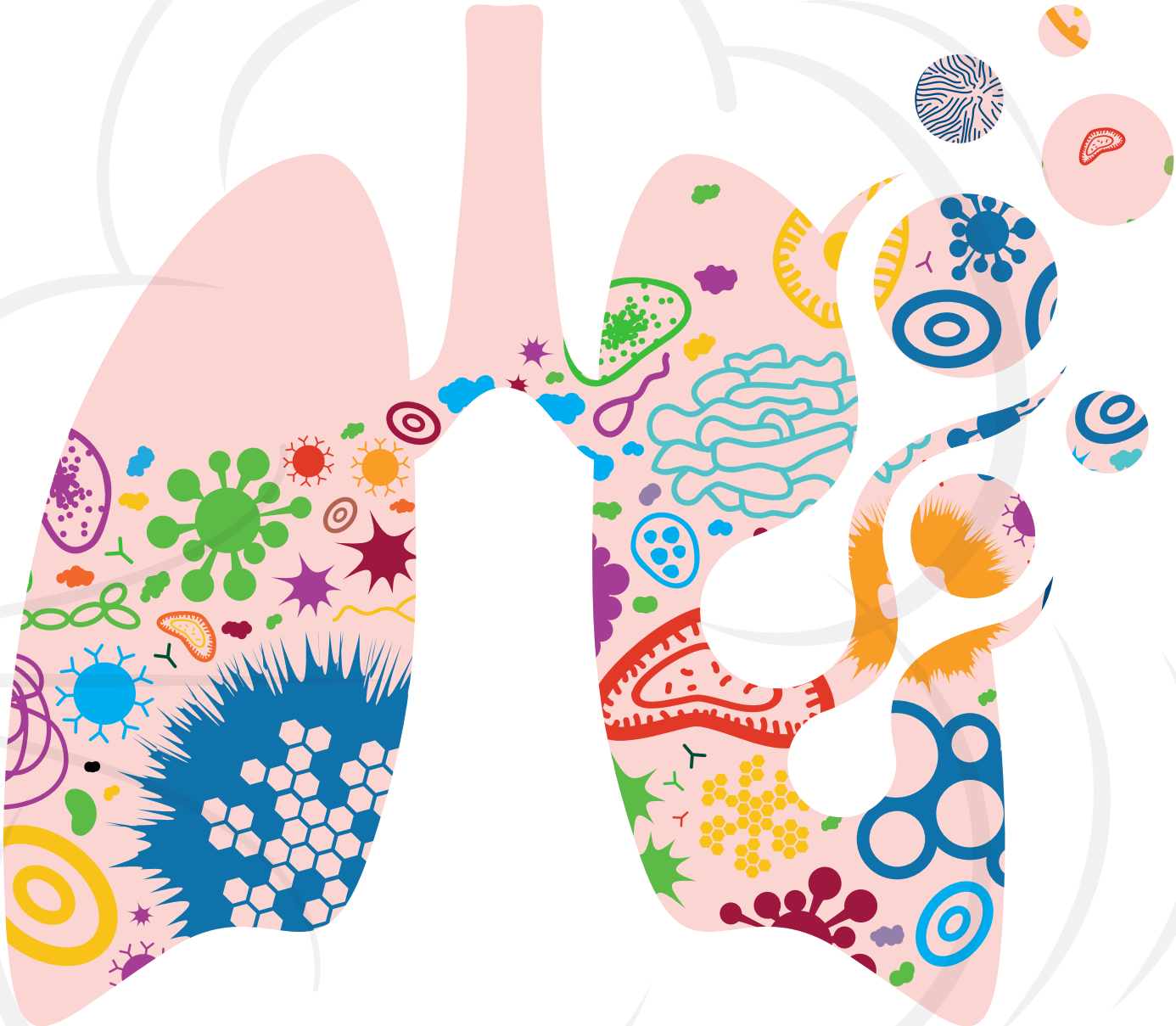
Clinical Care for Severe Acute Respiratory Infection

Toolkit

Update 2022



COVID-19 Adaptation

World Health Organization

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Clinical care for severe acute respiratory infection: toolkit, update 2022. COVID-19 adaptation

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Contents

Foreword

This toolkit is intended for clinicians working with adult and paediatric patients with severe forms of acute respiratory infection, including severe pneumonia, acute respiratory distress syndrome, sepsis and septic shock in low- and middle-income countries.

Its main objective is to provide some of the necessary tools that can be used to care for patients with respiratory conditions from hospital entry to hospital discharge. It is a hands-on practical guide for health care professionals involved in critical care management during the COVID-19 pandemic and outbreaks of influenza (seasonal or avian influenza), Middle East respiratory syndrome coronavirus (MERS-CoV) or other emerging respiratory viral epidemics.

The toolkit is structured by topic and follows the different levels of care required to manage the respiratory conditions. Each topic starts with a summary and follows with the tools; complementary references and resources are listed at the end of each section. The tools provide a framework for users and are to be adapted to local conditions.

The child icon identifies tools to be used and adapted when caring for paediatric patients.

The adult icon identifies tools to be used and adapted when caring for adult patients.

Tools without an icon can be used and adapted when caring for adult and paediatric patients.

Accompanying the toolkit there are several links and QR codes that clinicians can use to access materials for use in clinical settings.

Acknowledgements

In 2015 and 2016, a major revision of the toolkit and associated materials was conducted to include the most recent internationally peer-reviewed publications at that time. In 2020, the toolkit was adapted for the COVID-19 pandemic and, in 2022, the updated version was developed to add new evidence and improved content with new algorithms, infographics and tables to facilitate the management of patients with severe acute respiratory infections (SARI) (including specifications for influenza virus and SARS-CoV-2 infection).

Confidentiality undertakings and declaration of interests forms were collected and reviewed from all the collaborators for this toolkit and no conflict of interests were identified.

2022 version

This latest update of the toolkit, with practical and simplified materials to manage patients with SARI, is the product of the contribution of many individuals, under the coordination of the case management team from the WHO Health Emergency Programme and guidance from Janet Diaz. Major contributions were provided by Vanessa Cramond (WHO), Janet Diaz (WHO), Bharath Kumar (WHO), Krutika Kuppalli (WHO), Marta Lado (WHO), Michael Lipnick (Zuckerberg San Francisco General Hospital, United States of America [USA]), Kobus Preller (WHO), Pryanka Relan (WHO), Alejandra Velez Ruiz Gaitan (WHO) and Archana Seahwag (WHO consultant). Special thanks also go to our copyeditor Vivien Stone (Etchingham, United Kingdom of Great Britain and Northern Ireland [United Kingdom]) and for the design to Irene Lengui from L'IV Com Sàrl (Villars-sous-Yens, Switzerland).

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Abbreviations

ABCCs	airway, breathing, circulation, consciousness/convulsing
ABCDE	awakening, breathing coordination, delirium monitoring/management and early mobility (bundle)
ABG	air blood gases
AC	assist control
ACVPU	alert, confusion, verbal, pain, unresponsive
AGP	aerosol-generating procedure
Ag-RDT	antigen rapid diagnostic test
ALT	alanine aminotransferase
AMS	altered mental status
ANC	absolute neutrophil count
APRV	airway pressure release ventilation
ARDS	acute respiratory distress syndrome
ARI	acute respiratory infection
ASE	attention screening exam
AST	aspartate aminotransferase
AVPU	alert, verbal, pain, unresponsive (scale for assessing level of consciousness)
bCPAP	bubble continuous positive airway pressure
BEC	basic emergency care
BEE	basal energy expenditure
BID	twice a day
BiPAP	bilevel positive airway pressure
BMI	body mass index
BP	blood pressure
bpm	beats per minute
BPS	Behavioural Pain Scale
BS	British Standards
BSI	blood stream infection
BV filter	bacteria-virus filter
BVM	bag valve mask (Ambu)
CAM-ICU	confusion assessment method for the intensive care unit for adults
CAPA	coronavirus disease-associated pulmonary aspergillosis
CBC	cell blood count
CCB	calcium channel blockers
CCC	Clinical Care Committee
CDC	Centers for Disease Control and Prevention (United States of America)

CFR	case fatality ratio
CNS	central nervous system
CO	carbon monoxide/cardiac output
CO_2	carbon dioxide
COPD	chronic obstructive pulmonary disease
COVID-19	coronavirus disease
CPAP	continuous positive airway pressure
CPOT	Critical-Care Pain Observation Tool
CPP	cerebral perfusion pressure
CR	capillary refill
CRP	c-reactive protein
CPR	cardio-pulmonary resuscitation
CrAg	cryptococcal antigen
CRBSI	catheter-related blood stream infection
CSF	cerebrospinal fluid
CT	computerized tomography
CURB-65	confusion, urea, respiratory rate, blood pressure, 65 years (score)
CVC	central venous catheter
CVP	central venous pressure
CXR	chest X-ray
DBP	diastolic blood pressure
DKA	diabetic ketoacidosis
DM	diabetes mellitus
DVT	deep venous thrombosis
ECG	electrocardiogram
ECLS	extracorporeal life support
ECMO	extracorporeal membrane oxygenation
EIA	enzyme immunoassay
EIP	electromagnetic inductance plethysmography
EN	enteral nutrition
ENT	ear, nose and throat
EPAP	expiratory positive airway pressure
ESBL	extended spectrum beta-lactamase
ESI	emergency severity index
ESR	erythrocyte sedimentation rate
ETAT	emergency triage, assessment and treatment
$EtCO_2$	end-tidal carbon dioxide
ETT	endotracheal tube
EV-D68	Enterovirus D68
FFP2	filtering face pieces 92%

FiO_2	fraction of inspired oxygen
FLACC	face, legs, activity, cry, consolability
FM	face mask
GCS	Glasgow Coma Scale
GI	gastrointestinal
GMP	good manufacturing practices
Hb	haemoglobin
HBcAb	hepatitis B core antibody
HBsAg	hepatitis B surface antigen
HCAb	hepatitis C antibody
HCO_3	blood bicarbonate
HDL	high density lipoprotein
HEPA	high-efficiency particulate air (filter)
HFNC	high-flow nasal cannula
HFNO	high-flow nasal oxygen
HICS	hospital incident command system
HIV	human immunodeficiency virus
HME	heat moisture exchanger
HR	heart rate
ICP	intracranial pressure
ICRC	International Committee of the Red Cross
ICU	intensive care unit
IHR	International Health Regulations
IITT	Interagency Integrated Triage Tool
ILI	influenza-like illness
IL-6	Interleukin-6
IL-6 RB	Interleukin-6 receptor blockers
IM	intramuscular
IMAI	Integrated Management of Adolescent and Adult Illness
IMV	invasive mechanical ventilation
iNO	inhaled nitric oxide
IO	intraosseous
IPC	infection prevention and control
ISO	International Organization for Standardization
IU	international units
IV	intravenous
JVP	jugular venous pressure
LAT	latex agglutination test
LDH	lactate dehydrogenase
LDL	low density lipoprotein

LFA	lateral flow immunochromatographic assay
LOS	length of stay
LPM/L/min	litres per minute
LPV	lung protective ventilation
LR	lactated Ringer's
LRT	lower respiratory tract
MAP	mean arterial pressure
MDR	multidrug-resistant
MERS-CoV	Middle East respiratory syndrome coronavirus
MEWS	modified Early Warning Score
MI	myocardial infarction
MIS-C	multisystem inflammatory syndrome in children
MRI	magnetic resonance image
MRSA	methicillin-resistance *Staphylococcus aureus*
MSF	Médecins Sans Frontières
MV	minute ventilation
NAAT	nucleic acid amplification testing
NCD	noncommunicable disease
NEWS	National Early Warning Score (adults)
NG	nasogastric
NJ	nasojejunal
NIPPV	nasal intermittent positive pressure ventilation
NIV	non-invasive ventilation
NMB	neuromuscular blockers
NPA	nasopharyngeal airway
NRB	non-rebreather
NS	normal saline
NSAID	non-steroidal anti-inflammatory drugs
N95	filtering less 95%
OG	orogastric
OI	oxygenation index using SpO_2
OMD	Office of Medical Director
OPA	oropharyngeal airway
OSI	oxygen saturation index
PAD	pain, agitation and delirium
PALS	paediatric advanced life support
$PaCO_2$	partial pressure of carbon dioxide
PaO_2	partial pressure arterial oxygen
pARDS	paediatric acute respiratory distress respiratory
PBW	predicted body weight

pCAM-ICU	confusion assessment method for the intensive care unit for children
PCR	polymerase chain reaction
PDR	pressure driving
PEEP	positive end-expiratory pressure
PELOD	paediatric logistic organ dysfunction
PES	post-extubation stridor
PEWS	Paediatric Early Warning Score
P:F	ratio between arterial partial pressure of oxygen and the fraction of inspired oxygen
PIP	pressure inspiratory peak
PLR	passive leg raising
PLT	platelets
po	per os
POCT	point-of-care testing
PONV	post-operative nausea and vomiting
PPE	personal protective equipment
Pplat	plateau pressure
PPx	prophylaxis
PS	pressure support
PSA	pressure swing adsorption
PSI	pounds per square inch absolute
PSV	pressure support ventilation
PT	physical therapist
PTSD	post-traumatic stress disorder
QID	four times a day
qSOFA	quick sequential organ failure assessment
RASS	Richmond Agitation-Sedation Scale
RB	receptor blockers
RDT	Rapid diagnostic test
ROCM	rhino-orbito-cerebral mucormycosis
ROM	range of motion
RR	respiratory rate
RSBI	rapid shallow breathing index
RSI	rapid sequence intubation
RSV	respiratory syncytial virus
RT	respiratory therapist
RT-PCR	reverse transcription polymerase chain reaction
SARI	severe acute respiratory infection
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SAT	spontaneous awakening trial

SBP	systolic blood pressure
SBT	spontaneous breathing trial
SCI	spinal cord injury
$ScvO_2$	saturation of central venous blood
SD	standard deviation
S:F	ratio between saturation of oxygen and the fraction of inspired oxygen
SIMV	synchronized intermittent mandatory ventilation
SIRS	systemic inflammatory response syndrome
SmPC	Summary of Product Characteristics (European Union)
SOFA	sequential organ failure assessment
SOP	standard operating procedure
SpO_2	oxygen saturation
TB	tuberculosis
TBI	traumatic brain injury
TMJ	temporomandibular joint
TNF-inhibitors	tumoral necrosis factor inhibitors
TOF	train-of-four
TT	triage team
TV	tidal volume
ULN	upper limit of normal
URT	upper respiratory tract
US	ultrasound
USP	United States Prescribing Information
UTI	urinary tract infection
VA	veno-arterial
VAP	ventilator-associated pneumonia
VAS	Visual Analogue Scale
VOC	Variant of Concern
VOI	Variant of Interest
VPSA	vacuum pressure swing adsorption
VTE	venous thromboembolism
VTM	viral transport medium
VV	veno-venous
WBC	white cell count
WHO	World Health Organization

Executive summary

Description of updates and new tools in the SARI toolkit update 2022

1. EPIDEMIOLOGY OF SARI

- Updated epidemiological information on COVID-19 and other viral infections that produce SARI with pandemic potential.

