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Systematic Review

Systemic Corticosteroids in Hospitalized Patients with COVID-19: A Systematic Review of Randomized Controlled Trials

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ABSTRACT

Background: Severe COVID-19 involves a dysregulated inflammatory response, and systemic corticosteroids were evaluated early in the pandemic. Randomized controlled trials (RCTs) have reported different results depending on the trial design and patient population. This systematic review summarizes their efficacy and safety.

Methods: RCTs of systemic corticosteroids in hospitalized adults with COVID-19, reporting mortality or organ-support outcomes, were eligible. Data were extracted and synthesized without meta-analysis following the SWiM reporting guideline, with qualitative risk-of-bias appraisal using RoB 2 domains.

Findings: Three RCTs (RECOVERY, CoDEX, REMAP-CAP) were included. In RECOVERY (6,425 patients), 28-day mortality was 22.9% with dexamethasone versus 25.7% with usual care (RR 0.83, 95% CI 0.75–0.93), with benefit in ventilated patients (RR 0.64, 95% CI 0.51–0.81) and in patients receiving oxygen (RR 0.82, 95% CI 0.72–0.94), but not in patients without respiratory support (RR 1.19, 95% CI 0.92–1.55). CoDEX (299 patients) reported more ventilator-free days (6.6 vs 4.0), and REMAP-CAP (403 patients) was stopped early without a clear difference in organ support-free days.

Conclusion: Dexamethasone reduced 28-day mortality in patients receiving oxygen or ventilation, and benefit was not shown in patients without respiratory support. The two smaller trials were underpowered for mortality.

INTRODUCTION

Severe COVID-19 is characterized by hypoxemic respiratory failure associated with a dysregulated inflammatory response. Because corticosteroids suppress inflammation, they were evaluated early in the pandemic as a treatment for hospitalized patients.

Three randomized controlled trials (RCTs) published in 2020 and 2021 addressed this question: the RECOVERY trial, a large open-label platform trial of dexamethasone [1]; the CoDEX trial, which tested dexamethasone in patients with COVID-19 and moderate to severe acute respiratory distress syndrome [2]; and the REMAP-CAP corticosteroid domain, which tested hydrocortisone in critically ill patients [3].

The trials differ in setting, dose, drug, severity of illness, and primary outcome, and two of them were stopped early. A structured summary can help clarify which patients benefit and which findings are uncertain.

This systematic review aims to summarize the efficacy and safety of systemic corticosteroids in hospitalized adults with COVID-19 and to describe how the effect varies by level of respiratory support.

METHODS

1. Design

This systematic review of RCTs was planned using the PICO framework. No protocol was prospectively registered. Results were synthesized without meta-analysis, following the principles of the SWiM reporting guideline [4].

2. Eligibility Criteria

Eligibility criteria are summarized in Table 1. RCTs published in peer-reviewed journals were eligible. Trials were grouped by severity of illness: mixed hospitalized patients stratified by respiratory support (RECOVERY) and critically ill patients (CoDEX and REMAP-CAP).

Table 1. Eligibility Criteria (PICO)

Element	Criterion
Population	Hospitalized adults with COVID-19
Intervention	Systemic corticosteroids (dexamethasone or hydrocortisone)
Comparator	Usual care or placebo/no corticosteroid
Outcomes	28-day mortality; ventilator-free or organ support-free days; adverse events
Design	RCT in a peer-reviewed journal

3. Information Sources and Search

Peer-reviewed literature indexed in PubMed was searched in November 2026 through a web search interface, using the terms “corticosteroids,” “dexamethasone,” “COVID-19,” and “randomized trial”. Publisher abstracts and verified secondary records were used to confirm the content of each trial report.

4. Study Selection

Records were screened against the eligibility criteria by title, abstract, and available full-text information. Selection was performed by a single reviewer.

5. Data Items

Sample size, population, drug and dose, comparator, primary outcome and results, mortality by level of respiratory support, secondary outcomes, and adverse events were extracted.

6. Risk-of-Bias Appraisal

Risk of bias was appraised qualitatively using the domains of the RoB 2 tool [5] (randomization, deviations from intended interventions, missing outcome data, outcome measurement, and selective reporting), based on information in published abstracts and verified secondary records.

7. Effect Measures

Effect measures were reported as given by each trial, including hazard ratios, risk ratios, vaccine or treatment efficacy, absolute event rates, and mean differences, each with its 95% confidence interval where available. When a trial reported a confidence level other than 95%, this is stated in the text. Measures were not converted between scales, because conversion requires data that were not available in the records reviewed.

8. Missing and Unreported Data

When a result, confidence interval, or safety rate was not available in the records reviewed, it is stated as not available and was not estimated. Where a figure was derived by simple arithmetic from reported values, this is stated in the text and no confidence interval is given.

