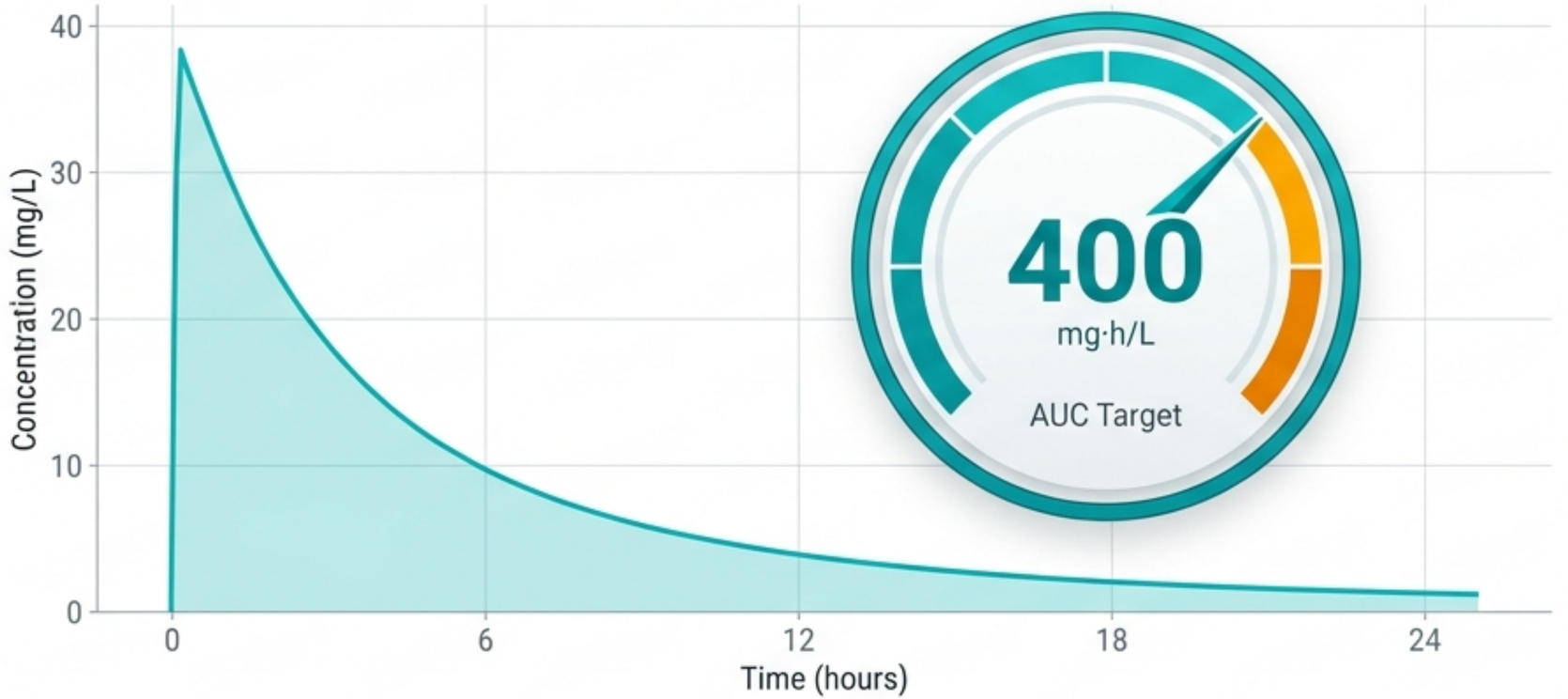
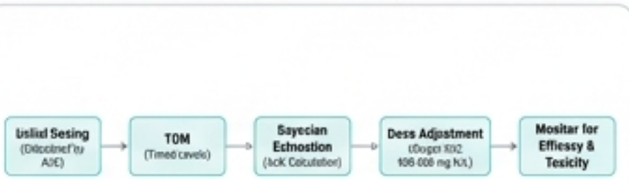
PRECISION VANCOMYCIN

The 2020 Consensus Guideline Implementation Dashboard.

Moving beyond trough-based dosing to maximize efficacy and eliminate acute kidney injury.

Based on joint guidelines by ASHP, IDSA, PIDS, and SIDP.





