

# INPLASY PROTOCOL

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None declared.

## Intravenous high-dose vitamin C monotherapy for sepsis and septic shock: a meta-analysis of randomized controlled trials

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**Review question / Objective:** Vitamin C has been used as an adjuvant in the treatment of sepsis and septic shock; however, its role remains controversial. This study aimed to assess the effectiveness of intravenous (IV) high-dose vitamin C monotherapy in sepsis and septic shock patients.

**Condition being studied:** Sepsis is a dysregulated systemic response to infection that causes organ dysfunction. Globally, sepsis remains one of the leading causes of death in intensive care units (ICUs) and continues to pose a major public health issue. Vitamin C has been used as an adjunctive therapy for sepsis because of its anti-inflammatory and antioxidant properties. Specifically, intravenous (IV) high-dose vitamin C therapy has recently become a popular research topic in adjuvant therapy for sepsis.

**INPLASY registration number:** This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 February 2023 and was last updated on 22 February 2023 (registration number INPLASY202320097).

### INTRODUCTION

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monotherapy in sepsis and septic shock patients.

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## METHODS

**Participant or population:** The patients had sepsis or septic shock according to Sepsis-1, -2, or -3 definitions.

**Intervention:** IV high-dose vitamin C ( $\geq 6$  g or 100- mg/kg every day) monotherapy was administered to the intervention group.

**Comparator:** Standard treatment for sepsis was administered to the control group.

**Study designs to be included:** RCTs.

**Eligibility criteria:** The patients were  $\geq 18$  years old.

**Information sources:** The PubMed, Embase, and Cochrane Library databases were systematically searched.

**Main outcome(s):** Short-term all-cause mortality.

**Quality assessment / Risk of bias analysis:** Two authors independently perform the methodological quality of the included studies by the Cochrane risk-of-bias tool.

**Strategy of data synthesis:** For dichotomous data, we calculated the pooled relative risk (RR) with corresponding 95% confidence intervals (CI); continuous data were expressed as mean difference (MD) with 95% CI, and if different unit were used between studies, standardised MD (SMD) with 95% CI was calculated. Differences were considered significant at  $p < 0.05$ . Statistical heterogeneity was estimated by calculating the  $I^2$  statistic where  $I^2 \geq 50\%$  indicates significant heterogeneity. A fixed-effects model was utilized if there was no

significant heterogeneity; otherwise, a random-effects model was applied.

**Subgroup analysis:** If high heterogeneity was observed and more than five studies were included, subgroup analysis will conduct using the leave-one-out approach to assess the reliability of the overall results and the impact of each study on the final outcome.

**Sensitivity analysis:** If high heterogeneity was observed and more than five studies were included, sensitivity analysis will conduct using the leave-one-out approach to assess the reliability of the overall results and the impact of each study on the final outcome.

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

**Keywords:** vitamin C, sepsis patient, septic shock patient.

### Contributions of each author:

Author 1 - Yiqian Zeng.

Author 2 - Zhao Liu.

Author 3 - Fei Xu.

Author 4 - Zhanhong Tang.