UPDATED

1.1 Differential diagnosis of SARI
1.2 COVID-19 (SARS-CoV-2) fact sheet
1.3 Influenza virus fact sheet
1.4 Middle East respiratory syndrome coronavirus (MERS-CoV) fact sheet

NEW

1.5 Risk factors for severe disease: influenza vs COVID-19

2. SCREENING, TRIAGE, CLINICAL ASSESSMENT AND MANAGEMENT OF SARI

- Detailed description to differentiate screening and triage for patients with SARI and recommended tools.
- Updated WHO classification of severity in COVID-19 as part of triage.
- Update of algorithms for the management of ARI and SARI in the community and in health facilities with consideration of influenza and COVID-19.
- Inclusion of medevac protocols for transfer of patients with SARI due to COVID-19.

UPDATED

2.5 Decision-making algorithm for patients presenting with acute respiratory infection (ARI) (influenza or COVID-19 suspected or known to be circulating)
2.6 Decision-making algorithm for hospitalization of patients with pneumonia (influenza or COVID-19 known to be circulating)
2.7 Decision-making support tool for hospitalization and ICU admission for patients with SARI and severe pneumonia

NEW

2.1 Screening for SARI
2.2 Triage for SARI
2.4 Classification of severity in patients with COVID-19
2.10 Transfer of critically ill patients: air medevac for COVID-19 patients

3. INFECTION PREVENTION AND CONTROL FOR PATIENTS WITH SARI

- Updated measures for IPC for SARI and specifically for COVID-19.
- Updates on PPE for SARI with special consideration of COVID-19.

UPDATED

3.1 How to implement infection control measures for SARI
3.3 Personal protective equipment (PPE)
3.6 Hand hygiene
3.9 Checklist for aerosol-generating procedures

NEW

3.2 How to implement infection control measures for ARIs of potential concern
3.4 How to improve medical mask fit in health care settings
3.7 The 5 moments for hand hygiene in health care facilities
3.8 The "Three Cs": settings where transmission of the COVID-19 virus spreads more easily

4. MONITORING PATIENTS WITH ACUTE RESPIRATORY INFECTION

- Updates on the description of monitoring of patients with SARI: pulse oximetry, blood gases, capnometry.
- New table on monitoring patients with COVID-19 depending on disease severity and patient disposition (home, health facility, etc.).
- Bundle of recommendations for health care workers to care for and monitor patients with mild COVID-19 at home.

UPDATED

4.2 Pulse oximetry monitoring
4.3 Blood gas analysis monitoring
4.5 National Early Warning Score (NEWS) for adults

NEW

4.4 Capnometry (capnography)
4.7 Routine monitoring and care framework for COVID-19 patients
4.8 WHO Mild COVID-19 home care bundle for health care workers

5. DIAGNOSTIC TESTING FOR PATIENTS WITH ARI

- Specifications for diagnostic testing in COVID-19.
- Link to videos with explanation of different specimen collection systems (nasopharyngeal and pharyngeal swabs).

UPDATED

5.3 Specimen collection kit for upper respiratory tract specimens

NEW

5.1 Diagnostic testing for SARS-CoV-2 infection
5.2 Use of antigen-detection rapid diagnostic testing for SARS-CoV-2

6. OXYGEN THERAPY

- Definition of concepts related to oxygen therapy: oxygen concentration, fraction of inspired oxygen, saturation of oxygen.
- Indications for oxygen therapy.
- Explanation of the different oxygen delivery devices for low and high flows of oxygen.
- Specifications for oxygen therapy in children.
- Algorithms and flowcharts to understand how to titrate oxygen therapy according to need in neonates, children and adults.
- Awake prone positioning as an adjunctive therapy to oxygen in SARI/ARDS: indications and tips.
- Addition of links to oxygen calculators.
- Explanation and description of different oxygen supply sources: PSA, cryogenic liquid oxygen, concentrators, cylinders.
- Recommended template document to check oxygen therapy in patients in health care facilities.

UPDATED

6.9 Checklist to troubleshoot warning signs during oxygen therapy delivery

NEW

6.1 Indications for oxygen therapy
6.2 Memory aid: oxygen delivery devices
6.3 Memory aid: oxygen delivery in children
6.4 Algorithm to escalate respiratory support in adults and children with pneumonia
6.5 Flowchart on how to titrate oxygen in neonates
6.6 Flowchart on how to titrate oxygen in children
6.7 Flowchart on how to titrate oxygen in adults
6.8 Key tips on awake prone positioning
6.10 Oxygen supply calculations.
6.11 Memory aids: oxygen supply sources and distribution
6.12 Respiratory care order template for oxygen therapy

7. THERAPIES FOR SARI (COVID-19, INFLUENZA, BACTERIAL PNEUMONIA): ANTIMICROBIALS AND IMMUNOMODULATORS

- Update on antimicrobial therapies for SARI.
- Updated tables for antimicrobials in ARI adapted to influenza and COVID-19.
- Summary of COVID-19 therapeutics approved for use.
- Tables with descriptions of and administration instructions for COVID-19 therapeutics: corticosteroids, IL-6 RB; monoclonal antibodies.
- New tables on identification and management of super-infection with invasive fungal infections in patients with COVID-19.

NEW

7.1 Memory aid: treatment for acute respiratory infections according to severity (when COVID-19 and influenza are circulating)
7.2 COVID-19 and therapeutics
7.3 Memory aid: invasive fungal infections in patients with COVID-19

8. SEPSIS AND SEPTIC SHOCK

- Updated definitions for sepsis and septic shock in adults and children.
- Description of different tools related to sepsis (SOFA, PELOD-2).
- Tables and algorithms for management of sepsis and shock, including use of vasopressors.

UPDATED

8.6 Algorithms on initial resuscitation, and on fluid and vasoactive-inotrope management for children with septic shock

8.7 Guide to the use of vasopressors in septic shock for adults and children

NEW

8.1 Sepsis and septic shock definitions

8.2 Sequential Organ Failure Assessment (SOFA) score

8.3 Quick Sequential Organ Failure Assessment (qSOFA)

8.4 Paediatric Logistic Organ Dysfunction (PELOD-2) score

8.5 Algorithm on targeted resuscitation in adults with shock

9. ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

- Algorithms to escalate respiratory support in patients with ARDS including principles for intubation and mechanical ventilation in adults and children.
- New list of commonly used medicines in ventilated patients.
- Update of the protocol to deliver lung protective ventilation and description of different types of ventilation.
- New tools: respiratory pocket cards to support clinicians with the fundamentals of respiratory support.
- Checklist to help with proning techniques for patients with ARDS.
- New section to explain the locations for ventilator circuits, filters and humidifiers for patients with invasive and non-invasive ventilation.

UPDATED

9.1 Memory aid: diagnosis and classification of ARDS in adults

9.2 Memory aid: diagnosis and classification of pARDS in children

NEW

9.3 Advanced non-invasive oxygen delivery in ARDS: algorithm to escalate supportive respiratory therapy

9.4 Checklist for rapid sequence intubation procedure in adults and children

9.5 Considerations for intubation and mechanical ventilation in children

9.6 List of commonly used medicines and dosage in ICU with ventilated patients (adults, children)

9.7 Choice of induction agents in adults

9.8 Choice of induction agents in children

9.9 Protocol to deliver lung protective ventilation (LPV)

9.10 Memory aid: comparison of normal waveforms during volume and pressure-limited ventilation

9.11 Memory aid: recognizing and interpreting abnormal pressure and flow waveforms during volume control ventilation

9.12 Guide to distinguishing between the causes of high peak airway pressures: resistance versus compliance

9.13 Troubleshooting high peak airway pressures, low tidal volumes, desaturation or haemodynamic instability in ventilated patients

9.14 Respiratory care pocket card reference
9.15 Adult ventilation order set (ARDS)
9.16 Checklist for proning in severe ARDS
9.17 Ventilator circuit types, filter and humidifier locations for SARI

10. MANAGE PAIN, SEDATION AND DELIRIUM

- Revised formatting of tables, but no new tools.

11. LIBERATION FROM INVASIVE MECHANICAL VENTILATION

- Updates in the algorithm for daily sedation interruption and daily spontaneous breathing trial, and the cuff leak test protocol.

NEW

11.1 Algorithm for daily sedation interruption and daily spontaneous breathing trial (SBT)
11.2 How to perform a cuff leak test
11.3 Respiratory care pocket card reference
11.4 Spontaneous breathing trial (SBT) order set

12. BEST PRACTICES TO PREVENT COMPLICATIONS

- Update on identification and management of complications in critical patients (ICU): tables.
- Addition of thromboembolic prophylaxis in COVID-19.

NEW

12.1 Interventions to prevent complications in hospitalized and critically ill patients with COVID-19
12.8 Thromboembolic prophylaxis in COVID-19

13. QUALITY IN CRITICAL CARE

- Revised formatting of the summary of principles for quality in critical care.
- New checklists for ICU daily best practices.

NEW

13.1 Checklist for ICU daily best practices

14. ETHICAL CONSIDERATIONS

- Updates in tables related to key ethical principles, triage decision process flow and algorithm for hospital scarce resources decision-making.

NEW

14.1 Ethical values and principles
14.2 Triage decision process flow
14.3 Hospital scarce resource decision-making

1 Epidemiology of SARI

1 Epidemiology of SARI

Summary

A global case definition for severe acute respiratory infection (SARI) for surveillance purposes, applicable to all age groups, was first published by the World Health Organization (WHO) in 2011. The current WHO case definition is:

> **Patients with acute respiratory infection who have history of fever (or measured fever of ≥ 38 °C), cough and onset within the last 10 days (symptoms within 10 days) and require hospitalization.**

The differential diagnoses for SARI include a wide spectrum of community-acquired pathogens, including respiratory viruses, bacteria and other less common micro-organisms. The ranking of differential diagnoses will vary by host factors (e.g. age, presence of chronic conditions, travel history, vaccination), environmental factors (e.g. geographic location, vectors), epidemiologic factors (e.g. the prevalence of the pathogen in the community) and pathogen factors (e.g. tropism for lungs). The differential diagnosis for SARI should also include endemic infections, such as malaria, arboviruses (dengue, chikungunya, yellow fever), tuberculosis (TB), or even human immunodeficiency virus (HIV) related opportunistic infections that can produce severe acute respiratory infections. See Tool 1.1 for a comprehensive differential diagnosis list that can be adapted to local settings.

Clinicians should be aware that in addition to the common viral and bacterial pathogens, an emerging respiratory virus may result in SARI and lead to a public health emergency of international concern. For example, influenza virus types A and B is a common respiratory virus that circulates worldwide and can cause seasonal influenza outbreaks and epidemics. Most people recover from fever and other symptoms within a week without requiring medical attention; however, hospitalization and death may mainly among high-risk groups. Worldwide, these annual epidemics are estimated to result in 3 to 5 million cases of severe illness, and 290 000 to 650 000 respiratory deaths. This estimate does not take in account deaths from other diseases such as cardiovascular disease, which can be influenza-related. Emerging respiratory viruses include: zoonotic influenza viruses, such as avian influenza, and coronaviruses, such as MERS-CoV and SARS-CoV-2. In addition, a new subtype of influenza A virus may also have pandemic potential. See Tools 1.2–1.4 for comprehensive information on these respiratory viruses.

Tools

1.1 Differential diagnosis of SARI
1.2 COVID-19 (SARS-CoV-2) fact sheet
1.3 Influenza virus fact sheet
1.4 Middle East respiratory syndrome coronavirus (MERS-CoV) fact sheet
1.5 Risk factors for severe disease: influenza vs COVID-19

1.1 Differential diagnosis of SARI

It is important to develop a differential diagnosis rapidly for all patients presenting with SARI. This will guide health care workers in the initial infection prevention and control (IPC), diagnostic and treatment measures.

The rate of co-infection among these pathogens is unknown. Therefore, a positive diagnostic test for another infection does not exclude the need for other micro-organism testing.

VIRAL PATHOGENS

Common viral pathogens

- Respiratory syncytial virus (RSV)
- Parainfluenza virus
- Rhinoviruses
- Adenovirus, enterovirus (EV-D68)
- Human metapneumovirus
- Bocavirus
- Seasonal influenza, known subtype

Less common viral pathogens

- Varicella zoster
- Measles
- Hantavirus

Virus that may constitute a public health emergency of international concern

- SARS
- SARS-CoV-2
- MERS
- New subtypes of influenza
- Other zoonotic viral infections

If immunosuppressed (i.e. people living with HIV)

- Cytomegalovirus,
- Herpes simplex viruses

BACTERIAL PATHOGENS

Most common bacterial pathogens

- *Streptococcus pneumoniae*
- *Hemophilus influenzae*
- *Moraxella catarrhalis*
- *Legionella pneumophila, non-pneumophila Legionella*
- *Chlamydia pneumonia*
- *Mycoplasma pneumoniae*
- *Klebsiella pneumonia*
- *Staphylococcus aureus*

Less common, unless at risk or in high-prevalence geographic area

- *Mycobacterium tuberculosis*
- *Burkholderia pseudomallei*
- Rickettsial infections
- *Coxiella burnetti* (Q fever)
- *Leptospira* spp.
- *Chlamydia psittaci*
- *Bortedella pertussis*
- *Salmonella* sp.

Resistant pathogens

Risk factors for multidrug-resistant pathogens: intravenous antimicrobial therapy within < 90 days.
Resistant pathogens include:

- Methicillin-resistant *S. aureus* (MRSA)
- Non-fermenters such as *Pseudomonas aeruginosa, Acinetobacter baumannii*
- Extended spectrum beta-lactamase (ESBL) producers such as *E. coli, Klebsiella, Enterobacter*

OTHER ENDEMIC INFECTIONS

Potential endemic infections

Can co-exist with respiratory infections in endemic areas.

- Malaria, dengue, chikungunya, tuberculosis, HIV

1.2 COVID-19 (SARS-CoV-2) fact sheet

COVID-19

Introduction

- The novel coronavirus SARS-CoV-2 is similar genetically to the SARS coronavirus.
- The first cases were reported in December 2019 in China, with SARS-CoV-2 identified in early January 2020.
- Since then, cases have been reported in virtually all countries, and the disease declared as a Public Health Emergency of International Concern by WHO on 30 January 2020 and described as a pandemic in March 2020.
- The latest epidemiology and case counts are available in the COVID-19 WHO situation reports: Coronavirus disease (COVID-19) weekly epidemiological and operational updates ().
- The latest technical guidance can be found in: Country & Technical Guidance – Coronavirus disease (COVID-19) ().