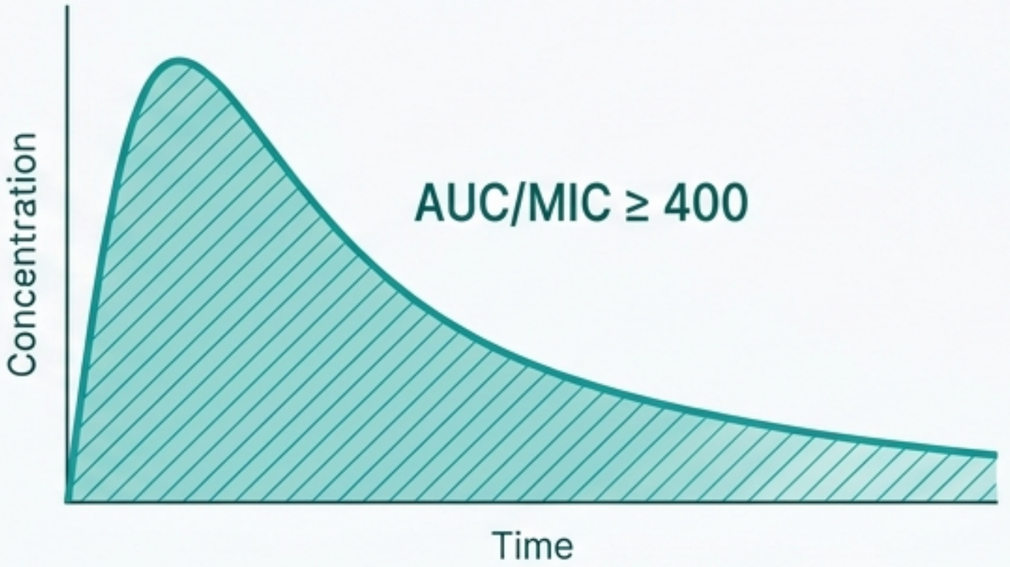
LEGEND: Muted Slate Gray = Old Paradigm (Trough Monitoring) | Vibrant Clinical Teal = New Standard (AUC Monitoring) | Sharp Medical Amber = Critical Alerts & Toxicity Risks

THE OLD PARADIGM

2009 Standard: Trough-only monitoring (15-20 mg/L).

Used as an imperfect surrogate for overall drug exposure.

THE NEW PARADIGM



2020 Standard: Area Under the Curve (AUC) monitoring.

Daily AUC values of 400-600 mg·h/L (assuming MIC of 1 mg/L) are now the universal target for serious MRSA infections.

