Table 5a. Systemic Corticosteroids: Selected Clinical Trial Data

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The clinical trials described in this table do not represent all the trials that the Panel reviewed while developing the recommendations for systemic corticosteroids. The studies summarized below are those that have had the greatest impact on the Panel's recommendations. Unless stated otherwise, the clinical trials listed below only included participants aged ≥18 years.

Methods	Results	Limitations and Interpretation
RECOVERY: Open-Label RCT of Dexamethasone in Hospitalized Patients With COVID-19 in the United Kingdom[1]		

Key Inclusion Criterion
• Hospitalized with suspected or laboratory-confirmed SARS-CoV-2 infection
Key Exclusion Criteria
• Physician determination, based on patient's medical history, that risk of participation was too great
• An indication for corticosteroid therapy outside of the study
Interventions
• DEX 6 mg IV or PO once daily plus SOC for up to 10 days or until hospital discharge, whichever came first (n = 2,104)
• SOC alone (n = 4,321)
Primary Endpoint
• All-cause mortality at 28 days
	Participant Characteristics
	• Mean age 66 years; 64% men; 73% White
	• 56% had ≥1 comorbidities; 24% with DM
	• 89% had laboratory-confirmed SARS-CoV-2 infection.
	• Median of 7 days of DEX therapy
	• At randomization:
	  • 16% received MV or ECMO.
	  • 60% required supplemental oxygen but not MV.
	  • 24% required no supplemental oxygen.
	• <1% in both arms received RDV.
	• Received tocilizumab or sarilumab: 2% in DEX arm vs. 3% in SOC arm
	Primary Outcome
	• All-cause mortality at 28 days in DEX arm vs. SOC arm:
	  • All patients: 23% vs. 26% (age-adjusted rate ratio 0.83; 95% CI, 0.75–0.93; $P < 0.001$)
	  • Patients who required MV or ECMO at randomization: 29% vs. 41% (rate ratio 0.64; 95% CI, 0.51–0.81)
	  • Patients who required supplemental oxygen but not MV at randomization: 23% vs. 26% (rate ratio 0.82; 95% CI, 0.72–0.94)
	  • Patients who did not require supplemental oxygen at randomization: 18% vs. 14% (rate ratio 1.19; 95% CI, 0.92–1.55)
		Key Limitations
		• Open-label study
		• Published data did not include results for key secondary endpoints (e.g., cause-specific mortality, need for renal replacement), AEs, and key subgroups (e.g., patients with comorbidities).
		• Patients who required supplemental oxygen (but not MV) had a range of disease severity. It is unclear whether all patients in this group benefited from DEX or whether benefit was restricted to those who required higher levels of supplemental oxygen.
		• Patients aged >80 years were preferentially assigned to receive supplemental oxygen therapy (and not MV).
		• The high mortality in this study may limit the generalizability of results to populations with a lower baseline mortality.
		Interpretation
		• In hospitalized patients with severe COVID-19 who required supplemental oxygen, the use of DEX reduced mortality at 28 days. The greatest benefit was seen in those who were receiving MV at randomization.
		• There was no survival benefit for DEX in patients who did not require supplemental oxygen at randomization.

Methods	Results	Limitations and Interpretation
CoDEX: Open-Label RCT of Dexamethasone in Patients With Moderate to Severe ARDS and COVID-19 in Brazil[2]		

