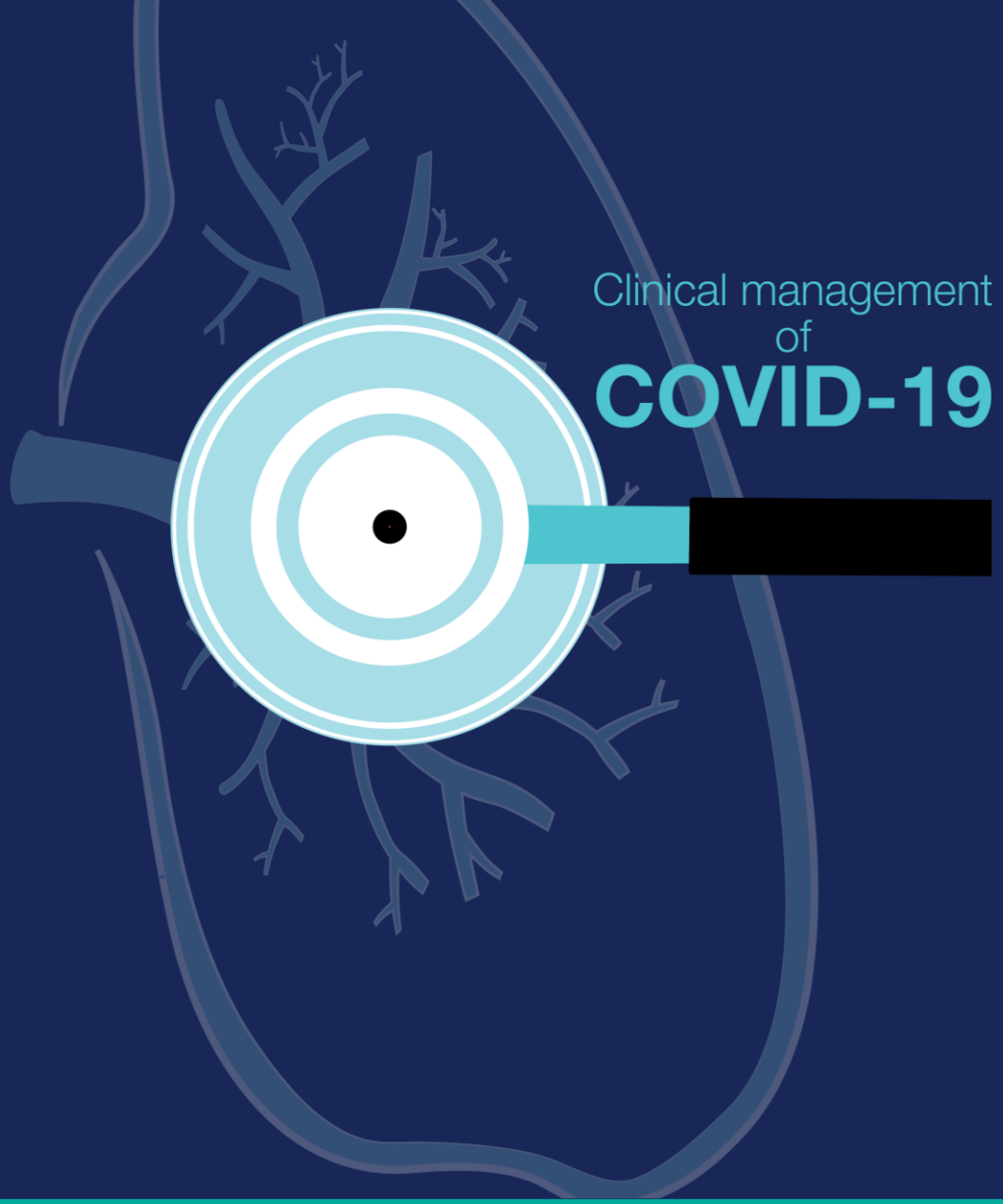
Management of critical **COVID-19**

Acute hypoxaemic respiratory failure and COVID-19: Recognize ARDS



World Health Organization

HEALTH EMERGENCIES programme

Learning objectives

At the end of this module, you will be able to:

- Describe the etiology and pathophysiology of hypoxaemia with COVID-19.
- Describe an algorithmic approach to escalation of oxygen therapy from supplemental oxygen to advanced respiratory support interventions.
- Recognize and diagnosis ARDS.

Definition of acute respiratory failure

- Respiratory system unable to meet the oxygen and ventilatory requirements of the patient.
- Commonly requires advanced respiratory support interventions.
- Types of acute respiratory failure include:
  - upper airway failure
  - hypoxaemic respiratory failure SpO_2 < 90 (PaO_2 ≤ 50-60 mm Hg) despite supplemental oxygen therapy (10–15 L/min)
  - hypercapnic $PaCO_2$ ≥ 50 mm Hg with pH < 7.35.

