



## Major publications in the critical care pharmacotherapy literature: 2025

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### ABSTRACT

**Objectives:** To summarize and provide clinical insights on the most impactful publications related to critical care pharmacotherapy in 2025.

**Methods:** A systematic search of PubMed/Medical Literature Analysis and Retrieval System Online (MEDLINE) was conducted between January 1, 2025 and October 5, 2025. Inclusion criteria consisted of randomized controlled trials with prospective study designs evaluating a critically ill adult patient population receiving pharmacotherapeutic interventions and reporting clinical endpoints. A multi-disciplinary and geographically diverse group of critical care clinicians was assembled and an a-priori defined three-round modified Delphi process was performed, with a focus on the publications determined to be the most impactful or novel.

**Results:** The systematic search yielded a total of 1609 articles for review and 1566 were excluded, leaving 43 articles to be included in the modified Delphi process. In each round, articles were scored based on their overall contribution to the literature and novelty with articles achieving a score at or above the median progressing to the next modified Delphi round. The six included articles are summarized. Article topics include alternative sedation options in mechanically ventilated patients, thrombolytic usage in acute ischemic strokes, management of coagulopathic bleeding following cardiac surgery, and use of corticosteroids in severe community-acquired pneumonia.

**Conclusions:** This concise review identified, summarized, and offered insights on the most relevant critical care pharmacotherapy publications in the year 2025.

### 1. Introduction

The rapid expansion of medical literature creates an increasing challenge for clinicians to remain current with evidence-based practices. [1,2] To manage this, many clinicians employ strategies such as utilizing

journal surveillance, membership in professional organizations, engagement with colleagues on social media, participating in continuing education, and reviewing literature summaries. [3] High-quality literature analysis and summation conducted by seasoned clinicians is crucial for helping critical care practitioners stay abreast of the

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literature. [4–16] Therefore, this review aims to assess and summarize the most influential publications related to the pharmacotherapeutic management of critically ill patients in 2025 to assist practitioners in staying informed.

## 2. Methods

This was a systematic search of PubMed/Medical Literature Analysis and Retrieval System Online (MEDLINE) conducted from January 1, 2025 to October 5, 2025 to identify articles relevant to critical care pharmacotherapy. This timeframe was selected to ensure timely review of the 2025 literature allowing for an early 2026 release. Following completion of the Delphi surveys, a post-hoc search for eligible articles was performed from October 6, 2025 to December 31, 2025 to ensure no articles were missed during the review process. The search criteria utilized mirrored previous reviews (Appendix A). [14–16] Articles were then reviewed by two independent reviewers (E.A.H. and A.M.E.) to assess for eligibility based on pre-specified parameters, including: 1. Randomized controlled trial (RCT) or prospective study design, 2. A patient population consisting of critically ill adults, 3. Assessment of a pharmacotherapeutic intervention 4. Evaluation of clinical endpoints. Articles that met these criteria were then included in a full-text review conducted to exclude remaining articles not meeting the aforementioned inclusion criteria. Eligible articles were then grouped into clinical categories and included in a modified Delphi survey (Appendix B).

An a priori defined three-round modified Delphi process was performed, consisting of a survey containing article titles and links to full-text files sent to a multiprofessional panel of reviewers ( $n = 14$ ). During rounds 1 and 2, reviewers were asked to score each article independently on a scale of 1 (lowest) to 5 (highest) based on the article's overall contribution to scientific knowledge and novelty to critical care pharmacotherapy literature. A response rate of  $>70\%$ , or  $\geq 10$  survey participants, was required to progress to the next round of surveying. For rounds 1 and 2, a mean score was calculated for each article from the submitted reviewer scores and any article scoring above the median progressed to subsequent rounds. The final Delphi round ranked articles from most impactful to least impactful. The selected articles were then

summarized, with an emphasis on highlighting the impact on critical care practice.