Key Inclusion Criteria
• Suspected or laboratory-confirmed SARS-CoV-2 infection
• Received MV within 48 hours of meeting criteria for moderate to severe ARDS (PaO_2/FiO_2 ≤200 mm Hg)
Key Exclusion Criteria
• Received immunosuppressive drugs in past 21 days
• Death expected within 24 hours
Interventions
• DEX 20 mg IV once daily for 5 days, then DEX 10 mg IV once daily for 5 days or until ICU discharge (n = 151)
• SOC alone (n = 148)
Primary Endpoint
• Number of days alive and free from MV by Day 28
Key Secondary Endpoints
• All-cause mortality by Day 28
• Number of ICU-free days by Day 28
• Duration of MV by Day 28
• Score on 6-point OS at Day 15
• SOFA score at Day 7
Key Exploratory Analysis
• Death or MV at Day 15
	Participant Characteristics
	• Mean age 61 years; 63% men
	• Comorbidities in DEX arm vs. SOC arm:
	  • Obesity: 31% vs. 24%
	  • DM: 38% vs. 47%
	• Vasopressor use: 66% in DEX arm vs. 68% in SOC arm
	• Mean PaO_2/FiO_2: 131 mm Hg in DEX arm vs. 133 mm Hg in SOC arm
	• Median of 10 days of DEX therapy
	• No patients received RDV or tocilizumab.
	• 35% in SOC arm received corticosteroids for indications such as bronchospasm or septic shock.
	Primary Outcome
	• Mean number of days alive and free from MV by Day 28: 7 in DEX arm vs. 4 in SOC arm ($P = 0.04$)
	Secondary Outcomes
	• No differences between arms by Day 28 in all-cause mortality (56% in DEX arm vs. 62% in SOC arm), number of ICU-free days, or duration of MV
	• No difference between arms at Day 15 in score on 6-point OS
	• Mean SOFA score at Day 7: 6.1 in DEX arm vs. 7.5 in SOC arm ($P = 0.004$)
	Other Outcome
	• Post hoc analysis of probability of death or MV at Day 15: 68% in DEX arm vs. 80% in SOC arm (OR 0.46; $P = 0.01$)
		Key Limitations
		• Open-label study
		• Underpowered; enrollment stopped after release of data from the RECOVERY trial.
		• Since no follow-up data were collected after hospital discharge for patients who were discharged before Day 28, no data on deaths or rehospitalization were available for these patients between day of discharge and Day 28.
		• The high mortality in this study may limit the generalizability of results to populations with a lower baseline mortality.
		• More than a third of those randomized to receive SOC also received corticosteroids.
		Interpretation
		• Compared with SOC alone, DEX increased the mean number of days alive and free of MV by Day 28 in patients with COVID-19 and moderate to severe ARDS.

Methods	Results	Limitations and Interpretation
Observational Cohort Study of Dexamethasone in Hospitalized Patients With COVID-19 Who Were Not on Intensive Respiratory Support in the United States[3]		

Key Inclusion Criterion
• Within 14 days of a positive SARS-CoV-2 test result
Key Exclusion Criteria
• Recent receipt of corticosteroids
• Receipt of IRS (defined as HFNC oxygen, NIV, or MV) within 48 hours
• Hospital LOS <48 hours
Interventions
• Corticosteroids (95% received DEX) administered within 48 hours of admission (n = 7,507)
• No corticosteroids administered (n = 7,433)
Primary Endpoint
• All-cause mortality at 90 days
	Participant Characteristics
	• Mean age 71 years; 95% men; 27% Black, 55% White
	• 77% did not receive IRS within 48 hours.
	• 83% were hospitalized within 1 day of a positive SARS-CoV-2 test result.
	• Median duration of DEX for patients who did not receive IRS: 5 days for those not on supplemental oxygen at baseline vs. 6 days for those on low-flow nasal cannula oxygen
	• Received RDV: 43% of those who received DEX vs. 13% of those who did not
	• Received anticoagulants: 46% of those who received DEX vs. 10% of those who did not
	Primary Outcome
	• Risk of all-cause mortality at 90 days was higher in those who received DEX.
	  • Combination of those not on supplemental oxygen and those on low-flow nasal cannula oxygen: HR 1.59; 95% CI, 1.39–1.81
	  • Those not on supplemental oxygen: HR 1.76; 95% CI, 1.47–2.12
	  • Those on low-flow nasal cannula oxygen: HR 1.08; 95% CI, 0.86–1.36
		Key Limitations
		• Retrospective observational study
		• Because nearly all patients on MV or HFNC oxygen received DEX, analysis was restricted to patients who did not receive IRS (i.e., those who received no supplemental oxygen or only low-flow nasal cannula oxygen).
		• There were differences between the arms in other therapies received. The investigators attempted to account for this using different approaches (e.g., propensity scoring, weighted analyses, subgroup/sensitivity analyses).
		Interpretation
		• In hospitalized patients with COVID-19, the use of DEX was not associated with a reduction in mortality among those who received low-flow nasal cannula oxygen during the first 48 hours after hospital admission, but it was associated with increased mortality among those who received no supplemental oxygen during the first 48 hours after admission.

