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**Methylene blue for the adjunctive therapy of septic shock: a systematic review and meta-analysis of randomized controlled study**

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**ADMINISTRATIVE INFORMATION**

**Support** - Funded by the Natural Science Foundation of Fujian Province (2023J01820).

**Review Stage at time of this submission** - Completed but not published.

**Conflicts of interest** - None declared.

**INPLASY registration number:** INPLASY202610083

**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 25 January 2026 and was last updated on 25 January 2026.

**INTRODUCTION**

**Review question / Objective** The current study was aimed to investigate the effect of methylene blue as adjunctive therapy on the clinical outcomes among this patient population.

**Condition being studied** Condition being studied The research team comes from the Department of Critical Care Medicine of a tertiary hospital in China, and all the team members have perfect clinical experience in critical care and resuscitation. Moreover, our team members have published more than 50 meta-analyses, which can guarantee the successful completion of the current research.

**METHODS**

**Participant or population** Adult patients diagnosed with septic shock, with the definition of

septic shock explicitly aligning with the relevant guidelines.

**Intervention** MB, with no restrictions on dosage, timing of administration, or duration of therapy.

**Comparator** Placebo or no intervention of MB.

**Study designs to be included** Not limited.

**Eligibility criteria** Randomized controlled study (RCT) that investigated the effectiveness of methylene blue in treating septic shock.

**Information sources** PubMed, Embase, Cochrane Library, Web of Science, and Chinese databases (Wanfang, VIP, and CNKI).

**Main outcome(s)** Mortality.

**Quality assessment / Risk of bias analysis** Cochrane risk of bias tool.

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**Strategy of data synthesis** Meta-analysis.

**Subgroup analysis** Subgroup analyses were conducted based on mortality risk ( $>40\%$  or  $\leq 40\%$ ), MB treatment ( $>24$  hours or  $\leq 24$  hours), MB solvents (saline or glucose solution), and race (Asian or non-Asian populations).

**Sensitivity analysis** (1) sample size  $>50$ ; (2) sepsis 3.0; (3) double-blind design; and (4) published after 2012.

**Country(ies) involved** China.

**Keywords** methylene blue, septic shock, mortality, meta-analysis.

**Contributions of each author**

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