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Systematic review

Predictors of ICU Admission and Mechanical Ventilation in Neuroleptic Malignant Syndrome and Malignant Catatonia Presenting to the Emergency Department: A Systematic Review

Hisham Alyahya[1], Abdulaziz Turki Alqabli[2], Anas Ghazi Fintyana[3], Omar Saeed Alzahrani[4], Ayman Ali Asiri[5], Rayhana Yousef Alsaif[6], Shatha Shabab Alghamdi[7], Hanan Salem Albalawi[8], Shahad Fahad Basamad[9], Shoug Khaled Albesher[10], Lanah Asim Alsuhim[11], Noor Hassan Albayat[12]

1. Emergency Medicine Consultant, Emergency Department, Riyadh First Health Cluster, Riyadh, Saudi Arabia. Email: hfiy.hf@gmail.com
2. Medical Intern, Faculty of Medicine, University of Tabuk, Tabuk, Saudi Arabia. Email: abdulaziz.alqabli@gmail.com
3. Medical Intern, College of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia. Email: anas.fintyana@gmail.com
4. Medical Intern, College of Medicine, Albaha University, Al-Baha, Saudi Arabia. Email: Omarbadawi202@gmail.com
5. Medical Intern, College of Medicine, King Khalid University, Abha, Saudi Arabia. Email: aimn20911@gmail.com
6. Medical Intern, College of Medicine, King Faisal University, Al-Ahsa, Saudi Arabia. Email: Rehana1387@gmail.com
7. Medical Intern, College of Medicine, Albaha University, Al-Baha, Saudi Arabia. Email: iiffoor@gmail.com
8. Medical Intern, College of Medicine, University of Tabuk, Tabuk, Saudi Arabia. Email: hanans.20020@gmail.com
9. Medical Intern, College of Medicine, Umm Al-Qura University, Makkah, Saudi Arabia. Email: shahadbasamad@hotmail.com
10. Medical Intern, College of Medicine, Qassim University, Burydah, Saudi Arabia. Email: shougalbesher.med@gmail.com
11. Medical Student, College of Medicine, Arabian Gulf University, Manama, Bahrain. Email: lanahas1@outlook.com
12. Medical Intern, College of Medicine, Alfaisal University, Riyadh, Saudi Arabia. Email: Albayatn@gmail.com

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Abstract

Background. Neuroleptic malignant syndrome and malignant catatonia are uncommon emergencies in which altered consciousness, autonomic instability, and respiratory deterioration complicate disposition, in this systematic review study we aimed to identify factors measured during emergency department assessment that were associated with intensive care unit admission or invasive mechanical ventilation. **Methods.** PubMed and supplementary searches identified original reports published through 31 May 2026. Reports describing at least two affected patients were eligible when they documented intensive care admission, endotracheal intubation, or mechanical ventilation during the index illness. Findings were synthesized narratively by syndrome, recruitment setting, and outcome. **Results.** Fifteen original reports contributed data. In a Japanese inpatient cohort of 1,585 patients with neuroleptic malignant syndrome, 408 entered intensive care and 193 underwent intubation. Intensive care admission occurred in 31.4% of typical antipsychotic users and 21.0% of atypical antipsychotic users in a matched inpatient comparison. An Australian adverse-event study showed the opposite numerical pattern. In a treatment-selected series of eight patients with malignant catatonia associated with autoimmune encephalitis, seven received intensive care and four required mechanical ventilation. **Conclusions.** The evidence describes critical care use and provides limited inpatient associations. Prospective emergency department cohorts with timed baseline measurements and explicit indications for intubation are needed.

Keywords Neuroleptic malignant syndrome, malignant catatonia, emergency department, intensive care unit, mechanical ventilation, prognosis.

Introduction

Neuroleptic malignant syndrome (NMS) is a rare fatal reaction associated with dopamine receptor antagonists, including antipsychotics and some antiemetics. The clinical picture commonly includes rigidity, elevated temperature, autonomic instability, and an altered level of consciousness, with variation in how these findings emerge over time (1). The international consensus diagnostic criteria recognize recent withdrawal of a dopamine agonist and incorporate creatine kinase (CK), tachycardia, tachypnea, and evaluation for alternative causes. Those criteria were developed for case identification (2). Estimating the subsequent need for intensive care unit (ICU) admission or invasive mechanical ventilation (IMV) requires additional information on baseline severity, the timing of deterioration, and the clinical decisions leading to organ support (1,2).