COVID-19: critically ill patients

Before vaccination, studies found that nearly 5% of patients with symptomatic COVID-19 have critical disease.

- 70% of these patients have ARDS
- 25% with acute organ injury (acute kidney injury [AKI], cardiac, liver or sepsis).

Mortality in patients with critical illness has varied substantially in different cohorts throughout the pandemic.

Early in the pandemic mortality amongst critically ill was described at 50-60% or higher. Now, mortality is described around 30-40%. Mortality in resource-limited settings remains high.

Mortality is impacted by various factors, including access to oxygen, and safe high-quality critical care services, which include trained, multidisciplinary staff and protocols.

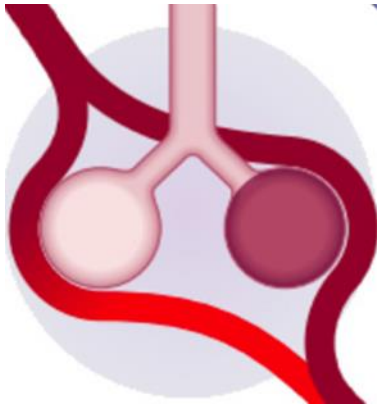
Example of data from patients admitted in African high-care or intensive care units (ACCOS)

- In a cohort of 3140 critically ill patients from 64 hospitals in 10 countries in Africa, in-hospital mortality within 30 days of hospital admission was 48.2%.
- Factors independently associated with mortality: age, HIV/AIDS, diabetes, chronic liver disease, chronic kidney disease, delay in admission due to a shortage of resources, quick sequential organ failure assessment score at admission, receipt of respiratory support or vasopressors.

African COVID-19 Critical Care Outcomes Study (ACCCOS) Investigators. Patient care and clinical outcomes for patients with COVID-19 infection admitted to African high-care or intensive care units: a multicentre, prospective, observational cohort study. Lancet. 2021;397(10288):1885-94