Transmission

- The SARS-CoV-2 virus is a zoonotic virus. The intermediary animal host and source of the virus has not yet been identified but is currently under study.
- The SARS-CoV-2 virus is spread mainly via inhalation of respiratory droplets coming from coughing or sneezing of an infected person to a person who is in close contact (within 1 m). Those respiratory droplets can reach or can be introduced in the mouth, nose or eyes of a susceptible person and can result in infection. Crowded closed indoor spaces with poor ventilation can be favourable environments for the virus to spread easily among people.
- Additionally, indirect contact transmission involving contact of a susceptible host with a contaminated object or surface (fomite transmission) may also be possible.
- Nosocomial transmission can occur where there are inadequate IPC measures, including personal protective equipment (PPE) to be used during close contact with infected individuals.
- Aerosol-generating procedures (AGP), such as open suctioning of airways, sputum induction, cardiopulmonary resuscitation, endotracheal intubation and extubation, non-invasive ventilation (e.g. bilevel positive airway pressure [BiPAP], continuous positive airway pressure [CPAP]), bronchoscopy, and manual ventilation, may present additional risk in health care settings for transmission and infection of health care workers, requiring higher levels of respiratory protection.
- The median incubation period is about 5–6 days (range: 1–14 days). The most infectious period is 1–2 days before symptoms appear. The infectious period can last up to 5–9 days for mild patients, up to 3 weeks for severe patients, and immunosuppressed patients can be infectious for many months, with high virus levels being detected in the upper respiratory tract early in the disease course or pre-symptomatic phase.
- SARS-CoV-2, as other viruses, may present changes and/or mutations. There have been emergences of several variants of the virus that could pose an increased risk to global public health which prompted the characterization of specific Variants of Interest (VOI) and Variants of Concern (VOC). For the latest updated list of variants see: WHO Tracking SARS-CoV-2 variants ().

Clinical features

- The most common clinical features include: fever, cough, malaise and shortness of breath and other symptoms included in the case definition: general weakness/fatigue, headache, myalgia, sore throat, coryza, anorexia/nausea/vomiting, diarrhoea, altered mental status. In children poor feeding, fussiness, vomiting and stiff neck can also be possible symptoms. The loss of taste and smell is a less common symptom, but seems to be quite specific to, although not exclusively associated with, COVID-19 compared with influenza.
- Clinical features range from mild, moderate ARI and, in some cases, SARI requiring oxygen, and critical disease with respiratory failure, sepsis, septic shock and ARDS with progressive multi-organ failure, thromboembolic disease, requiring intensive care interventions such as non-invasive or invasive mechanical ventilation, dialysis or vasopressors. Overall, the case fatality ratio (CFR) is around 1–2% of all infected patients. For more details per region and country, see the WHO Coronavirus (COVD-19) Dashboard ().
- According to data, approximately 80% of symptomatic patients will have mild (40%) to moderate (40%) disease and recover. Moderate disease may include a mild form of pneumonia. Approximately 15% of mild/moderate cases progress to severe disease and an additional approximately 5% become critically ill; 20% of cases will remain asymptomatic. With COVID-19 vaccination, the proportion of patients with severe disease and mortality is decreasing. VOC may also impact the disease severity in COVID-19, see WHO Tracking SARS-CoV-2 variants ().

Clinical features continued

- Severe/critical disease (20%) has a higher CFR and has been seen in older persons (> 60 years old) and those with chronic medical conditions, including noncommunicable diseases (NCDs) (e.g. hypertension, cardiac disease, diabetes, chronic lung disease, cerebrovascular disease, dementia, mental health disorders, chronic kidney disease) and some immunosuppressed conditions (e.g. cancer and HIV), obesity, smoking, pregnant or recently pregnant: women > 35 years old, obesity, with chronic medical conditions or pregnancy specific disorders (e.g. gestational diabetes and pre-eclampsia/eclampsia) and unvaccinated against COVID-19; with clinical deterioration occurring at around day 7 of illness.
- Complications such as thromboembolism, myocardial injury, arrhythmias, cardiomyopathy, heart failure and encephalopathy have been reported in severe/critical cases.
- Children appear to mainly have asymptomatic or mild disease, but there are reports of a small number of cases with multisystem inflammatory syndrome in children (MIS-C).
- Bilateral infiltrates and ground-glass changes are the most commonly reported signs on chest X-ray and CT imaging, with lymphopaenia frequently seen in blood tests and elevation of inflammatory markers (e.g. C-reactive protein [CRP], lactate dehydrogenase [LDH], ferritin, erythrocyte sedimentation rate [ESR], interleukin 6 [IL-6], D-dimer).

Prevention

Infection prevention and control and public health interventions

- For all individuals, proper hand washing techniques, respiratory hygiene, social distancing and limiting contact with symptomatic individuals are the main preventive measures (droplet and contact precautions). Universal masking and targeted continuous use of medical masks are recommended in specific transmission scenarios such as crowded indoor spaces with poor ventilation and inability to maintain the correct social distancing; WHO current guidance is provided in *Mask use in the context of COVID-19* ( ) ( ).
- In health care settings, enhanced IPC measures are required when caring for patients with suspected, probable or confirmed COVID-19; including appropriate use of PPE (gown, gloves, medical mask, eye protection), and addition of airborne precautions (N95/FFP2/3) when performing AGP. See also *WHO recommendations on mask use by health workers, in light of the Omicron variant of concern* ( ).

Vaccines and medications for prophylaxis

- Vaccines to protect from COVID-19 are in available and clinical trials and further developments are ongoing. See COVID-19 vaccines ( ) for the most up-to-date information.
- Prophylaxis: see *WHO Living guideline: drugs to prevent COVID-19* ( ) for the most up-to-date recommendations for the use of drugs to prevent COVID-19.

Treatment

- Early recognition of those patients with (or at risk of) severe disease, and access to critical care interventions are key (*Living guidance for clinical management of COVID-19*) ( ).
- The most updated recommended therapeutics for COVID-19 can be found in *Therapeutics and COVID-19: living guideline* ( ).
- Diagnosis and treatment of co-infections like respiratory viral, secondary bacterial infections or endemic diseases such as malaria or tuberculosis, which can cause febrile illness are important.
- For symptomatic patients: discharge from hospitals and/or removal of isolation measures can be done 10 days after symptom onset, plus at least 3 days without symptoms (without fever and respiratory symptoms).
- For asymptomatic patients: removal of isolation measures can be done 10 days after positive test for SARS-CoV-2.

1.3 Influenza virus fact sheet

SEASONAL INFLUENZA VIRUSES

Introduction

- Circulates worldwide causing outbreaks and seasonal epidemics.
- Some immunity already in the population, depending on age and vaccination status.
- Populations at higher risks of severe disease are patients > 65 years old, with chronic conditions: cardiac, respiratory, endocrine, neurological, renal, including metabolic and haematologic disorders, chronic liver disease and other immunosuppressed conditions, as well as children < 59 months, pregnant and post-partum period women.
- Health care workers are at high risk of acquiring influenza virus infection due to increased exposure to patients and risk further spread particularly to vulnerable individuals.
- For updated information on influenza see WHO Influenza (☝) and *Guidelines for the clinical management of severe illness from influenza virus infections* (☝).

Human infection

Seasonal influenza epidemics are caused by influenza A and B viruses.

- These circulate worldwide and spread easily from person to person.
- Can cause annual epidemics that peak during winter in temperate climates or may circulate year-round in tropical regions.
- Epidemics can result in high levels of work/school absenteeism and productivity losses. Clinics and hospitals can be overwhelmed during peak illness periods worldwide, these annual epidemics are estimated to result in about 3 to 5 million cases of severe illness, and about 290 000 to 650 000 deaths from respiratory causes.
- In high-income countries most deaths associated with influenza occur among people age 65 or older.
- The effects of seasonal influenza epidemics in developing countries are not fully known, but research estimates that 99% of deaths in children under 5 years of age with influenza-related lower respiratory tract infections are found in low-resource countries.

Transmission

- Influenza viruses are spread mainly via inhalation of respiratory droplets coming from coughing or sneezing of an infected person to a person who is in close contact (within 1 m). Those respiratory droplets can reach the mouth, nose or eyes of a susceptible person and can result in infection.
- Indirect contact transmission involving contact of a susceptible host with a contaminated object or surface (fomite transmission) may also be possible.
- The incubation period is about 2 days. Patients can be infectious 1 day before symptoms appear and up to 1 day after symptoms go away.
- Children shed virus longer than adults.
- The estimated attack rate is 5–20% and higher in densely populated communities and schools.

Clinical features

- Uncomplicated ARI with high fever, cough and viral syndrome that commonly lasts for 1 week and does not require medical attention.
- Can also cause severe illness with pneumonia, sepsis, ARDS; seen more in patients at high risk (children < 59 months of age, older patients, pregnant woman and those with chronic medical conditions).

Prevention

Infection prevention and control and public health interventions

- For all individuals, proper hand washing techniques, respiratory hygiene, social distancing and limiting contact with symptomatic individuals are the main preventive measures (droplet and contact precautions).
- In health care settings, enhanced IPC measures are required when caring for patients with suspected, probable or confirmed influenza infection; including appropriate use of PPE (gown, gloves, medical mask, eye protection) with the addition of airborne precautions (N95/FFP2/3) when performing AGP.

Vaccines and medications for prophylaxis

- Annual vaccination is recommended for pregnant women, children aged 6–59 months, older age (≥ 65 years), individuals with chronic medical conditions and health care workers.
- No medication for prevention has been recommended.

Treatment

- Neuraminidase inhibitors (i.e. oseltamivir) are active against all circulating strains of seasonal influenza and should be given as soon as possible to patients with SARI, and those high-risk patients with uncomplicated ARI. See *Guidelines for the clinical management of severe illness from influenza virus infections* ( ).

ZOONOTIC INFLUENZA

Introduction

- Depending on the origin host, humans can be infected with avian, swine and other zoonotic influenza viruses: such as avian influenza virus subtypes A(H5N1), A(H7N9) and A(H9N2), and swine influenza virus subtypes A(H1N1), A(H1N2) and A(H3N2).
- Human infections are rare and primarily acquired through direct contact with infected animals or contaminated environments; all these animal influenza type A viruses are distinct from human influenza viruses and have not acquired the ability of sustained transmission among humans.
- Aquatic birds are the primary natural reservoir for most subtypes of influenza A viruses. Most cause asymptomatic or mild infection in birds, where the range of symptoms depends on the virus properties.
- Human infections with these viruses need to be monitored closely. As the extent of virus circulation in animals is often not clear, epidemiological and virological surveillance and follow up of suspected human cases should remain high. Guidance on investigation of non-seasonal influenza and other emerging acute respiratory diseases can be found on the WHO website: Global Influenza Surveillance and Response System ( ).

Transmission

- Most human cases of influenza A(H5N1) and A(H7N9) virus infection have been associated with direct or indirect contact with infected live or dead poultry.
- Human infections with avian and other zoonotic influenza viruses, though rare, have been reported sporadically.
- Human infections are primarily acquired through direct contact with infected animals or contaminated environments, but do not result in efficient transmission of these viruses between people.

Clinical features

- Avian, swine and other zoonotic influenza virus infections in humans may cause disease ranging from mild upper respiratory tract infection (fever and cough), early sputum production and rapid progression to severe pneumonia, sepsis with shock, ARDS, and even death. Conjunctivitis, gastrointestinal symptoms, encephalitis and encephalopathy have also been reported to varying degrees depending on subtype.

Prevention

Infection prevention and control and public health interventions

- Proper hand washing techniques, respiratory hygiene, social distancing and limiting contact with symptomatic individuals are the main preventive measures (droplet and contact precautions).
- Disease control in animals, avoid direct and prolonged exposure to infected animals.
- In health care settings, enhanced IPC measures are required when caring for patients with suspected, probable or confirmed zoonotic influenza; including appropriate use of PPE (gown, gloves, medical mask, eye protection), and the addition of airborne precautions (N95/FFP2/3) when performing AGP.

Vaccines and medications for prophylaxis

- Not available.

Treatment

- Early treatment with neuraminidase inhibitor, as soon as possible. See *Guidelines for the clinical management of severe illness from influenza virus infections* ().

NEW INFLUENZA VIRUSES WITH PANDEMIC POTENTIAL

- Any new influenza virus is considered to have the potential to cause a pandemic if:
  - the virus has demonstrated the capacity to infect a human; and
  - the haemagglutinin (HA) gene or protein is not a variant or mutated form of those – A(H1) or A(H3) – circulating widely in the human population.
- A pandemic influenza virus may arise when genes from animal and human influenza viruses mix together to create a human-animal influenza reassortant virus (genetic reassortment); or genes in an animal influenza virus change allowing the virus to infect humans and transmit easily among them (genetic mutation).
- It is mandatory to notify a human influenza case caused by a new subtype to WHO, under the International Health Regulations (IHR) (2005). Because it is a new virus to which people have not been exposed, the population has no or little immunity and the virus is able to spread quickly between people and cause illness.
- Although we start with the assumption that the risk groups for infection and severe outcome are the same as in seasonal influenza, there might be differences. Historical knowledge from the 1918 and 2009 pandemics indicates that healthy, young adults can be disproportionately and more severely affected.
- Pandemic influenza might present differently from seasonal influenza and symptoms may be more severe and complications more frequent.

1.4 Middle East respiratory syndrome coronavirus (MERS-CoV) fact sheet

MERS-CoV

Introduction

- Type of coronavirus whose primary reservoir is dromedary camels, with origination in bats (similar strains isolated from camels in Egypt, Oman, Qatar and Saudi Arabia).
- First case reported in March 2012 (Saudi Arabia).
- Since then, cases have been reported in 27 countries. 83% of the cases have been in Saudi Arabia. There was a large outbreak in the Republic of Korea in 2015; and moderate numbers have occurred in Jordan, Oman, Qatar and the United Arab Emirates.
- To date, there are 2578 laboratory-confirmed cases and 888 deaths (October 2021).

Transmission

- Camel-human transmission route is unknown.
- Human-human transmission has been limited to health care settings when inadequate IPC measures occurred during close contact with infected individual (nosocomial transmission).
- No sustained community transmission reported.

Clinical features

- Ranges from asymptomatic to mild ARI: fever, cough and shortness of breath. Pneumonia is common, but not always present. Gastrointestinal symptoms, including diarrhoea, have also been reported. In some cases, it can present as SARI with progressive organ failure, sepsis and ARDS.
- Some laboratory-confirmed cases of MERS-CoV infection have been reported as asymptomatic, following aggressive contact tracing of a laboratory-confirmed case.
- Approximately 35% of reported patients with MERS-CoV infection died.
- More severe disease in older people, immunosuppressed and those with chronic medical conditions.

Prevention

Infection prevention and control and public health interventions

- Proper hand washing techniques, respiratory hygiene, social distancing and limiting contact with symptomatic individuals are the main preventive measures (droplet and contact precautions).
- When visiting areas where camels are present, use proper hand washing techniques.
- Avoid contact with sick camels.
- Avoid eating raw meat or unpasteurized milk.
- In health care settings, enhanced IPC measures are required when caring for patients with suspected, probable or confirmed MERS-CoV; including appropriate use of PPE (gown, gloves, medical mask, eye protection), and the addition of airborne precautions (N95/FFP2/3) when performing AGP.

Vaccines and medications for prophylaxis

- Not available.

Treatment

- Experimental protocols for treatment are available but no medication approved ( ).