9. Certainty of the Evidence

A formal certainty-of-evidence rating was not performed. Instead, the consistency of results across trials, the precision of estimates, the directness of the evidence, and the potential

for bias were considered narratively when interpreting the findings.

10. Ethical Considerations

This review used only published data from previously reported trials and did not involve new contact with patients. Ethical approval was therefore not required, and the original trials reported their own ethical approvals and participant consent.

11. Synthesis

Because drugs, populations, durations, comparators, and outcomes differed, a pooled estimate was not calculated. Results are reported as provided by each trial and are tabulated and described narratively.

RESULTS

1. Study Selection

The search identified three RCTs that met the eligibility criteria [1–3]. They differed in drug, dose, and population, and results are therefore presented by trial.

2. Characteristics of Included Trials

RECOVERY compared dexamethasone 6 mg once daily for up to 10 days (2,104 patients) with usual care (4,321 patients) [1]. CoDEX randomized 299 patients with COVID-19 and moderate to severe acute respiratory distress syndrome to dexamethasone 20 mg intravenously daily for 5 days then 10 mg daily for 5 days (n = 151) or standard care (n = 148) [2]. REMAP-CAP randomized 403 critically ill patients to a fixed-duration hydrocortisone course (n = 143), shock-dependent hydrocortisone (n = 152), or no hydrocortisone (n = 108) [3].

Table 2. Characteristics of Included Trials

Trial	Design and population
RECOVERY [1]	6,425 hospitalized patients; dexamethasone 6 mg daily for up to 10 days (n = 2,104) vs usual care (n = 4,321); open-label
CoDEX [2]	299 patients with moderate to severe ARDS; dexamethasone 20 mg daily for 5 days then 10 mg for 5 days vs standard care
REMAP-CAP [3]	403 critically ill patients; fixed-duration hydrocortisone (n = 143), shock-dependent hydrocortisone (n = 152), or none (n = 108); open-label

3. Mortality

3.1 RECOVERY

In RECOVERY, 28-day mortality was 22.9% (482 deaths) with dexamethasone and 25.7% (1,110 deaths) with usual care (RR 0.83, 95% CI 0.75–0.93) [1]. The effect differed by level of respiratory support at randomization: mortality was 29.3% versus 41.4% in patients receiving invasive mechanical ventilation (RR 0.64, 95% CI 0.51–0.81), 23.3% versus 26.2% in patients receiving oxygen without ventilation (RR 0.82, 95% CI 0.72–0.94), and 17.8% versus 14.0% in patients receiving no respiratory support (RR 1.19, 95% CI 0.92–1.55) [1].

Table 3. 28-Day Mortality in RECOVERY by Respiratory Support

Subgroup	Dexamethasone vs usual care
All patients	22.9% vs 25.7%; RR 0.83 (0.75–0.93)
Invasive ventilation	29.3% vs 41.4%; RR 0.64 (0.51–0.81)
Oxygen only	23.3% vs 26.2%; RR 0.82 (0.72–0.94)
No respiratory support	17.8% vs 14.0%; RR 1.19 (0.92–1.55)

3.2 CoDEX and REMAP-CAP

In CoDEX, 28-day mortality was 56.3% with dexamethasone and 61.5% with standard care (P = 0.31) [2]. In REMAP-CAP, in-hospital mortality was 30% with fixed-dose hydrocortisone, 26% with shock-dependent hydrocortisone, and 33% with no hydrocortisone [3].

4. Organ Support Outcomes

In CoDEX, dexamethasone increased the mean number of ventilator-free days during the first 28 days (6.6 vs 4.0 days; P = 0.02) [2]. In REMAP-CAP, the median number of organ support-free days was 0 in all three groups, and the trial was stopped early after

recommendations from RECOVERY became available [3].

5. Safety

In CoDEX, ventilator-associated pneumonia occurred in 12.6% with dexamethasone and 19.6% with standard care, and insulin use occurred in 31.1% and 28.4%, respectively [2]. The records reviewed did not provide detailed adverse event rates for RECOVERY or REMAP-CAP.

Table 4. Selected Findings from Smaller Trials

Trial	Finding
CoDEX [2]	Ventilator-free days 6.6 vs 4.0 (P = 0.02); mortality 56.3% vs 61.5% (P = 0.31)
REMAP-CAP [3]	Median organ support-free days 0 in all groups; mortality 30% / 26% / 33%

6. Risk-of-Bias Appraisal

RECOVERY, CoDEX, and REMAP-CAP were randomized and published in peer-reviewed journals. RECOVERY and REMAP-CAP were open-label, and CoDEX and REMAP-CAP were stopped early, which may lead to imprecise or exaggerated estimates. A domain-level RoB 2 judgement requires full-text and protocol review and was not completed.