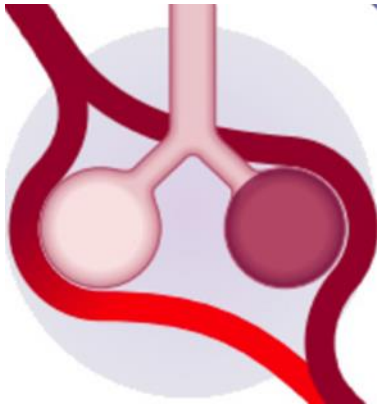
Basics of oxygenation

INSERT VIDEO HERE



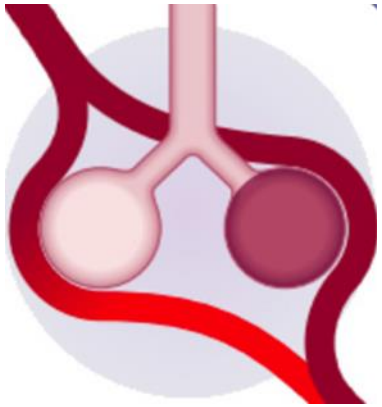
Causes of hypoxaemia

INSERT VIDEO HERE



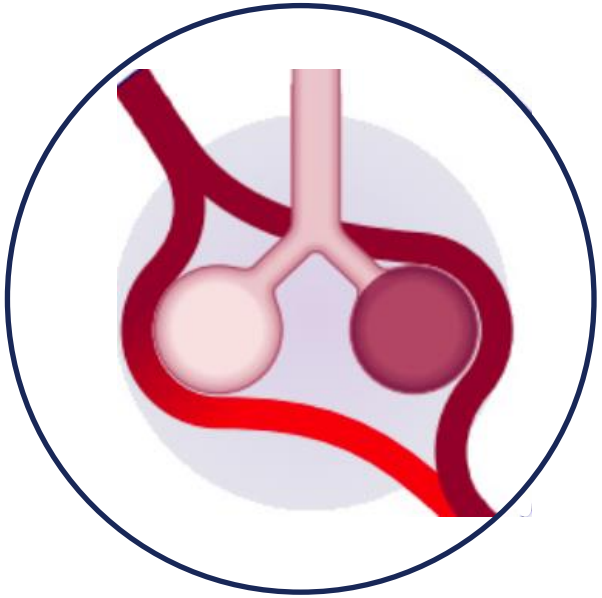
Causes of ARDS, including COVID-19

INSERT VIDEO HERE

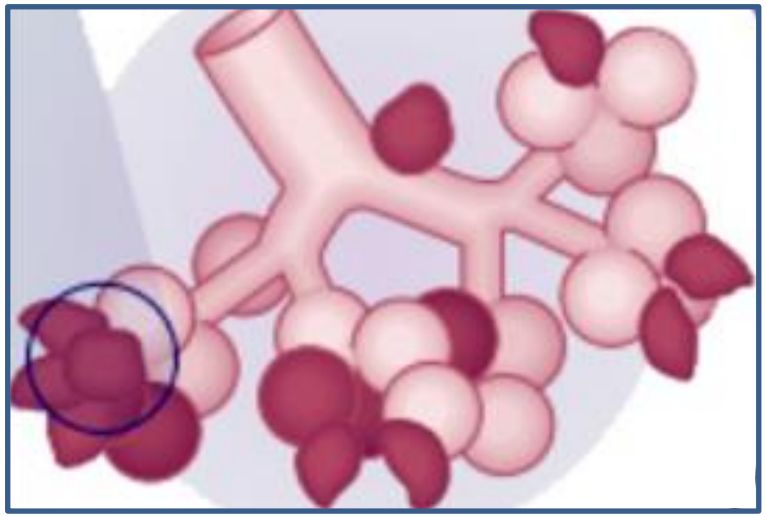


Intrapulmonary shunt

- Severe form of ventilation perfusion (V/Q) mismatch:
  - areas of lung perfused but not ventilated (V/Q < 1).



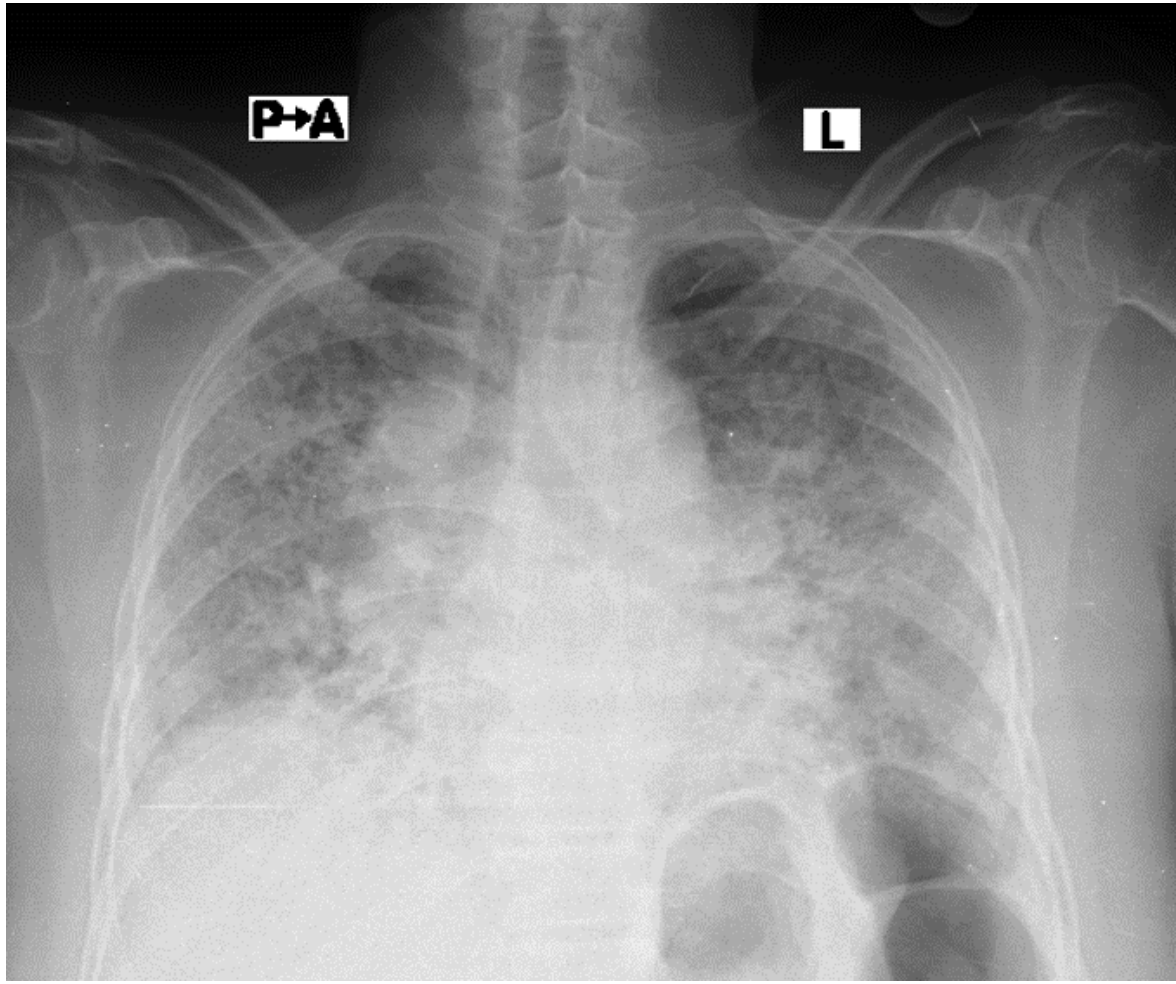
- Increasing FiO_2 does not readily improve hypoxaemia:
  - PEEP may recruit collapsed alveoli and improve shunt.