## 3. Results

The systematic search yielded 1609 articles for review. The title and abstract screening excluded 1558 studies and an additional 8 were excluded following full text review. Forty-three articles were included in the modified Delphi process and each Delphi round had a 100% response rate (Fig. 1). Of the 43 articles included in round 1, 24 met or exceeded the median of round 1 and progressed to round 2 (Appendix C). Thirteen articles from round 2 met or exceeded the median score and were included in round 3 (Appendix D). After 3 Delphi rounds, the 6 articles with the highest median ranking were included and are presented in order of the final ranking in Delphi round 3 (Appendix E). Brief summaries of additional potentially impactful articles included in round 3 are presented in Appendix F. The top 6 ranked articles resulting from the modified Delphi process are summarized in the body of this review.

The post-hoc search conducted from October 6, 2025 to December 31, 2025 yielded 449 articles. Of these articles, 4 met the inclusion criteria that would have enabled them to progress to the Delphi survey rounds. These 4 articles were sent to the multidisciplinary team for an approval vote, alongside an open call for additional articles to be included, and were approved by the review panel. The additional 4 articles were summarized. (Appendices G, H).

## 4. Discussion

### 4.1. Propranolol as an anxiolytic to reduce the use of sedatives for critically ill adults receiving mechanical ventilation (PROACTIVE): an open-label randomized controlled trial

The Propranolol as an Anxiolytic to Reduce the Use of Sedatives for Critically Ill Adults Receiving Mechanical Ventilation (PROACTIVE) trial was an open-label, multicenter RCT evaluating whether propranolol decreases intravenous sedative requirements in mechanically ventilated adults. Eligible patients were expected to require mechanical