Table 5. Qualitative Risk-of-Bias Summary

Trial	Appraisal
RECOVERY [1]	Randomized, open-label; very large sample
CoDEX [2]	Randomized, open-label; stopped early; small sample
REMAP-CAP [3]	Randomized, open-label; stopped early; small sample

DISCUSSION

1. Summary of Evidence

The largest trial, RECOVERY, showed a lower 28-day mortality with dexamethasone, and the benefit was concentrated in patients receiving ventilation or oxygen [1]. The two smaller trials were consistent in direction for some outcomes but were stopped early and were underpowered for mortality [2][3].

2. Differences by Respiratory Support

The RECOVERY subgroup results suggest a gradient: the greatest reduction in mortality in ventilated patients (RR 0.64), a smaller reduction in patients receiving oxygen (RR 0.82), and no benefit, with a point estimate suggesting possible harm, in patients without respiratory support (RR 1.19, 95% CI 0.92–1.55) [1]. This supports targeting corticosteroids to patients who need respiratory support.

3. Role of the Smaller Trials

CoDEX reported more ventilator-free days with dexamethasone but no clear mortality difference [2]. REMAP-CAP did not show a difference in organ support-free days and was stopped early [3]. Their sample sizes limit conclusions, and they do not contradict the large trial.

4. Drug and Dose

The trials used different drugs and doses (dexamethasone 6 mg daily in RECOVERY, higher-dose dexamethasone in CoDEX, hydrocortisone in REMAP-CAP) [1–3]. The records reviewed do not permit a direct comparison of dose or drug.

5. Safety

Safety data were limited in the records reviewed. CoDEX reported insulin use in about 30% of patients in both arms and fewer ventilator-associated pneumonia events with dexamethasone [2]. The potential for hyperglycemia and secondary infection should still be considered in clinical use.

6. Open-Label Design and Early Stopping

Two trials were open-label and two were stopped early [1–3]. Open-label designs may influence care co-interventions, and early stopping may lead to imprecise estimates. The large size of RECOVERY mitigates but does not remove these concerns.

7. Implications for Practice

Evidence supports systemic corticosteroids for hospitalized patients with

COVID-19 who require oxygen or ventilation, and does not support their use in patients without respiratory support. The records reviewed did not address Indonesian patients, newer variants, or concomitant antivirals; decisions should follow current national guidance.

8. Implications for Research

Future research should clarify optimal drug, dose, and duration, outcomes in vaccinated populations and with newer variants, and long-term outcomes after corticosteroid treatment.

9. Strengths of the Review

This review focused on randomized controlled trials published in major peer-reviewed journals, which are the strongest design for estimating intervention effects. Each trial result was cross-checked against the published abstract or a verified secondary record, and the numbers reported here are those given by the trial authors. The reporting of synthesis without meta-analysis followed a published guideline, and limitations in the methods are described openly.

10. Certainty and Consistency of the Evidence

Considered narratively, the certainty of the evidence depends on three features: the number and size of the trials, the consistency of the direction and size of effects between trials, and the precision of the estimates. Where trials agree in direction and have narrow confidence intervals, the evidence is stronger; where trials disagree or have wide confidence intervals, the evidence is weaker and conclusions should be more cautious. A formal grading of certainty was not undertaken and would be needed before the findings are used to support a guideline recommendation.

11. Generalizability

Trial participants are selected by eligibility criteria and often receive closer monitoring than patients in routine care, so effects seen in trials may differ in practice. The populations in the included trials may differ from patients in Indonesia in baseline risk, access to care, and background treatment, and the findings should be applied with attention to local circumstances.

12. Recommendations for an Updated Review

An updated review suitable for journal submission should register a protocol in a public registry before the search, search several databases such as PubMed, Embase, and the Cochrane Library with an exportable strategy, and screen records independently in duplicate. Data should be extracted from full-text reports and trial registries, risk of bias should be assessed domain by domain with RoB 2, and, where trials are sufficiently similar, a random-effects meta-analysis with an assessment of heterogeneity should be performed. The certainty of evidence for each outcome should then be graded using the GRADE approach.

13. Limitations

Several limitations should be acknowledged. Searching was performed through a web interface rather than an exportable multi-database search and no protocol was registered, so relevant trials may have been missed. Selection and extraction were performed by one reviewer, using published abstracts and verified secondary records. A formal RoB 2 assessment was not completed and no pooled estimate was computed. Only three trials were included, the trials evaluated different drugs, and the RECOVERY dexamethasone results are an arm of a larger platform trial. The review should be repeated with a documented multi-database search and independent duplicate review before the findings are used for clinical recommendations.

CONCLUSIONS

In hospitalized patients with COVID-19, dexamethasone reduced 28-day mortality in patients receiving oxygen or invasive ventilation in the largest trial, with no benefit and possible harm in patients without respiratory support.

The two smaller trials were underpowered for mortality.

Future work should include a pre-registered, multi-database systematic review with meta-analysis, formal risk-of-bias and certainty-of-evidence assessment, and evaluation of drug, dose, and duration in current clinical settings.

Author Contribution Statement

The author performed all aspects of this study.

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