Clinical presentation of patients with ARDS

Rapid progression of severe respiratory distress:

- severe shortness of breath
- inability to complete full sentences
- tachypnoea
- use of accessory muscles of respiration
- cyanosis (very severe)
- persistent severe hypoxaemia
- refractory to supplemental oxygen therapy.



Definition of ARDS: adults

Berlin definition

Acute respiratory distress syndrome (ARDS)	
Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms.
Chest imaging	Bilateral opacities not fully explained by effusions, lobar/lung collapse, or nodules.
Origin of oedema	Respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echocardiography) to exclude hydrostatic oedema if no risk factor present.
Oxygenation	
Mild	200 mm Hg < PaO_2/FiO_2 ≤ 300 mm Hg with PEEP or CPAP ≥ 5 cm H_2O
Moderate	100 mm Hg < PaO_2/FiO_2 ≤ 200 mm Hg with PEEP ≥ 5 cm H_2O
Severe	PaO_2/FiO_2 ≤ 100 mm Hg with PEEP ≥ 5 cm H_2O

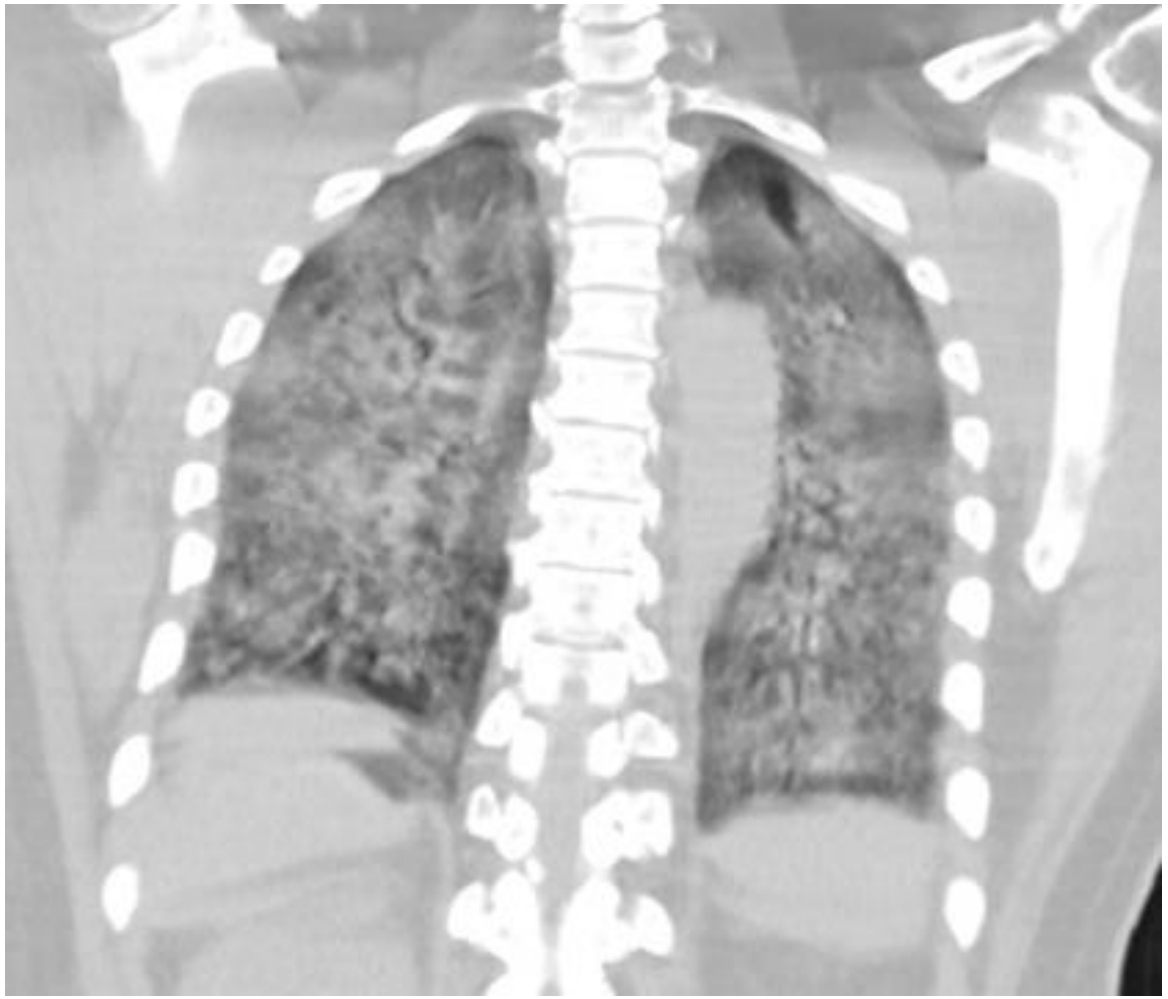
Kigali modifications of Berlin definition

