monotherapy has been launched for 2019-nCoV (ChiCTR2000029308). Future animal model and clinical studies should focus on assessing the effectiveness and safety of promising antiviral drugs, monoclonal and polyclonal neutralising antibody products, and therapeutics directed against immunopathologic host responses.

We have to be aware of the challenge and concerns brought by 2019-nCoV to our community. Every effort should be given to understand and control the disease, and the time to act is now.

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Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury

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The 2019 novel coronavirus (2019-nCoV) outbreak is a major challenge for clinicians. The clinical course of patients remains to be fully characterised, little data are available that describe the disease pathogenesis, and no pharmacological therapies of proven efficacy yet exist.

Corticosteroids were widely used during the outbreaks of severe acute respiratory syndrome (SARS)-CoV[1] and Middle East respiratory syndrome (MERS)-CoV,[2] and are being used in patients with 2019-nCoV in addition to other therapeutics.[3] However, current interim guidance from WHO on clinical management of severe acute respiratory infection when novel coronavirus (2019-nCoV) infection is suspected (released Jan 28, 2020) advises against the use of corticosteroids unless indicated for

	Outcomes of corticosteroid therapy*	Comment
MERS-CoV	Delayed clearance of viral RNA from respiratory tract[2]	Adjusted hazard ratio 0·4 (95% CI 0·2–0·7)
SARS-CoV	Delayed clearance of viral RNA from blood[5]	Significant difference but effect size not quantified
SARS-CoV	Complication: psychosis[6]	Associated with higher cumulative dose, 10 975 mg *vs* 6780 mg hydrocortisone equivalent
SARS-CoV	Complication: diabetes[7]	33 (35%) of 95 patients treated with corticosteroid developed corticosteroid-induced diabetes
SARS-CoV	Complication: avascular necrosis in survivors[8]	Among 40 patients who survived after corticosteroid treatment, 12 (30%) had avascular necrosis and 30 (75%) had osteoporosis
Influenza	Increased mortality[9]	Risk ratio for mortality 1·75 (95% CI 1·3–2·4) in a meta-analysis of 6548 patients from ten studies
RSV	No clinical benefit in children[10,11]	No effect in largest randomised controlled trial of 600 children, of whom 305 (51%) had been treated with corticosteroids

CoV=coronavirus. MERS=Middle East respiratory syndrome. RSV=respiratory syncytial virus. SARS=severe acute respiratory syndrome. *Hydrocortisone, methylprednisolone, dexamethasone, and prednisolone.

Table: **Summary of clinical evidence to date**

another reason.[4] Understanding the evidence for harm or benefit from corticosteroids in 2019-nCoV is of immediate clinical importance. Here we discuss the clinical outcomes of corticosteroid use in coronavirus and similar outbreaks (table).

Acute lung injury and acute respiratory distress syndrome are partly caused by host immune responses. Corticosteroids suppress lung inflammation but also inhibit immune responses and pathogen clearance. In SARS-CoV infection, as with influenza, systemic inflammation is associated with adverse outcomes.[12] In SARS, inflammation persists after viral clearance.[13,14] Pulmonary histology in both SARS and MERS infections reveals inflammation and diffuse alveolar damage,[15] with one report suggesting haemophagocytosis.[16] Theoretically, corticosteroid treatment could have a role to suppress lung inflammation.

In a retrospective observational study reporting on 309 adults who were critically ill with MERS,[2] almost half of patients (151 [49%]) were given corticosteroids (median hydrocortisone equivalent dose [ie, methylprednisolone 1:5, dexamethasone 1:25, prednisolone 1:4] of 300 mg/day). Patients who were given corticosteroids were more likely to require mechanical ventilation, vasopressors, and renal replacement therapy. After statistical adjustment for immortal time and indication biases, the authors concluded that administration of corticosteroids was not associated with a difference in 90-day mortality (adjusted odds ratio 0·8, 95% CI 0·5–1·1; p=0·12) but was associated with delayed clearance of viral RNA from respiratory tract secretions (adjusted hazard ratio 0·4, 95% CI 0·2–0·7; p=0·0005). However, these effect estimates have a high risk of error due to the probable presence of unmeasured confounders.

