	Preferred	Alternative (In consultation with Psychiatry)
Initiation Phase (first 24-48h post- intubation)	<ul> <li>Propofol IVCI (Start at 5 mcg/kg/min, ↑5-10mcg/kg/min q5min)</li> <li>Fentanyl IVCI (start at 25 mcg/hr, ↑25-50 mcg/hr q10min)</li> </ul>	<ul> <li>Hydromorphone IVCI (start at 0.4 mg/hr or 75% of converted fentanyl dose, ↑0.2 mg/hr q10min)</li> <li>1 mg IV hydromorphone = 100 mcg IV fentanyl</li> <li>Midazolam IVCI (Start at 1-4 mg/hr, ↑1 mg/hr q5min)</li> </ul>
Maintenance Phase (Target RASS –2 to –3)	<ul> <li>Propofol IVCI as noted in the initiation phase</li> <li>Continue fentanyl as above and add PRN fentanyl for nursing care related pain</li> <li>Dexmedetomidine IVCI (start at 0.2-0.4 mcg/kg/hr, ↑0.1 mcg/kg/hr q30min)</li> <li>Start quetiapine at 12.5mg po/NGT q12h</li> <li>Titrate quetiapine by 25-50 mg/day up to 200 mg/day</li> </ul>	<ul> <li>Hydromorphone IVCl as noted in the initiation phase</li> <li>Midazolam IVCl (Start at 1-4 mg/hr, ↑1 mg/hr q5min)</li> <li>Haloperidol 0.5 mg IV q8h</li> <li>Titrate haloperidol by 1 mg/day up to 5 mg daily</li> </ul>
De-escalation Phase (FiO2 0.5 and PEEP +10)	<ul> <li>Fentanyl IVCI (wean by 25 mcg/hr daily or q12h)</li> <li>Dexmedetomidine IVCI (start at 0.2-0.4 mcg/kg/hr, ↑0.1 mcg/kg/hr q30min)</li> <li>Continue/titrate quetiapine as noted in the Maintenance Phase.</li> </ul>	<ul> <li>Hydromorphone IVCI (wean by 0.2-0.4 mg/hr daily or q12h)</li> <li>Propofol IVCI as noted in the initiation phase</li> <li>Continue/titrate haloperidol as noted in the Maintenance Phase.</li> </ul>
Post-Extubation	<ul> <li>If patient is not agitated for 12 to 24 hours, reduce antipsychotic gradually.</li> <li>Discontinue antipsychotic before discharge or shortly after.</li> </ul>	<ul> <li>If patient is not agitated for 12 to 24 hours, reduce antipsychotic gradually.</li> <li>Discontinue antipsychotic before discharge or shortly after.</li> </ul>
Na	rcotics Sedatives	Antipsychotics

Daily EKG or QTc for ALL patients.

## For all patients with history of Parkinson's disease, parkinsonism, dementia, schizophrenia, intellectual disability, or bipolar disorder, consult Psychiatry for management of delirium

If QTc>500 msec, consult Psychiatry for recommendations on use of antipsychotics or other psychotropic agents.

If needed, increase sedatives overnight to ensure good day/night sleep cycle

Exercise caution when up titrating medications for geriatric patients (>70 years of age).

If using IV benzodiazepines for over a week: During the post-extubation stage, reduce standing benzodiazepine dose by 50%, and continue reduction by 20% daily until discontinuation (consider slower taper and using prn benzodiazepines if withdrawal is a concern).

Consult Psychiatry if: 1) agitation/delirium cannot be managed with above recommendations, 2) patient is a danger to self or staff or is in physical restraints, or 3) side effects develop (rigidity, akathisia, QTc prolongation).

Please refer to Institutional Delirium Screening, Assessment, and Management Standards for further information on delirium screening, assessment, and non-pharmacological management.

- By mid-April, we were informed by our Pharmacy that the medication supply shortages were no longer an imminent issue. Therefore, we updated the previous guidelines to allow for less benzodiazepine use, the use of opioids for pain only, and for return to pre-COVID dexmedetomidine use.
- We kept the guidelines as basic as possible, encouraging psychiatry consultation for the above listed indications and as needed.
- Critical care clinicians requested to use quetiapine instead of olanzapine as first line. The sedating effects of
  quetiapine were desired to adjust the sleep-wake cycle. During the weaning phase or the post-extubation phase,
  some of the patients on quetiapine were switched over to olanzapine to prevent sedation, or due to concerns
  for hypotension.
- C-L fellows assigned to each one of the critical care teams went over the guidelines with team members and
  provided guidance specifically for patients who were difficult to wean, severely agitated, requiring prolonged
  use of sedatives at high doses.
- For patients who did not respond to the guidelines above, additional medical work up, neurology consult, and a detailed review of drug-interactions were carried out. In select cases, chlorpromazine IV or ketamine infusion were utilized for management of acute agitation placing patient and staff at risk of harm. The use of ketamine for agitation management was limited to critical care setting only. The use of chlorpromazine was not made a part of the guidelines to save its use for cases where psychiatry was consulted due to side effects associated with use of IV chlorpromazine. We sparingly used valproic acid, for patients with known brain metastasis and seizures.
- We have noted parkinsonism more frequently at low doses of antipsychotics in COVID-19 patients. We therefore decided to see all patients in-person at least once a week, and more often if clinically indicated.
- In-person bedside rounds in critical care facilitated bedside education of Nursing who knew patients the best. Propofol, fentanyl, and midazolam are typically titrated by Nursing within a certain range. One-on-one discussions with Nursing, instructions on how to taper, what to taper first, were well-received by bedside Nursing.
- During the initiation phase, that is during the first 24 to 48 hours following intubation, patients were kept on fentanyl and propofol. Once the patients moved to the maintenance phase, if they continued require prone positioning, they were kept at RASS-4 to -5 along with use of paralytic agents. Once the spontaneous breathing and awakening trials were started, the sedation was lightened, the use of dexmedetomidine was preferred, benzodiazepines were minimized. As the spontaneous breathing trials were tolerated, sedation was further reduced. In COVID-19 patients, the maintenance phase and de-escalation phase were much longer than any other case of ARDS which meant patients were on benzodiazepines and opioids for extended periods of time. Abrupt discontinuation of these medications resulted in withdrawal symptoms, agitation, and prolonged intubation. Use of low dose antipsychotics, earlier in the course allowed for faster taper of sedatives and a smoother weaning period.
- We acknowledge that our experience in critically ill cancer patients with COVID-19 delirium is limited to around 20 to 30 patients, all seen in the last month. Therefore, our experience remains anecdotal, and not evidencebased. We are writing up our experience as a case-series to share our experience in more detail with the ACLP community.