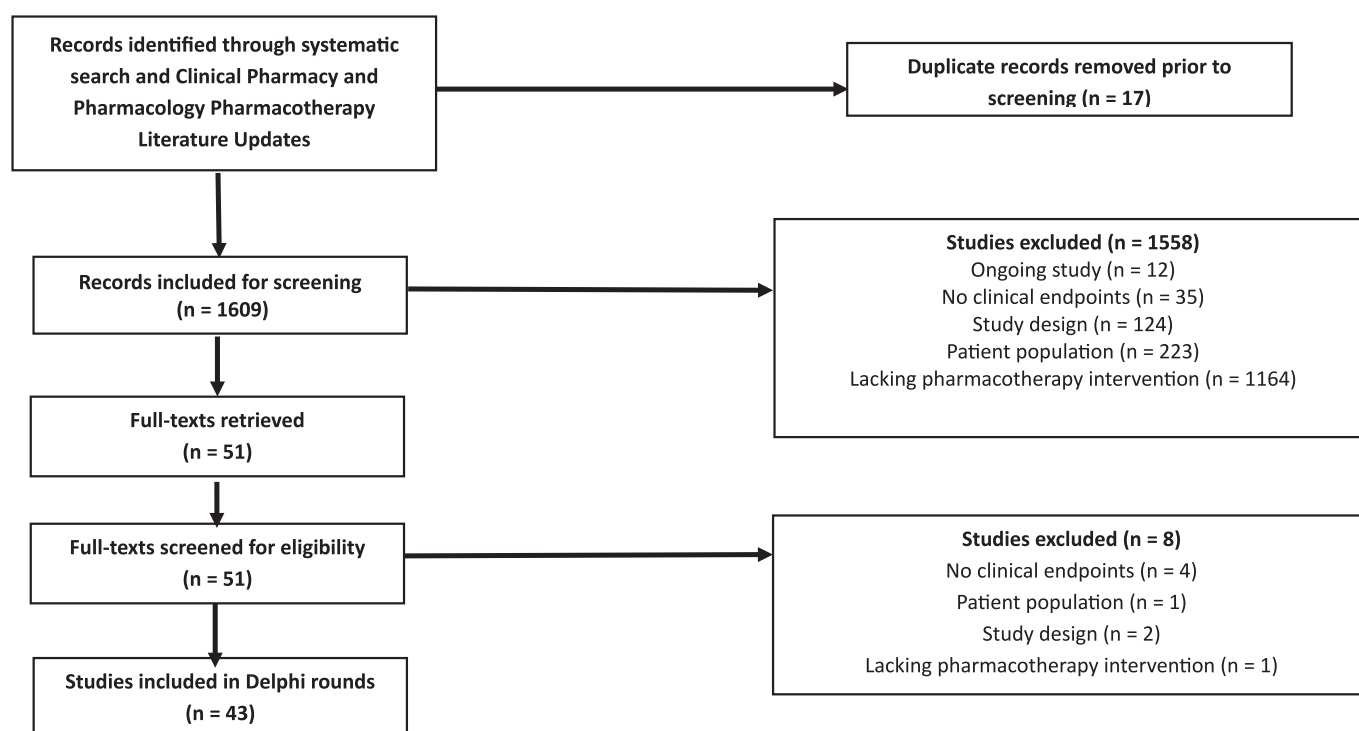


Fig. 1. Flow diagram of article screening.

ventilation for at least 48 h and had already received minimum doses of propofol ( $\geq 25 \mu\text{g/kg/min}$ ) or midazolam ( $\geq 3 \text{ mg/h}$ ) for at least 24 h. Exclusion criteria included contraindications to beta blockers, high-dose vasopressor support, and need for neuromuscular blockade at enrollment. Patients were randomized 1:1 to receive enteral propranolol 20 mg every 6 h, titrated daily by 10 mg increments to a maximum of 60 mg every 6 h, or standard open-label sedation alone. Seventy-one patients were included in the intention-to-treat population, with majority of the group being male (69%) and an average age of 54 years. The average daily dose of propranolol was 90 mg/day with a mean (SD) treatment duration of 10 days (6.86). Patients receiving propranolol had significantly lower sedation dosages by day 3 when compared to control (53.9% vs 33.9% reduction,  $p = 0.048$ ). More patients in the propranolol group had Richmond Agitation-Sedation Scale (RASS) assessments within target range (48% vs 35%,  $p < 0.0001$ ). No differences were observed in weaning to minimal sedative dose, opioid requirements, delirium incidence, ventilator-free days, or mortality. A similar rate of adverse reactions occurred in both groups, with more episodes of bradycardia in the control group (3 vs 1.5,  $p = 0.03$ ). [17]

Agitation and delirium are highly prevalent in critically ill patients and frequently prompt escalation of sedatives, potentially leading to negative downstream effects on duration of ventilation, delirium risk, and intensive care unit (ICU) stay. Propranolol serves as an inexpensive adjunct to traditional IV sedatives through mitigation of adrenergic hyperactivation and may thereby decrease doses of conventional sedation. Prior to PROACTIVE, supporting evidence was limited to small retrospective cohorts in mixed medical-surgical ICUs demonstrating reductions in fentanyl, midazolam, propofol, and haloperidol. [18] In the severe traumatic brain injury population, propranolol use has been associated with decreased mortality and improved functional outcomes at 6 months. [19] Notably, the Society of Critical Care Medicine (SCCM) guidelines for pain, anxiety, and delirium do not currently address beta blockers as anxiolytic adjuncts. [20]

PROACTIVE provides an important prospective signal that modulation of sympathetic overactivity can meaningfully influence sedation trajectories. Strengths of the PROACTIVE trial include well-balanced groups comprised of patients at a moderate risk for mortality. However, several methodological considerations should be noted. The open-label design likely influenced sedation titration behaviors. In addition, the PROACTIVE trial did not elucidate target RASS for patients, which is central to interpreting sedative dose reductions. [21] Furthermore, while safety findings are reassuring, the study was underpowered to detect uncommon but clinically important beta blocker related adverse events. Nonetheless, the trial demonstrates operational feasibility and suggests that propranolol may be a reasonable, low-cost adjunct in select mechanically ventilated patients with agitation or adrenergic hyperarousal despite guideline-directed analgesia and sedation. Larger blinded trials with protocolized sedation targets are needed before propranolol is routinely incorporated into ICU analgesedation bundles.

