RECOVERY
Randomised Evaluation of COVID-19 Therapy

## Intervention

Dexamethasone 6mg by mouth, nasogastric tube or intravenously for 10 days or until discharge, whichever is sooner. Pregnant women should receive oral prednisolone 40mg once daily or intravenous hydrocortisone 80mg twice daily instead of dexamethasone.

## Summary of information on dexamethasone in influenza

RECOVERY and other randomised trials have demonstrated the benefit of corticosteroids in hypoxic COVID-19 patients, which reduce the risk of dying by around a fifth.[1] A similar benefit may be seen in patients hospitalised with influenza, but their role in this setting remains uncertain. Corticosteroids have been widely used in hospitalised influenza patients for many years, without good evidence of any benefit or safety.[2,3] Although observational studies have reported higher mortality associated with corticosteroids use, these are prone to biases that make them unreliable, particularly if sicker patients are more likely to have received steroid treatment.[2] A large randomised trial of corticosteroids is needed to identify, or rule out, worthwhile benefits.

## Eligibility

- Hospitalised with viral pneumonia syndrome (e.g. fever, cough and/or shortness of breath with compatible chest X-ray changes)
- Confirmed influenza infection (laboratory test or point-of-care test if performed by a healthcare worker)
- Hypoxia (requiring supplemental oxygen or $SpO_2$ <92% on air)

## Contraindications

- Recent or planned use of a systemic corticosteroid at a dose equivalent to ≥10mg of prednisolone per day
- Current SARS-CoV-2 infection

## Frequently asked questions

1. ***Can someone on a regular low-dose oral corticosteroid be enrolled in the dexamethasone arm?***
   Yes, but only if they are taking <10 mg/day prednisolone or equivalent. The usual steroid should be stopped if allocated to dexamethasone, and care taken to ensure it is restarted after the RECOVERY dexamethasone is stopped.

2. ***Can someone on inhaled corticosteroids be enrolled in the dexamethasone arm?***
   Yes, and this can continue regardless of treatment allocation.

3. ***Can someone who requires initiation of oral corticosteroids for treatment of a co-existing medical condition (e.g. COPD) be enrolled in the dexamethasone arm?***
   No. They should receive corticosteroids as clinically indicated.

4. ***Can someone who is diabetic be enrolled in the dexamethasone arm?***
   Yes. Patients with diabetes (diet, drug or insulin controlled) can be enrolled. However, it may not be appropriate to enrol patients with unstable diabetes, or with acute complications of diabetes.

5. ***For patients with diabetes who are enrolled in the dexamethasone arm, is any additional monitoring required?***
   Patients with diabetes will require regular glucose monitoring according to usual clinical practice with appropriate adjustment of diabetic therapy to prevent/treat any emergent hyperglycaemia***.***

6. ***If dexamethasone-induced hyperglycaemia cannot be controlled, what should be done?***
   Dexamethasone may be stopped if causing uncontrollable hyperglycaemia.

7. ***Is dexamethasone safe when given during pregnancy?***
   Yes, but prednisolone (40 mg once daily) or hydrocortisone (80 mg twice daily IV) should be used instead of dexamethasone.

8. ***Are tablet and liquid preparations of dexamethasone inter-changeable?***
   Yes. For the purposes of the trial, the tablet and liquid preparations of dexamethasone are dose-equivalent.

9. ***Can liquid dexamethasone be administered down an NG tube?***
   Yes.

10. ***Are IV preparations of dexamethasone dose equivalent to oral preparations?***
    Yes. Vials of IV dexamethasone may come in concentrations that make it difficult to draw up 6 mg of dexamethasone exactly (e.g. 3.33 or 3.8 mg per ml). An approximate 10% over or under dosing is reasonable as a practical measure e.g. accept 1.5 ml of 3.8 mg per ml solution (slight under dose of 5.7 mg) or 2 ml of 3.33 mg per ml (slight over dose of 6.6 mg) as being acceptable for a dexamethasone 6 mg dose.

11. ***In renal impairment, is any dose adjustment required?***
    No.

12. ***In hepatic impairment, is any dose adjustment required?***
    No.

13. ***Can dexamethasone be stopped abruptly after 10 days of treatment?***
    Yes. At the dose and duration prescribed in RECOVERY, acute adrenal insufficiency upon withdrawal is unlikely. BNF advice is that “systemic corticosteroids may be stopped abruptly in those whose disease is unlikely to relapse and who have received treatment for 3 weeks or less and who are not included in the patient groups described below:

- received more than 40 mg prednisolone (or equivalent) daily for more than 1 week;
- been given repeat doses in the evening;
- received more than 3 weeks' treatment;
- recently received repeated courses (particularly if taken for longer than 3 weeks);
- taken a short course within 1 year of stopping long-term therapy;
- other possible causes of adrenal suppression

***14. If the patient is being discharged before day 10 after randomisation, should dexamethasone be prescribed as take-home medication?***

No. The trial dexamethasone is stopped on the day of hospital discharge, or at day 10 whichever is sooner.

***15. Can dexamethasone be continued beyond day 10 from randomisation?***

Use of dexamethasone beyond day 10 is outside the trial protocol and is a matter of individualised clinical judgement.

## References

1. RECOVERY Collaborative Group, Horby P, Lim WS, et al. Dexamethasone in Hospitalized Patients with Covid-19. N Engl J Med. 2021 Feb 25;384(8):693-704. PMID: 32678530
2. Lansbury L, Rodrigo C, Leonardi-Bee J. Corticosteroids as adjunctive therapy in the treatment of influenza. Cochrane Database Syst Rev. 2019 Feb 24;2(2):CD010406. PMID: 30798570
3. Lim WS, Brittain C, Duley L. Blinded randomised controlled trial of low-dose Adjuvant Steroids in Adults admitted to hospital with Pandemic influenza (ASAP): a trial 'in hibernation', ready for rapid activation. Health Technol Assess. 2015 Feb;19(16):1-78, vii-viii. PMID: 25716702