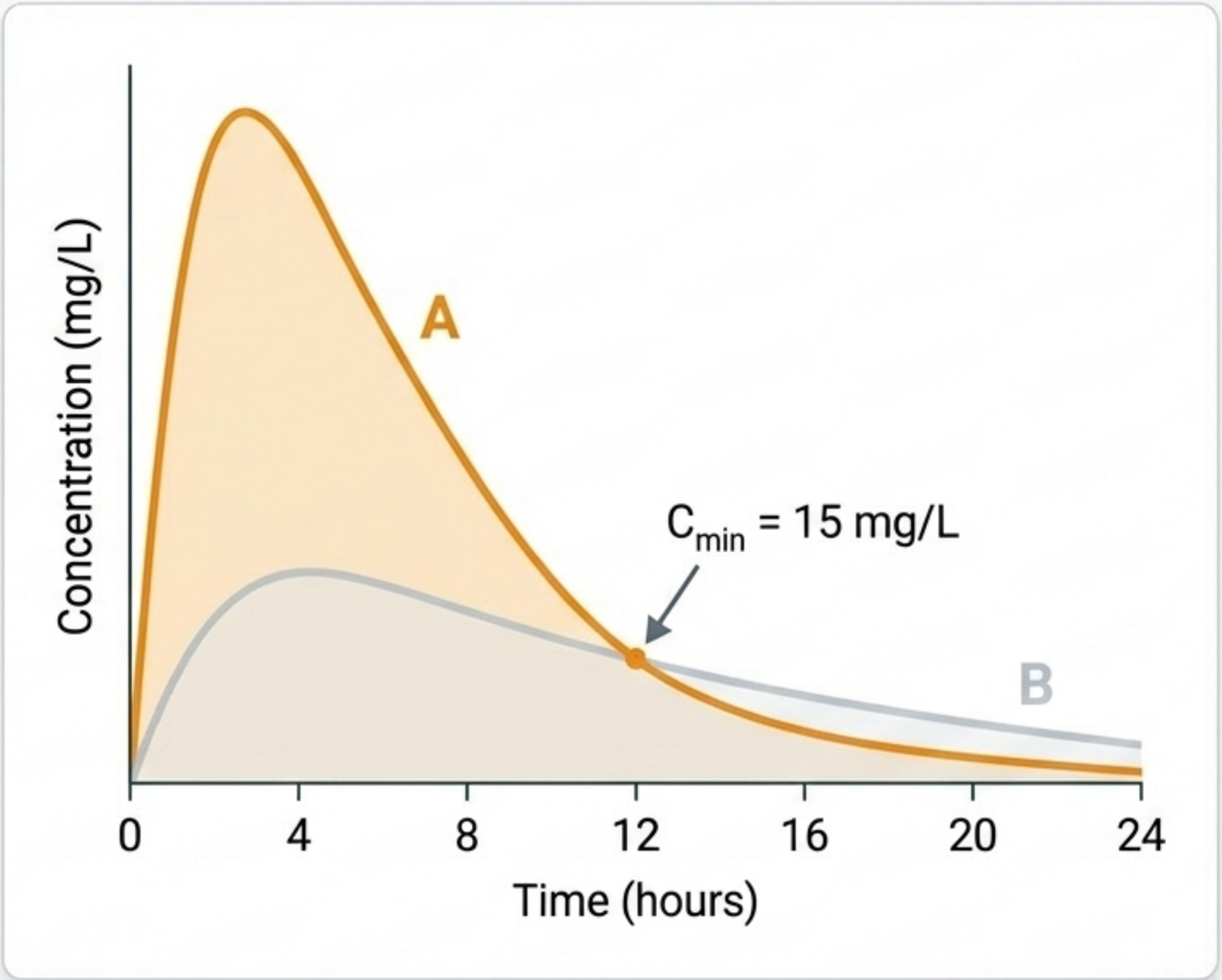
The Catalyst

Trough targets failed to consistently predict true exposure, leading to unnecessary vancomycin-induced Acute Kidney Injury (AKI).

Comparing the diagnostic accuracy of dosing paradigms

	Trough Monitoring	AUC Monitoring
Primary Target	15-20 mg/L	**400-600 mg·h/L**
Pharmacokinetic Accuracy	⚠ **Low** (Represents a single end-of-interval exposure point)	✓ **High** (Represents integrated cumulative drug exposure over 24 hours)
AKI Risk	⚠ **Elevated** (Risk increases sharply at >15 mg/L)	✓ **Minimized** (Carefully controlled beneath the 600 mg·h/L toxicity threshold)
Adaptive Capability	⚠ **Reactive** (Waits for steady-state)	✓ **Proactive** (Bayesian forecasting adapts within the first 24-48 hours)

The inherent danger of the trough illusion

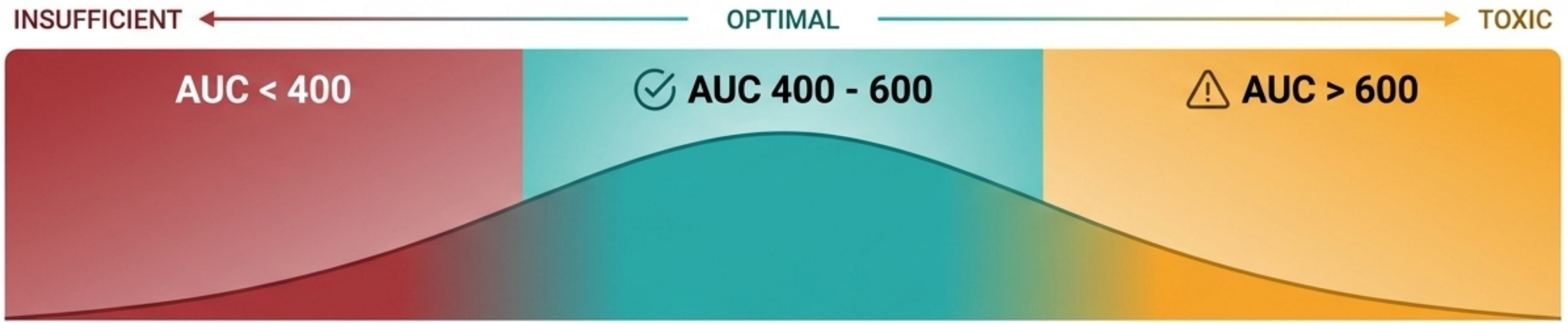


The Flaw: A single trough value can represent vastly different total body exposures.

The Consequence: Two patients with the exact same trough level of 15 mg/L can have wildly different AUCs.
One patient is experiencing clinical failure; the other is experiencing severe nephrotoxicity.

Conclusion:
Trough is a mathematically insufficient safety gauge.

Navigating the therapeutic Goldilocks zone



Treatment Failure & Resistance

Fails to achieve a 1- to 2-log reduction in bacterial inoculum.

The Efficacy Zone

Clears the infection while preserving renal function. The universal target.

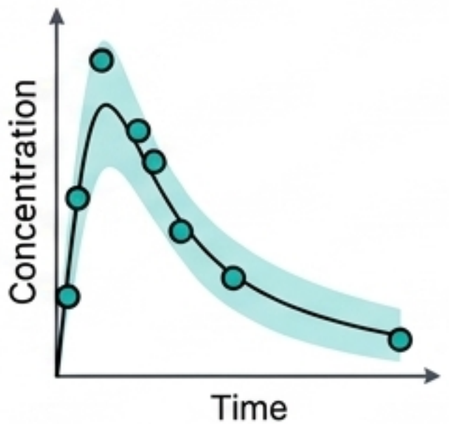
Acute Kidney Injury (AKI)

Toxicity probability increases stepwise as daily AUC approaches 800-1300 mg·h/L.