Methods	Results	Limitations and Interpretation
COVID STEROID 2: Blinded RCT of Dexamethasone 12 mg Versus 6 mg in Hospitalized Adults With COVID-19 and Severe Hypoxemia in Denmark, India, Sweden, and Switzerland[4,5]		

Key Inclusion Criteria
• Laboratory-confirmed SARS-CoV-2 infection
• Required oxygen ≥10 L/min, NIV, CPAP, or MV
Key Exclusion Criteria
• Treated with DEX >6 mg (or equivalent)
• Treated with corticosteroid within past 5 days
• Invasive fungal infection or active TB
Interventions
• DEX 12 mg IV once daily for up to 10 days (n = 497)
• DEX 6 mg IV once daily for up to 10 days (n = 485)
Primary Endpoint
• Number of days alive without life support (MV, circulatory support, or kidney replacement therapy) at 28 days
Key Secondary Endpoints
• Number of days alive without life support at 90 days
• Number of days alive and out of hospital at 90 days
• Mortality at 90 days
• Mortality at 28 days
• SAEs at 28 days
	Participant Characteristics
	• Median age 65 years; 31% women
	• DM: 27% in 12 mg arm vs. 34% in 6 mg arm
	• Median of 7 days from symptom onset to hospitalization in both arms
	• Received ICU care: 78% in 12 mg arm vs. 81% in 6 mg arm
	• Oxygen requirements:
	  • 54% on oxygen via nasal cannula or face mask (median flow rate 23 L/min)
	  • 25% on NIV
	  • 21% on MV
	• 63% received RDV; 12% received IL-6 inhibitors or JAK inhibitors.
	• Median of 7 days of DEX therapy in both arms
	Primary Outcome
	• Median number of days alive without life support at 28 days: 22.0 in 12 mg arm vs. 20.5 in 6 mg arm (adjusted mean difference 1.3 days; 95% CI, 0.0–2.6; $P = 0.07$)
	  • 63.9% Bayesian probability of clinically important benefit and 0.3% Bayesian probability of clinically important harm for DEX 12 mg
	Secondary Outcomes
	• At 90 days:
	  • Median number of days alive without life support: 84 in 12 mg arm vs. 80 in 6 mg arm ($P = 0.15$)
	  • Median number of days alive and out of hospital: 62 in 12 mg arm vs. 48 in 6 mg arm ($P = 0.09$)
	  • Mortality: 32% in 12 mg arm vs. 38% in 6 mg arm (adjusted relative risk 0.87; 99% CI, 0.70–1.07; $P = 0.09$)
	• At 28 days:
	  • Mortality: 27% in 12 mg arm vs. 32% in 6 mg arm (adjusted relative risk 0.86; 99% CI, 0.68–1.08; $P = 0.10$)
	  • SAEs, including septic shock and invasive fungal infections: 11% in 12 mg arm vs. 13% in 6 mg arm (adjusted relative risk 0.83; 99% CI, 0.54–1.29; $P = 0.27$)
		Key Limitation
		• The randomized intervention period was <10 days for some patients because the trial allowed up to 4 days of DEX before enrollment.
		Interpretation
		• Among patients with COVID-19 and severe hypoxemia, the use of DEX 12 mg once daily did not result in more days alive without life support at 28 days than the use of DEX 6 mg once daily.
		• A preplanned Bayesian analysis showed that DEX 12 mg had a higher probability of benefit and a lower probability of harm than DEX 6 mg.[5]

