# INPLASY PROTOCOL

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**Corresponding author:**
**Jing Li**

**lijing7112@126.com**

**Author Affiliation:**
**The Affiliated Hospital of Qingdao University.**

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**None declared.**

# Carbapenems versus β-lactam and β-lactamase inhibitors for treatment of Nosocomial Pneumonia: a systematic review and meta-analysis

Cang, HQ[1]; Quan, XH[2]; Chu, XH[3]; Liang, Y[4]; Yang, X[5]; Li, J[6].

**Review question / Objective:** **Carbapenems and β-lactam and β-lactamase inhibitors (BLBLIs) have been used empirically in nosocomial pneumonia, but their efficacy and safety are controversial. We carried out a systematic review with meta-analysis to evaluate the efficacy and safety of carbapenems versus BLBLIs against nosocomial pneumonia.**
**Condition being studied:** **Hospital-acquired pneumonia (HAP) is one of the most common types of infection of pulmonary parenchyma and includes ventilator-associated pneumonia (VAP). HAP (particularly VAP) has become a major public-health issue due to its high morbidity and mortality rates. Carbapenems have become a common option in nosocomial pneumonia caused by Gram-negative bacteria. However, several studies have demonstrated that use of carbapenems is resistance to their effects. Administration of inappropriate initial antibiotic therapy in a patient with HAP is a high-risk factor causing multidrug-resistant (MDR) Gram-negative bacteria. Inadequate antibiotic therapy has been associated with significantly increased mortality. Identifying the appropriate initial antibiotic therapy for HAP is very important. We undertook a meta-analysis of the effects and safety of carbapenems versus BLBLIs in patients with HAP.**

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 30 April 2023 and was last updated on 05 May 2023 (registration number INPLASY202340113).

## INTRODUCTION

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**Condition being studied:** Hospital-acquired pneumonia (HAP) is one of the most common types of infection of pulmonary parenchyma and includes ventilator-associated pneumonia (VAP). HAP (particularly VAP) has become a major public-health issue due to its high morbidity and mortality rates. Carbapenems have become a common option in nosocomial pneumonia caused by Gram-negative bacteria. However, several studies have demonstrated that use of carbapenems is resistance to their effects. Administration of inappropriate initial antibiotic therapy in a patient with HAP is a high-risk factor causing multidrug-resistant (MDR) Gram-negative bacteria. Inadequate antibiotic therapy has been associated with significantly increased mortality. Identifying the appropriate initial antibiotic therapy for HAP is very important. We undertook a meta-analysis of the effects and safety of carbapenems versus BLBLIs in patients with HAP.

## METHODS

**Participant or population:** Patients had to be diagnosed with HAP (including VAP). Pneumonia had to be diagnosed based on clinical and radiographic criteria: purulent tracheal secretions with at least one respiratory sign or symptom of pneumonia, including new-onset fever or hypothermia, leukocytosis, or decline in oxygenation and including new or worsening infiltrates on chest radiographs within 48 h of hospital admission. HAP was defined as a patient with pneumonia who remained in hospital ≥48 h after hospital admission. VAP was defined as pneumonia with onset ≥48 h after endotracheal intubation and mechanical ventilation.

**Intervention:** The experimental group had to be treated with carbapenems.

**Comparator:** The control group had to be treated with BLBLIs.

**Study designs to be included:** A randomized control trial (RCT).

**Eligibility criteria:** 1) Participants: Patients had to be diagnosed with HAP (including VAP). Pneumonia had to be diagnosed based on clinical and radiographic criteria: purulent tracheal secretions with at least one respiratory sign or symptom of pneumonia, including new-onset fever or hypothermia, leukocytosis, or decline in oxygenation and including new or worsening infiltrates on chest radiographs within 48 h of hospital admission. HAP was defined as a patient with pneumonia who remained in hospital ≥48 h after hospital admission. VAP was defined as pneumonia with onset ≥48 h after endotracheal intubation and mechanical ventilation. (2) Interventions: The experimental group had to be treated with carbapenems. (3) Comparaors: The control group had to be treated with BLBLIs. (4) Outcomes: mortality , clinical response, microbiologic response , Side-effects of antibiotic treatment. (5) Study design: a randomized control trial (RCT).
Exclusion criteria
(1) abstracts, conference papers; (2) studies with incomplete data or using different control drugs.

**Information sources:** PubMed, Embase, and Cochrane Central Register of Controlled Trials, CNKI, Wanfang databases, VIP, Sinomed were searched systematically for clinical trials comparing carbapenems with BLBLIs for treatment of nosocomial pneumonia.There will not language restriction.

**Main outcome(s):** mortality , clinical response.

**Additional outcome(s):** microbiologic response, side-effects.

**Quality assessment / Risk of bias analysis:** Cochrane Collaboration's risk of bias tools. We evaluated the confidence in the evidence for each outcome by employing the GRADE approach, which considers study design, risk of bias, inconsistency, indirectness, imprecision.

**Strategy of data synthesis:** Review Manager 5.4 was used for this meta-

analysis . Treatment effects were calculated with the risk ratio (RR) and the corresponding 95% confidence interval for dichotomous outcomes. Cochran's Q statistic (significance level, $P < 0.01$) and I2 statistic were employed to assess heterogeneity. According to the Cochrane Handbook, I2 can be considered "non-important" (60%) . Heterogeneity can be xategorized into three types: clinical heteogeneity, methodological heterogeneity and statistical heterogeneity. Although statistical heterogeneity was not present, there was still clinical heterogeneity, and therefore, the radom-effects model was employed to improve the reliability of the result. Results were assessed using forest plots.

**Subgroup analysis:** Subgroup analyses were conducted according to the type of carbapenems, the classification of microorganisms and categorization of AEs.

**Sensitivity analysis:** Sensitivity analysis was undertaken to ascertain the results of the meta-analysis by excluding each individual study.

**Country(ies) involved:** China.

**Keywords:** carbapenem antibiotics, β-lactam, β-lactamase inhibitors, nosocomial pneumonia, systematic review meta-analysis.

**Contributions of each author:**

Author 1 - Huai Qin Cang.
Email: chq200709@163.com
Author 2 - Xiang Hua Quan.
Author 3 - Xiang Hua Chu.
Author 4 - Yu Liang.
Author 5 - Xue Yang.
Author 6 - Jing Li.