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INPLASY

Protocol for a systematic review and core meta-analysis of parenteral antipsychotic strategies for adult acute agitation in the emergency department

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 March 2026 and was last updated on 26 March 2026.

INTRODUCTION

Review question / Objective To evaluate, in adults presenting to the emergency department (ED) with acute agitation, how parenteral antipsychotic strategies—particularly olanzapine, haloperidol, and droperidol—compare with respect to additional/rescue sedation, early adequate sedation, and adverse events.

Rationale Existing reviews often mix psychiatric emergency settings, inpatient wards, prehospital care, multiple routes of administration, and different pharmacologic classes. As a result, they do not directly answer the pragmatic bedside question most relevant to ED clinicians: among parenteral antipsychotic strategies used for adult acute agitation in the ED, which options are associated with faster adequate sedation, less need for rescue medication, and acceptable safety.

Condition being studied Adult acute agitation in the emergency department, including undifferentiated agitation managed in routine ED practice. The review focuses on the acute pharmacologic management of agitation requiring parenteral medication.

METHODS

Search strategy The search strategy will combine terms related to:
(1) agitation (e.g., agitation, agitated, violent, combative, acute behavioral disturbance, excited delirium);
(2) emergency setting (e.g., emergency department, emergency room);
(3) route/management approach (e.g., parenteral, intramuscular, intravenous, rapid tranquilization, chemical restraint);
(4) target drugs (e.g., olanzapine, haloperidol, droperidol, midazolam, lorazepam, ziprasidone).
Reference lists and citing articles of eligible studies will also be reviewed.

Participant or population Adults treated in the emergency department for acute agitation or acute

behavioral disturbance requiring parenteral sedation/tranquilization.

Intervention Parenteral antipsychotic strategies used in the ED, including intramuscular or intravenous olanzapine, haloperidol, and droperidol, either as monotherapy or in clinically relevant ED regimens.

Comparator Other parenteral antipsychotic strategies or clinically relevant direct comparators used for acute agitation management in the ED, including haloperidol-, olanzapine-, droperidol-, benzodiazepine-, or combination-based regimens when directly compared.

Study designs to be included Randomized controlled trials and non-randomized comparative studies (prospective or retrospective cohort studies and other comparative observational designs).

Eligibility criteria Inclusion criteria:
(1) original comparative studies;
(2) adult patients managed in the ED for acute agitation;
(3) parenteral sedation/tranquilization as the core intervention;
(4) at least one extractable outcome relevant to this review.

Exclusion criteria:
(1) non-ED settings;
(2) non-original articles;
(3) conference abstracts without full text;
(4) studies with ineligible intervention/comparator structures;
(5) studies without extractable core outcome data;
(6) duplicate or overlapping datasets.

Information sources PubMed, Embase, Web of Science, Cochrane Library, and Scopus will be searched from inception to March 2026. Additional records will be identified through manual searching, reference checking, and citation tracking.

Main outcome(s) Primary outcomes will be:
(1) additional/rescue sedation;
(2) adequate sedation at 15 minutes;
(3) adequate sedation at 30 minutes;
(4) any reported adverse event.
For pooled binary outcomes, risk ratios (RRs) with 95% confidence intervals will be used.

Additional outcome(s) Time to sedation, time to arousal, repeat dosing, oxygen use, airway interventions, extrapyramidal symptoms, QTc-related events, and other study-reported safety outcomes.

Data management Search results will be imported into reference management software for de-duplication. Records will then undergo title/abstract screening and full-text eligibility assessment. Data extraction will be performed using a standardized extraction form capturing study design, setting, sample size, regimens compared, outcome definitions, and outcome data.

Quality assessment / Risk of bias analysis Randomized studies will be assessed using the Cochrane RoB 2 tool. Non-randomized comparative studies will be assessed using ROBINS-I. Certainty of evidence for the core meta-analytic outcomes will be evaluated using the GRADE framework.

Strategy of data synthesis A systematic review with a core meta-analysis approach will be used. Quantitative synthesis will be performed only when at least two studies address a sufficiently similar clinical question with comparable outcome definitions and time points. Dichotomous outcomes will be pooled as risk ratios with 95% confidence intervals, primarily using a random-effects model. Comparisons supported by only a single study, by markedly different routes of administration, or by predominantly continuous outcomes will be summarized narratively.

Subgroup analysis If sufficient data are available, analyses will be grouped according to clinically comparable comparisons and time points. Formal subgroup meta-analysis is not anticipated for most non-core comparisons because of limited study numbers and clinical heterogeneity.

Sensitivity analysis Sensitivity analyses will be considered according to study design and clinical comparability, particularly when randomized and non-randomized evidence contribute to related questions or when IV regimens and combination regimens may influence interpretability.

Language restriction No language restriction.

Country(ies) involved China.

Other relevant information This review uses a "systematic review + core meta-analysis" framework. Quantitative synthesis is deliberately restricted to repeatable and clinically pragmatic ED comparisons, while heterogeneous single-study or

route-specific comparisons are retained for narrative synthesis.

Keywords acute agitation; emergency department; olanzapine; haloperidol; droperidol; parenteral antipsychotics; systematic review; meta-analysis.

Dissemination plans The findings will be submitted to a peer-reviewed journal and may also be presented at academic conferences related to emergency medicine, psychiatry, or evidence synthesis.

Contributions of each author

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