Malignant catatonia (MC) is a life-threatening form of catatonia characterized by clinically significant autonomic disturbance accompanying psychomotor abnormalities. Catatonia occurs in psychiatric, neurologic, and general medical illness, and its motor manifestations range from stupor, mutism, and posturing to severe excitement (3). Earlier clinical descriptions emphasized the sequence of symptoms, including antecedent psychomotor excitement in some cases of lethal catatonia and early rigidity in NMS (4). Overlapping signs make medication history, the evolution of motor findings, and the evaluation for underlying illness important during emergency department (ED) assessment (3,4).

In the ED, the disposition decision often arises before diagnostic clarification, particularly when agitation or depressed consciousness limits the initial examination (1,5). In either syndrome, impaired airway protection, aspiration, respiratory compromise, and systemic complications are relevant to decisions about monitoring and organ support (3,5,6). The clinical significance of a finding depends on its timing, since respiratory failure present on arrival informs immediate management, while respiratory failure developing later reflects the subsequent course (5,6). The ICU literature on MC also describes patients whose catatonic signs coexist with delirium or coma, complicating the interpretation of findings recorded after escalation (6).

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Much of the published literature concerns diagnostic recognition, complications, or response to treatment (1,3,6). The Cochrane review of benzodiazepines for catatonia in schizophrenia and other serious mental illnesses identified one trial with usable data on changes in catatonic symptoms among 17 participants. Intensive care disposition and use of ventilation were outside the outcomes available from that trial (7). The primary question in this review was whether characteristics available during ED evaluation were associated with subsequent ICU admission or IMV in patients with NMS or MC (2,5,6). A secondary objective was to describe ICU admission and ventilation in hospital studies that documented these outcomes for affected patients.

Methods

We used the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 framework to structure reporting. PubMed was searched on 11 November 2026 for reports first published through 31 May 2026, including articles released online before their print issue. Four searches combined controlled vocabulary and title or abstract terms for NMS, MC, and related terminology with terms for emergency care, intensive care, ventilation, study design, or clinical outcomes. One search used broad catatonia and acute-care terms to identify reports in which the malignant subtype appeared in the full text. Publisher searches and citation checks supplemented the database search. The review was unregistered and used data from published reports.

Original human studies with at least two affected patients were eligible when they reported ICU admission, tracheal intubation, or mechanical ventilation during an episode of NMS or MC. Study authors' diagnostic criteria were accepted and the case definition was extracted, including author-classified NMS associated with dopaminergic medication withdrawal. ED studies were assessed for characteristics documented before a disposition or ventilation decision. Hospital and ICU studies were eligible for descriptive evidence when they documented critical care use or respiratory support during the syndrome. Single-patient reports, secondary reviews, nonmalignant catatonia without extractable MC data, and reports limited to mortality, noninvasive ventilation, ventilation duration, or routine anesthesia were excluded.

Records were de-duplicated by PubMed identifier, with supplementary records checked by title and digital object identifier. Titles and abstracts were assessed for eligibility, and relevant reports were evaluated using accessible full texts or explicit data in published abstracts. Extracted variables included setting, sample size, diagnostic ascertainment, syndrome onset, candidate factors, timing of measurement, outcome definitions, event denominators, and the indication for respiratory support. Overlapping case series were checked by institution, clinical characteristics, and recruitment period, with preference given to the more informative report when independence was unclear.

ICU admission was defined as documented admission or transfer to a medical or surgical ICU. IMV required explicit reporting of ventilation through an artificial airway. Intubation and mechanical ventilation of unspecified mode were recorded as reported. Recruitment, diagnostic and outcome ascertainment, timing, and confounding were assessed in relation to each study design. The synthesis used counts and estimates with their original denominators, distinguishing patients from episodes and recording unreported outcomes as unavailable. No estimates were pooled because ED-based predictor data were absent and hospital studies differed in population, outcome measurement, and analysis.

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Results

Study selection and comparative findings

The four PubMed searches retrieved 1,085 records. Removal of 194 duplicates left 891 unique records for screening. Fifteen original reports entered the synthesis, including 13 identified through the database searches and two through supplementary searches. Twelve described NMS and three described MC, as shown in Tables 1 and 2.