1.5 Risk factors for severe disease: influenza vs COVID–19

INFLUENZA	COVID-19
Chronic conditions, including: • cardiac conditions (hypertension and cardiovascular disease) • chronic lung conditions (asthma or chronic obstructive pulmonary disease [COPD]), endocrine disorders (diabetes) • neurological disorders (stroke and neurodevelopmental conditions) • chronic kidney disease • metabolic disorders • haematologic disorders • chronic liver disease • other immunosuppressed conditions, including cancer and HIV/AIDS and chronic conditions requiring immunosuppressive therapy, such as chronic steroid treatment or chemotherapy	**Chronic conditions, including:** • cardiac conditions (hypertension and cardiovascular disease) • chronic neurological disorders (e. g. stroke) • dementia or mental health disorders • chronic lung disease (e.g. COPD) • endocrine disorders (diabetes) • chronic kidney disease • some immunosuppressed conditions (e.g. cancer, HIV)[a]
Obesity	Obesity
Pregnancy and post-partum period (up to 6 weeks)	Smoking
Older persons (> 65 years old)	In pregnant or recently pregnant: women > 35 years old, obesity, with chronic medical conditions or pregnancy specific disorders (e.g. gestational diabetes and pre-eclampsia/eclampsia)
Young children (< 59 months)	Unvaccinated against COVID-19
	Older persons (> 60 years old)

Note:
[a] List of risk factors to be updated as evidence emerges.

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- Clinical care
- Country-level coordination, planning, and monitoring
- Critical preparedness, readiness and response actions for COVID-19
- Essential resource planning
- Guidance for schools, workplaces and institutions
- Health workers
- Humanitarian operations, camps, refugees/migrants in non-camps and other fragile settings
- Infection prevention and control/WASH
- Maintaining essential health services and systems
- Naming the coronavirus disease (COVID-19)
- National laboratories
- Risk communication and community engagement
- Serology and early investigation protocols
- Surveillance, rapid response teams, and case investigation
- Travel, points of entry and border health
- Virus origin/reducing animal-human transmission

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2 Screening, triage, clinical assessment and management of SARI

2 Screening, triage, clinical assessment and management of SARI

Summary

The screening and identification of patients with acute respiratory symptoms, mainly SARI, at all points of access to the health system, including primary health centres, clinics, hospital emergency units and community settings, is a priority when such symptoms may be due to pathogens of high concern, such as influenza and/or SARS-CoV-2.

At all first points of access to the health system, it is important to always apply appropriate IPC precautions to prevent the spread of illness to health care workers or other patients. See Chapter 3 for details.

1. It is fundamental to set up **systems for reporting and referral of cases from the community** to the appropriate destination for triage, clinical assessment, testing, and/or treatments as per local clinical care pathways and protocols.

2. **After screening at the point of access, triage should be done** with a validated acuity-based triage tool to identify and treat patients needing immediate care. Do not delay emergency care.

3. **After triage, care for all patients should be delivered in designated areas, according to disease severity and acute care needs.** Generally, patients with SARI need acute hospital care because of possible complications such as severe pneumonia, sepsis, organ dysfunction, and/or exacerbation of chronic disease or co-infections. These patients can progress to acute organ failure that may require critical care and admission to ICU for closer monitoring and supportive therapies that cannot be delivered on a general ward. Do not delay ICU admission for these patients.

For example, suspected COVID-19 patients with **mild or moderate disease and without risk factors** should be instructed to self-isolate and contact the COVID-19 information line or a health care provider for advice on testing and referral if needed. These patients can be isolated (or cohorted) at a health facility (if resources allow), community facility with rapid access to health advice, or at home (see WHO guidance) according to local care pathways.

Patients with suspected or confirmed COVID-19 with **mild or moderate disease and with risk factors** should be instructed to self-isolate and call the COVID-19 information line or a health care provider for advise on testing and referral if needed. These patients can be isolated (or cohorted) at a health facility (if resources allow), community facility with rapid access to health advice, or at home (see WHO guidance) according to local care pathways.

Patients with suspected or confirmed COVID-19 with **severe or critical disease** should be instructed to call the emergency hotline (such as the COVID-19 information line for emergency referrals) as soon as possible and be isolated and transferred to designated hospital for inpatient care.

See WHO guidance for more details:

- *Home care for patients with suspected or confirmed COVID-19 and management of their contacts* ();
- *COVID-19 home care bundle for health care workers* ();
- *Coronavirus disease (COVID-19): home care for families and caregivers* ();
- *Living guidance for clinical management of COVID-19* ().

Tools

2.1 Screening for SARI
  2.1.1 Case definition for suspected cases of COVID-19
  2.1.2 Clinical classification for respiratory infection due to influenza
2.2 Triage for SARI
  2.2.1 Setting up a triage/resuscitation area in a health care facility: rationale and requirements
  2.2.2 Examples of acuity-based triage tools: Interagency Integrated Triage Tool
2.3 Clinical assessment of acutely ill patients – basic emergency care: ABCDE approach
2.4 Classification of severity in patients with COVID-19
2.5 Decision-making algorithm for patients presenting with acute respiratory infection (ARI) (influenza or COVID-19 suspected or known to be circulating)
2.6 Decision-making algorithm for hospitalization of patients with pneumonia (influenza or COVID-19 known to be circulating)
2.7 Decision-making support tool for hospitalization and ICU admission for patients with SARI and severe pneumonia
2.8 Checklist for admission
2.9 Checklist for transfer
2.10 Transfer of critically ill patients: air medevac for COVID-19 patients

2.1 Screening for SARI

Screening is the process by which a patient is evaluated to see whether they meet a standardized case definition. It can be performed by different types of health workers and in many different areas such as the emergency unit, outpatient department/primary care clinic, in the community by a community health worker or by telemedicine.

During an epidemic, screening protocols should be established at all health care access points and during contact tracing activities. The screening questions may need to be adjusted for certain settings and guided by epidemiological considerations.

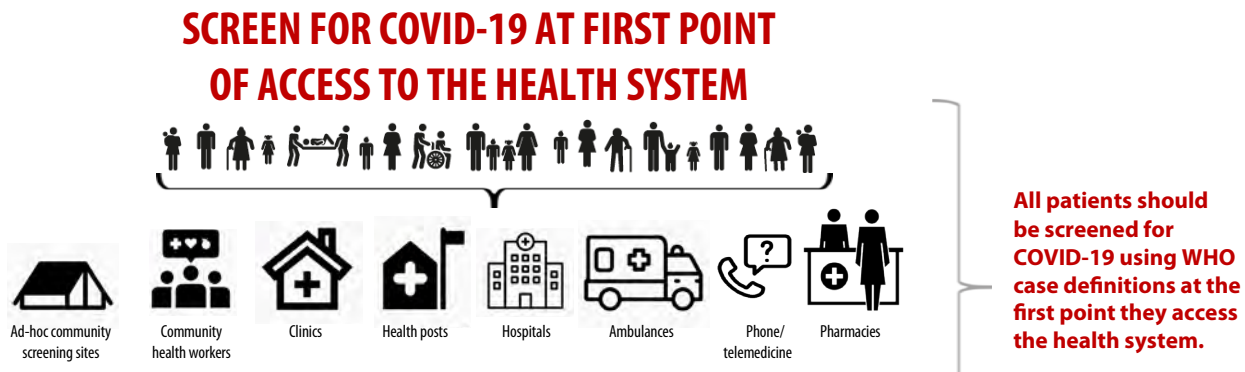
As a precaution, screening should always be done at a distance (> 1 m), with no physical contact.

For example, in the context of a COVID-19 outbreak, screening consists of a simple set of questions based on the WHO COVID-19 case definition (fever, cough, dyspnoea) (). This screening has a simple binary outcome: yes or no.

A person screened positive becomes a suspected case and enters the COVID-19 care pathway. The patient should immediately be given a medical mask and referred to the next appropriate site (health facility for medical care and/or isolation, community facility for medical care or isolation, home for self-isolation, laboratory site for testing, and medical care).

A person screened negative can continue on the normal patient pathway (non-COVID-19) within the health care system without any special precaution.

COVID-19 screening helps ensure the safety of patients, staff and the community and is the first step in the COVID-19 care pathway.



Patients suspected to have COVID-19	Patients NOT suspected to have COVID-19
Refer to appropriate facility or testing site as per local protocol	Management as per local protocol (routine management or referral as per reorganization of service delivery)

Source: Operational considerations for case management of COVID-19 in health facility and community: interim guidance (WHO, 2020).

2.1.1 Case definition for suspected cases of COVID-19

A. Clinical and epidemiological criteria

Clinical criteria:

- Acute onset of fever AND cough; *or*
- Acute onset of any three or more of the following signs or symptoms: fever, cough, general weakness/fatigue, headache, myalgia, sore throat, coryza, dyspnoea, anorexia/nausea/vomiting, diarrhoea, altered mental status.

Epidemiological criteria:

- Residing in or working in an area with high risk of transmission of virus: closed residential settings, humanitarian settings such as camps and camp-like settings for displaced persons; any time within the 14 days prior to symptom onset; *or*
- Residing in or travel to an area with community transmission any time within the 14 days prior to symptom onset; *or*
- Working in any health care setting, including within health facilities or within the community; any time within the 14 days prior of symptom onset.

B. A patient with severe acute respiratory illness (SARI)

- acute respiratory infection with history of fever or measured fever of ≥ 38 °C;
- cough;
- onset within the last 10 days; and
- requires hospitalization.

C. A person NOT meeting the clinical AND epidemiological criteria

- Asymptomatic person not meeting epidemiological criteria with **a positive SARS-CoV-2 antigen-RDT**.

Source: WHO COVID-19: Case definitions (WHO, 2020).

Checklist for COVID–19 neurological screening

COVID-19 may present with neurological symptoms with or without respiratory signs, and patients with COVID-19 are at increased risk for neurological manifestations.

How to use this screening checklist:

- In addition to standardized screening questions, the COVID-19 neurological screening checklist may be used to identify patients who may present with non-respiratory symptoms of COVID-19.
- Additionally, this checklist may be used while monitoring patients with COVID-19 for new or emerging neurological symptoms.

Adult screening checklist

- ☐ Loss (ageusia) or decreased sense of taste (dysgeusia)
- ☐ Loss (anosmia) or decreased sense of smell (hyposmia)
- ☐ New onset headache
- ☐ New onset dizziness (including pre-syncopal symptoms or syncope)
- ☐ Confusion (delirium), behavioural changes including agitation, or psychotic symptoms
- ☐ Decreased consciousness (e.g. somnolence, stupor, unresponsiveness)
- ☐ New focal or diffuse muscle pain (myalgias) with or without weakness
- ☐ Worsening of underlying neurological condition
- ☐ Myoclonus
- ☐ New onset seizures or increased seizure activity
- ☐ New onset weakness (paresis, hemiparesis)
- ☐ Neck stiffness (meningismus)
- ☐ Trouble with speech
- ☐ Numbness/tingling (sensory symptoms)
- ☐ New onset of fatigue
- ☐ Blurring/loss of vision
- ☐ Problems passing urine or with bowel movements
- ☐ Problems with balance in standing or walking

Special considerations in infants and children

- COVID-19 infection is frequently asymptomatic and requires a high index of suspicion when screening.
- Neurologic symptoms of COVID-19 infection in children include poor feeding, fussiness, vomiting, stiff neck.
- Multisystem inflammatory syndrome in children (MIS-C) due to COVID-19 may present with serious neurological symptoms.

This checklist was developed by members of the WHO Neurology and COVID-19 Forum Acute Clinical Care and Support Working Group. Working group members generated a list of symptoms based on their clinical and academic experience with COVID-19. In order to identify all relevant symptoms for inclusion in this checklist, an auditing process was carried out using meta-analytic data from a forthcoming WHO review (manuscript in progress) with a pre-defined threshold for inclusion and exclusion. Symptoms for which there are at least five cases reported in peer-reviewed literature in at least two different sites met the threshold for inclusion. After this process, each symptom was discussed within the working group and final decisions were reached by consensus.

2.1.2 Clinical classification for respiratory infection due to influenza

Clinical syndrome	Definition
Influenza-like infection (ILI)	Acute onset within the last 10 days following respiratory symptoms, measured fever of ≥ 38 °C and cough.
Acute respiratory infection (ARI)	Sudden onset of respiratory infection symptoms (cough, sore throat shortness of breath, or coryza).
Severe acute respiratory infection (SARI)	Acute respiratory infection with a history of fever or measured fever of ≥ 38 °C and cough with onset within the last 10 days and requires overnight hospitalization.

Signs and symptoms of uncomplicated influenza-like illness (ILI)

- Fever
- Cough
- Sore throat
- Rhinorrhoea or nasal congestion
- Headache
- Muscle pain or malaise
- Gastrointestinal illness such as diarrhoea or vomiting, but **no** evidence of dehydration
- **No** shortness of breath.

Note: Older people and immunosuppressed may present with atypical symptoms. Symptoms due to physiologic adaptations of pregnancy and adverse pregnancy events, such as dyspnoea, fever, gastrointestinal symptoms or fatigue, may overlap with ILI.

Signs and symptoms of complicated ARI (SARI)

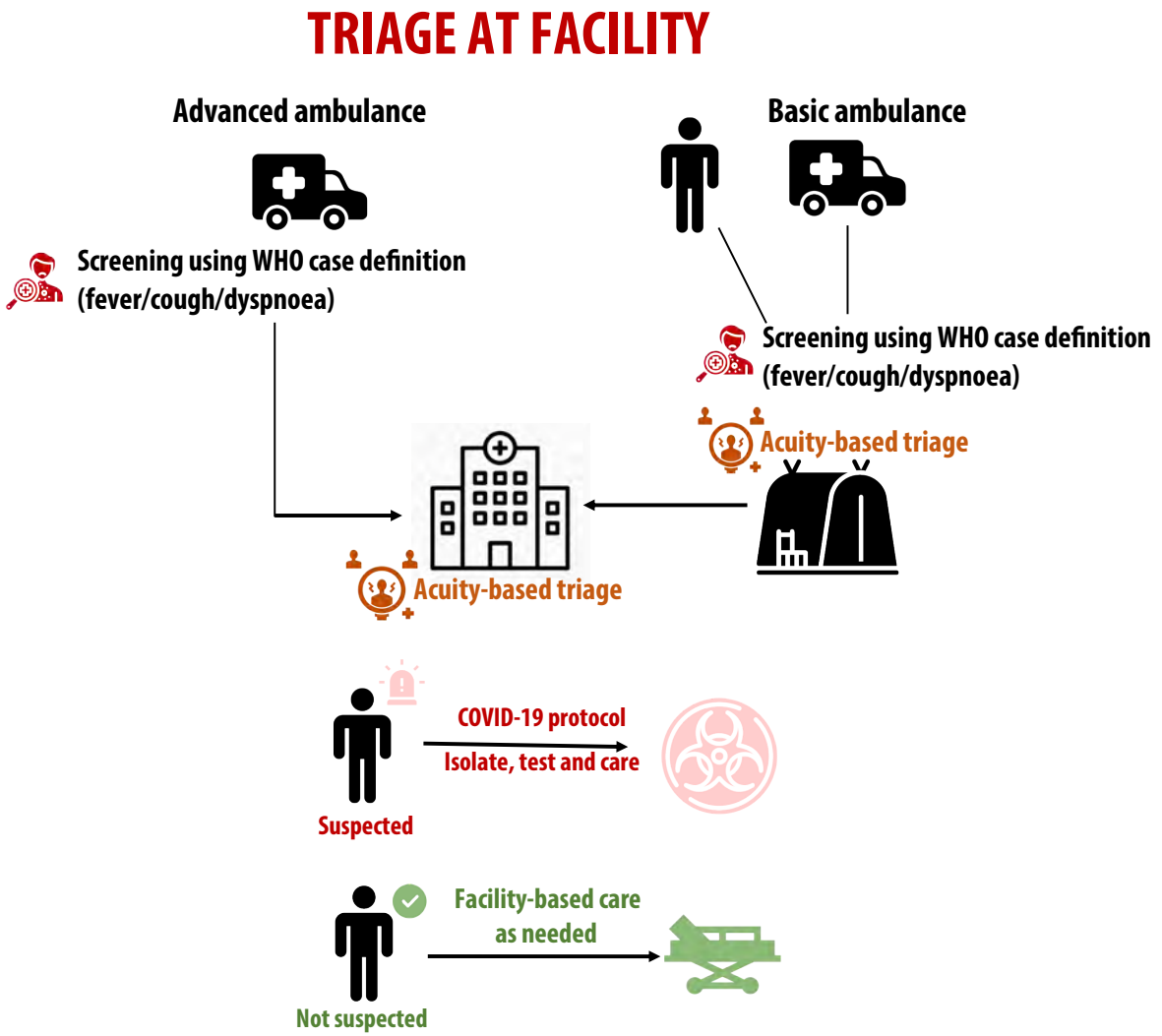
- Respiratory distress: fast breathing, shortness of breath, accessory muscle use, cyanosis.
  - **In children:** central cyanosis, severe distress, grunting, severe chest indrawing or danger signs of lethargy, convulsions or inability to breastfeed or drink.
- Cardiovascular distress:
  - **Adult:** low blood pressure (SBP < 100); delayed capillary refill (> 3 sec < 65 years or > 4.5 sec in older people); fast and weak pulse.
  - **Child:** delayed capillary refill (> 3 sec); fast and weak pulse; or cool extremities or hypotension.
- Neurologic distress: alteration in mental status such as coma, lethargy, confusion, seizures, agitation.
- Dehydration:
  - **In children:** diarrhoea plus any two of the following signs: lethargy, sunken eyes, very slow skin pinch, unable to drink or drinks poorly.
- Persistent fever that is not responding after 3 days.