Methods	Results	Limitations and Interpretation
CAPE COVID: Double-Blind RCT of Hydrocortisone in Critically Ill Patients With COVID-19 in France[6]		

Key Inclusion Criteria
• Laboratory-confirmed SARS-CoV-2 infection or radiographically suspected COVID-19 with ≥1 of the following:
  • MV with PEEP ≥5 cm H_2O
  • PaO_2/FiO_2 <300 mm Hg and FiO_2 ≥50% on HFNC
  • PaO_2/FiO_2 <300 mm Hg on reservoir mask oxygen
  • Pulmonary severity index score >130
Key Exclusion Criteria
• Septic shock
• Do-not-intubate orders
Interventions
• Continuous IV infusion of hydrocortisone 200 mg per day for 7 days, then 100 mg per day for 4 days, then 50 mg per day for 3 days; if patient improved by Day 4, then IV infusion of hydrocortisone 200 mg per day for 4 days, then 100 mg per day for 2 days, then 50 mg per day for 2 days (n = 76)
• Placebo (n = 73)
Primary Endpoint
• Treatment failure (death or dependency on MV or high-flow oxygen) by Day 21
Key Secondary Endpoints
• Need for intubation, prone positioning, ECMO, or inhaled nitric oxide
• Nosocomial infection by Day 28
• Clinical status by Day 21, as measured by a 5-item scale:
  • Death
  • In ICU and on MV
  • Required high-flow oxygen therapy
  • Discharged from ICU
  • Required low-flow oxygen therapy
	Participant Characteristics
	• Mean age 62 years; 70% men; median BMI 28
	• 96% had laboratory-confirmed SARS-CoV-2 infection.
	• Median symptom duration of 9–10 days
	• 81% required MV at baseline.
	• Received vasopressors: 24% in hydrocortisone arm vs. 18% in placebo arm
	• <5% received RDV or tocilizumab.
	• Median duration of treatment with study drug: 11 days in hydrocortisone arm vs. 13 days in placebo arm ($P = 0.25$)
	Primary Outcome
	• Treatment failure by Day 21: 42% in hydrocortisone arm vs. 51% in placebo arm ($P = 0.29$)
	Secondary Outcomes
	• No difference between arms in need for intubation or prone positioning (too few received ECMO or inhaled nitric oxide for comparison)
	• Need for intubation in those not on MV at baseline: 50% in hydrocortisone arm vs. 75% in placebo arm
	• No difference between arms in proportion of patients with nosocomial infection by Day 28
	• No difference between arms in clinical status by Day 21, but 15% died in hydrocortisone arm vs. 27% in placebo arm ($P = 0.06$)
	• Discharged from ICU by Day 21: 57% in hydrocortisone arm vs. 44% in placebo arm; 23% in both arms still required MV
		Key Limitations
		• Underpowered; enrollment stopped after release of data from the RECOVERY trial.
		• Limited information about comorbidities
		Interpretation
		• The use of hydrocortisone did not reduce the proportion of patients with COVID-19 and acute respiratory failure who experienced treatment failure by Day 21.

Methods	Results	Limitations and Interpretation
REMAP-CAP: Randomized, Open-Label, Adaptive Trial of Hydrocortisone in Patients With Severe COVID-19[7]		

