

**Table 1S. Search strategy**

<p><b>Review question</b> What is the clinical effectiveness of carbapenem therapeutic drug monitoring (TDM) in the critically ill patient?</p>
<p><b>PICO format</b>  <b>Population:</b> Patients with sepsis, septic shock o critically ill treated with carbapenems  <b>Intervention:</b> Therapeutic drug monitoring  <b>Comparator:</b> Not performing therapeutic drug monitoring  <b>Outcomes:</b> Clinical Effectiveness (Antimicrobial drug resistance; antibiotic resistance; Mortality; Morbidity; Treatment Outcome; Length of Stay; Hospitalization; Patient Readmission; Drug-Related Side Effects and Adverse Reactions; Pharmacokinetics; clinical cure; microbiological eradication; target plasma concentration)  <b>Study design:</b> Any type of study design</p>
<p><b>Filters</b> Adult: 19+ years; Humans</p>
<p><b>Data Bases</b>  <a href="#">Pubmed/Medline</a>  <a href="#">Embase</a>  <a href="#">ClinicalTrials.gov</a>  <a href="#">Cochrane Central Register of Controlled Trials (CENTRAL)</a></p>
<p><b>Key words</b> Critical illness, septic shock, sepsis, carbapenems, drug monitoring, treatment outcome</p>
<p><b>Terms</b>  <u>Patients with sepsis, septic shock o critically ill treated with carbapenems</u> <ul style="list-style-type: none"> <li>• Care, critical</li> <li>• Critical illness</li> <li>• Septic shock</li> <li>• Sepsis</li> <li>• Carbapenems</li> <li>• Panipenem</li> <li>• Ertapenem</li> <li>• Meropenem</li> <li>• Meropenem and vaborbactam</li> <li>• Doripenem</li> <li>• Imipenem</li> <li>• Cilastatin Imipenem Drug Combination</li> <li>• Imipenem, cilastatin and relebactam</li> <li>• Sanfetrinem</li> <li>• Sanfetrinem cilexetil</li> </ul>   <u>Therapeutic drug monitoring</u> <ul style="list-style-type: none"> <li>• Drug Monitoring</li> <li>• Therapeutic drug monitoring</li> </ul>   <u>Clinical Effectiveness</u> <ul style="list-style-type: none"> <li>• Antimicrobial drug resistance</li> <li>• Antibiotic resistance</li> <li>• Mortality</li> <li>• Morbidity</li> </ul> </p>

- Treatment Outcome
- Length of Stay
- Hospitalization
- Patient Readmission
- Drug-Related Side Effects and Adverse Reactions
- Pharmacokinetics
- Clinical cure
- Microbiological eradication
- Target plasma concentration

#### **Search algorithm**

1. Care, critical
2. Critical illness
3. Septic shock
4. Sepsis
5. 1 OR 2 OR 3 OR 4
6. Carbapenems
7. Panipenem
8. Ertapenem
9. Meropenem
10. Meropenem and vaborbactam
11. Doripenem
12. Imipenem
13. Cilastatin Imipenem Drug Combination
14. Imipenem, cilastatin and relebactam
15. Sanfetrinem
16. Sanfetrinem cilexetil
17. 6 OR 7 OR 8 OR 9 OR 10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16
18. 5 AND 17
19. Drug Monitoring
20. Therapeutic drug monitoring
21. 19 OR 20
22. Antimicrobial drug resistance
23. Antibiotic resistance
24. Mortality
25. Morbidity
26. Treatment Outcome
27. Length of Stay
28. Hospitalization
29. Patient Readmission
30. Drug-Related Side Effects and Adverse Reactions
31. Pharmacokinetics
32. Clinical cure
33. Microbiological eradication
34. Target plasma concentration
35. 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33 OR 34
36. 18 AND 21 AND 35
37. Humans
38. Adult: 19+ years
39. 36 AND 37 AND 38
40. Apply limits if applicable

**Search strategy for Embase**

('critically ill patient'/exp OR 'critical illness'/exp OR 'sepsis'/exp OR 'septic shock'/exp) AND ('carbapenem'/exp OR 'ertapenem'/exp OR 'meropenem'/exp OR 'meropenem plus vaborbactam'/exp OR 'imipenem'/exp OR 'cilastatin plus imipenem'/exp OR 'doripenem'/exp OR 'cilastatin sodium plus imipenem plus relebactam'/exp OR 'sanfetrinem'/exp OR 'sanfetrinem cilxetil'/exp OR 'panipenem'/exp) AND ('drug monitoring'/exp OR 'therapeutic drug monitoring') AND ('antibiotic resistance'/exp OR 'mortality'/exp OR 'morbidity'/exp OR 'treatment outcome'/exp OR 'hospitalization'/exp OR 'hospital readmission'/exp OR 'length of stay'/exp OR 'side effect'/exp OR 'pharmacokinetics'/exp OR 'cure rate'/exp OR 'microbiological eradication' OR 'target plasma concentration')

**Search strategy for Pubmed/Medline**

(((((care, critical[MeSH Terms]) OR (critical illness[MeSH Terms])) OR (septic shock[MeSH Terms])) OR (sepsis[MeSH Terms])) AND (((("Carbapenems"[Mesh] OR "panipenem" [Supplementary Concept]) OR "Ertapenem"[Majr]) OR "Doripenem"[Majr]) OR ("Meropenem"[Mesh] OR "meropenem and vaborbactam" [Supplementary Concept] )) OR ("Imipenem"[Mesh] OR "Cilastatin, Imipenem Drug Combination"[Mesh] OR "imipenem, cilastatin and relebactam" [Supplementary Concept] )) OR ("sanfetrinem" [Supplementary Concept] OR "sanfetrinem cilxetil" [Supplementary Concept] ))) AND (((("Drug Monitoring"[Mesh]) OR (therapeutic drug monitoring))) AND ((antimicrobial drug resistance[MeSH Terms]) OR (((((((("Mortality"[Mesh]) OR "Morbidity"[Mesh]) OR "Treatment Outcome"[Mesh]) OR "Length of Stay"[Mesh]) OR "Hospitalization"[Mesh]) OR "Patient Readmission"[Mesh])) OR "Drug-Related Side Effects and Adverse Reactions"[Mesh]) OR "Pharmacokinetics"[Mesh]) OR (((clinical cure) OR (microbiological eradication)) OR (target plasma concentration))))

**Search strategy for ClinicalTrials.gov**

Critical Illness | drug monitoring | Adult, Older Adult

**Search strategy for CENTRAL**

"carbapenems" OR "Ertapenem" OR "Meropenem" OR "Imipenem" OR "Doripenem" OR "Panipenem" OR "Sanfetrinem" in Title Abstract Keyword AND "drug monitoring" in Title Abstract Keyword

**Eligibility criteria**Inclusion criteria

- Eligible studies compared carbapenem TDM to empiric care in adult critically ill or sepsis/septic shock patients.
- Randomized controlled trials (RCTs)
- Comparative prospective or retrospective cohort studies
- Included studies had to report an effect estimate for at least one of the following outcomes of effectiveness determined by the authors: mortality, morbidity, clinical cure, microbiological eradication, antimicrobial resistance, drug-related side effects and adverse reactions and achievement of target plasma concentrations.

Exclusion criteria

- Cross sectional studies
- Intervention or observational studies without control group
- Research carried out in pediatric population