Source: Revision of clinical case defintions: influenza-like illness and severe acute respiratory infection (WHO, 2020).

2.2 Triage for SARI

Triage refers to the sorting of patients by priority after screening, based on specific criteria (e.g. severity) and can be performed at any point of access to the health care system, including in both pre-hospital and facility-based settings.

Acuity-based triage is the action of sorting and prioritizing patients based on the estimation of their severity. This is used as the basis for identification of those patients who require immediate medical intervention and those who can safely wait, or those who may need to be transported to a specific destination based on their condition. The concept of triage has been around for a long time and different triage tools have been created over the years. Acuity-based triage is the standard method of sorting patients in medical settings.



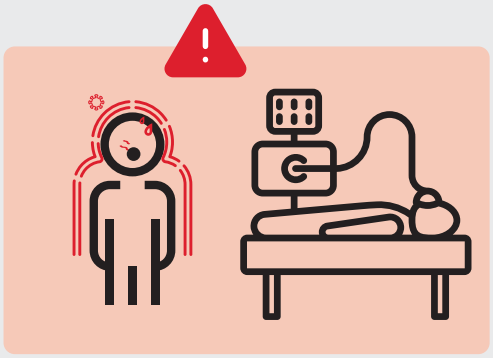
Source: Operational considerations for case management of COVID-19 in health facility and community: interim guidance (WHO, 2020).

2.2.1 Setting up a triage/resuscitation area in a health care facility: rationale and requirements

DESIGNATING A RESUSCITATION AREA IN THE EMERGENCY UNIT

Rationale: Early recognition of conditions requiring time-sensitive management saves lives. A standardized approach in a designated resuscitation area ensures that the sickest patients in the emergency unit are clearly identified and receive necessary life-saving care. Dedicated resuscitation areas ensure that essential resources are accessible and providers are aware of critical patients as soon as possible.

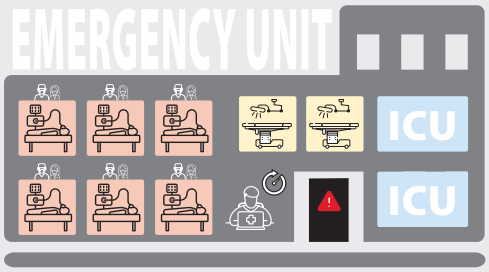
Use of the resuscitation area ⚠



- Upon arrival to the emergency unit, all patient are triaged.
- Patients triaged as "red" are immediately transferred to the resuscitation area.
- Triage personnel alert emergency unit staff as patients are transferred to the resuscitation area (e.g. overhead announcement).
- Pre-hospital providers or bystanders remain until report is given to the receiving medical team.
- Patients in the resuscitation area are the top staff priority.
- The emergency unit ideally has other staff not assigned to the resuscitation area that continue to care for lower acuity patients.
- Initial assessment and resuscitation are followed by monitoring and re-evaluation.
- After initial resuscitation, team leader releases additional providers to care for other patients.
- Care plan (diagnostic, management and disposition) is developed before the team leaves the resuscitation area.

Staff

- Staff trained in resuscitation respond immediately to the resuscitation area.
- At the beginning of each shift, resuscitation area providers (doctors, nurses, technicians) are clearly identified and this information is communicated on a centrally visible whiteboard, chalkboard or monitor).



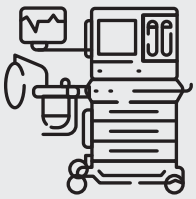
Space

- For rapid reception of patients, the resuscitation area is easily accessible to the main emergency unit entry areas including the ambulance entrance, main entrance and triage area.
- The resuscitation area is easily visible from the main nurses' station and physicians' work area, and staff are aware of its location and function.
- The resuscitation area has enough space to accommodate multiple providers and equipment.
- Easy access to radiology, operating theatre and ICU.

Equipment and supplies

The resuscitation area is equipped to handle critically ill patients at all times:

- Equipment to check and monitor vital signs.
- Mediations cart equipped with key medications for critically ill patients (e.g. fluids, glucose, pain meds).
- Supplies (e.g. blood vials, IV kits, bandages, needles).
- Equipment for critical procedures (e.g. instruments, ultrasound if available).
- Equipment for airway emergencies (e.g. nasal and oral airways, intubation supplies, oxygen, bag valve masks).
- Crash/code cart with advanced life support medications and defibrillator.
- Essential utilities (e.g. electricity, lights, running water).
- Charting and documentation equipment and supplies.
- PPE for providers (e.g. gloves, gowns) and disposal area for sharps, infectious and non-infectious waste.
- Patient gowns and bed linens.



2.2.2 Examples of acuity-based triage tools: Interagency Integrated Triage Tool

Interagency Integrated Triage Tool (IITT) is a novel triage tool developed in collaboration between WHO, the International Committee of the Red Cross (ICRC) and Médecins Sans Frontières (MSF) to provide an integrated set of protocols for routine triage of adults and children. It can be utilized for facility-based triage, facility-based mass casualty triage and pre-hospital triage.

The tool was developed in 2019 and focuses on a three-tier triage system:

- high-acuity resuscitation area
- clinical treatment area
- low-acuity or waiting room.

based on red, yellow and green criteria.

Interagency Integrated Triage Tool: ≥ 12 years

1 CHECK FOR RED CRITERIA

- Unresponsive

AIRWAY & BREATHING
- Stridor
- Respiratory distress* or central cyanosis

CIRCULATION
- Capillary refill >3 sec
- Weak and fast pulse
- Heavy bleeding
- HR <50 or >150

DISABILITY
- Active convulsions
- Any two of:
  - Altered mental status
  - Hypothermia or fever
  - Stiff neck
  - Headache
- Hypoglycaemia

OTHER
- High-risk trauma*
- Poisoning/ingestion or dangerous chemical exposure*
- Threatened limb*
- Snake bite
- Acute chest or abdominal pain (>50 years old)
- ECG with acute ischaemia (if done)
- Violent or aggressive

PREGNANT WITH ANY OF:
- Heavy bleeding
- Severe abdominal pain
- Seizures or altered mental status
- Severe headache
- Visual changes
- SBP ≥160 or DBP ≥110
- Active labour
- Trauma

YES

MOVE TO HIGH ACUITY RESUSCITATION AREA IMMEDIATELY

*See Reference Card

NO

2 CHECK FOR YELLOW CRITERIA

AIRWAY & BREATHING
- Any swelling/mass of mouth, throat or neck
- Wheezing (no red criteria)

CIRCULATION
- Vomits everything or ongoing diarrhoea
- Unable to feed or drink
- Severe pallor (no red criteria)
- Ongoing bleeding (no red criteria)
- Recent fainting

DISABILITY
- Altered mental status or agitation (no red criteria)
- Acute general weakness
- Acute focal neurologic complaint
- Acute visual disturbance
- Severe pain (no red criteria)

OTHER
- New rash worsening over hours or peeling (no red criteria)
- Visible acute limb deformity
- Open fracture
- Suspected dislocation
- Other trauma/burns (no red criteria)
- Known diagnosis requiring urgent surgical intervention
- Sexual assault
- Acute testicular/scrotal pain or priapism
- Unable to pass urine
- Exposure requiring time-sensitive prophylaxis (eg. animal bite, needlestick)
- Pregnancy, referred for complications

YES

MOVE TO CLINICAL TREATMENT AREA

NO

Patients with high-risk vital signs or clinical concern need up-triage or immediate review by supervising clinician

YES

3 CHECK FOR HIGH-RISK VITAL SIGNS

HR <60 or >130
RR <10 or >30
Temp <36° or >39°C
SpO2 <92%
AVPU other than A

NO

MOVE TO LOW ACUITY OR WAITING AREA

Developed by World Health Organization, The International Committee of the Red Cross, Médecins Sans Frontières

Interagency Integrated Triage Tool: < 12 years

1 CHECK FOR RED CRITERIA

- Unresponsive

AIRWAY & BREATHING
- Stridor
- Respiratory distress* or central cyanosis

CIRCULATION
- Capillary refill >3 sec
- Weak and fast pulse
- Heavy bleeding
- Cold extremities
- Any two of:
  - Lethargy
  - Sunken eyes
  - Very slow skin pinch
  - Drinks poorly

DISABILITY
- Active convulsions
- Altered mental status (confused, restless, continuously irritable or lethargic) with stiff neck, hypothermia or fever
- Hypoglycaemia (if known)

OTHER
- Any infant <8 days old
- Age <2 months and temp <36 or >39°C
- High-risk trauma*
- Threatened limb*
- Acute testicular/scrotal pain or priapism
- Snake bite
- Poisoning/ingestion or dangerous chemical exposure*
- Pregnant with adult red criteria

YES

MOVE TO HIGH ACUITY RESUSCITATION AREA IMMEDIATELY

NO

2 CHECK FOR YELLOW CRITERIA

AIRWAY & BREATHING
- Any swelling/mass of mouth, throat or neck
- Wheezing (no red criteria)

CIRCULATION
- Unable to feed or drink
- Vomits everything
- Ongoing diarrhoea
- Dehydration
- Severe pallor (no red criteria)

DISABILITY
- Restless, continuously irritable or lethargy
- Severe pain

OTHER
- Any infant 8 days to 6 months old
- Malnutrition with visible severe wasting OR oedema of both feet
- Trauma/burn (no red criteria)
- Sexual assault
- Known diagnosis requiring urgent surgical intervention
- New rash worsening over hours or peeling (no red criteria)
- Exposure requiring time-sensitive prophylaxis (e.g. animal bite)
- Pregnancy (no red criteria)
- Headache (no red criteria)

YES

MOVE TO CLINICAL TREATMENT AREA

NO

Patients with high-risk vital signs or clinical concern need up-triage or immediate review by supervising clinician

YES

3 CHECK FOR HIGH-RISK VITAL SIGNS

Temp <36° or >39°C

SpO2 < 92%

AVPU other than A

RR	< 1 year	1-4 years	5-12 years
High	50	40	30
Low	25	20	10
HR	**< 1 year**	**1-4 years**	**5-12 years**
High	180	160	140
Low	< 90	< 80	< 70

NO

MOVE TO LOW ACUITY OR WAITING AREA

*See Reference Card

Developed by World Health Organization, International Committee of the Red Cross, Médecins Sans Frontières

High-Risk Trauma Criteria

General Trauma	Road Traffic
Fall from twice person's height	High speed motor vehicle crash
Penetrating trauma excluding distal to knee/ elbow with bleeding controlled	Pedestrian or cyclist hit by vehicle
Crush injury	Other person in same vehicle died at scene
Polytrauma (injuries in multiple body areas)	Motor vehicle crash without a seatbelt
Patient with bleeding disorder or on anticoagulation	Trapped or thrown from vehicle (including motorcycle)
Pregnant	

Major Burns

(the below criteria refer to partial or full thickness burns) Greater than 15% body surface area	Inhalation injury
Circumferential or involving face or neck	Any burn in age < 2 or age > 70

Threatened Limb

A patient presenting with a limb that is:

- Pulseless OR
- Painful and one of the following: pale, weak, numb, or with massive swelling after trauma.

Other High-Risk Criteria

Signs of Respiratory Distress

Adult	Child
Very fast or very slow breathing	Very fast breathing
Inability to talk or walk unaided	Inability to talk, eat or breastfeed
Confused, sleepy or agitated	Nasal flaring, grunting
Accessory muscle use (neck, intercostal, abdominal)	Accessory muscle use (e.g. head nodding, chest indrawing)

Ingestion/exposure

Use of clinical signs alone may not identify all those who need time-dependent intervention. Patients with high risk ingestion or exposure should initially be up-triaged to Red for early clinical assessment.

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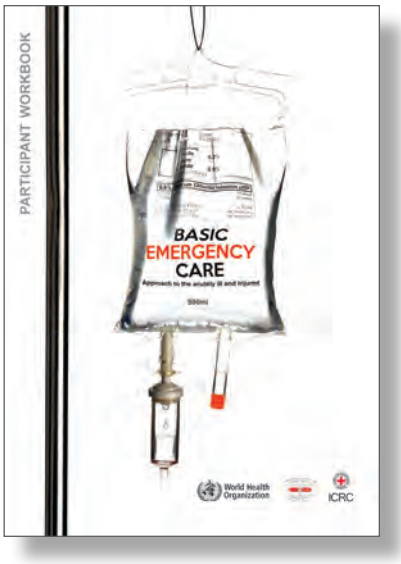
Source: Interagency Integrated Triage Tool (WHO, MSF, ICRC, 2019).

2.3 Clinical assessment of acutely ill patients – basic emergency care: ABCDE approach

Basic emergency care (BEC): ABCDE approach to the acutely ill

Developed by WHO and ICRC in collaboration with the International Federation for Emergency Medicine, ***Basic emergency care (BEC): approach to the acutely ill and injured*** is an open-access training course for frontline health care providers who manage acute illness and injury with limited resources, including students, nurses, pre-hospital technicians, clinical officers and doctors who are working in field (pre-hospital) or hospital settings.