Methodologies for clinical AUC calculation

GRADING SYSTEM	
Category and Grade	**Definition**
Level A-II	**Early intervention.** Does not require steady-state conditions (can be used in first 24-d8h), Evidence Accounts for dynamic pathophysiological changes in critically ill patients.

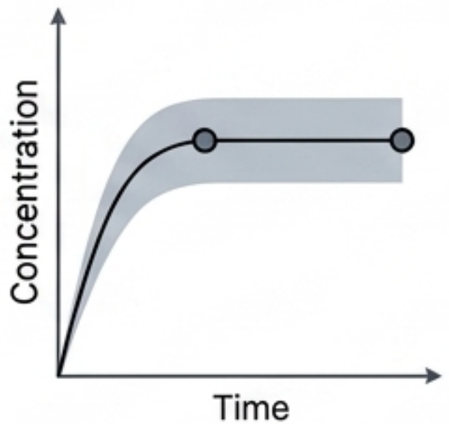
Bayesian Software (Preferred)



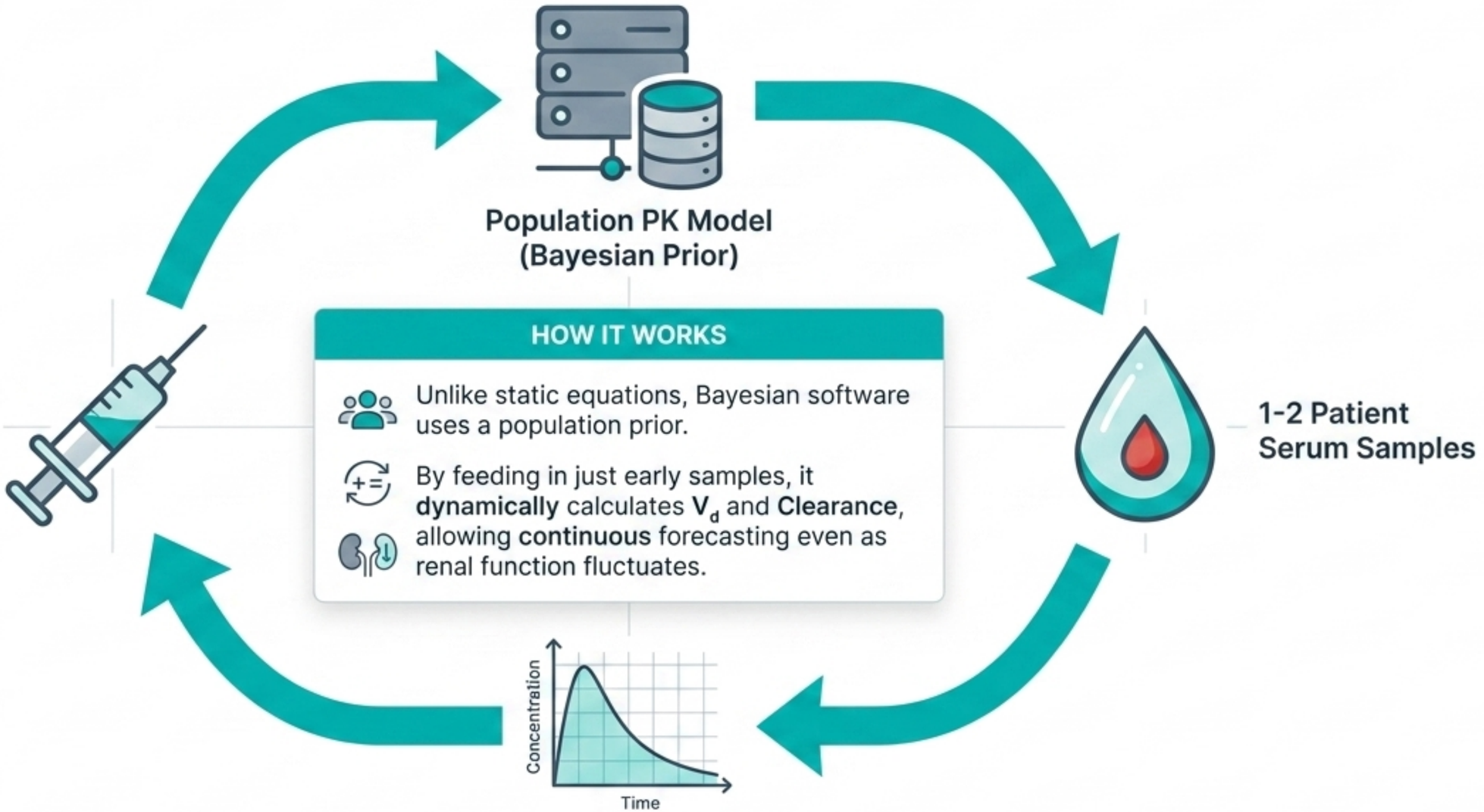
- **Inputs:** 1 or 2 drug concentrations (at least 1 trough).
- **Timing:** Early intervention. Does not require steady-state conditions (can be used in first 24-48h).
- **Adaptability:** High. Accounts for dynamic pathophysiological changes in critically ill patients.

