's minimum inhibitory concentration, expressed as the ratio of the 24-hour area under the concentration-time curve to the MIC (AUC_{24}/MIC) (Onita et al., 2025).

Vancomycin represents the classic paradigm of personalized AUC/MIC optimization. Historically, trough-only monitoring (aiming for 15–20 mg/L) was used as a surrogate for exposure. However, extensive clinical evidence has demonstrated that trough concentrations are a poor predictor of actual AUC and are independently associated with an increased risk of nephrotoxicity. Modern precision guidelines mandate direct **AUC_{24}/MIC monitoring**, aiming for a narrow therapeutic window of **400 to 600** (Onita et al., 2025). This specific exposure window maximizes clinical cure against Methicillin-Resistant *Staphylococcus aureus* (MRSA) while minimizing the risk of vancomycin-induced acute kidney injury (AKI).

IV. PRACTICAL IMPLEMENTATION STRATEGIES AT THE BEDSIDE



Transitioning from theoretical PK/PD targets to clinical implementation requires a structured, multi-step operational workflow at the bedside.

Step 1: Optimizing the Initial Loading Dose

Because the volume of distribution (V_d) is expanded during the hyperinflammatory phase of early sepsis, the conventional practice of delaying or reducing the initial dose based on renal impairment is a dangerous clinical error (Abdul-Aziz et al., 2020). The loading dose must be calculated independently of organ function, focusing entirely on overcoming the expanded V_d to achieve immediate therapeutic target concentrations. For example, a critically ill patient with septic shock and concurrent anuric AKI should still receive a full, high-dose initial loading of meropenem (2 g) or amikacin (30 mg/kg) to ensure rapid, effective serum and tissue sterilization.

Step 2: Continuous and Extended Infusions

For time-dependent β -lactams, altering the method of administration is a highly effective structural approach to personalizing therapy. Traditional intermittent infusions (administered over 30 minutes) generate high peaks but rapid declines, resulting in significant periods of subtherapeutic troughs, especially in patients with augmented renal clearance (Lonsdale & Lipman, 2021).

By extending the infusion duration either via **extended infusions** (over 3 to 4 hours) or **continuous infusions** (over 24 hours) clinicians can maintain stable, prolonged serum concentrations well above the MIC throughout the entire dosing interval (Fratoni et al., 2021). Continuous infusions are particularly advantageous in the ICU; they consistently achieve higher target attainment rates (100% $fT > MIC$), require lower total daily doses, and facilitate simplified TDM sampling, as a single blood draw at any point during steady-state accurately reflects the average drug concentration (Schrader et al., 2021).

Step 3: Therapeutic Drug Monitoring (TDM)

Therapeutic drug monitoring forms the operational backbone of personalized antimicrobial therapy. The international consensus position paper endorsed by the European Society of Intensive Care Medicine (ESICM) and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID) strongly recommends **routine TDM for aminoglycosides, β -lactams, linezolid, teicoplanin, and vancomycin** in critically ill adult patients (Abdul-Aziz et al., 2020).

The logistical challenges of a TDM service involve sample timing and rapid laboratory turnaround. For intermittent infusions, a "peak" sample is typically drawn 30 minutes after completing the infusion to assess efficacy (C_{max}/MIC), while a "trough" sample is drawn immediately prior to the next scheduled dose to evaluate target attainment ($fT > MIC$) or safety limits (Legg et al., 2023). For continuous infusions, a steady-state sample can be obtained at any point after 4 to 5 drug half-lives. Crucially, standard laboratory assays measure *total* drug concentrations. If a patient exhibits severe hypoalbuminemia, the clinician must ideally order an equilibrium dialysis assay to measure the *unbound, free concentration*, or apply validated mathematical correction formulas to prevent misinterpreting a low total concentration as subtherapeutic when the free active fraction is actually adequate (Abdul-Aziz et al., 2020).

Step 4: Model-Informed Precision Dosing (MIPD)

While traditional TDM relies on reactive dose adjustments based on retrospective trough or peak data, Model-Informed Precision Dosing (MIPD) represents a proactive paradigm shift. MIPD utilizes sophisticated **Bayesian forecasting software** (e.g., InsightRX, BestDose, TDMx) integrated with robust population pharmacokinetic models tailored for critical illness (Onita et al., 2025).

