DRAFT BRIGHTON COLLABORATION CASE DEFINITION LEVELS OF DIAGNOSTIC CERTAINTY (LOC) FOR ACUTE MULTI-ORGAN DYSFUNCTION (aMOD)

LOC	**Criteria -** Recent onset (≤7 days) required
1	>2 organs with definite dysfunction (LOC 1)
2	[1 organ with definite dysfunction (LOC 1) **AND** ≥1 organs with probable dysfunction (LOC 2)] **OR** ≥2 organs with probable dysfunction (LOC 2)
3	[1 organ with definite dysfunction (LOC 1) **AND** ≥1 organs with possible dysfunction (LOC 3)] **OR** [1 organ with probable dysfunction (LOC 2) **AND** ≥1 organs with possible dysfunction (LOC 3)] **OR** ≥2 organs with possible dysfunction (LOC 3)
4	Reported as a case of acute MOD but insufficient information to meet any defined level (i.e. LOC 1, 2, 3 or 5) of the case definition
5	NOT a case of acute MOD **OR** because not of recent (≤7 days) onset

Organ Dysfunction	Population	Level 1 - Definite	Level 2 - Probable	Level 3 - Possible
Respiratory dysfunction	Adult	Two consecutive measures (≥ 1hr apart) of one of the following: • PaO_2/FiO_2 (mmHg) <300 • SaO_2/FiO_2 <315 **OR** Mechanical ventilation required for respiratory dysfunction	(Need for supplemental oxygen of at least > 4L/min via nasal canula **AND** requiring increasing respiratory support (any type) for > 1hr) to maintain saturation >94%	Two or more clinical signs of respiratory dysfunction: tachypnea, cyanosis, grunting, chest wall retractions, increased use of accessory respiratory muscles, newly identified SaO2 <94%
	Pediatric	Two consecutive measures (≥ 1hr apart) of one of the following: • PaO_2/FiO_2 (mm Hg) <300 • SaO_2/FiO_2 <264 **OR** Mechanical ventilation required for respiratory dysfunction	(Need for supplemental oxygen of at least > 4L/min via nasal canula **AND** requiring increasing respiratory support (any type) for > 1hr) to maintain saturation >94%	Two or more clinical signs of respiratory dysfunction: tachypnea, cyanosis, grunting, chest wall retractions, increased use of accessory respiratory muscles, newly identified SaO2 <94%
Cardiovascular dysfunction	Adult	Sustained administration of vasoactive agents[1] (for ≥ 30 minutes) to maintain MAP ≥65mmHg	Administration of intravenous fluids resuscitation of at least 500 ml intravenously for the purpose of maintaining MAP ≥65mmHg	MAP ≤65 mmHg **OR** Two or more of the following: Low volume/ thready/ absent peripheral pulses, cold/clammy extremities, capillary refill time >3 sec
	Pediatric	Any need for vasoactive agents[1] to maintain age specific MAP: <46 (<1 mo), <55 (1–11 mo), < 60 (12–23 mo), <62 (24–59 mo), <65 (60–143 mo), <67 (>144 mo)	Fluid resuscitation of at least 10ml/kg to maintain age specific MAP	One MAP less than age specific value **OR** Two or more of the following: Low volume/ thready/ absent peripheral pulses, cold/clammy extremities, capillary refill time >3 sec
Renal dysfunction	Adult	Increase in serum creatinine ≥2x patient's baseline **OR** Increase in serum creatinine by ≥0.3 mg/dL (≥26.5 micromol/L) within 48 hrs **OR** Sustained reduction in urine output[2] to <0.5 mL/kg/hour for ≥12 hours	Any serum creatinine to greater than 1.2 (in absence of baseline) **OR** Sustained reduction in urine output[2] to <0.5 mL/kg/hour for at least 6 hours	Sustained reduced urine output for at least 6 hours[2]

