

# Is Beta-lactam Effectiveness Impacted by the Duration of Drug Infusion in Critically Ill Septic Patients? A Systematic Review of Clinical Pharmacokinetics Studies

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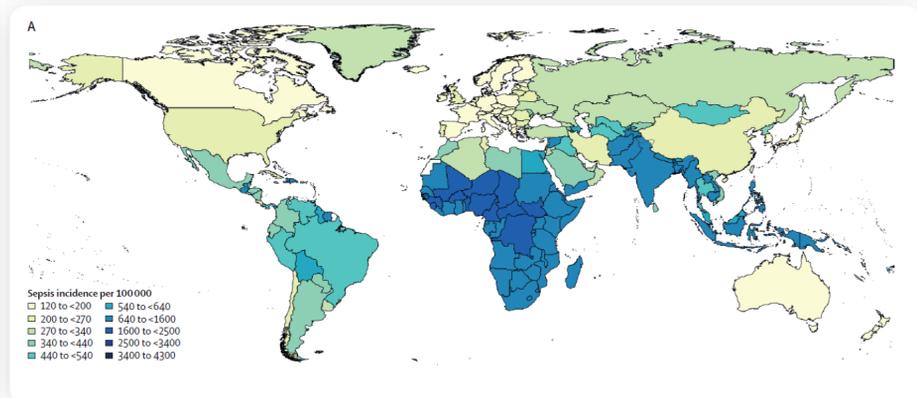
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## Introduction

### Incidence and Mortality of Septic Patients Annually in 2020

47-50 M → 11 M → 1 death every **2,8 s**

### Geographic Distribution of Sepsis Incidence in 2020



Meropenem (MEM) and piperacillin/tazobactam (PTZ) have been prescribed to septic patients with nosocomial infection caused by susceptible Gram-negative bacteria (GNB) in the intensive care unit (ICU) mainly by intermittent 0.5 h infusion. It was demonstrated that beta-lactam effectiveness against GNB is reached only up to MIC 2 mg/L after the intermittent 0.5 h infusion.

## Objective

The aim of the present review was to investigate MEM and PTZ effectiveness after recommended dose regimens by comparison of intermittent 0.5 h with extended (2-4 h) and continuous infusion.

## Casuistry and Methods

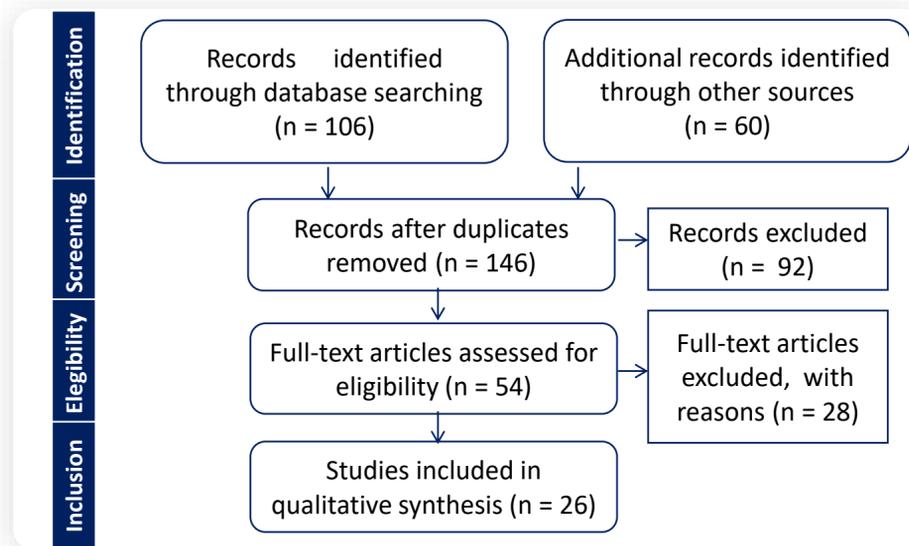
A systematic review of the literature was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and PICO strategy:

**PATIENT:** Septic with normal renal function  
**INTERVENTION:** MEM or PTZ  
**COMPARISON:** Infusion: intermittent, extended, continuous  
**OUTCOME:** 1º: - PD (PTA target 100% $f\Delta T > MIC$ )  
 2º: - PK alterations vs healthy volunteers  
 - Microbioly of isolates

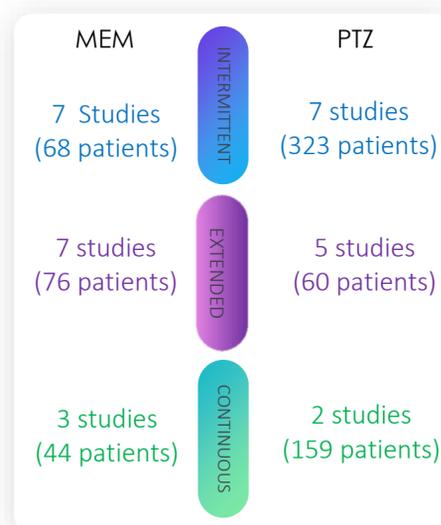
A systematic search was performed on Embase and MEDLINE databases until April 2020, without restrictions of publication date or language. Outcomes were considered according to pharmacokinetic/pharmacodynamic (PK/PD) approach.

## Results

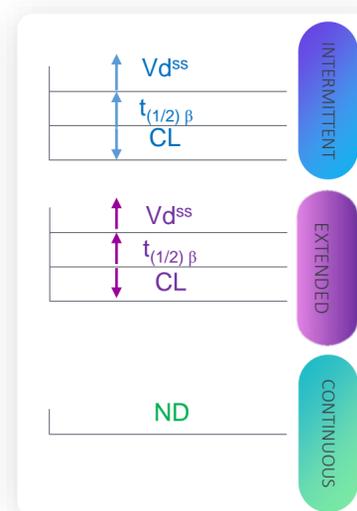
### Flow Diagram According to PRISMA Statement



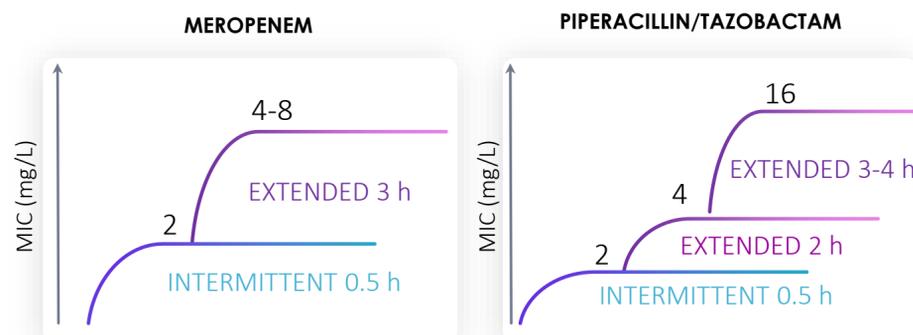
### Distribution of Studies



### PK Septic vs Healthy



### Effectiveness by Infusion Duration (target 100% $f\Delta T > MIC$ )



## Conclusion

Superiority of extended 3 h over intermittent 0.5 h infusion was demonstrated for both beta-lactam agents, MEM and PTZ. Further pharmacokinetic studies are required to clarify beta-lactam's profile data in ICU patients undergoing the continuous infusion. It is important to highlight that an implementation of therapeutic drug serum monitoring done in real-time followed by PK/PD approach may provide clinical support for a rational individualization of therapy in septic shock to avoid mutant selection by antimicrobial resistance development and, consequently, reduce mortality of ICU septic patients.