BEC integrates guidance from WHO *Emergency triage assessment and treatment (ETAT)* and the *Integrated management of adolescent and adult illness (IMAI) district clinician manual* and teaches a systematic approach to the initial assessment and management of four time-sensitive conditions – difficulty in breathing, shock, altered mental status and injury – where early intervention saves lives.

Because emergency care providers must respond to "undifferentiated" patients, those with acute symptoms for which the cause may not be known, BEC teaches a **simple, systematic ABCDE approach to managing acute, potentially life-threatening conditions** even before a diagnosis is known.

Patients who are acutely ill due to a SARI may present with any of three life-threatening conditions: difficulty in breathing, shock or altered mental status. The following "quick cards" from BEC summarize the initial approach to assessment and management of key findings from the ABCDE approach.

See: *Basic emergency care (BEC): approach to the acutely ill and injured* (☞) or *WHO Emergency care* (☞) or contact emergencycare@who.int for more information.

	ASSESSMENT FINDINGS	IMMEDIATE MANAGEMENT
Airway 	Unconscious with limited or no air movement	If **NO TRAUMA**: head-tilt and chin-lift, use OPA or NPA to keep airway open, place in recovery position or position of comfort. If possible **TRAUMA**: use jaw thrust with c-spine protection and place OPA to keep the airway open (no NPA if facial trauma).
	Foreign body in airway	Remove visible foreign body. Encourage coughing. • If **unable** to cough: chest/abdominal thrusts/back blows as indicated. • If patient becomes unconscious: CPR.
	Gurgling	Open airway as above, suction (avoid gagging).
	Stridor	Keep patient calm and allow position of comfort. • For signs of anaphylaxis: give IM adrenaline. • For hypoxia: give oxygen.
Breathing 	Signs of abnormal breathing or hypoxia	Give oxygen. Assist ventilation with BVM if breathing NOT adequate.
	Wheeze	Give salbutamol. For signs of anaphylaxis: give IM adrenaline.
	Signs of tension pneumothorax (absent sounds/hyperresonance on one side WITH hypotension, distended neck veins)	Perform needle decompression, give oxygen and IV fluids. Will need chest tube.
	Signs of opiate overdose (AMS and slow breathing with small pupils)	Give naloxone.
Circulation 	Signs of poor perfusion/shock	If **no pulse**, follow relevant CPR protocols. Give oxygen and IV fluids.
	Signs of internal or external bleeding	Control external bleeding. Give IV fluids.
	Signs of pericardial tamponade (poor perfusion with distended neck veins and muffled heart sounds)	Give IV fluids,oxygen. Will need rapid pericardial drainage.
Disability 	Altered mental status (AMS)	If NO TRAUMA, place in recovery position.
	Seizure	Give benzodiazepine.
	Seizure in pregnancy (or after recent delivery)	Give magnesium sulphate.
	Hypoglycaemia	Give glucose if < 3.5 mmol/L or unknown.
	Signs of opiate overdose (AMS with slow breathing with small pupils)	Give naloxone.
	Signs of life-threatening brain mass or bleed (AMS with unequal pupils)	Raise head of bed, monitor airway. Will need rapid transfer for neurosurgical services.
Exposure 	Remove wet clothing and dry skin thoroughly	
	Remove jewellery, watches and constrictive clothing	
	Prevent hypothermia and protect modesty	
	Snake bite	Immobilize extremity. Send picture of snake with patient. Call for anti-venom if relevant.

If cause unknown, remember trauma: Examine the entire body and always consider hidden injuries [see also TRAUMA card]

REMEMBER: PATIENTS WITH ABNORMAL ABCDE FINDINGS MAY NEED RAPID HANDOVER/TRANSFER. PLAN EARLY.

NORMAL ADULT VITAL SIGNS

Pulse rate: 60–100 beats per minute
Respiratory rate: 10–20 breaths per minute
Systolic blood pressure > 90 mmHg
Oxygen saturation > 92%

Estimating systolic blood pressure
(not reliable in children and the elderly):
Carotid (neck) pulse → SBP ≥ 60 mmHg
Femoral (groin) pulse → SBP ≥ 70 mmHg
Radial (wrist) pulse → SBP ≥ 80 mmHg

SAMPLE History

Signs & symptoms
Allergies
Medications
PMH
Last oral intake
Events

SPECIAL CONSIDERATIONS IN THE ASSESSMENT OF CHILDREN

- Children have bigger heads and tongues, and shorter, softer necks than adults. Position airway as appropriate for age.
- Always consider foreign bodies.

- Look for signs of increased work of breathing (e.g. chest indrawing, retractions, nasal flaring).
- Listen for abnormal breath sounds (e.g. grunting, stridor, or silent chest).

AGE	RESPIRATORY RATE (breaths per minute)
< 2 months	40–60
2–12 months	25–50
1–5 years	20–40

- Signs of poor perfusion in children include: slow capillary refill, decreased urine output, lethargy, sunken fontanelle, poor skin pinch.
- Look for signs of anaemia and malnourishment (adjust fluids).
- Remember that children may not always report trauma and may have serious internal injury with few external signs.

AGE (in years)	NORMAL HEART RATE (beats per minute)
<1	100–160
1–3	90–150
4–5	80–140

- Always check AVPU (alert, verbal, pain, unresponsive).
- Hypoglycaemia is common in ill children.
- Check for tone and response to stimulus.
- Look for lethargy or irritability.

INFANTS AND CHILDREN HAVE DIFFICULTY MAINTAINING TEMPERATURE

- Remove wet clothing and dry skin thoroughly. Place infants skin-to-skin when possible.
- For hypothermia, cover the head (but be sure mouth and nose are clear).
- For hyperthermia, unbundle tightly wrapped babies.

DANGER SIGNS IN CHILDREN

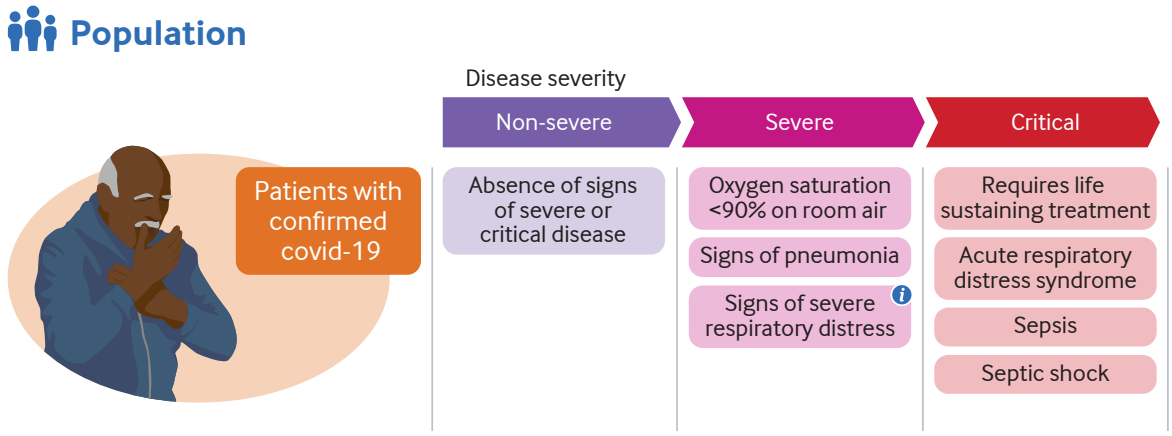
- Signs of airway obstruction (unable to swallow saliva/ drooling or stridor).
- Increased breathing effort (fast breathing, nasal flaring , grunting, chest indrawing or retractions).
- Cyanosis (blue colour of the skin, especially at the lips and fingertips).
- Altered mental status (including lethargy or unusual sleepiness, confusion, disorientation).
- Moves only when stimulated or no movement at all (AVPU other than "A").
- Not feeding well, cannot drink or breastfeed or vomiting everything.
- Seizures/convulsions.
- Low body temperature (hypothermia).

ESTIMATED WEIGHT in KILOGRAMS for CHILDREN 1–10 YEARS OLD:

[age in years + 4] x 2

Source: WHO/IFRC/IFEM Basic emergency care (BEC): approach to the acutely ill and injured, quick cards (2018).

2.4 Classification of severity in patients with COVID-19



Source: A living WHO guideline on drugs for COVID-19 (BMJ, 2020).

Mild disease	
	Symptomatic patients meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia.

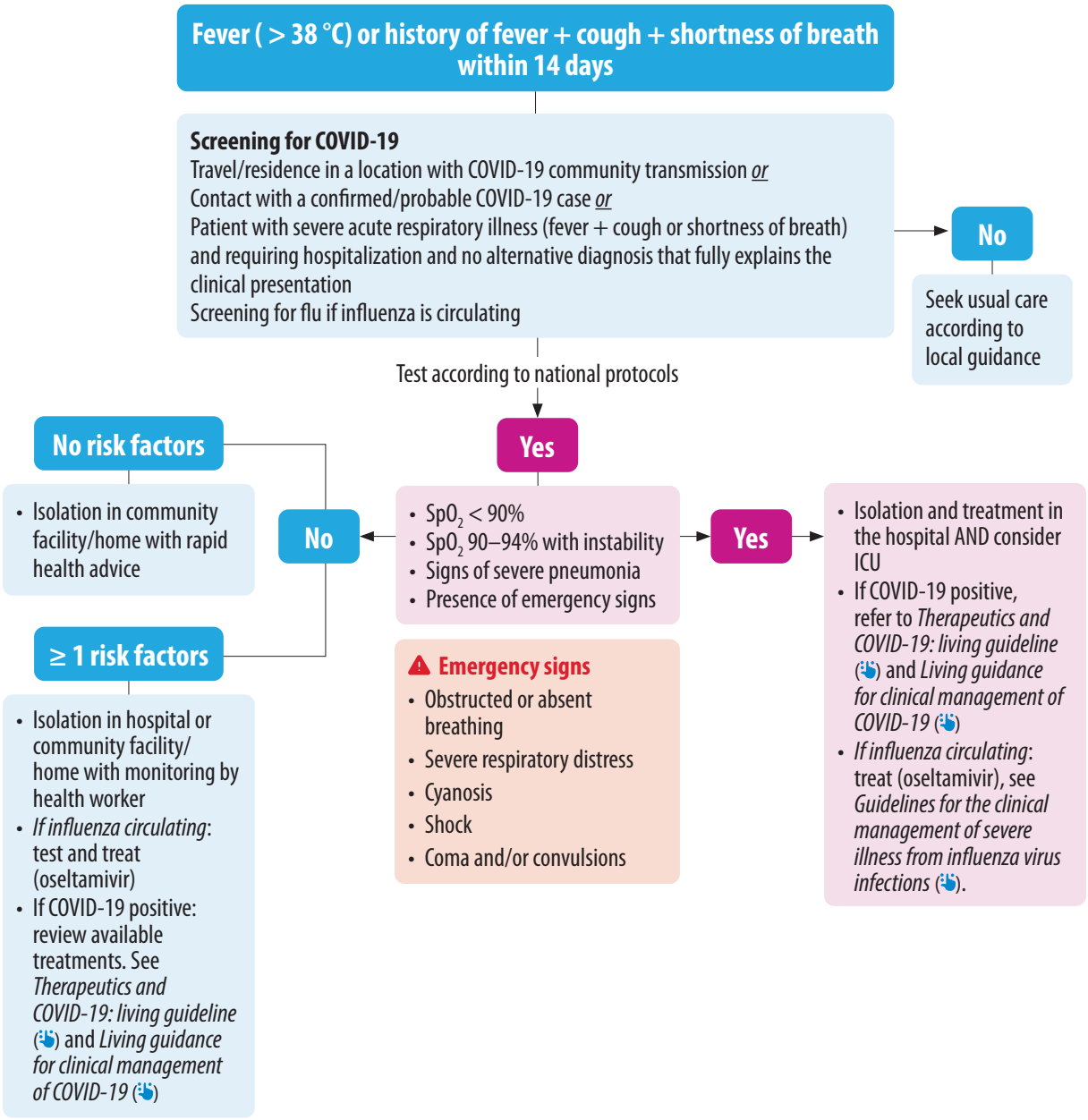
Moderate disease	
Pneumonia	**Adolescent or adult** with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) but no signs of severe pneumonia, including $SpO_2 \geq 90\%$ on room air. **Child** with cough or difficulty breathing + fast breathing and/or chest indrawing and no signs of severe pneumonia. Fast breathing: < 2 months: ≥ 60 breaths/min; 2–11 months: ≥ 50; 1–5 years: ≥ 40. The diagnosis can be made on clinical grounds; chest imaging (radiograph, CT scan, ultrasound) may assist in diagnosis and identify or exclude pulmonary complications. **Caution:** The oxygen saturation threshold of 90% to define severe COVID-19 is arbitrary and should be interpreted cautiously. For example, clinicians must use their judgment to determine whether a low oxygen saturation is a sign of severity or is normal for a given patient with chronic lung disease. Similarly, a saturation between 90–94% on room air may be abnormal (in patient with normal lungs) and can be an early sign of severe disease, mainly if patient is on a downward trend. Generally, if there is any doubt, the panel suggested erring on the side of considering the illness as severe.

Severe disease	
Severe pneumonia	**Adolescent or adult** with clinical signs of pneumonia (fever, cough, dyspnoea) plus one of the following: respiratory rate > 30 breaths/min, severe respiratory distress, or $SpO_2 < 90\%$ on room air. **Child:** with clinical signs of pneumonia (cough or difficulty breathing + fast breathing or chest wall indrawing) + at least one of the following: • $SpO_2 < 90\%$ • Very severe chest indrawing, grunting, central cyanosis, or presence of any other general danger sign (inability to breastfeed or drink, lethargy or unconsciousness or convulsions). The diagnosis can be made on clinical grounds; chest imaging (radiograph, CT scan, ultrasound) may assist in diagnosis and identify or exclude pulmonary complications.

