Supplementary table 1: Delirium protocol.

Step 1: Non-pharmacological interventions for delirium prevention and treatment

General

- Perform daily sedation holidays, unless contraindicated
- Avoid over-treatment and under-treatment of pain

Orientation

- Encourage communication
- Have familiar objects from the patient's home in the hospital room
- Frequently re-orient the patient to date, time, and caretakers
- Attempt consistency in staff
- Provide visual and auditory aids
- Allow television during the day with daily news or non-verbal music

Environment

- Encourage early mobilization (e.g. ambulation, range of motion exercises, minimize use of immobilizing equipment, ensure timely removal of catheters, order physical therapy and occupational therapy consults)
- Optimize sleep hygiene
  - Minimize noise and interruption
  - Keep lights on and window shades up during the day
  - Keep lights off and window shades closed at night

Clinical parameters

- Maintain euvolemia
- Maintain adequate systolic blood pressure
- Maintain adequate oxygen saturation
- Treat underlying metabolic derangements and infections

Step 2: Patient assessment

Nursing responsibilities

- Assess delirium using Confusion Assessment Method for the Intensive Care Unit (CAM-ICU)[45] every nursing shift, during sedation holidays if applicable
- Document screening results in the electronic medical record
- Report delirium positive results to the physician or advanced practitioner
- Assess for other causes of neurological status changes (e.g. hypoxia, vasospasm, stroke, seizure, infection, hypoglycemia, myocardial

infarction, pulmonary embolism)

- Assess patient for extra-pyramidal symptoms (e.g. acute dystonia, akathisia, parkinsonism, tardive dyskinesia), drug-induced rigidity, and high fever at least twice daily (every nursing shift) and when there is a change in clinical status

Physician or advanced practitioner responsibilities

- Assess the patient for non-delirium causes of neurological status changes
- Order appropriate delirium intervention(s) if applicable (Step 3)

Step 3: Interventions by CAM-ICU assessment result

Unable to assess delirium (Richmond Agitation Sedation Scale (RASS)[46] score -4 or -5)

- Lighten sedation, if applicable, to obtain goal level of sedation
- Continue non-pharmacological interventions for delirium prevention
- Continue daily sedation holidays, unless contraindicated

CAM-ICU delirium negative

- If applicable, continue sedation and analgesia protocols for treatment of anxiety and pain
- Continue non-pharmacological interventions for delirium prevention
- Continue twice daily delirium assessments

CAM-ICU delirium positive

All delirium positive patients

- Implement non-pharmacologic interventions for the prevention and treatment of delirium
- Assess patient for non-delirium causes of neurological status changes
- Ensure adequate pain control
- Discontinue or minimize use of potentially deliriogenic drugs
  - Avoid the use of benzodiazepines
  - Consider the use of propofol if sedation is required

-AND-

Tailored delirium treatment based on RASS score

- Delirium positive and RASS +2 to +4 [agitated]

- Assess pain
  - Pain: treat with analgesics and reassess for delirium
  - No pain: consider treatment with an antipsychotic agent (see next section)
- Provide adequate sedation for protection of the patient and staff

- Delirium positive and RASS 0 or +1 [awake and alert]
  - Ensure adequate pain control
  - Consider treatment with an antipsychotic agent (see next section)

- Delirium positive and RASS -1 to -3 [sedated]
  - Reassess sedation goal and consider adjustment of sedation regimen
  - Perform daily sedation holidays

Treatment of delirium with antipsychotic medications

General considerations

- For patients with alcohol withdrawal delirium (delirium tremens) or traumatic brain injury, use protocols specific for those disease processes
- For transplant patients, discuss with the transplant service before ordering medications
- For pregnant patients, carefully assess risks and benefits of medications and discuss with the Obstetrics and Gynecology service prior to ordering medications
- Use lower antipsychotic doses for elderly patients
- Prior to initiation of antipsychotics, obtain baseline QTc and monitor regularly thereafter
  - If QTc >490 mSec on bedside monitor, obtain 12-lead electrocardiogram
  - If QTc >500 mSec on 12-lead electrocardiogram
    - Alert physician or advanced practitioner
    - Hold all non-essential QTc prolonging medications and do not administer atypical antipsychotics
    - Repeat electrocardiogram in 6-12 hours
    - Consider supplemental magnesium administration
- Perform regular assessments for extra-pyramidal symptoms, drug-induced rigidity, and high fever
- Obtain liver function tests at baseline and at regular intervals according to the pharmacologic profile of the medication in use
- Consider consultation with the Psychiatry service if:

- Antipsychotic agents are ineffective
- The patient has a contraindication to antipsychotic use
- The patient has a baseline psychiatric disorder for which the patient is already receiving antipsychotics

Antipsychotic discontinuation

Once delirium has resolved, taper to the minimum effective dose over 3 to 5 days. Therapy should be discontinued approximately two weeks after discharge from the ICU or prior to discharge home to avoid the development of long-term adverse effects, including:

- Sedation/fatigue
- Weight gain
- Glucose intolerance
- Dyslipidemia
- Sudden cardiac death
- Increased mortality among elderly patients with dementia