#### 4.2. Tenecteplase thrombolysis for stroke up to 24 h after onset with perfusion imaging selection: the CHABLIS-T II randomized clinical trial

Chinese Acute Tissue-Based Imaging Selection for Lysis In Stroke-Tenecteplase II (CHABLIS-T II) was a multicenter, block-randomized, open-label, blinded-end point, phase 2b trial that randomized acute ischemic stroke (AIS) patients who presented within 4.5–24 h after last known normal (LKN) to 0.25 mg/kg tenecteplase (TNK) ( $n = 111$ ) or best medical treatment (BMT) ( $n = 113$ , 23% received alteplase). [22] Adult patients with a pre-stroke modified Rankin Scale (mRS) of 0–2, a clinically significant neurological deficit, an anterior large or medium vessel occlusion, and a favorable penumbral mismatch profile were eligible for enrollment. The average patient was 64 years old with large artery atherosclerosis (LAA) related stroke (76.4%) and had a National Institutes of Health Stroke Scale score (NIHSS) of 9. Based on the provider's discretion, 54.9% underwent preplanned endovascular treatment

(EVT). The primary outcome was major reperfusion without symptomatic intracranial hemorrhage (sICH) within 24–48 h post-randomization, with major reperfusion defined as restoration of blood flow of  $>50\%$  of the involved ischemic territory. The primary outcome was achieved in 33.3% in the TNK group vs 10.8% of patients who were randomized to BMT (adjusted relative risk [aRR], 3.0; 95% CI, 1.6–5.7;  $p = 0.001$ ). Recanalization was achieved in 35.8% (TNK) vs 14.3% (BMT) (aRR, 2.5; 95% CI, 1.4–4.4;  $p = 0.002$ ). There was no significant difference in secondary or safety outcomes. The preplanned subgroup analysis found TNK patients with preplanned EVT had a trend towards larger infarct growth and worse functional outcomes.

Intravenous thrombolysis and EVT remain the most effective treatment for AIS, therefore extending the time window has been a primary focus for recent studies. [22] Current guidelines include TNK as an alternative to alteplase in patients eligible for mechanical thrombectomy and given TNK's advantages over alteplase, including single-bolus administration, longer half-life, and greater fibrin specificity, it is an attractive option for clinicians treating AIS. [23,24] Previous studies demonstrated noninferiority of TNK to alteplase for AIS treated within 4.5 h and TRACE-III found less disability and similar survival with TNK in patients without access to EVT, while the TIMELESS study found no significant difference in outcomes in patients with access to EVT. [25–27]

CHABLIS-T II is the first study to find significantly higher reperfusion with TNK in extended-window stroke with access to EVT, however no improvement in functional outcomes was found and the trend towards worse functional outcomes raises concerns for TNK's role in patients with access to EVT. Limited by the sample size, the study may have been underpowered to detect a difference with the secondary outcomes. The utilization of delay time  $> 3 \text{ s}$  for defining hypoperfusion lesion, predominance in LAA-related stroke, and having only 54.9% of patients undergo preplanned EVT limit the generalizability, however, the mismatch volume threshold allowed for inclusion of a larger patient population. It remains uncertain if TNK improves functional outcomes in patients with access to EVT, and in extended-window AIS patients, TNK might be best utilized in patients awaiting transfer to comprehensive stroke centers for EVT. Larger trials focused on both patient groups with and without immediate access to EVT are warranted.

