

Supplementary Table 3. Outcome definitions

Outcome	Definition
<i>Primary outcome</i>	
Duration of invasive mechanical ventilation (IMV)	The duration of mechanically assisted breathing via endotracheal tube or tracheostomy tube from initiation (endotracheal intubation, initiation of assisted breathing on patients with chronic tracheostomy) until first successful extubation, measured in hours.
<i>Secondary outcomes</i>	
Duration of non-invasive mechanical ventilation	Duration of mechanically assisted breathing from extubation until termination of ventilator support, measured in hours.
Mortality	Death of participant from any cause in any reported form.
Length of stay in the intensive care unit	Duration from admission to the intensive care unit to PICU discharge, measured in days.
Length of stay in the hospital	Duration from hospital admission to hospital discharge, measured in days.
<i>Adverse events</i>	
Inadequate pain management	Measured with any type of pain score or by clinical judgement
Iatrogenic withdrawal syndrome	Clinical signs of withdrawal using any type of standardized measurement or need for rescue therapy (a bolus or an increased dose of infusion of either benzodiazepine or opioid medication).
Delirium	Measured with any type of standardized measurement.
Unplanned extubation	Unplanned removal of the endotracheal tube.
Extubation failure	Reintubation within 24 hours of being extubated.
Post-extubation stridor	Stridor (harsh or high-pitched tone during inspiration) with chest-wall retractions after extubation.
Unplanned removal of catheter or invasive device	Unplanned removal of any type of invasive tube or device (e.g.: arterial access, central venous access, peripheral venous access, nasogastric drainage tube, bladder catheter, chest tube).
Ventilator-associated pneumonia	Novum pneumonia during artificial ventilation confirmed by any clinical, microbiological, or radiological criteria.
Catheter-associated bloodstream infection	Bloodstream infection confirmed by microbiological sampling.
Pressure ulcers	Measured by any standardized criteria.
Tracheostomy	New tracheostomy tube inserted during current ICU admission.
<i>Long-term outcomes</i>	
Memory function after hospital discharge	Reported using any valid type of validated measurement.
Psychological recovery after hospital discharge	Reported using any valid type of validated measurement.

Cognitive recovery after hospital discharge	Reported using any valid type of validated measurement.
Quality of life after hospital discharge	Reported using any valid type of validated measurement.
<i>Sedative and opioid exposure</i>	
Duration of sedation Duration of benzodiazepines Duration of opioids Mean daily-, peak daily- and cumulative doses of benzodiazepines and opioids	<p>Doses of opioid analgesics were calculated as morphine equivalents[1] and were measured in micrograms per bodyweight kilograms (mcg/kg). Opioids include morphine (1), fentanyl (0.015), remifentanyl (0.015), sufentanyl (0.0015), methadone (0.3), butorphanol (0.2), enteral codeine (20), hydromorphone (0.15), meperidine (10), enteral oxycodone (3), and enteral tramadol (10).</p> <p>Doses of benzodiazepines were calculated as midazolam equivalents[2] and were measured in milligrams per bodyweight kilograms (mg/kg). Benzodiazepines include midazolam (1), clonazepam (0.2), lorazepam (0.3), and diazepam (2).</p> <p>Duration was measured in days.</p>

ICU, intensive care unit; PICU, pediatric ICU.