The Bayesian optimization workflow follows a structured sequence:

1. **Prior Information:** The software utilizes an established population PK model that incorporates specific patient covariates (e.g., age, weight, serum creatinine, presence of CRRT/ECMO, albumin levels) to generate an initial predicted concentration-time curve.

2. **Likelihood Data:** The clinician inputs the exact times of antibiotic administration and blood sampling, alongside the measured serum concentration from the TDM laboratory.
3. **Posterior Estimation:** Using Bayes' theorem, the software mathematically reconciles the population characteristics with the patient's real-time data to calculate the individual's exact pharmacokinetic parameters (V_d and CL).
4. **Adaptive Simulation:** The clinician can simulate various dosing regimens (e.g., changing a dose from 1 g every 8 hours to an extended infusion of 2 g every 12 hours) to determine the exact strategy that maximizes the probability of target attainment (PTA) while minimizing toxicity risks (Onita et al., 2025).

V. SYNTHESIS OF CLINICAL EVIDENCE AND LANDMARK TRIALS

The clinical utility of personalized antibiotic therapy has been rigorously evaluated across multiple cohort studies, registries, and randomized controlled trials (RCTs).

5.1. The DALI Study (2014)

The **Defining Antibiotic Levels in Intensive care unit patients (DALI)** study was a landmark, multicenter, prospective pharmacokinetic point-prevalence study across 68 ICUs worldwide (Roberts et al., 2012). The study evaluated eight distinct β -lactams and demonstrated profound PK variability among critically ill patients. Crucially, the DALI study revealed that **one in seven patients failed to achieve even the basic target of 50% $fT > MIC$** , and target non-attainment was directly linked to a significant decrease in clinical cure rates and a higher risk of treatment failure (Lonsdale & Lipman, 2021; Wieringa et al., 2023). This trial provided the definitive, large-scale epidemiological justification for abandoning empirical dosing in favor of individualized, targeted strategies.

5.2. The DOLPHIN Trial (2020–2024)

To assess whether routine TDM improves hard clinical outcomes, the **DOLPHIN trial** was conducted as a prospective, multicenter randomized controlled trial in the Netherlands (Abdulla et al., 2020). The trial investigated whether early, model-based TDM of β -lactams and fluoroquinolones could shorten the ICU length of stay (LOS) compared to standard of care dosing.

While the protocol was highly optimized, the primary analysis highlighted the profound logistical complexities of implementing TDM in multi-center clinical trials. Delays in sample transportation, variable laboratory turnaround times, and lower-than-expected clinician compliance with software dosing recommendations attenuated the intervention's impact (Pai Mangalore et al., 2024). The DOLPHIN trial served

as a vital lesson: for personalized antibiotic therapy to successfully translate into improved survival or shortened hospital stays, a seamless, rapid, and highly compliant institutional infrastructure must be established at the institutional level.

5.3. The ADAPT-TDM Trial and Modern Registries

Recent trials, including the ADAPT-TDM trial protocol, have focused heavily on the feasibility and fidelity of early TDM implementation, initiating dose adjustments within the first 24 to 48 hours of ICU admission (Pai Mangalore et al., 2024). Retrospective analyses focusing on specific broad-spectrum agents, such as piperacillin/tazobactam, have demonstrated that implementing standardized operating procedures for TDM leads to a significant reduction in extreme, unpredictable serum levels (Schrader et al., 2021).

In a descriptive analysis of piperacillin TDM, it was observed that unadjusted dosing regularly resulted in either highly toxic serum concentrations (>100 mg/L, primarily in patients with unrecognized renal impairment or advanced age) or severely subtherapeutic levels (<22.5 mg/L, predominantly in young patients with intact renal function and augmented clearance) (Schrader et al., 2021). The systematic correction of these dosing errors through TDM-guided adjustments has consistently resulted in enhanced microbiological clearance and a lower rate of secondary resistance emergence (Pai Mangalore et al., 2024).

VI. FUTURE HORIZONS IN PRECISION ANTIMICROBIAL STEWARDSHIP

As personalized antibiotic therapy evolves, several cutting-edge technological advancements are poised to redefine precision dosing at the ICU bedside.