#### 4.3. Alteplase for posterior circulation ischemic stroke at 4.5 to 24 h

The Extending the Time Window for Thrombolysis in Posterior Circulation Stroke without Early CT Signs (EXPECTS) trial was a Chinese multicenter, open-label, randomized trial that evaluated extended administration of alteplase (4.5–24 h from LKN) to standard of care in patients with a posterior circulation stroke (PCS). [28] Adult patients ( $n = 234$ ) were included if they were diagnosed with a PCS confirmed either with imaging or clinical signs without alternative cause and were 4.5 to 24 h from LKN with posterior circulation Acute Stroke Prognosis Early CT score (PC-ASPECTS)  $\geq 7$ , NIHSS  $\geq 1$ , and pre-stroke mRS of 0–1. Key exclusion criteria were planned EVT or contraindication to alteplase other than time from LKN. The average patient was 64 years old and majority (56.5%) were on dual antiplatelet therapy (DAPT) at baseline with a NIHSS of 3 and imaging confirmed PCS in 61.5% of those enrolled. Functional independence (defined as mRS 0–2) at 90 days was observed more in the alteplase group (89.6% vs 72.6%; risk ratio [RR], 1.16; 95% CI, 1.03–1.30). All-cause mortality at 90 days and major secondary outcomes were similar between groups apart from functional improvement based on ordinal distribution of mRS scores (OR 2.12; 95% CI, 1.31–3.43). Rates of both sICH and any ICH were similar between the two groups.

PCS account for 20–25% of ischemic strokes and historically was thought to have more favorable outcomes compared to strokes of the anterior circulation. [29] Current guidelines for AIS recommend alteplase administration for all eligible patients and list no specific recommendations pertaining to infarcts of the posterior circulation. Extended

thrombolysis with alteplase (4.5–24 h from LKN) is recommended only when features of recent infarct are identified using perfusion imaging. [23] More recent trials have evaluated thrombolysis with TNK with similar efficacy and safety, primarily in patients with anterior circulation infarcts. [26,27]

The EXPECTS trial offers the first evaluation of extended-window thrombolysis exclusively in patients with PCS, with findings similar to previous studies that largely included patients with strokes of the anterior circulation. A recent meta-analysis found patients with PCS had lower median NIHSS scores (7 vs 13) compared to anterior circulation strokes, despite having similar clinical outcomes and lower risk of intracranial bleeding. [30] While guidelines do not recommend alteplase administration in patients presenting with mild, nondisabling stroke (NIHSS 0–5), the lack of grading of symptoms in the NIHSS that are more prominent in PCS may lead to underestimation of stroke severity. [23] The results of EXPECTS highlight the importance of identifying the unique characteristics of PCS strokes, and the potential benefit of thrombolysis outside of the standard windows validated primarily in patients with strokes in the anterior circulation. Eligibility for thrombectomy and stroke severity should be evaluated when applying these findings to clinical practice.

#### 4.4. Prothrombin complex concentrate vs frozen plasma for coagulopathic bleeding in cardiac surgery: the FARES-II multicenter randomized clinical trial

The Factor Replacement in Surgery (FARES-II) trial, based on the FARES pilot trial, was a multicenter, non-blinded, randomized, non-inferiority trial comparing 4-factor prothrombin complex concentrate (PCC) (1500 IU if  $\leq 60$  kg, 2000 IU if  $> 60$  kg;  $n = 265$ ) with fresh frozen plasma (FFP) (3 units if  $\leq 60$  kg, 4 units if  $> 60$  kg;  $n = 263$ ) in adult patients with bleeding after cardiac surgery with cardiopulmonary bypass (CPB). [31,32] Key exclusion criteria included heart transplant, insertion or removal of ventricular assist devices, repair of a thoracoabdominal aneurysm, or any concomitant noncardiac surgery. The average patient was 65 years old and majority were male (73.5%). The primary outcome was hemostatic efficacy within 4 h, defined as no additional hemostatic intervention required from 60 min to 24 h after first investigational medicinal product dose. This was achieved in 77.9% in the PCC group and 60.4% in the FFP group, corresponding to a hemostatic response failure of 17.6% (95% CI, 8.7%–26.4%) lower in the PCC group (RR, 0.56; 95% CI, 0.41–0.75,  $p < 0.001$ ). Key secondary outcomes showed PCC significantly reduced red blood cell transfusions in the 24 h post dose (45.5% vs 63.8%; RR, 0.71; 95% CI, 0.60–0.85,  $p < 0.001$ ) and the rate of severe or massive bleeding was significantly lower in the PCC group (14.1% vs 27.5%; RR, 0.51; 95% CI, 0.34–0.76,  $p = 0.001$ ). While thromboembolic events, intubation duration, and ICU and hospital length of stay were similar, serious adverse events (36.2% vs 47.3%; RR, 0.76; 95% CI, 0.61–0.96,  $p = 0.02$ ) and acute kidney injury (AKI) incidence (10.3% vs 18.8%; RR, 0.55; 95% CI, 0.34–0.89,  $p = 0.02$ ) were significantly higher in the FFP group.