Analytic PK Equations

- **Inputs:** Requires 2 timed steady-state concentrations (post-distributional peak at 1-2h, and trough).
- **Timing:** Must wait for steady-state, delaying early assessment.
- **Adaptability:** Low. Provides only a static snapshot; invalid if renal function changes abruptly.



The adaptive power of Bayesian forecasting



The MIC denominator: why we assume 1 mg/L

Clinical guidelines

- **The Baseline Rule:** For empiric dosing, assume the vancomycin Minimum Inhibitory Concentration (MIC) is 1 mg/L.
- **Testing Variability:** Automated MIC testing methods have a ±1 doubling dilution error rate compared to gold-standard Broth Microdilution (BMD).
- **Clinical Action:** Do NOT decrease the dose if the lab reports an MIC < 1 mg/L.
- **Clinical Warning:** If true BMD MIC > 1 mg/L, achieving an AUC of 400 is unlikely without risking extreme toxicity. Consider alternative agents.

Adult baseline protocol: normal renal function

Loading Dose

20 to 35 mg/kg based on Actual Body Weight.

Max dose: 3,000 mg.

Purpose: Rapid attainment of targeted concentrations in critically ill patients.

Maintenance Dose

15 to 20 mg/kg (Actual Body Weight).

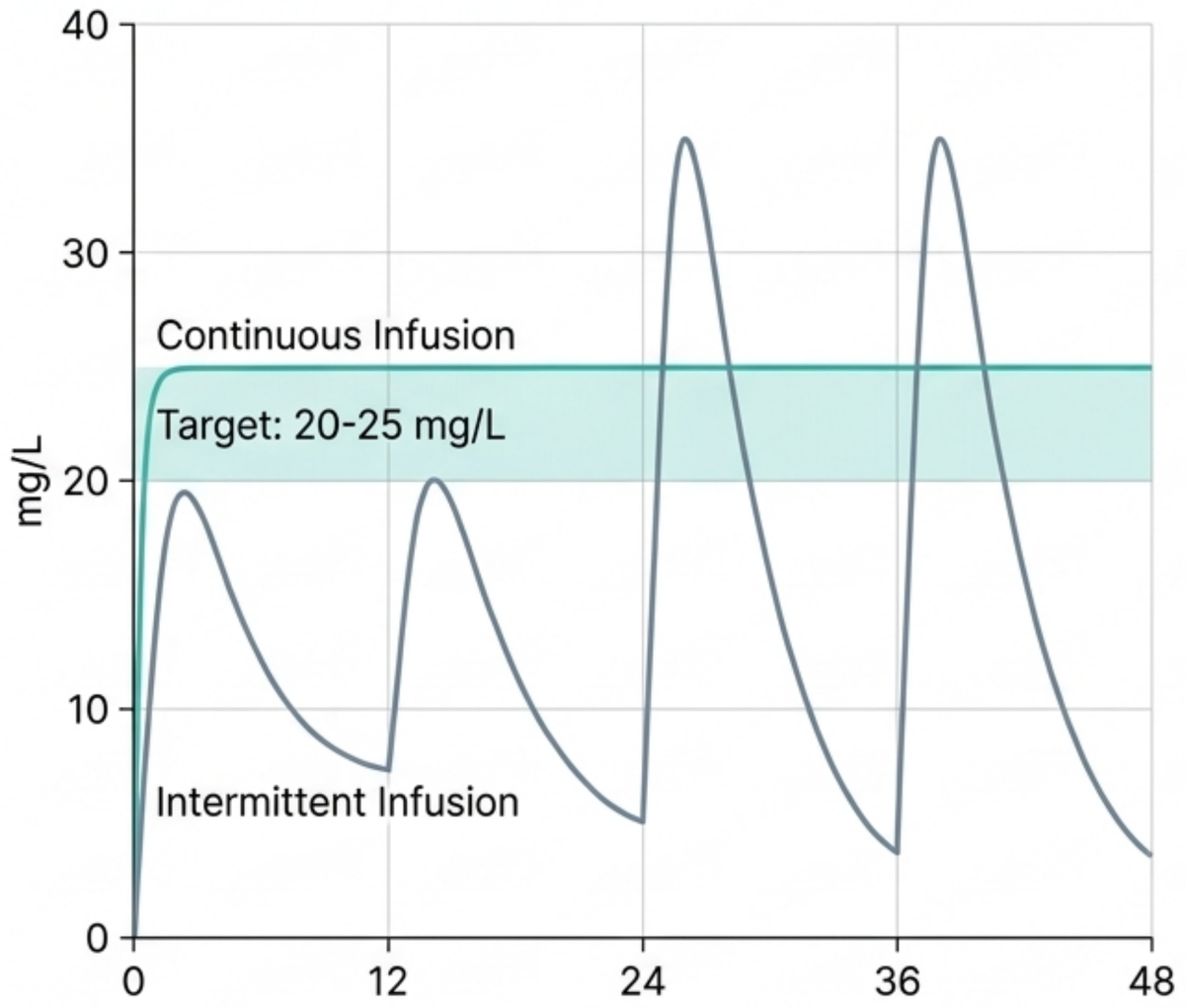
Administered every 8 to 12 hours as an intermittent infusion.