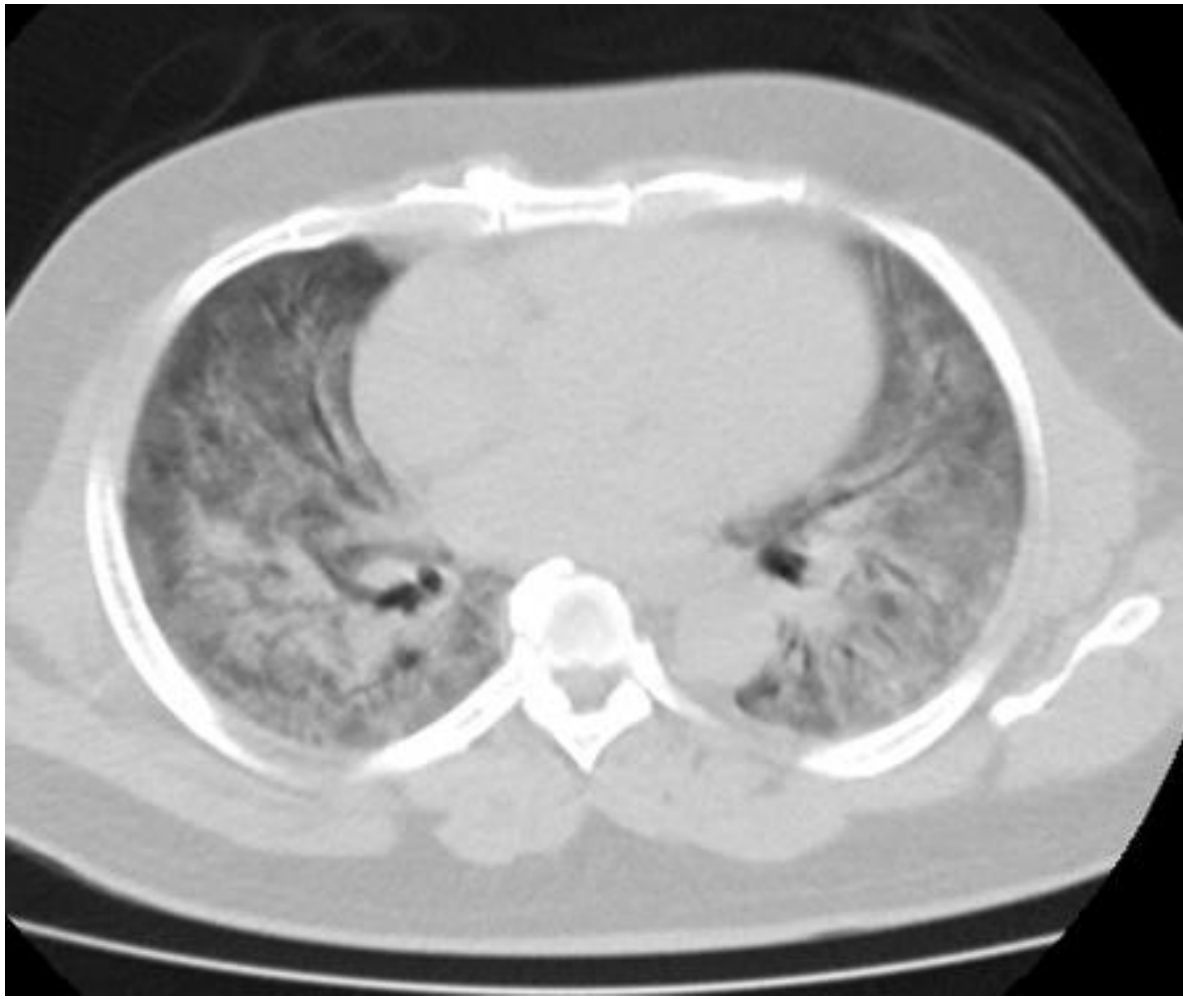
Acute respiratory distress syndrome (ARDS)	
Timing	Same
Chest imaging	Bilateral opacities not fully explained by effusions, lobar/lung collapse or nodules by chest radiograph or **ultrasound.**
Origin of oedema	Same
Oxygenation	SpO_2/FiO_2 ≤ 315 No PEEP or CPAP requirement

Challenge: Arterial blood gas analysis less commonly used in children and in resource-limited settings; SpO_2 can be used instead.

ARDS Definition Task Force, et al. Acute respiratory distress syndrome: the Berlin definition. JAMA. 2012;307(23):2526-33.
Riviello ED, et al. Hospital incidence and outcomes of ARDS using the Kigali modification of the Berlin definition. Am J Respir Crit Care Med. 2016;193(1):52-9.