Excessive bleeding surrounding cardiac surgery is common, occurring in 15% of cases, and is associated with increased morbidity, mortality, and cost. [33–35] To date, FFP has been the traditional therapy for managing these events but requires large volumes and carries safety risks including allergic transfusion reactions and volume overload. [36] Prior studies suggested that PCC provides faster factor repletion with less volume, but high-quality randomized data are limited and earlier studies were smaller in size, involved heterogeneous dosing, and raised concerns about thrombotic risk. [31,37] This trial differs by utilizing standardized dosing and prospective thrombotic adjudication. Current guidelines recommend PCC as a reasonable alternative to FFP for refractory post-CPB bleeding, but stop short of a strong first-line endorsement due to previously limited randomized evidence. [38]

FARES-II adds to the body of literature surrounding correction of post-cardiac surgery bleeding, specifically PCC having greater efficacy

than FFP for bleeding, with no clear harm signal. Its strengths include randomized multicenter design, protocolized dosing, and well-defined hemostatic endpoints. It was limited by the open-label design and potential for transfusion practice bias. Additionally, short follow-up may have underestimated late thromboembolic events. Generalizability is strongest for typical post-CPB bleeding, but weaker for those with recent thrombotic events, and other surgical populations. These results support PCC as a potential first-line option for factor replacement in post-CPB bleeding, particularly in patients at risk for volume overload, right heart failure, or pulmonary edema. From a stewardship standpoint, PCC may reduce FFP utilization, transfusion complications, and ICU resource use.

#### 4.5. Dexmedetomidine- or clonidine-based sedation compared with propofol in critically ill patients: the A2B randomized clinical trial

The Dexmedetomidine- or Clonidine-Based Sedation Compared with Propofol in Critically Ill Patients (A2B) trial was a randomized, multicenter, pragmatic, open-label trial comparing dexmedetomidine-based sedation (DEX group,  $n = 457$ ) and clonidine-based sedation (CLON group,  $n = 476$ ) vs. propofol-based sedation (PROP group,  $n = 471$ ) in mechanically ventilated adults. [39] Eligible patients had to be enrolled within 48 h of intubation and expected to receive mechanical ventilation for at least 24 h after randomization. Key exclusion criteria were acute brain injury, neuromuscular paralysis, severe bradycardia, and expected death within 24 h. The average patient was a 59-year-old male (64.9%) with an average APACHE II score of 20.3. Weight-based intravenous infusions were initiated within 2 h of randomization and titrated to a target RASS of  $-2$  to  $+1$ , unless deeper sedation was requested per clinician discretion. Propofol was permitted in the DEX and CLON groups if the maximum dose was reached (1.4  $\mu\text{g/kg/h}$  and 2  $\mu\text{g/kg/h}$ , respectively), or dose-limiting adverse effects occurred, in order to reach targeted RASS goals, which occurred over 75% of the time. There was no difference in the primary outcome of time from randomization to successful extubation between DEX 136 h (95% CI, 117–150), CLON 146 h (95% CI, 124–168), and PROP 162 h (95% CI, 136–170). The hazard ratios comparing DEX vs. PROP groups (Hazard ratio [HR], 1.99; 95% CI, 0.96–1.25;  $p = 0.2$ ) and CLON vs. PROP groups (HR, 1.05; 95% CI, 0.95–1.17;  $p = 0.34$ ) further indicate no significant differences. Compared to the PROP group, higher rates of agitation were observed in the DEX (RR, 1.54; 95% CI, 1.21–1.97) and CLON (RR, 1.55; 95% CI, 1.22–1.97) groups. Severe bradycardia occurred more frequently in the DEX (RR, 1.62; 95% CI, 1.36–1.93) and CLON (RR, 1.58; 95% CI, 1.33–1.88) groups compared to the PROP group. There were no significant differences in mortality, ICU length of stay, or rates of delirium or coma.