6.1. Machine Learning and Artificial Intelligence

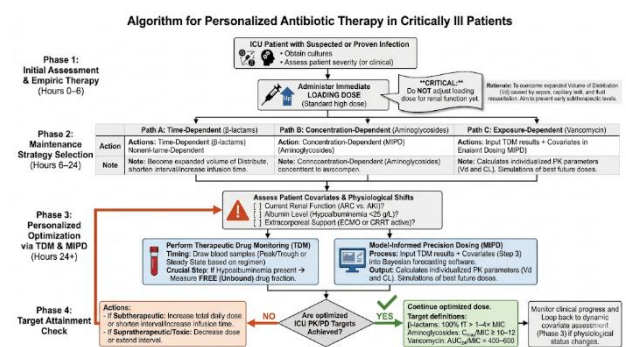
Traditional Bayesian software requires precise covariate input and predefined structural PK models. The future lies in integrating machine learning (ML) and artificial intelligence (AI) directly into Electronic Health Records (EHR) to automate this process (Wieringa et al., 2023). Advanced multivariable prediction models, utilizing Random Forest (RF), Logistic Regression (LR), and Naive Bayes (NB) architectures, have been developed and externally validated to predict a patient's risk of antibiotic target non-attainment *at the exact moment* a clinician writes the initial empirical prescription (Wieringa et al., 2023). By instantly processing real-time clinical variables such as mechanical ventilation parameters, vasopressor requirements, fluid balance metrics, and inflammatory markers these AI tools can automatically flag high-risk patients and prompt clinicians to initiate proactive continuous infusions or immediate TDM scheduling (Wieringa et al., 2023).

6.2. Point-of-Care Biosensors and Continuous Monitoring

The primary logistical bottleneck of current TDM practices is the delay associated with centralized laboratory testing (e.g., Liquid Chromatography-Mass Spectrometry or Immunoassays), which often takes 12 to 24 hours to return results. To achieve true real-time personalized therapy, research is actively focused on the development of **point-of-care biosensors** and microfluidic devices capable of quantifying antibiotic concentrations within minutes from a single drop of whole blood or interstitial fluid (Pai Mangalore et al., 2024). Furthermore, wearable microneedle arrays are being developed for continuous, real-time antibiotic monitoring, functioning similarly to continuous glucose monitors. This will provide clinicians with a continuous visual profile of a patient's antibiotic concentration curve, allowing for instant adjustments to infusion rates at the bedside.

6.3. Pharmacogenomics and Host-Pathogen Multi-Omics

Finally, precision antibiotic therapy will increasingly integrate host genomics and pathogen multi-omics. Variations in host genes encoding drug-metabolizing enzymes (such as the Cytochrome P450 superfamily) or drug transporters (such as P-glycoprotein) can explain residual pharmacokinetic variability not captured by standard clinical organ function scores. Simultaneously, rapid metagenomic next-generation sequencing (mNGS) can identify pathogen-specific resistance genes within hours of ICU admission, allowing for immediate adjustments to both the spectrum of the antibiotic and the precise PK/PD target value required to suppress that specific enzymatic mechanism of resistance (Onita et al., 2025).



VII. CONCLUSION

Personalized antibiotic therapy represents a critical evolutionary leap in the management of severe infections within the intensive care unit. The traditional approach of uniform, static dosing is fundamentally incompatible with the extreme, volatile pathophysiological landscape of critical illness. Capillary leakage, augmented renal clearance, erratic protein binding, and the application of extracorporeal

life support systems render antibiotic plasma concentrations highly unpredictable, frequently resulting in clinical failure or profound organ toxicity.

Optimizing clinical outcomes requires a proactive, multi-pronged approach: administering aggressive initial loading doses, utilizing extended or continuous infusions for time-dependent agents, implementing routine therapeutic drug monitoring, and deploying model-informed precision dosing through Bayesian forecasting software. While structural and logistical barriers to widespread implementation remain, the integration of emerging technologies such as machine learning prediction models, real-time point-of-care biosensors, and pharmacogenomics promises to solidify precision antimicrobial dosing as an indispensable standard of care in modern intensive care medicine.

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