Key Inclusion Criteria
• Presumed or laboratory-confirmed SARS-CoV-2 infection
• ICU admission for respiratory or cardiovascular support
Key Exclusion Criteria
• Presumed imminent death
• Systemic corticosteroid use
• >36 hours since ICU admission
Interventions
• Hydrocortisone 50 mg IV every 6 hours for 7 days (n = 137)
• Shock-dependent hydrocortisone 50 mg IV every 6 hours for duration of shock for up to 28 days (n = 146)
• No hydrocortisone (n = 101)
Primary Endpoint
• Number of days free of respiratory and cardiovascular organ support by Day 21
Key Secondary Endpoint
• In-hospital mortality
	Participant Characteristics
	• Mean age 60 years; 71% men; 53% White
	• Mean BMI range of 29.7–30.9 for the 3 arms
	• 50% to 64% required MV.
	Primary Outcome
	• Median number of days free of organ support by Day 21: 0 in both arms
	• Median adjusted ORs for hydrocortisone arms vs. no hydrocortisone arm:
	  • OR 1.43 (95% CrI, 0.91–2.27) with 93% Bayesian probability of superiority for fixed-dose hydrocortisone arm
	  • OR 1.22 (95% CrI, 0.76–1.94) with 80% Bayesian probability of superiority for shock-dependent hydrocortisone arm
	Key Secondary Outcome
	• No difference between arms in in-hospital mortality (30% in fixed-dose hydrocortisone arm vs. 26% in shock-dependent hydrocortisone arm vs. 33% in no hydrocortisone arm)
		Key Limitations
		• Open-label study
		• Enrollment stopped after release of data from the RECOVERY trial.
		Interpretation
		• The use of hydrocortisone did not increase the median number of days free of organ support in either the fixed-dose or the shock-dependent hydrocortisone arms; however, early termination limited the power to detect differences between the arms.

Methods	Results	Limitations and Interpretation
Single-Blind RCT of Methylprednisolone in Hospitalized Patients With COVID-19 Pneumonia in China[8]		

Key Inclusion Criteria
• Laboratory-confirmed SARS-CoV-2 infection
• Pneumonia confirmed by chest CT scan
• Hospitalized on general ward for <72 hours
Key Exclusion Criteria
• Severe immunosuppression
• Corticosteroid use for other diseases
Interventions
• Methylprednisolone 1 mg/kg IV per day for 7 days (n = 43)
• Saline (n = 43)
Primary Endpoint
• Clinical deterioration at 14 days
Key Secondary Endpoints
• Clinical cure at 14 days
• Time to clinical cure
• ICU admission
• In-hospital mortality
• Number of days hospitalized
	Participant Characteristics
	• Mean age 56 years; 48% men
	• Median of 8 days from symptom onset to randomization
	• At randomization, 71% were receiving oxygen via nasal cannula.
	Primary Outcome
	• Clinical deterioration at 14 days: 4.8% in both arms (OR 1.0; 95% CI, 0.134–7.442; $P = 1.00$)
	Secondary Outcomes
	• No difference (all $P > 0.05$) between methylprednisolone arm and placebo arm for:
	  • Clinical cure at 14 days: 51% vs. 58%
	  • Median number of days to clinical cure: 14 vs. 12
	  • ICU admission: 4.8% in both arms
	  • In-hospital mortality: 0% vs. 2.3%
	  • Median number of days hospitalized: 17 vs. 13
		Key Limitations
		• Small sample size
		• Terminated early because of decreasing incidence of COVID-19 pneumonia at study sites
		Interpretation
		• The use of methylprednisolone did not reduce the incidence of clinical deterioration among hospitalized patients with COVID-19.

Methods	Results	Limitations and Interpretation
COVIDICUS: RCT of High-Dose Dexamethasone Versus Standard of Care Dexamethasone in Patients With COVID-19–Related Respiratory Failure in the Intensive Care Unit in France[9]		
Key Inclusion Criteria • Suspected or laboratory-confirmed SARS-CoV-2 infection • ICU admission in past 48 hours • Respiratory failure (defined as PaO_2 <70 mm Hg, SpO_2 <90% on room air, >30 breaths/min, labored breathing, respiratory distress, or need for oxygen ≥6 L/min) **Key Exclusion Criteria** • Decision to limit life-sustaining treatment • Therapy with ≥0.5 mg/kg per day of prednisone equivalent for ≥3 weeks • Active and untreated bacterial, fungal, or parasitic infection **Interventions** • High dose: DEX 20 mg IV once daily for 5 days, then DEX 10 mg IV once daily for 5 days (n = 270) • SOC: DEX 6 mg IV once daily for 10 days (n = 239) or placebo (n = 37) **Primary Endpoint** • All-cause mortality by Day 60	**Participant Characteristics** • Median age 67 years; 76% men • Median of 9 days from symptom onset to randomization • 81% had ≥1 comorbidities. • 17% received RDV; <1% received tocilizumab. **Primary Outcome** • All-cause mortality by Day 60: 26% in high-dose arm vs. 27% in SOC arm (HR 0.96; 95% CI, 0.69–1.33; *P* = 0.79)	**Key Limitation** • Comparator arm was initially a placebo but was changed to a standard dose of DEX after the RECOVERY trial results were released. **Interpretation** • Among ICU patients with COVID-19–related respiratory failure, high-dose DEX did not significantly improve 60-day survival.