Radiographic findings consistent with ARDS: bilateral opacities





Definition of ARDS: paediatrics

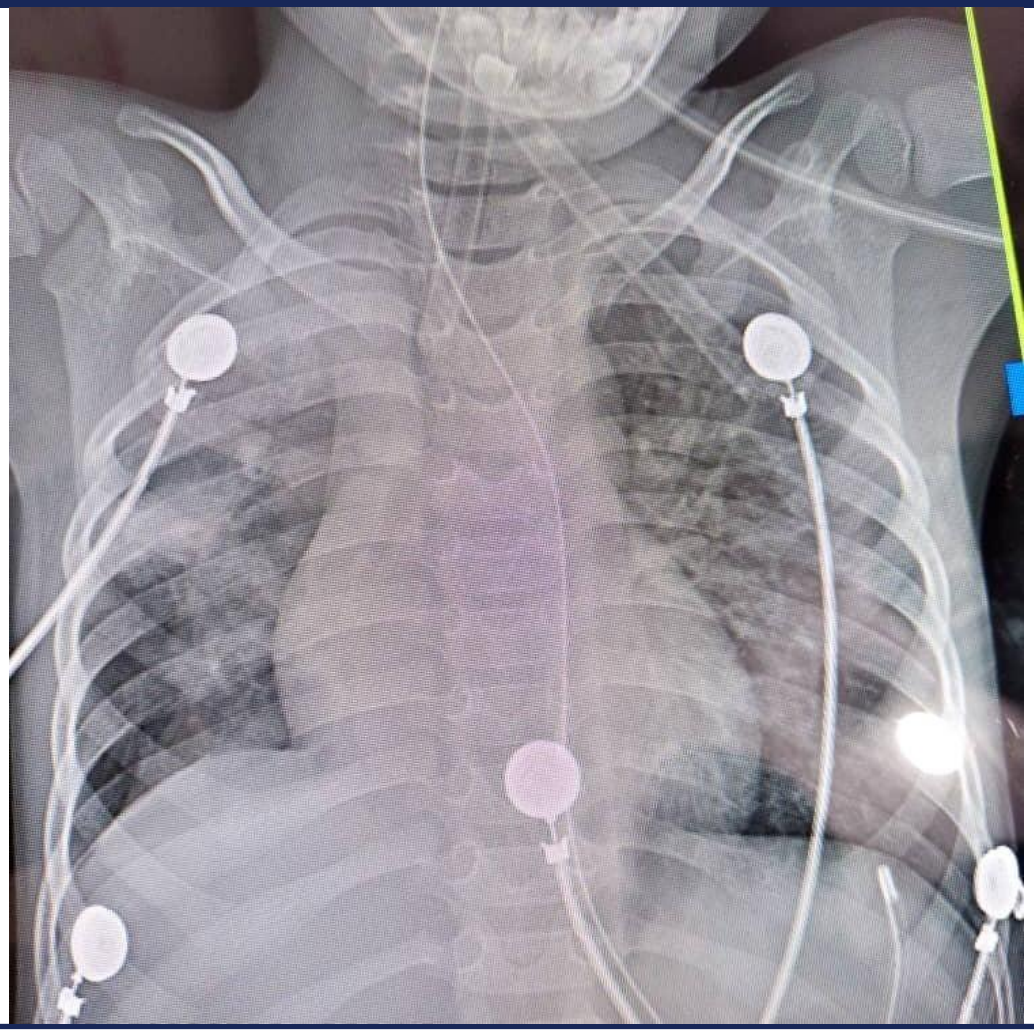
Age	Exclude patients with peri-natal related lung disease.	
Timing	Within 7 days of known clinical insult.	
Origin of oedema	Respiratory failure not fully explained by cardiac failure or fluid overload.	
Chest imaging	New infiltrate(s) consistent with acute pulmonary parenchymal disease.	
Oxygenation	Non-invasive mechanical ventilation PARDS (no severity stratification) Full face mask bi-level ventilation OR CPAP ≥ 5 cm H_2O PF ratio ≤ 300 SF ratio ≤ 264	Invasive mechanical ventilation Mild: 4 ≤ OI < 8 or 5 ≤ OSI < 7.5 Moderate: 8 ≤ OI < 16 or 7.5 ≤ OSI < 12.3 Severe: OI > 16 or OSI > 12.3

PF ratio: PaO_2:FiO_2 ratio. SF ratio: SpO_2:FiO_2 ratio.
OI: oxygenation index = (FiO_2 × mean airway pressure × 100)/PaO_2.
OSI: oxygen saturation index = (FiO_2 × mean airway pressure × 100)/SpO_2.

Challenge: Arterial blood gas analysis less commonly used in children; SpO_2 can be used instead.

Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: consensus recommendations from the Pediatric Acute Lung Injury Consensus Conference. Pediatr Crit Care Med. 2015;16(5):428-439.

Radiographic findings consistent with ARDS: bilateral opacities



WHO recommendations for COVID-19

WHO recommends prompt recognition of progressive acute hypoxaemic respiratory failure when a patient with respiratory distress is failing to respond to standard oxygen therapy and adequate preparation to provide advanced oxygen/ventilatory support.

