SECTION 1: REMAP-CAP CORTICOSTEROID DOMAIN INTERVENTIONS

This domain aims to determine the effectiveness of different strategies of corticosteroid utilisation in the treatment of severe CAP. In this domain, patients are randomised to receive:

- No corticosteroid, including Hydrocortisone (without administration of placebo)
- Fixed duration Hydrocortisone for 7 days
- Shock-dependent Hydrocortisone while the patient is in septic shock

Your site may be participating in all three interventions in this domain or only two, depending on local practice.

NO CORTICOSTEROID INTERVENTION

**Intervention**

In this intervention, patients are not to receive any systemic corticosteroid (including hydrocortisone) for this episode of Community-Acquired Pneumonia (CAP) or its direct complications.

**Discontinuation of Intervention**

The withholding of corticosteroids for this episode of CAP or its complications is to continue until the end of study day 28 or hospital discharge, whichever occurs first. Administration of corticosteroids after discharge from ICU will not be considered a protocol deviation.

**Corticosteroid strategy**

Administration of a systemic corticosteroid is permitted for the treatment of new illnesses that develop in the course of a patient’s ICU stay (e.g. asthma, treatment of an allergic reaction, new episode of septic shock from hospital-acquired infection). For patients in this domain who remain in ICU after study day 28, administration of corticosteroids is at the discretion of the treating clinician.

FIXED DURATION CORTICOSTEROID INTERVENTION

**Intervention**

In this intervention, patients are to receive a course of hydrocortisone 50mg IV every 6 hours, for 7 days.

**Commencement of Intervention**

Administration is to commence immediately after allocation is revealed at the time of randomisation. It will be considered a protocol deviation if during the 7 day course more than two sequential doses of hydrocortisone are missed, or if three or more individual doses are missed.

**Discontinuation of Intervention**

The seven-day course will be administered until at least the end of study day 7, and no longer than the end of study day 8 (i.e. it is intended that 28 doses are administered). For patients discharged from hospital before the end of the seven day course, Hydrocortisone should be discontinued at hospital discharge.

**Corticosteroid strategy**

From completion of the 7-day course of Hydrocortisone, patients allocated to this intervention are not to receive any systemic corticosteroid (including Hydrocortisone) for this episode of CAP or its direct complications, up until study day 28 or hospital discharge, whichever occurs first. For patients in this domain who remain in ICU after study day 28, administration of corticosteroids is at the discretion of the treating clinician.

Administration of a systemic corticosteroid (including hydrocortisone) after the end of the seven-day course is only permitted for the treatment of new illnesses that develop during the course of the patient’s ICU stay (e.g. asthma, treatment of an allergic reaction, or new episode of septic shock from hospital-acquired infection).

For patients who are discharged from ICU before the end of the seven-day course of Hydrocortisone, it is the responsibility of ICU staff to prescribe Hydrocortisone to complete the seven-day course. However, it is not the responsibility of ICU medical or research staff to ensure continuation of the Hydrocortisone after discharge from ICU. It is not a protocol deviation if the seven-day course of Hydrocortisone is not completed after ICU discharge.
SHOCK-DEPENDENT HYDROCORTISONE INTERVENTION

Intervention
Patients randomised to the shock-dependent hydrocortisone intervention are to receive 50mg IV Hydrocortisone every 6 hours while the patient is in septic shock.

Commencement of Intervention
The intervention is to commence as soon as septic shock is diagnosed, including immediately after randomisation if septic shock has already been diagnosed.

Definition of shock
For the purposes of this intervention, septic shock is defined as:

- Administration of any vasopressor by continuous infusion, AND
- The treating clinician believes that the vasopressor requirement is due to the CAP, and not for another reason such as untreated hypovolaemia or solely to offset the effects of other ICU interventions (such as administration of sedation or mechanical ventilation).

The exact dose of vasopressor that defines septic shock is not defined by the protocol, but is based on the judgement of the treating clinician.

Discontinuation of Intervention
Hydrocortisone administration is to cease when the clinician believes that septic shock has resolved. Septic shock would always be regarded as being resolved if vasopressor infusion has not been administered in the preceding 24 hours.

A clinician may regard septic shock to have resolved if vasopressors are being administered intermittently or at a low dose.

If, during the same ICU admission and within 28 days of randomisation, hydrocortisone is ceased and shock due to CAP or its direct complications reoccurs, then the intervention is to be recommenced until resolution of shock.

Hydrocortisone should be ceased prior to ICU discharge.

Corticosteroid strategy
Administration of a systemic corticosteroid while the patient is not in septic shock is only permitted for the treatment of new illnesses that develop during the course of the patient’s ICU stay (e.g. asthma, treatment of an allergic reaction, or new episode of septic shock from hospital-acquired infection).

Patients allocated to this intervention are not to receive any systemic corticosteroid (including Hydrocortisone) for this episode of CAP or its direct complications while the patient is not in septic shock, up until study day 28 or hospital discharge, whichever occurs first. For patients who remain in ICU after study day 28, administration of corticosteroids is at the discretion of the treating clinician.

SECTION 2. CONCOMITANT CARE

The administration of Etomidate after enrolment is not permitted and will be considered a protocol deviation. There are no other restrictions on concomitant care.