In a meta-analysis of corticosteroid use in patients with SARS, only four studies provided conclusive data, all indicating harm.[1] The first was a case-control study of SARS patients with (n=15) and without (n=30) SARS-related psychosis; all were given corticosteroid treatment, but those who developed psychosis were given a higher cumulative dose than those who did not (10 975 mg hydrocortisone equivalent *vs* 6780 mg; p=0·017).[6] The second was a randomised controlled trial of 16 patients with SARS who were not critically ill; the nine patients who were given hydrocortisone (mean 4·8 days [95% CI 4·1–5·5] since fever onset) had greater viraemia in the second and third weeks after infection than those who were given 0·9% saline control.[5] The remaining two studies reported diabetes and avascular necrosis as complications associated with corticosteroid treatment.[7,8]

A 2019 systematic review and meta-analysis[9] identified ten observational studies in influenza, with a total of 6548 patients. The investigators found increased mortality in patients who were given corticosteroids (risk ratio [RR] 1·75, 95% CI 1·3–2·4; p=0·0002). Among other outcomes, length of stay in an intensive care unit was increased (mean difference 2·1, 95% CI 1·2–3·1; p<0·0001), as was the rate of secondary bacterial or fungal infection (RR 2·0, 95% CI 1·0–3·8; p=0·04).

Corticosteroids have been investigated for respiratory syncytial virus (RSV) in clinical trials in children, with no conclusive evidence of benefit and are therefore not recommended.[10] An observational study of 50 adults with RSV infection, in which 33 (66%) were given

corticosteroids, suggested impaired antibody responses at 28 days in those given corticosteroids.[17]

Life-threatening acute respiratory distress syndrome occurs in 2019-nCoV infection.[18] However, generalising evidence from acute respiratory distress syndrome studies to viral lung injury is problematic because these trials typically include a majority of patients with acute respiratory distress syndrome of non-pulmonary or sterile cause. A review of treatments for acute respiratory distress syndrome of any cause, based on six studies with a total of 574 patients,[19] concluded that insufficient evidence exists to recommend corticosteroid treatment.[20]

Septic shock has been reported in seven (5%) of 140 patients with 2019-nCoV included in published reports as of Jan 29, 2020.[3,18] Corticosteroids are widely used in septic shock despite uncertainty over their efficacy. Most patients in septic shock trials have bacterial infection, leading to vasoplegic shock and myocardial insufficiency.[21,22] In this group, there is potential that net benefit might be derived from steroid treatment in severe shock.[21,22] However, shock in severe hypoxaemic respiratory failure is often a consequence of increased intrathoracic pressure (during invasive ventilation) impeding cardiac filling, and not vasoplegia.[23] In this context, steroid treatment is unlikely to provide a benefit.

No clinical data exist to indicate that net benefit is derived from corticosteroids in the treatment of respiratory infection due to RSV, influenza, SARS-CoV, or MERS-CoV. The available observational data suggest increased mortality and secondary infection rates in influenza, impaired clearance of SARS-CoV and MERS-CoV, and complications of corticosteroid therapy in survivors. If it is present, the effect of steroids on mortality in those with septic shock is small, and is unlikely to be generalisable to shock in the context of severe respiratory failure due to 2019-nCoV.

Overall, no unique reason exists to expect that patients with 2019-nCoV infection will benefit from corticosteroids, and they might be more likely to be harmed with such treatment. We conclude that corticosteroid treatment should not be used for the treatment of 2019-nCoV-induced lung injury or shock outside of a clinical trial.

JKB is a member of the WHO panel on clinical management for 2019-nCoV. CDR and JEM declare no competing interests.

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