Critical disease	
ARDS	**Onset:** within 1 week of a known clinical insult (i.e. pneumonia) or new or worsening respiratory symptoms. **Chest imaging:** radiograph,CT scan or lung ultrasound: bilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules. **Origin of pulmonary infiltrates:** respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echocardiography) to exclude hydrostatic cause of infiltrates/oedema if no risk factors present. Oxygenation impairment in adults: **Air blood gases (ABG) available** • Mild ARDS: 200 mmHg < PaO_2/FiO_2 ≤ 300 mmHg (with PEEP or CPAP ≥ 5 cmH_2O) • Moderate ARDS: 100 mmHg < PaO_2/FiO_2 ≤ 200 mmHg (with PEEP ≥ 5 cmH_2O) • Severe ARDS: PaO_2/FiO_2 ≤ 100 mmHg (with PEEP ≥ 5 cmH_2O). **ABG not available (Kigali modification)** • SpO_2/FiO_2 < 315 suggests ARDS (including non-ventilated patients) Oxygen impairment in children: note OI and OSI.[a] Use OI when available. If PaO_2 not available, wean FiO_2 to maintain SpO_2 ≤ 97% to calculate OSI or SpO_2/FiO_2 ratio: • Bilevel (NIV or CPAP) ≥ 5 cmH_2O via full face mask: PaO_2/FiO_2 ≤ 300 mmHg or SpO_2/FiO_2 ≤ 264 • Mild ARDS (invasively ventilated): 4 ≤ OI < 8 or 5 ≤ OSI < 7.5 • Moderate ARDS (invasively ventilated): 8 ≤ OI < 16 or 7.5 ≤ OSI < 12.3 • Severe ARDS (invasively ventilated): OI ≥ 16 or OSI ≥12.3. [a] Oxygenation Index (OI) is an invasive measurement of the severity of hypoxaemic respiratory failure and may be used to predict outcomes in paediatric patients. It is calculated as follows: percentage of fraction of inhaled oxygen multiplied by the mean airway pressure (in mmHg), divided by the partial pressure of arterial oxygen (in mmHg), divided by the partial pressure of arterial oxygen (in mmHg). Oxygen Saturation Index (OSI) is a non-invasive measurement and has been shown to be a reliable surrogate marker of OI in children and adults with respiratory failure. OSI replaces PaO_2 with oxygen saturation as measured by pulse oximetry (SpO_2) in the OI equation.
Sepsis	**Adults:** acute life-threatening organ dysfunction caused by a dysregulated host response to suspect or proven infection. Signs of organ dysfunction include: altered mental status (delirium), difficult or fast breathing, low oxygen saturation, reduced urinary output, fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate or hyperbilirubinaemia. **Children:** suspected or proven infection and ≥ 2 age-based systemic inflammatory response syndrome (SIRS) criteria,[b] of which one must be abnormal temperature or white blood cell count. [b] SIRS criteria: abnormal temperature (> 38.5 °C or < 36 °C); tachycardia for age or bradycardia for age if < 1 year; tachypnoea for age or need for mechanical ventilation; abnormal white blood cell count for age or > 10% bands.
Septic shock	**Adults:** persistent hypotension despite volume resuscitation, requiring vasopressor to maintain MAP ≥ 65 mmHg and serum lactate level > 2 mmol/L. **Children:** any hypotension (SBP < 5th centile or 2SD below normal for age) or two or three of the following: altered mental status; bradycardia or tachycardia (HR < 90 beats/min [bpm] or < 160 bpm in infants and heart rate < 70 bpm or > 150 bpm in children); prolonged capillary refill (> 2 sec) or weak pulse; fast breathing; mottled or cool skin or petechial or purpuric rash; high lactate; reduced urine output; hyperthermia or hypothermia.
Acute thrombosis	Acute venous thromboembolism (i.e. pulmonary thromboembolism), acute coronary syndrome, acute stroke.
MIS-C	Preliminary case definition: children and adolescents 0–19 years of age with fever ≥ 3 days AND two of the following: rash or bilateral non purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet); hypotension or shock; features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated troponin/NT-proBNP); evidence of coagulopathy (PT, PTT, elevated D-dimers); acute gastrointestinal problems (diarrhoea, vomiting or abdominal pain); AND elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin AND no other obvious microbial cause of shock syndrome AND evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19. (See scientific brief, 15 May 2020, WHO: *Multisystemic inflammatory syndrome in children and adolescents temporally related to COVID-19*.)

Abbreviations: BP – blood pressure; bpm – beats/min; CPAP – continuous positive airway pressure; CT – computed tomography; FiO_2 – fraction of inspired oxygen; MAP – mean arterial pressure; NIV – non-invasive ventilation; OI – Oxygenation Index using SpO_2; OSI – Oxygen Saturation Index; PaO_2 – partial pressure of oxygen; PEEP – positive end-expiratory pressure; SBP – systolic blood pressure; SD – standard deviation; SIRS – systemic inflammatory response syndrome; SOFA – sequential organ failure assessment; SpO_2 – oxygen saturation.

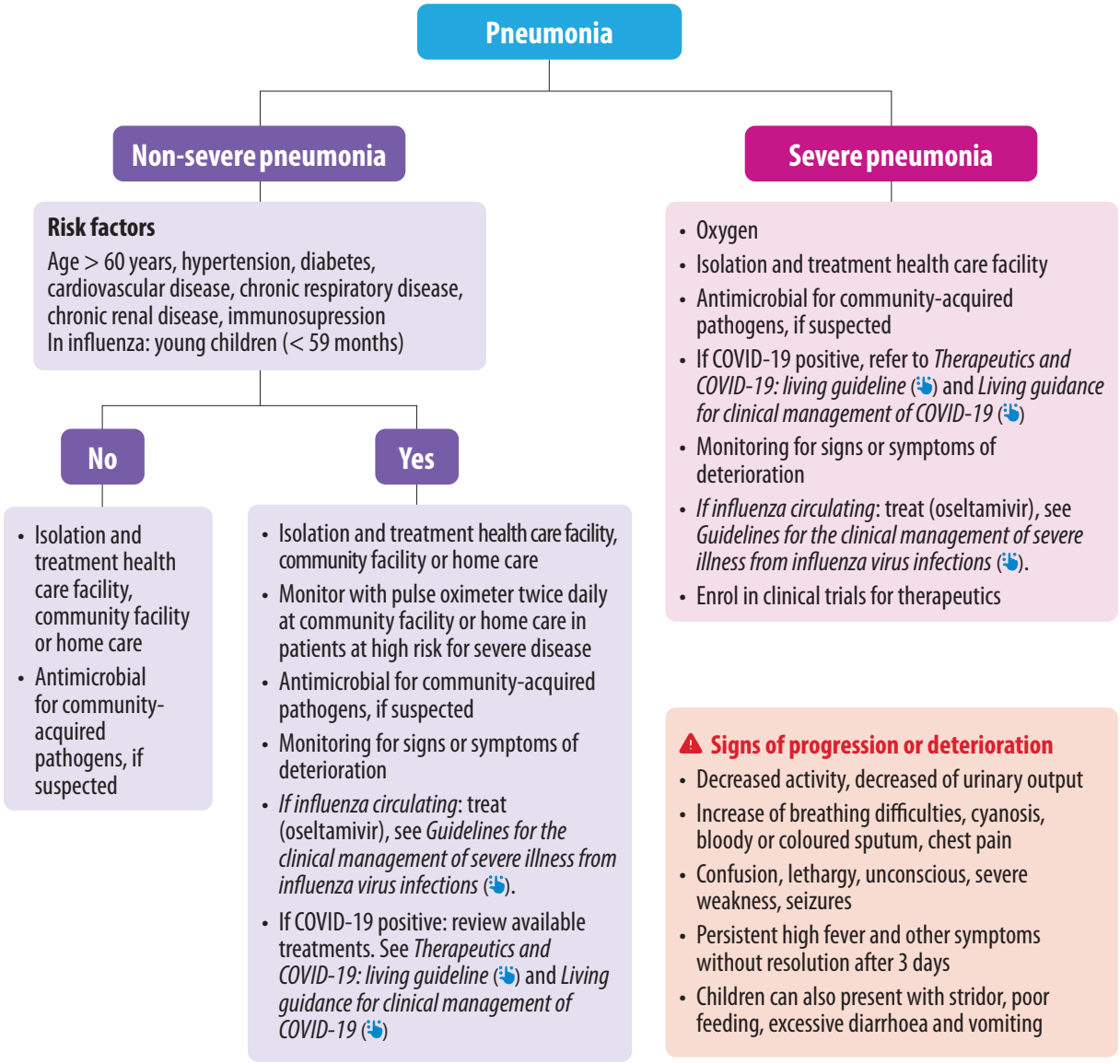
2.5 Decision-making algorithm for patients presenting with acute respiratory infection (ARI) (influenza or COVID-19 suspected or known to be circulating)



Risk factors associated with severe disease

- Age more than 60 years (increasing with age).
- Underlying noncommunicable diseases (NCDs): diabetes, hypertension, cardiac disease, chronic lung disease, cerebrovascular disease, dementia, mental disorders, chronic kidney disease, immunosuppression (including HIV), obesity and cancer.
- In pregnant or recently pregnant: women > 35 years old, obesity, with chronic medical conditions or pregnancy specific disorders (e.g. gestational diabetes and pre-eclampsia/eclampsia).
- Smoking.
- Unvaccinated against COVID-19.
- In influenza: young children (< 59 months).

2.6 Decision-making algorithm for hospitalization of patients with pneumonia (influenza or COVID-19 known to be circulating)



WHO criteria for severe pneumonia

Children: *Pocket book of hospital care for children* (WHO, 2013).

- Cough or difficulty breathing with at least one of the following:
  - central cyanosis or oxygen saturation (SpO_2) < 90%
  - severe respiratory distress (e.g. grunting, very severe chest indrawing)
  - general danger sign (e.g. inability to breastfeed or drink, lethargy or unconscious, convulsions).
- Any or all of the following may also be present:
  - fast breathing (< 2 months ≥ 60 breaths/min; 2–11 months ≥ 50; 1–5 years ≥ 40; 5–15 years ≥ 30).
  - chest indrawing.

Adults: *IMAI district clinician manual: hospital care for adults and adolescents* (WHO, 2011).

- RR > 30 breaths/min
- SpO_2 < 90%
- Signs of severe respiratory distress (e.g. inability to speak, use of accessory muscles).

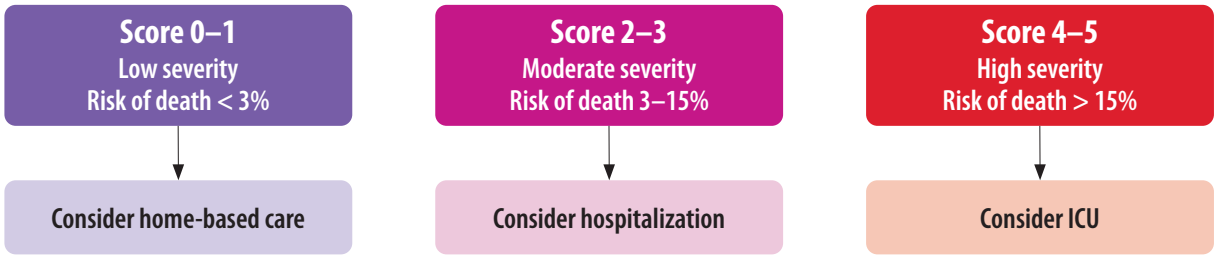
2.7 Decision-making support tool for hospitalization and ICU admission for patients with SARI and severe pneumonia

Patients should be admitted to ICU based on severity of clinical condition and resource availability. In hospitals where oxygen therapy is only available in the ICU, admit all SARI patients to the ICU. In hospitals where oxygen therapy can also be delivered on wards, admit less severe SARI patients to wards but with increased monitoring. During outbreaks, a surge of patients may exhaust resources; less severe cases may need to be managed outside the ICU.

In adults, the CURB-65 score is a validated tool that, when combined with clinical judgments can be used to predict mortality and aid in determining admission for adult patients with pneumonia. This is adapted from the *British Thoracic Society guidelines for the management of community acquired pneumonia in adults* (BTS, 2009).

CURB-65 score: one point for each feature present	**Total points**
Confusion	1
Urea > 7 mmol/L	1
RR ≥ 30/min	1
Blood pressure (SPB < 90 or DPB ≤ 60 mmHg)	1
Age ≥ **65** years	1

Level of severity, risk of death and management according to score



2.8 Checklist for admission

☑ Once you have decided to admit a patient with **severe acute respiratory infection (SARI)** to the hospital, consider using this checklist to ensure the following have been done in preparation for admission.

This is adapted from the *IMAI district clinician manual: hospital care for adults and adolescents* (WHO, 2011).

Checklist for admission

- ☐ **Essential diagnostic tests obtained, e.g. complete blood cell count, chemistry panel, glucose, chest radiograph, upper respiratory tract specimens for viral testing (COVID-19 and during influenza season include influenza testing), blood sample for culture (when possible, before first dose of antimicrobials), but do not delay antimicrobials.**
- ☐ **Emergency treatments given and patient's response checked, e.g. oxygen therapy, insertion of peripheral IV (use appropriate antisepsis for the skin to prevent catheter-related infections), initial fluid therapy (and vasopressors if in shock).**
- ☐ **For patients with SARI and sepsis or septic shock: administer appropriate antimicrobials immediately for the suspected or confirmed pathogen, ideally within 1 hour of recognition (see Chapter 7).**
- ☐ **Give steroids (if suspected or confirmed severe or critical COVID-19).**
- ☐ **Documentation completed.**
- ☐ **Determined the level of care the patient needs, e.g. ICU, high dependency unit, general ward.**
- ☐ **Determined IPC measures and proper PPE health care workers need to manage the patient.**
- ☐ **Verbal communication with ward staff completed to ensure continuity of care.**
- ☐ **Patient prepared for safe transfer.**

2.9 Checklist for transfer

Transport of the critically ill patient can be risky as complications during this process can be life threatening and may be related to clinical, organizational, or equipment issues.

☑ Consider using this checklist to ensure the safe transport of the patient to the designated unit.

This is adapted from the *IMAI district clinician manual: hospital care for adults and adolescents* (WHO, 2011).

Checklist for transfer

- ☐ **Patient is stabilized.**
- ☐ **Adequate IPC measures and proper PPE needed, e.g. medical mask for patients with ARI.**
- ☐ **Everything secured: airway, NG tube, IV lines, monitors, endotracheal tubes, ventilator.**
- ☐ **Enough drugs: e.g. vasopressors, sedatives.**
- ☐ **Enough oxygen: adequate oxygen saturation (SpO_2).**
- ☐ **Enough IV fluids: blood pressure adequate.**
- ☐ **Health care workers (e.g. transporters, receiving staff) and receiving unit/ward prepared.**

2.10 Transfer of critically ill patients: air medevac for COVID-19 patients

Air ambulance services are facing multiple challenges when transporting highly infectious patients for several hours in enclosed spaces. The preference is to treat patients on site rather than transporting them from an outbreak area. However, an evacuation may be needed if patients require care beyond what can be provided in the current facility/location. Moving patients closer to hospital facilities is likely to increase the chance of a good outcome and relocating them will take the load off overburdened and under-resourced health care facilities during an outbreak. While there is no single standardized scoring system on emergency aeromedical evacuations, the patient's clinical condition, age, local resources and locations have been found to be the criteria that inform decision-making.

This overview is meant to provide a simplified guidance to clinicians that will facilitate air medevac and does not deliver detailed recommendations for necessary equipment, medications, flight physiology specific ventilation, waste management, IPC considerations, etc.

