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The effect of ciprofol on the incidence of postoperative delirium in adult surgical patients: A Meta-analysis and Meta-regression

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ADMINISTRATIVE INFORMATION

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

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202610019

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 5 January 2026 and was last updated on 5 January 2026.

INTRODUCTION

Review question / Objective P: adult surgical patients. I: ciprofol. C: Not applicable. O: postoperative delirium. S: randomized controlled trials (RCTs).

Rationale There is a pressing need for a comprehensive quantitative analysis to synthesize the available evidence, thereby providing a more precise and reliable assessment of the effect of ciprofol on POD. Meta-analysis serves as a powerful statistical tool that can enhance sample size and increase statistical power by pooling results from multiple independent studies, leading to more generalizable conclusions. Furthermore, meta-regression can be employed to explore potential sources of heterogeneity among study findings.

Condition being studied This study aims to conduct a systematic review and critical appraisal of the existing literature to perform a meta-analysis and meta-regression, with the following core objectives: to systematically evaluate the impact of ciprofol versus propofol on the incidence of postoperative delirium in adult surgical patients, and to explore potential sources of heterogeneity—including patient age, surgical type, and anesthesia

technique—via subgroup analysis and meta-regression.

METHODS

Search strategy Given the limited volume of literature in this specific field, the search strategy was designed using "Ciprofol" as the primary search term, incorporating MeSH terms and other relevant keywords. Key search terms included "Ciprofol", "HSK3486", and "2-((1R)-1-cyclopropyl)ethyl-6 -isopropyl-phenol" which were combined using Boolean operators. A systematic search was conducted across authoritative databases, including PubMed, Web of Science, OVID, EMBASE, and the Cochrane Library. Retrieved records were imported into EndNote 2025 for management. Two researchers independently performed an initial screening of the identified articles based on the relevance of their references. Any discrepancies encountered during the article selection process were resolved through consultation with a third investigator. The search was updated until October 2025.

Participant or population Patients anesthetized with ciprofol.

Intervention Ciprofol.

Comparator Not applicable.

Study designs to be included Randomized controlled trials (RCTs).

Eligibility criteria

Inclusion and Exclusion Criteria

The inclusion criteria were as follows: (1) surgical patients undergoing general anesthesia; (2) studies in which ciprofol was utilized as the primary anesthetic agent; (3) studies that assessed the incidence of POD in patients anesthetized with ciprofol; (4) randomized controlled trials (RCTs).

The exclusion criteria were as follows: (1) literature reviews, case reports, commentaries, letters, and conference abstracts; (2) duplicate publications or studies with overlapping patient populations; (3) studies not published in English; (4) studies that did not report or from which data on delirium events in surgical patients receiving ciprofol anesthesia could not be extracted.

Information sources Electronic databases.

Main outcome(s) Seven studies involving 4,171 patients were included. The overall POD incidence in the ciprofol group was 11.30% (95% CI: 0.77%–21.83%), which was significantly lower than that in the propofol group (19.51%; 95% CI: 2.51%–36.50%). Subgroup analysis revealed that the advantage of ciprofol in reducing POD incidence was more pronounced in patients undergoing trunk surgery (19.29% vs. 0.56%) and in those receiving total intravenous anesthesia (2.93% vs. 14.33%). Meta-regression did not identify significant correlations between POD incidence and age, sex distribution, or intraoperative hypotension. Significant heterogeneity was observed across studies ($I^2 > 85\%$), but sensitivity analysis confirmed the robustness of the results.

Quality assessment / Risk of bias analysis The quality of the included studies was assessed using the Newcastle-Ottawa Scale (NOS), accessible at http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Studies achieving an NOS score greater than 5 were deemed to meet the quality threshold for inclusion in this meta-analysis.

Strategy of data synthesis Meta-analysis was performed using the 'meta' and 'metafor' packages in R software (version 4.2.2) (8). Raw incidence data were first subjected to logarithmic, logit, arcsine, and Freeman-Tukey double arcsine transformations. The normality of the distribution was assessed using the Shapiro-Wilk test, and the most appropriate transformation method was selected based on the results. The incidence of POD in surgical patients receiving ciprofol anesthesia, along with its 95% confidence interval (CI), was calculated. Heterogeneity among the included studies was evaluated using Cochrane's Q test and the I^2 statistic. Significant heterogeneity was considered present if the p-value from Cochrane's Q test was ≤ 0.05 or if $I^2 \geq 50\%$. In such cases, subgroup analysis was employed to observe whether heterogeneity decreased within specific subgroups. Sensitivity analysis was conducted by iteratively omitting individual studies to assess the robustness of the pooled results. Studies identified as exerting an unduly influential effect on the analysis were considered for exclusion to determine if their removal resolved the heterogeneity.

If substantial heterogeneity persisted after these steps, a random-effects model was used to calculate the pooled incidence and its 95% CI, and sources of heterogeneity were further investigated. In the absence of significant heterogeneity, a fixed-effects model was applied to pool the overall incidence. Publication bias was assessed using funnel plots and Egger's test. If obvious outliers were identified, their potential sources of bias were

carefully analyzed before considering exclusion. Meta-regression analysis was performed to examine the relationship between reported continuous variables and the incidence of POD.

The conduct of this meta-analysis adhered to the guidelines outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement.

Subgroup analysis Subgroup analyses were conducted based on surgery type (trunk vs. peripheral), patient age (adults vs. elderly), and anesthesia technique (total intravenous anesthesia [TIVA] vs. balanced intravenous-inhalational anesthesia).

Sensitivity analysis The sensitivity analysis demonstrated that sequentially omitting any single study from the various meta-analyses did not significantly alter the overall results. This indicates that the high degree of heterogeneity observed in the results was not driven by any individual study, suggesting other origins for the heterogeneity. Further analysis pertaining to this finding will be elaborated upon in the Discussion section.

Country(ies) involved China.

Keywords Ciprofol, Postoperative Delirium, Anesthesia, Meta-Analysis.

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