	Pediatric	Increase in serum creatinine to 2x patients' baseline **OR** Serum creatinine higher than the upper limit of age specific value (in absence of patients' baseline): 1.0–1.1 (<1 mo), 0.5–0.7 (-11 mo), 0.6–1.0 (12–23 mo), 0.9–1.5 (24–59 mo), 1.1–1.7 (60–143 mo), 1.7–2.8 (144–216 mo), 2.0–3.4 (>216 mo) **OR** Sustained reduction in urine output[2] to <0.5 mL/kg/hour for ≥12 hours.	Any serum creatinine to greater than 1.2 **OR** Sustained reduction in urine output[2] to <0.5 mL/kg/hour for at least 6 hours	Sustained reduction in urine output for at least 6 hours[2]
Encephalopathy	Adult	[GCS <= 13 **OR** any one of the following: • Decreased or absent response to environment, as defined by response to loud noise or painful stimuli • Decreased or absent eye contact • Inconsistent or absent response to external stimuli • Decreased arousability • New onset seizure associated with loss of consciousness] **AND** Any one of the following for >24h: depressed level of consciousness, acute personality/behavior change[3]	[GCS <= 13 **OR** any one of the following: • Decreased or absent response to environment, as defined by response to loud noise or painful stimuli • Decreased or absent eye contact • Inconsistent or absent response to external stimuli • Decreased arousability • New onset seizure associated with loss of consciousness] **AND** Any one of the following for 6-24 hrs: depressed level of consciousness, acute personality/behavior change[3]	GCS <= 13 **OR** Deviation from alert status, including response only to verbal or painful stimuli, or complete unresponsiveness **OR** Any one of the following for >2hrs and <6 hrs: depressed level of consciousness, acute personality/behavior change[3], new onset of seizure
	Pediatric	GCS <= 13 **AND** Any one of the following for >24h: depressed level of consciousness, irritability, new onset of seizure	GCS <= 13 **AND** Any one of the following for 6-24 hrs: depressed level of consciousness, irritability, new onset of seizure	Any one of the following for >2hrs and <6 hrs: depressed level of consciousness, irritability, new onset of seizure
Hepatic dysfunction	All ages: ages and pediatric	Total bilirubin ≥2x ULN (1.2 mg/dL or 20.5 micromol/L) **OR** ALT ≥3x ULN	Increased total bilirubin **AND** ALT/AST any value above normal range	Jaundice **OR** scleral icterus
Hemostatic dysfunction / Coagulopathy	All ages: ages and pediatric	Platelet count < 100,000 cells/µL **OR** INR: >1.5	Platelet count below normal range for the reporting lab **OR** INR above normal range	Any of the following occurring spontaneously: purpura (i.e. petechiae, purpura sensu stricto, ecchymosis), hemorrhagic oozing of skin lesions including rashes, hematoma, bruising, hematemesis, hematochezia/melena, occult bleeding per rectum, epistaxis, hemoptysis, hematuria, vaginal bleeding other than menstruation, conjunctival bleeding, intracranial bleeding

[1] Dopamine or Epinephrine or Norepinephrine or Vasopressin

[2] Reduction of urine output as observed by a clinician

[3] Definition of personality/behavior change: irritability, aggression, impulsivity, disinhibition, and emotional lability

[4] Matics TJ, Sanchez-Pinto LN. Adaptation and Validation of a Pediatric Sequential Organ Failure Assessment Score and Evaluation of the Sepsis-3 Definitions in Critically Ill Children. JAMA Pediatr. 2017;171(10):e172352. doi:10.1001/jamapediatrics.2017.2352

ALT = Alanine Aminotransferase, **AST** = Aspartate Aminotransferase, **FiO_2** = Fraction of inspired oxygen, **GCS** = Glasgow Coma Scale, **MAP** = Mean Arterial Pressure, **PaO_2** = Partial pressure of oxygen in arterial blood, **pSOFA** = Pediatric Sequential Organ Failure Assessment, **PT/INR** = Prothrombin Time / International Normalized Ratio, **SaO_2** = Arterial Oxygen Saturation, **ULN** = Upper limit normal