Methods	Results	Limitations and Interpretation
RECOVERY: Open-Label RCT of 2 Doses of Dexamethasone in Hospitalized Patients With COVID-19 in the United Kingdom, Asia, and Africa[10]		
Key Inclusion Criteria • Hospitalized with suspected or laboratory-confirmed SARS-CoV-2 infection • SpO_2 <92% on room air **Key Exclusion Criteria** • Physician determination, based on patient's medical history, that risk of participation was too great • Contraindication for short-term corticosteroids • Suspected or confirmed influenza • Current use of ritonavir-boosted nirmatrelvir (Paxlovid), ritonavir, or other potent CYP3A inhibitor **Interventions** • High dose: DEX 20 mg once daily plus SOC for 5 days followed by DEX 10 mg once daily for 5 days or until hospital discharge, whichever came first (n = 659) • SOC: DEX 6 mg once daily plus SOC for 10 days or until hospital discharge, whichever came first (n = 613) **Primary Endpoint** • All-cause mortality at 28 days **Key Secondary Endpoints** • Time to discharge from hospital • Composite of MV (including ECMO) or death **Key Safety Endpoints** • Infections other than COVID-19 • Metabolic complications	**Participant Characteristics** • Enrollment for the subgroup of patients who received conventional oxygen or did not receive supplemental oxygen was stopped prematurely due to safety concerns. The results reported for this analysis only include patients from this subgroup. • Mean age 61 years; 60% men; 54% Asian, 36% White • 51% had ≥1 comorbidities; 19% with DM. • 53% received ≥1 COVID-19 vaccine doses. • 34% received RDV; 12% had received tocilizumab or were going to receive tocilizumab within 24 hours of randomization. **Primary Outcome** • All-cause mortality at 28 days: 19% in high-dose arm vs. 12% in SOC arm (rate ratio 1.59; 95% CI, 1.20–2.10; $P = 0.0012$) **Secondary Outcomes** • Time to discharge from hospital: 9 days in both arms • Composite of MV or death: 20% in high-dose arm vs. 13% in SOC arm (risk ratio 1.52; 95% CI, 1.18–1.97) **Safety Outcomes** • Pneumonia not due to COVID-19: 10% in high-dose arm vs. 6% in SOC arm (absolute difference 3.7%; 95% CI, 0.7–6.6) • Hyperglycemia requiring new or increased insulin dose: 22% in high-dose arm vs. 14% in SOC arm (absolute difference 7.4%; 95% CI, 3.2–11.5)	**Key Limitations** • Open-label study • The larger RECOVERY trial stopped enrollment of patients in this subgroup (i.e., those who received conventional oxygen or did not receive supplemental oxygen) due to safety concerns. **Interpretation** • In patients hospitalized with COVID-19 who had clinical hypoxemia (SpO_2 <92%) and did not require supplemental oxygen or required only conventional oxygen, the use of high-dose DEX increased the risk of death and hyperglycemia when compared with the use of standard doses of corticosteroids.