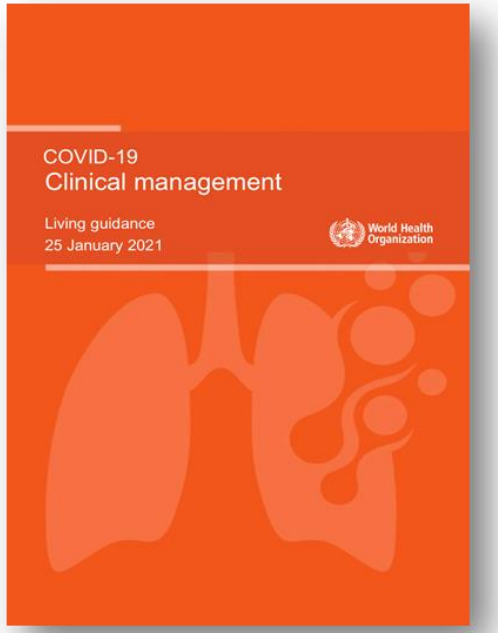
Hypoxaemic respiratory failure in ARDS commonly results from intrapulmonary ventilation-perfusion mismatch or shunt and usually requires mechanical ventilation.

At any time, if there are urgent or emergent indications for intubation, do not delay.

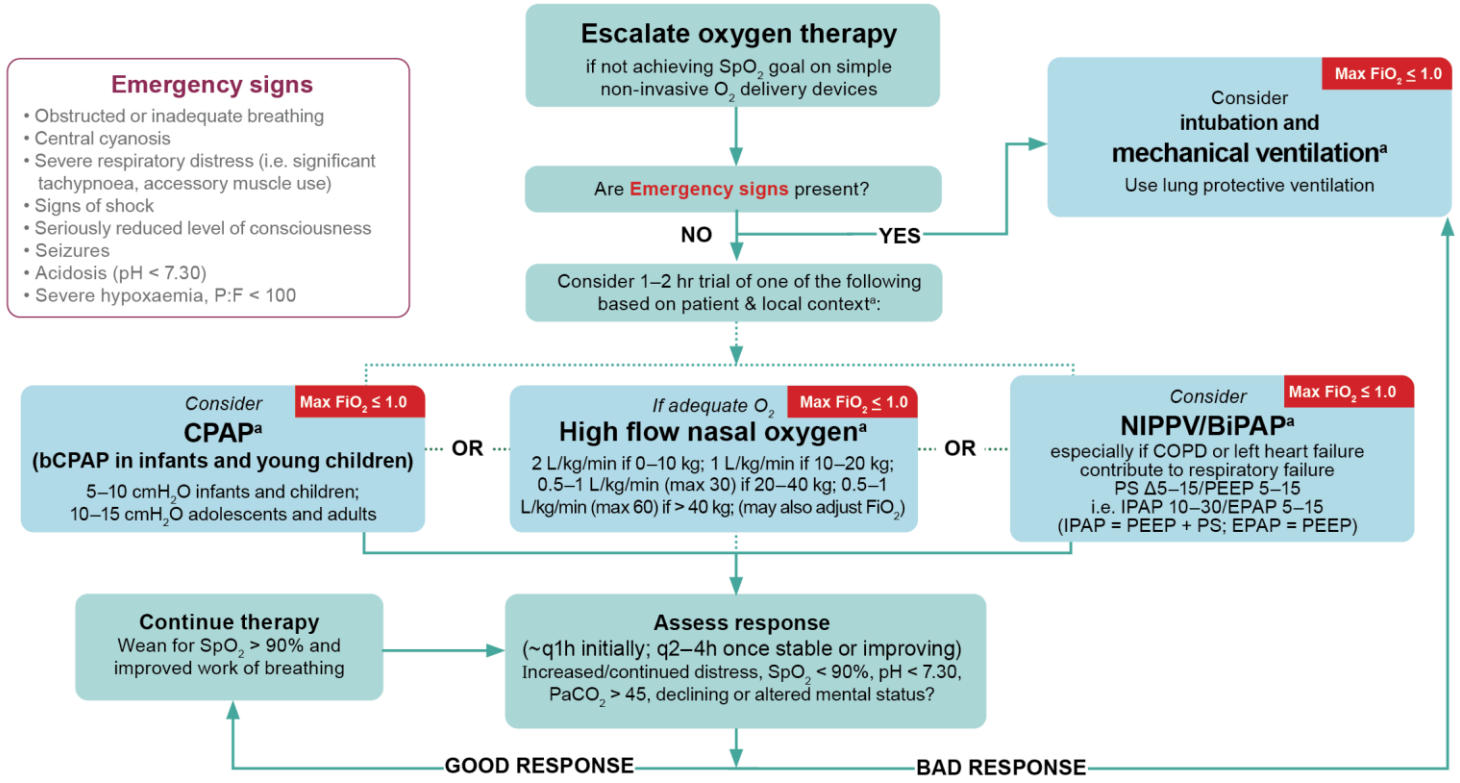
We recommend prompt recognition of progressive acute hypoxaemic respiratory failure when a patient with respiratory distress is failing to respond to standard oxygen therapy and adequate preparation to provide advanced oxygen/ventilatory support.