Nakamura et al. identified 1,585 NMS inpatients in Japan, of whom 408 (25.7%) entered the ICU and 193 (12.2%) underwent tracheal intubation (8). Of the 193 patients who underwent intubation, 133 were also admitted to intensive care (8). Among 210 propensity-matched pairs, ICU admission was more frequent with typical than with atypical antipsychotics (31.4% vs 21.0%, P = 0.020) (8). In Australia, Trollor et al. documented ICU admission in 1 of 43 first-generation cases and 13 of 165 second-generation cases (2.3% vs 7.9%, P = 0.309), with treatment details available in 149 of 208 adverse-event reports (9). ICU admission was reported in the characteristics or treatment data of the two studies, and their multivariable analyses addressed mortality (8,9).

Neuroleptic malignant syndrome

In three ED cases reported by Akın Şen et al., fever, impaired consciousness, and elevated CK were present at assessment, with two ICU admissions explicitly documented and one patient intubated on hospital day five (10). Rigidity was absent at presentation in all three patients in that series (10). In a five-patient parkinsonism series, one patient entered the ICU after worsening consciousness and hyperthermia, and another required ventilation in the ED for respiratory failure following withdrawal of dopaminergic medication (11). These reports describe the sequence leading to escalation in individual patients, with neither a contemporaneous comparison group nor a factor-specific estimate (10,11).

Among patients enrolled in ICUs, Özdemir et al. reported IMV in 25 of 42 patients, and Touzani et al. documented mechanical ventilation in 4 of 20 (12,13). At ICU assessment in the Turkish cohort, 39 of 42 patients had altered mental status and 20 of 42 had hyperthermia (12). At Mayo Clinic, mechanical ventilation was reported in 9 of 20 patients who fulfilled diagnostic criteria after review of 332 coded records (14). Three of nine older inpatients received intubation and ventilatory support (15). Two historical series reported ventilatory support in two of five patients referred to an intensive toxicology unit and artificial ventilation in four of seven episodes complicated by acute renal failure and rhabdomyolysis (16,17). A dementia cohort documented ICU care in two of 15 patients, and two patients with concurrent COVID-19 pneumonia required ICU transfer and IMV after deterioration on medical wards (18,19).

Malignant catatonia

Dessens et al. described four ICU patients with MC who received electroconvulsive therapy (ECT) after an inadequate response to intravenous benzodiazepines (20). Park et al. described two patients with MC and aspiration pneumonia, including one intubated and admitted to ICU following cardiac arrest during ECT (21). Kraiter et al. described eight ECT-treated patients who developed MC during admission for anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis, with ICU care in seven and mechanical ventilation in four (22). Three of the eight had catatonic signs at initial presentation (22). Across these reports, recruitment after ICU admission, selection for ECT, and uncertainty about when clinical factors were measured limited inference about risk at ED presentation (20-22).