Key: AE = adverse event; ARDS = acute respiratory distress syndrome; BMI = body mass index; CPAP = continuous positive airway pressure; CT = computed tomography; CYP = cytochrome P450; DEX = dexamethasone; DM = diabetes mellitus; ECMO = extracorporeal membrane oxygenation; FiO_2 = fraction of inspired oxygen; HFNC = high-flow nasal cannula; ICU = intensive care unit; IL = interleukin; IRS = intensive respiratory support; IV = intravenous; JAK = Janus kinase; LOS = length of stay; MV = mechanical ventilation; NIV = noninvasive ventilation; OS = ordinal scale; the Panel = the COVID-19 Treatment Guidelines Panel; PaO_2 = arterial partial pressure of oxygen; PEEP = positive end-expiratory pressure; PO = oral; RCT = randomized controlled trial; RDV = remdesivir; SAE = serious adverse event; SOC = standard of care; SOFA = sequential organ failure assessment; SpO_2 = oxygen saturation; TB = tuberculosis

References

1. RECOVERY Collaborative Group. Dexamethasone in hospitalized patients with COVID-19. *N Engl J Med*. 2021;384(8):693-704. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32678530.
2. Tomazini BM, Maia IS, Cavalcanti AB, et al. Effect of dexamethasone on days alive and ventilator-free in patients with moderate or severe acute respiratory distress syndrome and COVID-19: the CoDEX randomized clinical trial. *JAMA*. 2020;324(13):1307-1316. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32876695.
3. Crothers K, DeFaccio R, Tate J, et al. Dexamethasone in hospitalised COVID-19 patients not on intensive respiratory support. *Eur Respir J*. 2022;60(1):2102532. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34824060.
4. COVID STEROID 2 Trial Group. Effect of 12 mg vs 6 mg of dexamethasone on the number of days alive without life support in adults with COVID-19 and severe hypoxemia: the COVID STEROID 2 randomized trial. *JAMA*. 2021;326(18):1807-1817. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34673895.
5. Granholm A, Munch MW, Myatra SN, et al. Dexamethasone 12 mg versus 6 mg for patients with COVID-19 and severe hypoxaemia: a pre-planned, secondary Bayesian analysis of the COVID STEROID 2 trial. *Intensive Care Med*. 2022;48(1):45-55. Available at: https://www.ncbi.nlm.nih.gov/pubmed/34757439.
6. Dequin PF, Heming N, Meziani F, et al. Effect of hydrocortisone on 21-day mortality or respiratory support among critically ill patients with COVID-19: a randomized clinical trial. *JAMA*. 2020;324(13):1298-1306. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32876689.
7. Angus DC, Derde L, Al-Beidh F, et al. Effect of hydrocortisone on mortality and organ support in patients with severe COVID-19: the REMAP-CAP COVID-19 corticosteroid domain randomized clinical trial. *JAMA*. 2020;324(13):1317-1329. Available at: https://www.ncbi.nlm.nih.gov/pubmed/32876697.
8. Tang X, Feng YM, Ni JX, et al. Early use of corticosteroid may prolong SARS-CoV-2 shedding in non-intensive care unit patients with COVID-19 pneumonia: a multicenter, single-blind, randomized control trial. *Respiration*. 2021;100(2):116-126. Available at: https://www.ncbi.nlm.nih.gov/pubmed/33486496.
9. Bouadma L, Mekontso-Dessap A, Burdet C, et al. High-dose dexamethasone and oxygen support strategies in intensive care unit patients with severe COVID-19 acute hypoxemic respiratory failure: the COVIDICUS randomized clinical trial. *JAMA Intern Med*. 2022;182(9):906-916. Available at: https://www.ncbi.nlm.nih.gov/pubmed/35788622.
10. RECOVERY Collaborative Group. Higher dose corticosteroids in patients admitted to hospital with COVID-19 who are hypoxic but not requiring ventilatory support (RECOVERY): a randomised, controlled, open-label, platform trial. *Lancet*. 2023;401(10387):1499-1507. Available at: https://pubmed.ncbi.nlm.nih.gov/37060915.