WHO suggests that patients with severe or critical COVID-19 with acute hypoxaemic respiratory failure that do not require emergent intubation be treated with HFNO, or CPAP or NIV (BiPAP) over standard oxygen therapy.

WHO recommends in patients with critical COVID-19 that require intubation, implementation of mechanical ventilation using lower tidal volumes (4–8 mL/kg predicted body weight [PBW]) and lower inspiratory pressures (plateau pressure < 30 cm H_2O).



If patient does not respond to escalating oxygen therapy, then consider advanced respiratory support interventions



[a] Selection of optimal delivery device should be based on local clinician's judgment and risk-benefit assessment tailored to the individual patient, global and local outcomes data, as well as local resources including O_2 supply, skill of personnel, availability of consumables, monitoring and therapeutic adjuncts, among other factors.
[b] Venturi/entrainment face masks deliver FiO_2 24–60%, depending on flow rate and device setup

LPM (litres per minute), **EPAP** (expiratory positive airway pressure), **PS** (pressure support), **COPD** (chronic obstructive pulmonary disease), **SpO_2** (oxygen saturation), **$PaCO_2$** (arterial partial pressure of carbon monoxide), **P:F** (ratio between arterial partial pressure of oxygen and the fraction of inspired oxygen - **FiO_2**), **CPAP** (continuous positive airway pressure), **bCPAP** (bubble CPAP), **NIPPV** (non-invasive positive pressure ventilation), **BiPAP** (bi-level positive airway pressure); Δ - change.

If patient is getting worse or the same, be systematic in your response:

- Is measurement correct?
- Is there a technical difficulty in delivering treatment?
- Is the patient getting appropriate therapy?
- Is there an alternate diagnosis?
- Is the treatment causing harm?

Choose best next intervention systematically:

- Does patient need urgent intubation and invasive ventilation?
- Is patient good candidate for non-invasive modalities?
- What advanced device is available to use?
- Is there a preference for a certain device over another? See Module 5 Part 1 for more details.

Reminder: always consider other causes of diffuse alveolar infiltrates

- Acute heart failure.
- Other acute pneumonias (not primary infection):
  - e.g. acute interstitial pneumonia, hypersensitivity pneumonitis, cryptogenic organizing pneumonia, eosinophilic pneumonia.
- Diffuse alveolar haemorrhage:
  - e.g. associated with autoimmune diseases.
- Malignancy:
  - e.g. bronchoalveolar cell carcinoma.

Key points

In patients with critical COVID-19, severe hypoxaemia related to ARDS is the leading cause of acute respiratory failure.

The most common pathophysiologic mechanism for hypoxaemic respiratory failure is ventilation/perfusion and, in its extreme, pulmonary shunt.

Thus, despite escalation of supplemental oxygen therapy, advanced respiratory support is crucial to deliver the accurate amount of oxygen at higher levels and with positive pressure ventilation.

Experience in using advanced respiratory support interventions is necessary to ensure safe and high-quality care is delivered to these patients.

WHO has conditional recommendations for the use of HFNO, CPAP and NIV for patients that have severe or critical COVID-19 and do not require emergent intubation.

Acknowledgements

Contributors

Dr Carlos Grijalva, Vanderbilt University, Nashville, USA
Dr Neill Adhikari, Sunnybrook Health Sciences Centre, Toronto, Canada
Dr Shevin Jacob, University of Washington, Seattle, USA
Dr Niranjan Bhat, Johns Hopkins University, Baltimore, USA
Dr Timothy Uyeki, Centers for Disease Control and Prevention, Atlanta, USA
Dr Steve Webb, Royal Perth Hospital, Australia
Dr Paula Lister, Great Ormond Street Hospital, London, UK
Dr Michael Matthay, University of California San Francisco, USA
Dr Christopher Seymour, University of Pittsburgh Medical Center, USA
Dr Derek Angus, University of Pittsburgh Medical Center, USA
Dr Niranjan "Tex" Kissoon, British Colombia Children's Hospital and Sunny Hill Health Centre for Children
Dr Stephen Playfor, Royal Manchester Children's Hospital, UK
Dr Leo Yee Sin, Tan Tock Seng Hospital, National Centre for Infectious Diseases, Singapore
Dr Janet V Diaz, WHO, Geneva, Switzerland
Dr John Adabie Appiah, WHO Consultant, Kumasi, Ghana
Vanessa Cramond, WHO, Geneva, Switzerland
Dr Marta Lado, WHO, Geneva, Switzerland
Dr Bharath Kumar Tirupakuzhi Vijayaraghavan, Consultant, WHO