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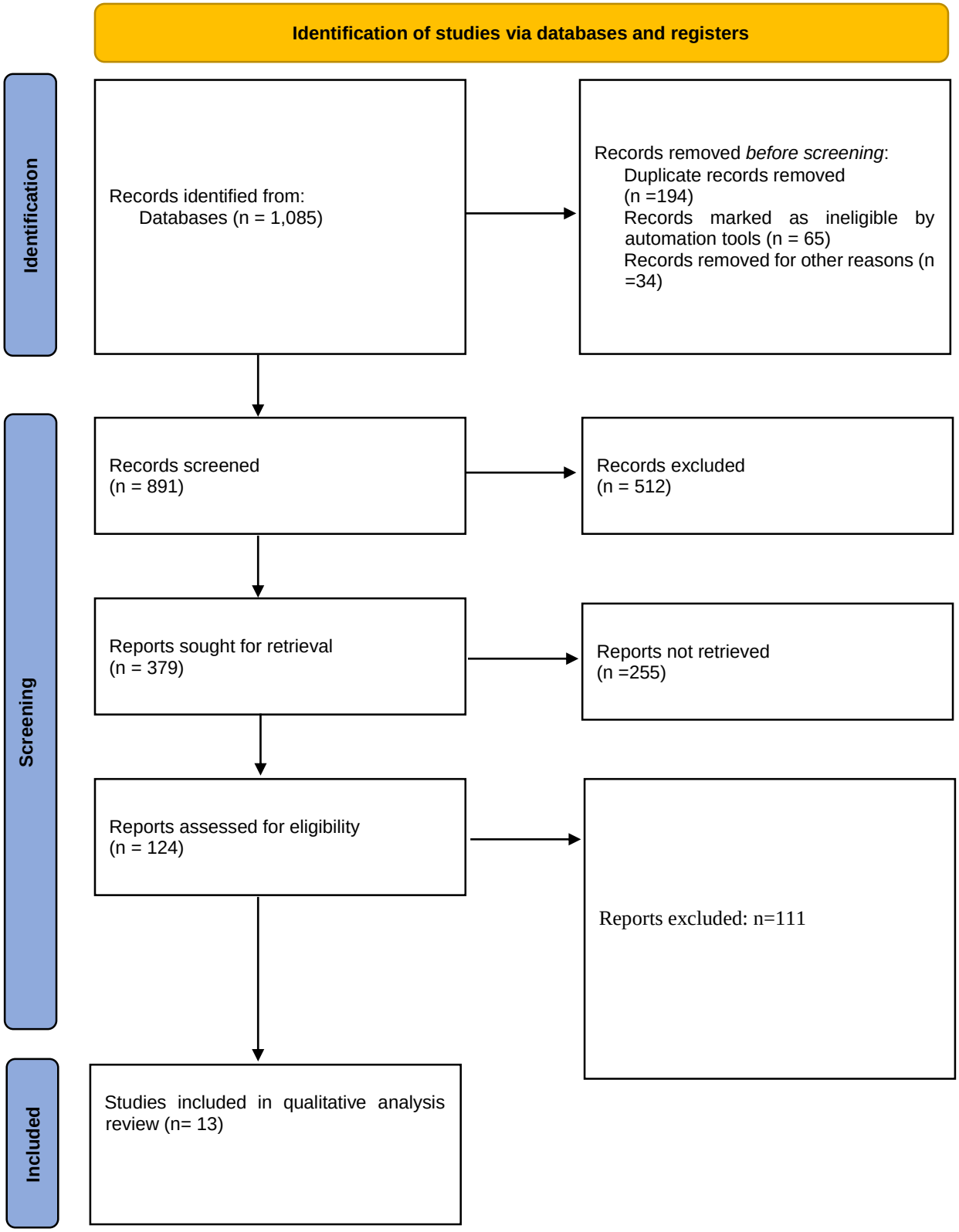


Figure 1: PRISMA flow chart

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Table 1. Original studies included

Study and population	ICU admission and respiratory support	Main limitation for ED prediction
Nakamura et al., Japanese inpatient database, 1,585 patients	ICU admission in 408/1,585 and tracheal intubation in 193/1,585. Matched ICU admission rates were 31.4% with typical and 21.0% with atypical antipsychotics (P = 0.020) (8).	Inpatient prescribing and claims-based ascertainment (8).
Trollor et al., Australian pharmacovigilance database, 208 reports	ICU admission documented in 1/43 first-generation and 13/165 second-generation reports (P = 0.309) (9).	Voluntary reporting and incomplete treatment information (9).
Akın Şen et al., Turkish ED series, 3 patients	Two documented ICU admissions and one intubation after deterioration on hospital day five (10).	Selected cases and incomplete disposition reporting (10).
Paul et al., Indian parkinsonism series, 5 patients	One documented ICU transfer after declining consciousness and one emergency ventilation event for respiratory failure in a different patient (11).	Mixed precipitants and descriptive reporting (11).
Özdemir et al., Turkish adult ICU cohort, 42 patients	IMV in 25/42 (59.5%) (12).	Clinical variables recorded at ICU entry (12).
Touzani et al., Moroccan ICU cohort, 20 patients	Mechanical ventilation in 4/20 (20.0%) (13).	Recruitment restricted to ICU patients (13).
Lopez et al., US hospital system, 20 confirmed cases	Mechanical ventilation in 9/20 (45.0%) (14).	Mixed onset settings and absence of an ED-specific estimate (14).
Pewloungsawat et al., Thai hospital, 9 NMS cases	Intubation and ventilation in 3/9 (33.3%) (15).	Small sample of older inpatients (15).
Chodorowski et al., Polish intensive toxicology unit, 5 patients	Ventilatory support in 2/5 after acute respiratory failure, with mode unspecified (16).	Referral from psychiatric units (16).
Kleinknecht et al., French series, 7 episodes in 6 patients	Artificial ventilation in 4/7 episodes, with mode unspecified (17).	Selection for rhabdomyolysis and acute renal failure (17).
Isik et al., Turkish memory clinic, 15 patients with 19 episodes	ICU care in 2/15 patients (18).	Dementia cohort with mixed medication-related precipitants (18).
Costa et al., Portuguese hospital series, 2 patients	Both required ICU transfer and IMV after ward deterioration (19).	Concurrent COVID-19 pneumonia and ward-onset NMS (19).

