Quality Academy Knowledge & Evidence Team

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| **Your request for evidence:**  Our enquirer would like to know if the administration of cortisone injections would put patients at risk of having more severe symptoms and complications of coronavirus.Top of Form  Bottom of Form | **Date of literature search: 19/03/2020**  **Search conducted by:** Ramona Naicker  **Contact details:** [ramona.naicker@nhs.net](mailto:ramona.naicker@nhs.net) x5338 |
| **In Summary:**   * **Extremely limited studies regarding COVID-19 and corticosteroids suggest corticosteroids are not beneficial and may be harmful** * **Recommendations about corticosteroids and COVID-19 are based on results of earlier higher-level studies relating to MERS-CoV, SARS, CoV and Influenza.**   The World Health Organisation1 and Centers for Disease Control and Prevention2 both **do not recommend the use of corticosteroids** for COVID-19 patients due to the lack of effectiveness and possible harm. The basis of this recommendation is that as **no clinical data exist to support use of corticosteroid therapy in the treatment of respiratory infection due to SARS-CoV or MERS-CoV**, patients with COVID-19 may also be unlikely to benefit from corticosteroid regimens.  WHO state in their [COVID 19 Public Health Emergency of International Concern (PHEIC)](https://www.who.int/blueprint/priority-diseases/key-action/Global_Research_Forum_FINAL_VERSION_for_web_14_feb_2020.pdf?ua=1) document, that they have prioritised the evaluation of corticosteroids in clinical trials to assess safety and efficacy and the [US clinical trial register shows a trial](https://clinicaltrials.gov/ct2/show/NCT04273321) to be completed in May 2020.  I’ve included 2 **small** studies3,4 on COVID-19, both of which assess the use of corticosteroids. One study suggested that corticosteroids could be linked **to increased mortality,3** the second noted **no benefits in patients**.4 | |