Monitoring Timing

Target AUC exposures must be achieved early: within the first 24 to 48 hours.

A. ADULTS AND PEDIATRIC PATIENTS Primary recommendation table
9. Doses of 15 to 20 mg/kg (based on actual body weight) administered every 8 to 12 hours as an intermittent infusion are recommended for most patients with normal renal function when assuming a MIC_BMD of 1 mg/L (A-II).

Continuous infusion for the critically ill



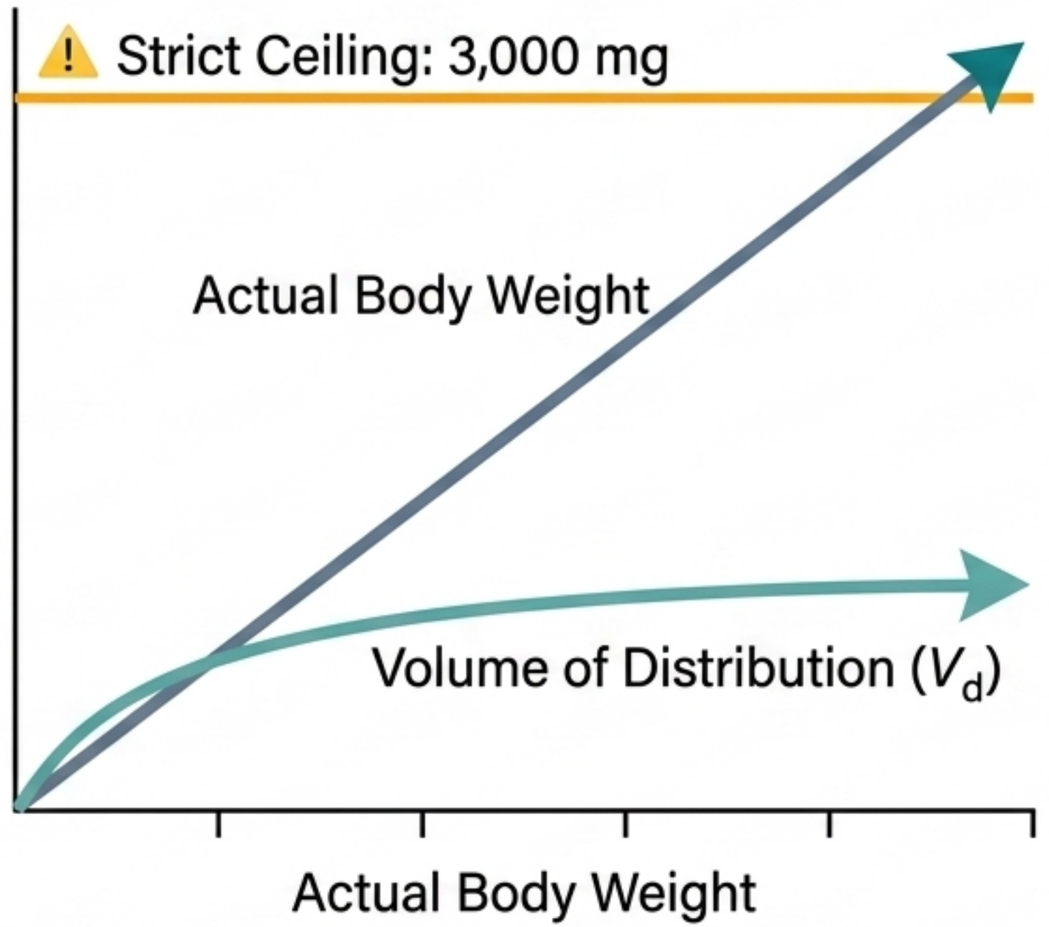
The Strategy: Continuous Infusion (CI) is a valid alternative to Intermittent Infusion (II) when AUC targets cannot be stabilized.