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Table 2. Studies reporting intensive care or respiratory support in malignant catatonia

Study and population	ICU admission and respiratory support	Main limitation for ED prediction
Dessens et al., Dutch ICU series, 4 patients	Four ICU patients received ECT after an unsuccessful benzodiazepine trial (20).	ICU recruitment prevents estimation of admission risk from the source population (20).
Park et al., US hospital series, 2 patients	One documented ICU admission and emergency intubation after cardiac arrest, with critical care consultation documented for the second patient (21).	Escalation occurred during the hospital course (21).
Kraiter et al., US ECT-treated anti-NMDAR encephalitis series, 8 patients	ICU care in 7/8, mechanical ventilation in 4/8, and tracheostomy in 3/8 (22).	ECT selection and overlapping indications for organ support (22).

Discussion

The Japanese comparison suggests that antipsychotic class warrants investigation, given the difference in ICU admission after propensity matching (8). The Australian estimates ran in the opposite direction and were imprecise, with incomplete care information in both medication groups (9). Differences in ascertainment, prescribing data, and the measurement of illness severity limit the use of either estimate for ED disposition (8,9).

In the ED literature, Şahin et al. analyzed 18 presentations with NMS and compared age, blood pressure, and laboratory results between survivors and nonsurvivors, using mortality as the outcome (23). Luccarelli et al. estimated 51,671 US ED visits coded for catatonia in 2019-2021, with an 82.6% hospital admission rate for catatonia overall and no estimate specific to ICU admission in MC (24). These studies characterize serious illness in ED populations and illustrate why the disposition endpoint and malignant subtype require explicit recording (23,24).

Respiratory findings deserve attention in NMS because they appear across administrative, ICU, and case-level data (12,14,19,25). In the US Nationwide Inpatient Sample, Modi et al. reported acute respiratory failure in 16.1% of 1,346 NMS hospitalizations and identified it as a predictor of death (25). Guinart et al. likewise found an association between respiratory problems and mortality in a pooled analysis of 683 published cases (26). In the Portuguese series, pneumonia and persistent coma complicated ventilator use, illustrating the value of recording pulmonary failure and airway protection as distinct indications (19). A clinical sign documented at intubation has a different prognostic interpretation from the same sign documented during the initial ED evaluation (12,19,25,26).

For MC, Cronemeyer et al. assembled 117 published and institutional cases and described greater intensive care use in the severe group (27). Among 105 cases with ICU data, the linked dissertation reported ICU treatment in 46.3% of severe cases and 23.4% of moderate cases (P = 0.02), using a severity definition requiring at least two of three findings: rigidity, temperature of at least 39 °C, and impaired consciousness (27,28). This comparison

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classified severity retrospectively across recorded illness episodes, leaving the timing of the qualifying signs relative to the ICU decision uncertain (27,28). In anti-NMDAR encephalitis, concurrent seizures, dysautonomia, and the underlying neurologic disorder complicate attribution of ventilation to MC alone (6,22).

A multicenter ED cohort would enroll consecutive patients at first assessment and record temperature, consciousness, oxygen requirement, blood pressure, and CK before sedation or escalation where feasible (2,3,29). Follow-up would document admission timing, the indication for intubation, and whether ventilation began in the ED or after transfer (8,19,29). Patients who receive ventilation during a procedure or after a later complication represent different clinical trajectories, so a documented indication is necessary for interpreting the outcome (19,21,29).

Conclusion

The available literature documents substantial critical care uses in selected populations with neuroleptic malignant syndrome and malignant catatonia. Inpatient comparisons of antipsychotic class produced inconsistent findings for intensive care admission, and emergency department reports described deterioration without estimating the independent contribution of presenting characteristics. Thresholds for disposition or invasive ventilation based on the initial assessment remain undefined. A multicenter emergency department cohort with standardized diagnostic adjudication, measurements recorded before treatment escalation, and clearly timed intensive care and ventilation outcomes would permit estimation of absolute risks and assessment of whether the same predictors apply reliably to both syndromes.

Abbreviations

CK, creatine kinase. ECT, electroconvulsive therapy. ED, emergency department. ICU, intensive care unit. IMV, invasive mechanical ventilation. MC, malignant catatonia. NMDAR, N-methyl-D-aspartate receptor. NMS, neuroleptic malignant syndrome. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

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