Optimizing sedation in mechanically ventilated patients is central to minimizing delirium, prolonged ventilation time, and downstream morbidity. This study sought to determine if  $\alpha_2$ -agonist-based sedation offers clinically meaningful advantages over propofol in ventilated patients. Earlier trials demonstrated that dexmedetomidine reduced delirium and mechanical ventilator duration compared with benzodiazepines, which influenced guideline recommendations. [40,41] However, studies directly comparing dexmedetomidine with propofol showed mixed results, with no consistent improvement in mechanical ventilation duration or mortality, and higher rates of bradycardia and hypotension. [42,43] Evidence for clonidine is limited and largely observational. Current guidelines recommend either propofol or dexmedetomidine over benzodiazepines, while suggesting dexmedetomidine when light sedation or delirium reduction are priorities. [20,44]

The A2B trial clarifies that routine substitution of propofol with  $\alpha_2$ -agonists does not meaningfully shorten the duration of mechanical ventilation or improve survival in a general ICU population. Major strengths of the study include its large sample size and multicenter, pragmatic design. The open-label conduct, heterogeneity within the DEX and CLON groups, and frequent use of rescue propofol may blunt



detectable differences. Generalizability is strongest for mixed medical–surgical ICUs targeting light sedation and limited for deeply sedated patients. These results align with prior studies and guidelines emphasizing that sedation choice should be individualized, considering patient sedation depth goals, delirium risk, hemodynamic tolerance, and adverse effect profiles. Dexmedetomidine may be reserved for selected patients prioritizing light sedation or delirium mitigation, with careful cardiovascular monitoring.

#### 4.6. Effect of hydrocortisone on mortality in patients with severe community-acquired pneumonia: the REMAP-CAP corticosteroid domain randomized clinical trial

The Effect of Hydrocortisone on Mortality in Patients with Severe Community-Acquired Pneumonia Trial (REMAP-CAP) is a randomized, embedded, multi-factorial, adaptive platform trial evaluating several treatments for patients with community-acquired pneumonia (CAP). [45] This study reports the results of the corticosteroid domain for non-COVID pneumonia. Adult patients admitted to an ICU for respiratory or cardiovascular support within 48 h of hospital presentation for CAP were eligible for enrollment. Patients ( $n = 658$ ) were randomized to receive either fixed-duration hydrocortisone (HCT) at a dose of 50 mg every 6 h for 7 days or until hospital discharge ( $n = 536$ ) or no corticosteroid ( $n = 122$ ). The primary endpoint was 90-day all-cause mortality. At baseline, the average patient was 60.5 years old with an APACHE II score of 18. The majority of patients required either invasive mechanical ventilation (38.7%) or high-flow nasal cannula (35.8%). By day 90, 15% of patients randomized to HCT had died compared to 9.8% of control patients (adjusted odds ratio [aOR] 1.56, 95% CI 0.80–3.31). There was a 10% probability of superiority of HCT, 90% probability of harm, and 3.4% probability of a  $> 20\%$  reduction in the odds of death.