Protocol: Loading dose of 15-20 mg/kg, followed by a daily maintenance CI of 30-40 mg/kg.

The Math: Steady-state concentration × 24 = 24-hour AUC. A steady 20 mg/L perfectly equates to an AUC of 480 mg·h/L.

⚠️ **Warning:** Requires independent IV lines due to incompatibility with other common ICU drugs.

Navigating altered pharmacokinetics in adult obesity



The PK Challenge:
Vancomycin Volume of Distribution (V_d) increases with actual body weight, but not proportionately. Linear dosing causes supratherapeutic exposure.

Loading Rule:
20 to 25 mg/kg using Actual Body Weight, **strictly capped** at a maximum of 3,000 mg.

Maintenance Rule:
Empiric maintenance doses **rarely exceed 4,500 mg/day** because vancomycin clearance rarely exceeds 9 L/h.

Dosing parameters for renal replacement therapies

Intermittent Hemodialysis (IHD)

- **Load:** 25 mg/kg (Low perm) or 35 mg/kg (High perm).
- **Maintenance:** Administer AFTER dialysis ends (7.5-10 mg/kg) or DURING final 60-90 min (10-15 mg/kg).
- **Target:** Predialysis concentrations of 15-20 mg/L correlate to AUC 400-600.

Hybrid Dialysis (SLED)

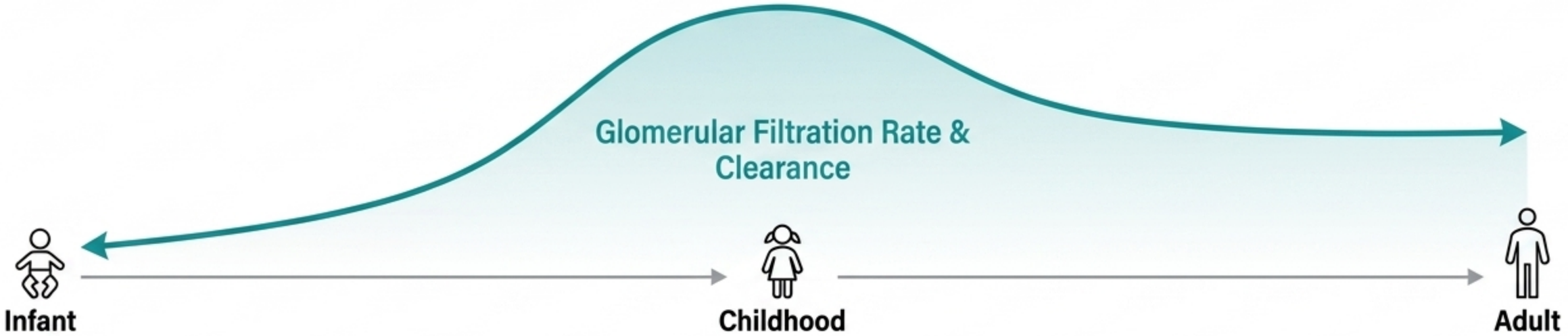
- **Load:** 20-25 mg/kg (Actual Body Weight). Do not delay for dialysis to end.
- **Maintenance:** 15 mg/kg given after hybrid dialysis ends.

Continuous RRT (CRRT)

- **Load:** 20-25 mg/kg.
- **Maintenance:** 7.5 to 10 mg/kg every 12 hours (based on effluent rates of 20-25 mL/kg/h).

Pristine Clinical Dashboard

Pediatric pharmacokinetics: the clearance challenge



Age-dependent changes in renal function and vancomycin clearance.

The Physiological Reality

- School-aged children have significantly higher glomerular filtration rates than adults, leading to rapid vancomycin clearance.

The Dosing Impact

- Standard adult dosages (45-60 mg/kg/day) are often insufficient.
- Children frequently require 60-80 mg/kg/day.

The Trough Disconnect

- Because of rapid clearance, a low trough of 7-10 mg/L in a child frequently correlates to a successful AUC of 400. Pushing pediatric troughs to adult levels (15-20 mg/L) **exponentially increases AKI risk.**

Pediatric Dosing	Target
60-80 mg/kg/day AUC-guided monitoring	AUC 400-600 mg·h/L

The pediatric baseline dosing staircase

Neonates & Infants
(< 3 months)

- **Dose**: 10 to 20 mg/kg every 8 to 48 hours.
- **Variables**: Highly dependent on postmenstrual age, weight, and serum creatinine.

Children
(3 months to < 12 years)

- **Dose**: 60 to 80 mg/kg/day.
- **Frequency**: Divided doses given every 6 hours.

Adolescents
(≥ 12 years)

- **Dose**: 60 to 70 mg/kg/day.
- **Frequency**: Divided doses given every 6 to 8 hours.

Universal Rule: Maximum empiric daily dose is 3,600 mg. Most children will not require more than 3,000 mg/day.

