

# INPLASY PROTOCOL

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**Support:** No.

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**Conflicts of interest:**  
None declared.

## Impact of area under the curve-based vancomycin dosing combination with anti-pseudomonal beta-lactam antibiotics: a systematic review and meta-analysis

Chiu, CY<sup>1</sup>; Sarwal, A<sup>2</sup>.

**Review question / Objective:** Did AUC-based vancomycin dosing reduce acute kidney injury than trough-based dosing when combined with anti-pseudomonal beta-lactam antibiotic?

**Condition being studied:** Patients received Vancomycin combined with anti-pseudomonal beta-lactam antibiotics and monitor with either trough-base dosing or AUC-based dosing vancomycin.

**Information sources:** All study types except case reports, case series, and conference abstracts were considered. PubMed, Embase, Cochrane Library, and ClinicalTrials.gov were searched from inception to November 2022.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 December 2022 and was last updated on 23 December 2022 (registration number INPLASY2022120025).

**Rationale:** Vancomycin combined with piperacillin/tazobactam (VPT) has a higher risk of acute kidney injury (AKI) than vancomycin combined with cefepime or meropenem. However, it is uncertain if area under the curve (AUC)-based vancomycin dosing is superior to trough-based dosing in these combinations.

### INTRODUCTION

**Review question / Objective:** Did AUC-based vancomycin dosing reduce acute kidney injury than trough-based dosing when combined with anti-pseudomonal beta-lactam antibiotic?

**Condition being studied:** Patients received Vancomycin combined with anti-pseudomonal beta-lactam antibiotics and monitor with either trough-base dosing or AUC-based dosing vancomycin.

## METHODS

**Search strategy:** ((Vancomycin area under the concentration-time curve) OR (Vancomycin AUC)) AND ((piperacillin-tazobactam) OR (ceftazidime) OR (cefoperazone-sulbactam) OR (cefepime) OR (imipenem-cilastatin) OR (doripenem) OR (meropenem) OR (beta-lactam)).

**Participant or population:** Patients received Vancomycin combined with anti-pseudomonal beta-lactam antibiotics and monitor with either trough-base dosing or AUC-based dosing vancomycin. Patients received Vancomycin combined with piperacillin/tazobactam (VPT) and monitor with either trough base dosing or AUC based dosing vancomycin.

**Intervention:** AUC based vancomycin dosing.

**Comparator:** Trough based vancomycin dosing.

**Study designs to be included:** Retrospective, prospective, randomized controlled trial.

**Eligibility criteria:** vancomycin combined with anti-pseudomonal beta-lactam antibiotics.

**Information sources:** All study types except case reports, case series, and conference abstracts were considered. PubMed, Embase, Cochrane Library, and ClinicalTrials.gov were searched from inception to November 2022.

**Main outcome(s):** The primary outcome is the odds ratio (OR) of AKI in patients who received VPT or the control using the AUC-based vancomycin dosing.

**Additional outcome(s):** The secondary outcomes are (1) the OR of AKI in patients

received VPT using AUC-based vancomycin dosing or trough-based dosing and (2) daily vancomycin dose in patients who received VPT using AUC-based dosing or trough-based dosing.

**Data management:** A random effects model was employed. Between-trial heterogeneity was determined by using I<sup>2</sup> tests; an I<sup>2</sup> > 50% was considered statistically significant heterogeneity. Funnel plots and Egger's test were used to examine potential publication bias. Statistical significance was defined as p values < 0.05, except for the determination of publication bias that employed p < 0.10. All analyses were performed using comprehensive meta-analysis (CMA) software, version 3 (Biostat, Englewood, NJ, USA).

**Quality assessment / Risk of bias analysis:** The methodological quality of enrolled studies was evaluated using Newcastle-Ottawa Quality Assessment Scale. Newcastle-Ottawa Quality Assessment Scale contains nine items in three categories: participant selection, comparability, and exposure.

**Strategy of data synthesis:** All eligible articles were reviewed. First author, year, sample size, number and type of treatment arms, and participant characteristics were recorded.

**Subgroup analysis:** The secondary outcomes are (1) the OR of AKI in patients received VPT using AUC-based vancomycin dosing or trough-based dosing and (2) daily vancomycin dose in patients who received VPT using AUC-based dosing or trough-based dosing.

**Sensitivity analysis:** Between-trial heterogeneity was determined by using I<sup>2</sup> tests; an I<sup>2</sup> > 50% was considered statistically significant heterogeneity. Funnel plots and Egger's test were used to examine potential publication bias.

**Language restriction:** Only English literature.

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**Country(ies) involved:** USA (The University of Texas Health Science Center at Houston).

**Keywords:** vancomycin, piperacillin-tazobactam, area under the curve, vancomycin trough, acute kidney injury.

**Dissemination plans:** officially publish.

**Contributions of each author:**

**Author 1 - Chia-Yu Chiu - Chia-Yu Chiu and Amara Sarwal** were responsible for conceptualization, data curation, and manuscript writing. Chia-Yu Chiu was also responsible for software. All authors critically revised and approved the final version of the manuscript.

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**Author 2 - Amara Sarwal - Chia-Yu Chiu and Amara Sarwal** were responsible for conceptualization, data curation, and manuscript writing. Chia-Yu Chiu was also responsible for software. All authors critically revised and approved the final version of the manuscript.