The potent anti-inflammatory and immunomodulatory effects of glucocorticoids make them an attractive therapeutic option for pneumonia, a state in which pulmonary and systemic inflammation can occur, resulting in impaired gas exchange, organ failure, and an increased risk of death. Corticosteroid utilization in CAP has been evaluated in several clinical trials with conflicting results on mortality. [46–51] The CAPE COD trial demonstrated a reduction in 28-day mortality in patients randomized to receive hydrocortisone compared to placebo for severe CAP (absolute difference,  $-5.6\%$ , 95% CI,  $-9.6$  to  $-1.7$ ). [50] These findings were corroborated in a meta-analysis showing a 32% reduction in the risk of hospital mortality with the utilization of corticosteroids for severe CAP (RR, 0.62, 95% CI, 0.45–0.85) leading to the SCMM and European Society of Intensive Care Medicine Guideline recommendation in favor of corticosteroid therapy in this population. [52]

The results of the corticosteroid domain of the REMAP-CAP platform trial are in contrast to most previously published literature, meta-analyses, and guideline recommendations. This discrepancy could be multifaceted. The REMAP-CAP trial was designed to trigger futility if a  $< 5\%$  probability of a  $> 20\%$  reduction in mortality was detected, thus, this trial was not designed to rule out smaller benefits of therapy. Moreover, the CAPE COD trial enrolled eligible patients within 24 h of ICU admission, whereas the REMAP-CAP study had a broader window of inclusion via platform enrollment, and indeed the CAPE COD trial detected a 5.6% absolute reduction in mortality in patients randomized to corticosteroids. [45,50] Consequently, smaller but clinically meaningful effects were not adequately assessed. Additionally, a transcription error during data collection resulted in several participants having group allocation mislabeling. This temporarily biased the response-adaptive randomization algorithm towards greater allocation to HCT contributing to a markedly imbalanced randomization. Although the subsequent adaptive analyses used correctly labeled data, the imbalanced randomization likely impacted the study's ability to detect modest effects. Overall, the corticosteroid domain of the REMAP-CAP platform adds to the literature regarding this clinical question. It reveals that

fixed-dose HCT is unlikely to provide a  $> 20\%$  reduction in mortality, but cannot exclude that smaller, clinically meaningful improvements in mortality may still be seen.

## 5. Conclusion

This review highlights and provides insight into the most impactful studies relevant to critical care pharmacotherapy published in 2025. The selected studies build upon the existing literature and contribute novel perspectives for clinicians to consider when managing critically ill patients.

## CRedit authorship contribution statement

**Emily A. Highsmith:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Validation, Visualization, Writing – original draft, Writing – review & editing. **Daniel Arellano:** Investigation, Visualization, Writing – review & editing. **Kathryn Bash:** Investigation, Visualization, Writing – review & editing. **Brady John Bielewicz:** Investigation, Visualization, Writing – review & editing. **Lauren M. Dehne:** Investigation, Visualization, Writing – original draft, Writing – review & editing. **Bradley J. Erich:** Investigation, Visualization, Writing – original draft, Writing – review & editing. **Kalle Fjeld:** Investigation, Visualization, Writing – review & editing. **Ivan Garcia:** Investigation, Visualization, Writing – review & editing. **Colman Hatton:** Investigation, Visualization, Writing – review & editing. **Matthew Li:** Investigation, Visualization, Writing – original draft, Writing – review & editing. **Kendall Mores:** Investigation, Visualization, Writing – original draft, Writing – review & editing. **Gretchen L. Sacha:** Investigation, Visualization, Writing – original draft, Writing – review & editing. **Sara Saldana:** Investigation, Visualization, Writing – original draft, Writing – review & editing. **Alyson M. Esteves:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Resources, Supervision, Validation, Visualization, Writing – original draft, Writing – review & editing.

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## Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.jcrc.2026.155508>.

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