Pediatric edge cases: obesity and neonates

Pediatric Obesity

Unlike adults, differences in volume of distribution are not sufficient to require alternate mg/kg rules.

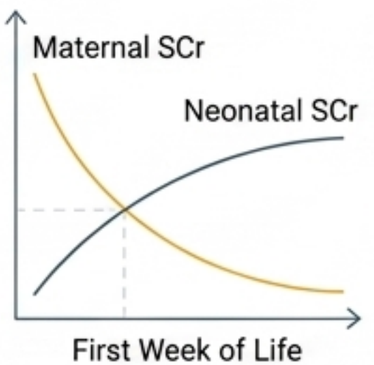
Loading Dose: 20 mg/kg based on Total Body Weight.

Maintenance: Dose using Total Body Weight (matches normal-weight children), but aggressive Bayesian therapeutic monitoring is mandatory due to high variance and AKI risk.

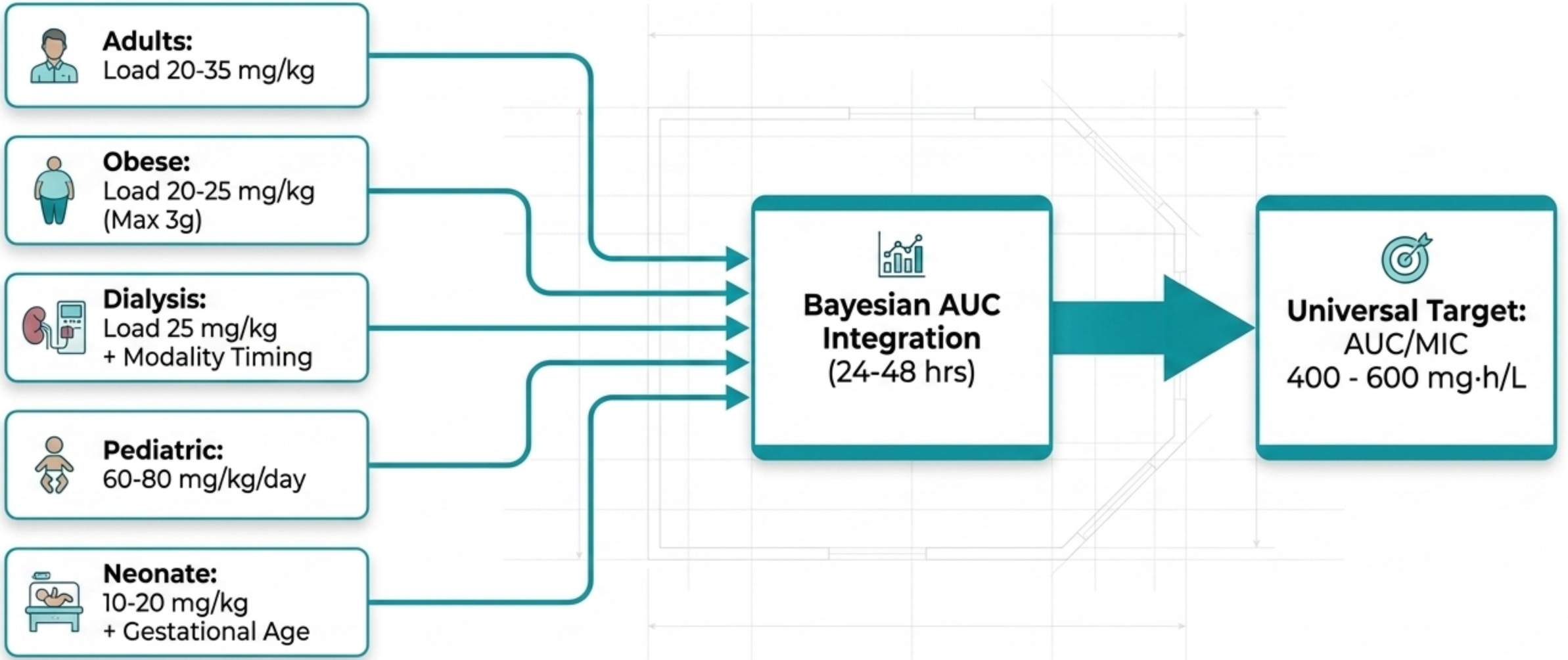
Neonatal Serum Creatinine

Warning: Serum creatinine (SCr) based dosing is inaccurate during the first week of life due to transplacental transfer of maternal creatinine.

Solution: Rely strictly on Bayesian AUC-guided estimation integrating postmenstrual age and weight during this critical window.



Synthesis: the master dosing pathway



Regardless of the patient population, body habitus, or renal function, **precision intervention** using **early Bayesian feedback aligns all clinical pathways to a single, unified therapeutic window.**