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| **No.** | **Key information** | **Document** |
| 1. | World Health Organisation. **Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected. Interim guidance**. [Published 13 March 2020]  **Key finding:**   * **Given lack of effectiveness and possible harm, routine corticosteroids should be avoided unless they are indicated for another reason**   10. Adjunctive therapies for COVID-19: corticosteroids  WHO advise to not routinely give systemic corticosteroids for treatment of viral pneumonia outside clinical trials.   * A systematic review of observational studies of corticosteroids administered to patients with SARS reported **no survival benefit and possible harms** (avascular necrosis, psychosis, diabetes, and delayed viral clearance) (62). * A systematic review of observational studies in influenza found a **higher risk of mortality and secondary infections** with corticosteroids; the evidence was judged as very low to low quality owing to confounding by indication (63). * A subsequent study of the above that addressed its limitation by adjusting for time-varying confounders **found no effect on mortality** (64). * A recent study of patients receiving corticosteroids for MERS used a similar statistical approach and found **no effect of corticosteroids on mortality but delayed LRT clearance of MERS-CoV** (65).   Given the lack of effectiveness and possible harm, routine corticosteroids should be avoided unless they are indicated for another reason. Other reasons may include exacerbation of asthma or COPD, septic shock, and risk/benefit analysis needs to be conducted for individual patients.   * A recent guideline issued by an international panel and based on the findings of two recent large RCTs makes a conditional recommendation for **corticosteroids for all patients with sepsis (including septic shock)** (66). * Surviving Sepsis guidelines, written before these RCTs were reported, recommend **corticosteroids only for patients in whom adequate fluids and vasopressor therapy do not restore hemodynamic stability** (5). * Clinicians considering corticosteroids for a patient with **COVID19 and sepsis must balance the potential small reduction in mortality with the potential downside of prolonged shedding of coronavirus in the respiratory tract**, as has been observed in patients with MERS (65). * If corticosteroids are prescribed, **monitor and treat hyperglycaemia, hypernatraemia, and hypokalaemia**. Monitor for recurrence of inflammation and signs of adrenal insufficiency after stopping corticosteroids, which may have to be tapered. Because of the risk of strongyloides stercoralis hyper-infection with steroid therapy, diagnosis or empiric treatment should be considered in endemic areas if steroids are used (67).   62. Stockman et al., 2006. **SARS: systematic review of treatment effects**. *PLoS Med*; 3(9): e343.  63. Rodrigo et al., 2016. **Corticosteroids as adjunctive therapy in the treatment of influenza**. *Cochrane Database Syst Rev*  64. Delaney et al., 2016. **The influence of corticosteroid treatment on the outcome of influenza A(H1N1pdm09)-related critical illness**. *Crit Care*; 20: 75.  65. Arabi et al., 2018. **Corticosteroid therapy for critically ill patients with Middle East respiratory syndrome**. *Am J Respir Crit Care Med*; 197(6): 757-767.  66. Lamontagne et al., 2018. **Corticosteroid therapy for sepsis: a clinical practice guideline**. *BMJ*.  67. CDC. **Resources for health professionals: parasites - strongyloides**. | A copy of this paper can be obtained upon request |
| 2. | Centers for Disease Control and Prevention, 2020. **Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease (COVID-19)** [Updated 7th March 2020].  **Key finding:**   * **Clinical management of COVID-19 patients includes avoidance of corticosteroids**   Clinical Management and Treatment:  Corticosteroids should be avoided, because of the **potential for prolonging viral replication as observed in MERS-CoV patients**,\* unless indicated for other reasons. For example, for a chronic obstructive pulmonary disease exacerbation or for septic shock per guidelines.  \*Zumla et al., 2015. **Middle East respiratory syndrome**. *Lancet*; 386(9997): 995-1007.  Arabi et al., 2018. Saudi Critical Care Trial Group. **Corticosteroid Therapy for Critically Ill Patients with Middle East Respiratory Syndrome**. *Am J Respir Crit Care Med*;197(6): 757-767.  Russell et al., 2020. **Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury**. *Lancet*. | Available to read online [here](https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html) |
| 3. | Zhou et al., 2020. **Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study**. *The Lancet* (published online March 9. 2020).  **Key finding:**   * **A higher percentage of non-survivors that survivors of COVID-19 received corticosteroids (48% vs 23% of survivors)**   Data comprised of:   * Retrospective, multicentre cohort study including 191 patients, Wuhan. * This is the largest retrospective cohort study among patients with COVID-19 who have experienced a definite outcome   Systematic corticosteroid and intravenous immunoglobulin use differed significantly between non-survivors and survivors; 48% of non-survivors recevied corticosteroids whereas only 23% of survivors did.    Limitations:   * Lack of effective antivirals, inadequate adherence to standard supportive therapy, and high-dose corticosteroid use might have also contributed to the poor clinical outcomes in some patients | Available to read online [here](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(20)30566-3/fulltext) |
| 4. | Liu et al., 2020. **Clinical characteristics of novel coronavirus cases in tertiary hospitals in Hubei Province**. *Chinese Medical Journal* [Published 7th February 2020].  **Key informtion:**   * **Systemic** **corticosteroid treatment did not show significant benefits in patients with novel coronavirus**   Data comrpised of:   * 137 patients (61 males, 76 females, aged 20–83 years, median age 57 years) * 9 tertiary hospitals in Hubei province from December 30, 2019 to January 24, 2020   This study aimed to investigate its epidemiologic history, and analyse the clinical characteristics, treatment regimens, and prognosis of patients infected with 2019-nCoV during the outbreak.  Based on the mechanism of action of the drug, it was expected that systemic corticosteroid treatment could inhibit a cytokine storm and promote the absorption of exudative lesions. However, **this treatment neither significantly shortened the disease course nor improved the prognosis**.  An example is given of a patient who was treated with 40 mg intravenously (iv) every day (qd) methylprednisolone after admission. On day 6 of treatment, review of the lung computed tomography scan showed significant lesion progression and the patient ultimately died, indicating that lung changes caused by the 2019-nCoV were not inhibited by corticosteroid as was expected. | A copy of this paper can be obtained upon request |

**Search Strategy:** *covid-19* **OR** *coronavirus* **AND** *corticosteroid\** **OR** *cortisone*

**Sources searched:** AMED, BNI, CINAHL, EMBASE, HMIC, Medline, NICE, NICE Evidence Search, UpToDate, Cochrane, BMJ, TRIP, advanced Google search