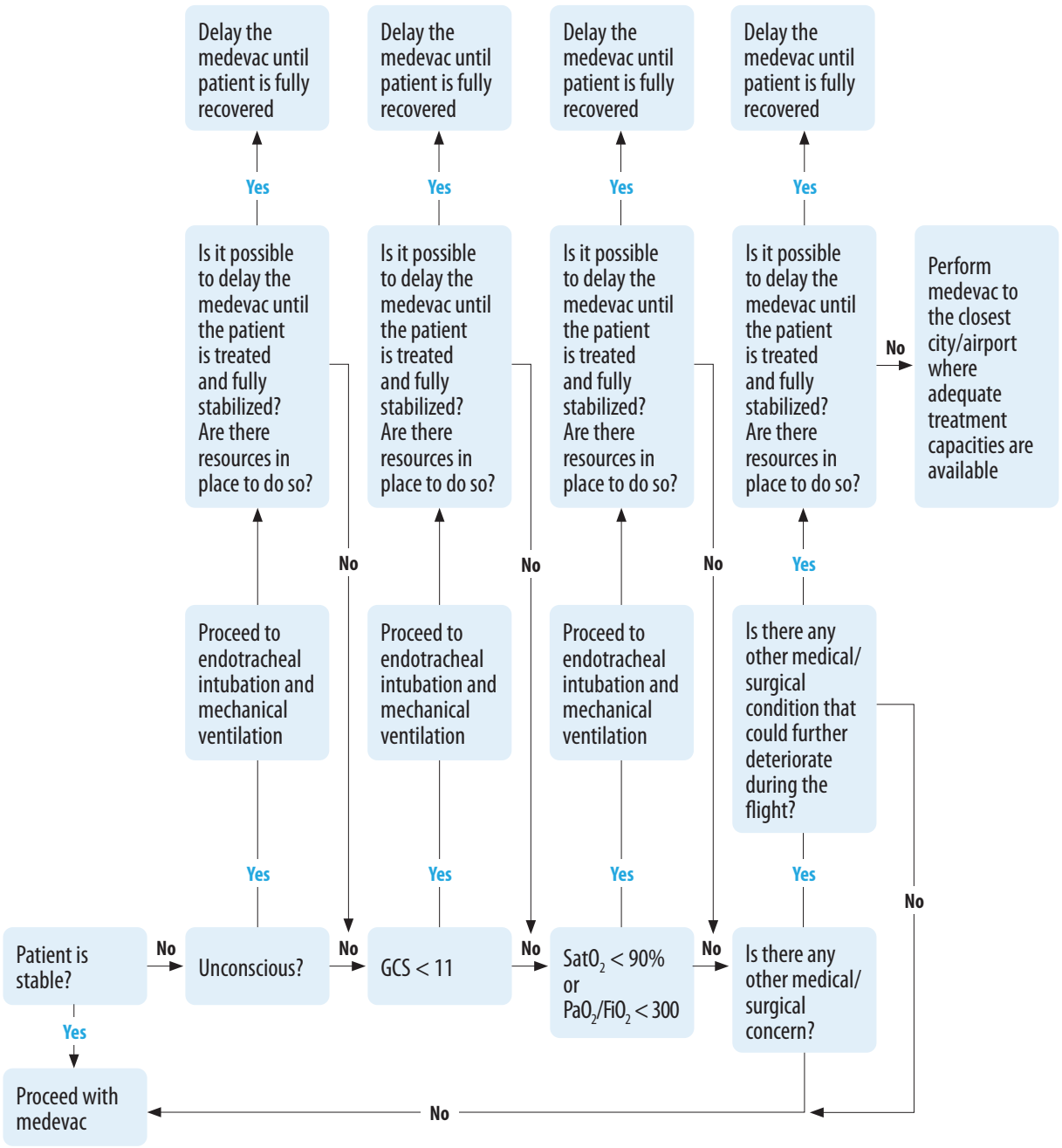
Pre-flight patient assessment

Presenting signs and symptoms of COVID-19 vary. When considering a medevac transportation, pre-clarification of the severity of the disease is crucial.

Pre-flight physiological considerations	Altitude exposure imposes hypoxia and gas expansion in body cavities. • Consider supplemental oxygen, ventilation and low-altitude flight paths. • Prepare for any deterioration and for conditions induced by the aerospace environment. • Plan for early endotracheal intubation: – Pre-emptive intubation is recommended for patients with the potential of respiratory decompensation during aeromedical transport. • Anaemia: fit to fly if Hb ≥ 95g/L. If, due to chronic disease and compensation, Hb ≥ 80 g/L is acceptable. If lower or if concurrent lung or cardiac disease, consider transfusion.
Pre-flight checklist	• Allocate key roles. • Flight crew must include a specialized intensive care flight physician and nurse, that are knowledgeable about flight physiology, experienced in inter-facility air-transfer and the management of critical care patients/ intubated patients. • Precise SOPs (e.g. correct use and handling of PPE/environmental cleaning and decontamination); every crew member and service staff (e.g. aircraft cleaning) strictly adhere to SOPs. • Medevac personnel to ensure that patient receives instruction on in-flight IPC measures. • Written informed consent and signed liability waiver forms from patient and/or relatives along with outline of intention to transfer must occur before the transfer. • Clear communication and agreement between coordination mechanism, transferring and receiving facility: – Formal agreement from the receiving facility. – Ensure full and up-to-date medical records on patient's clinical condition, treatment received, intention to transfer, mode and timeline of transfer and communicate them to flight crew and receiving facility. • Equipment check: monitoring devices (ECG, blood pressure, pulse oximetry, capnography, defibrillators, pacing devices, aeronautical oxygen systems, oxygen, suction, face mask, filter, breathing circuit, respiratory support device, equipment to manage sedation, intubation, ventilation, cardiovascular support, infusion devices, medications including resuscitation drugs, point-of-care testing (POCT) for e.g. arterial blood gases analysis, etc. All equipment must be certified for aeronautical use. • Check resuscitation medications. • Be prepared to deepen anaesthesia and administer additional catecholamines during transport.

In-flight checklist	• Precise SOPs (e.g. correct use and handling of PPE/environmental cleaning and decontamination); every crew member and service staff (e.g. aircraft cleaning) strictly adhere to SOPs. • Medevac personnel to ensure that patient receives instruction on in-flight IPC measures. • Avoid aerosol-generating procedures such as non-invasive ventilation, high-flow oxygen therapy, tracheal suction or nebulization. • Clear SOPs in place to ensure safe sharps/waste management.
Post-flight checklist	• SOPs on decontamination. • SOPs on safe equipment handling. • SOPs on safe waste disposal. • SOPs on personnel monitoring.

Medevac algorithm



Notes: GCS – Glasgow Coma Scale; PaO_2/FiO_2 – ratio of partial pressure arterial oxygen and fraction of inspired oxygen; $SatO_2$ – oxygen saturation.

Minimize risk of in-flight transmission

The risk of transmission in the confined environment of a helicopter or aircraft, potentially over long distances with prolonged transport times can be minimized by isolating the patient during transportation.

Rotary wing	• The cockpit should be isolated through use of the aircraft blind.
Fixed wing	• Use of barriers such as screens or curtains may provide some level of protection for personnel positioned in the cockpit, and their effectiveness is reliant on airflow and the movement of airborne particles within the aircraft. • Air-conditioning (if applicable) should be selected in non-recirculating mode. – Pressurized aircraft: if available, aircraft recirculation should be deselected. – If cabin air recirculation is selected, then HEPA filtration is preferred. Aircraft ventilation should remain on at all times during transport of respiratory patients, including during ground delays.

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3 Infection prevention and control for patients with SARI

3 Infection prevention and control for patients with SARI

Summary

Administrative and engineering measures and PPE work in harmony to prevent the spread of infection and keep health care workers and patients safe. For health care facility readiness for COVID-19 see *Severe acute respiratory infections treatment centre* (☝).

When providing health care for any patients in a health care facility, one must implement **standard precautions**, which should include hand hygiene according to the WHO 5 moments, respiratory hygiene, use of appropriate PPE according to a risk assessment, safe injection practices and sharps management, waste management, safe handling and cleaning of soiled linens, environmental cleaning, and safe handling, cleaning and disinfection of patient care equipment. Standard precautions apply to all patients regardless of their diagnosis or presumed infection status.

When caring for patients with certain types of ARI, such as avian influenza, MERS, SARS-CoV-2, seasonal influenza or another novel viral infection, it is also recommended to use **droplet and contact precautions**.

When carrying out certain high-risk procedures such as aerosol-generating procedures like open suctioning of airways, sputum induction, cardiopulmonary resuscitation, endotracheal intubation and extubation, non-invasive ventilation (e.g. BiPAP, CPAP), bronchoscopy and manual ventilation, one should use **airborne precautions** in addition to contact and droplet precautions.

In the context of the current COVID-19 epidemic, there are some specificities of SARS-CoV-2 in its transmission that have implications for the infection prevention precautions. The virus SARS-CoV-2 can spread from an infected person's mouth or nose in small liquid particles when they cough, sneeze, speak, sing or breathe. These particles range from larger respiratory droplets to smaller aerosols.

- Current evidence suggests that the virus spreads mainly between people who are in close contact with each other, typically within 1 m (short range). A person can be infected when aerosols or droplets containing the virus are inhaled or come directly into contact with the eyes, nose or mouth.
- The virus can also spread in poorly ventilated and/or crowded indoor settings, where people tend to spend longer periods of time. This is because aerosols remain suspended in the air or travel farther than 1 m (long range).
- People may also become infected by touching surfaces that have been contaminated by the virus when touching their eyes, nose or mouth without cleaning their hands (fomite transmission).

These different ways of transmission of COVID-19 can be prevented by following basic transmission-based precautions (*Coronavirus disease (COVID-19): How is it transmitted?*) (☝):

- Social distance: keep at least 1 m from others.
- Wear a mask (*Mask use in the context of COVID-19*) (☝).

- Ventilation: avoid crowded places, poorly ventilated, indoor locations and avoid prolonged contact with others.
- Spend more time outdoors than indoors; and avoid the three Cs: Crowded places; Close-contact settings; Confined and enclosed spaces ().
- Avoid touching surfaces, especially in public settings or health facilities, in case people infected with COVID-19 have touched them. Clean surfaces regularly with standard disinfectants.
- Clean hands with soap and water, or an alcohol-based handrub.
- Respiratory hygiene: cover nose and mouth during coughing or sneezing with tissue or flexed elbow.
- Vaccination against COVID-19 whenever possible (*COVID-19 vaccines*) ().

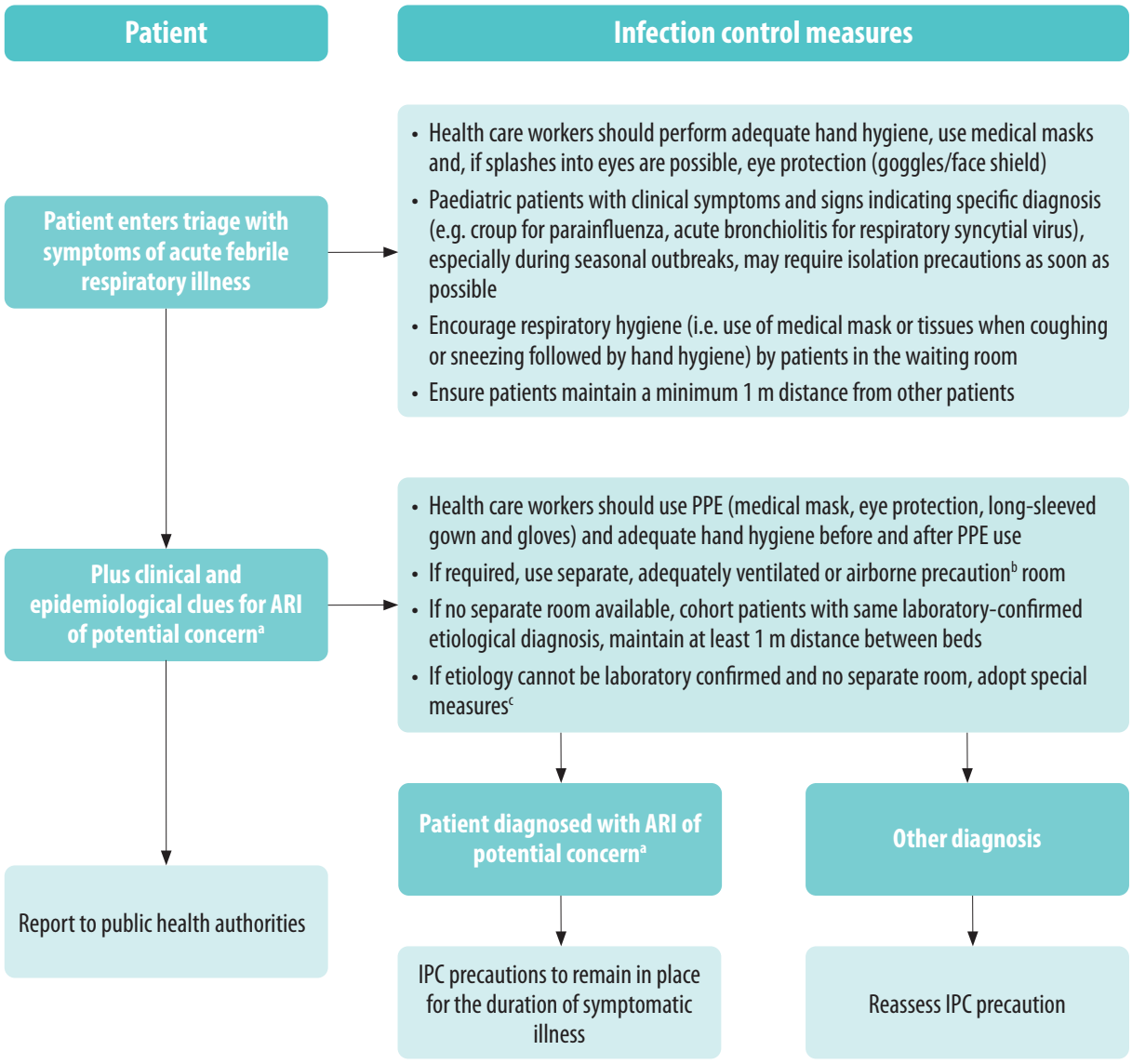
Tools

3.1 How to implement infection control measures for SARI
3.2 How to implement infection control measures for ARIs of potential concern
3.3 Personal protective equipment (PPE)
3.4 How to improve medical mask fit in health care settings
3.5 Steps to perform a particulate respirator seal check during the putting on of PPE
3.6 Hand hygiene
3.7 The 5 moments for hand hygiene
3.8 The "Three Cs": settings where transmission of the COVID-19 virus spreads more easily
3.9 Checklist for aerosol-generating procedures

3.1 How to implement infection control measures for SARI

These algorithms are adapted from the WHO guidelines, *Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care* (WHO, 2014).

Decision-tree for IPC measures for patients known or suspected to have an acute respiratory infection



[a] ARIs of potential concern include SARS, COVID-19, new influenza virus causing human infection (e.g. human cases of avian influenza) and novel pathogens causing ARIs that can cause outbreaks with high morbidity and mortality. Clinical and epidemiological clues include severe disease in a previously healthy host, exposure to household member or close contact with severe ARI, cluster of cases, travel, exposure to ill animals or laboratory.
[b] Airborne precaution rooms include both mechanically and naturally ventilated rooms with ≥ 12 air changes per hour and controlled direction of airflow.
[c] The term "special measures" means allowing patients with epidemiological and clinical information suggestive of a similar diagnosis to share a room, but with a spatial separation of at least 1 m.

3.2 How to implement infection control measures for ARIs of potential concern

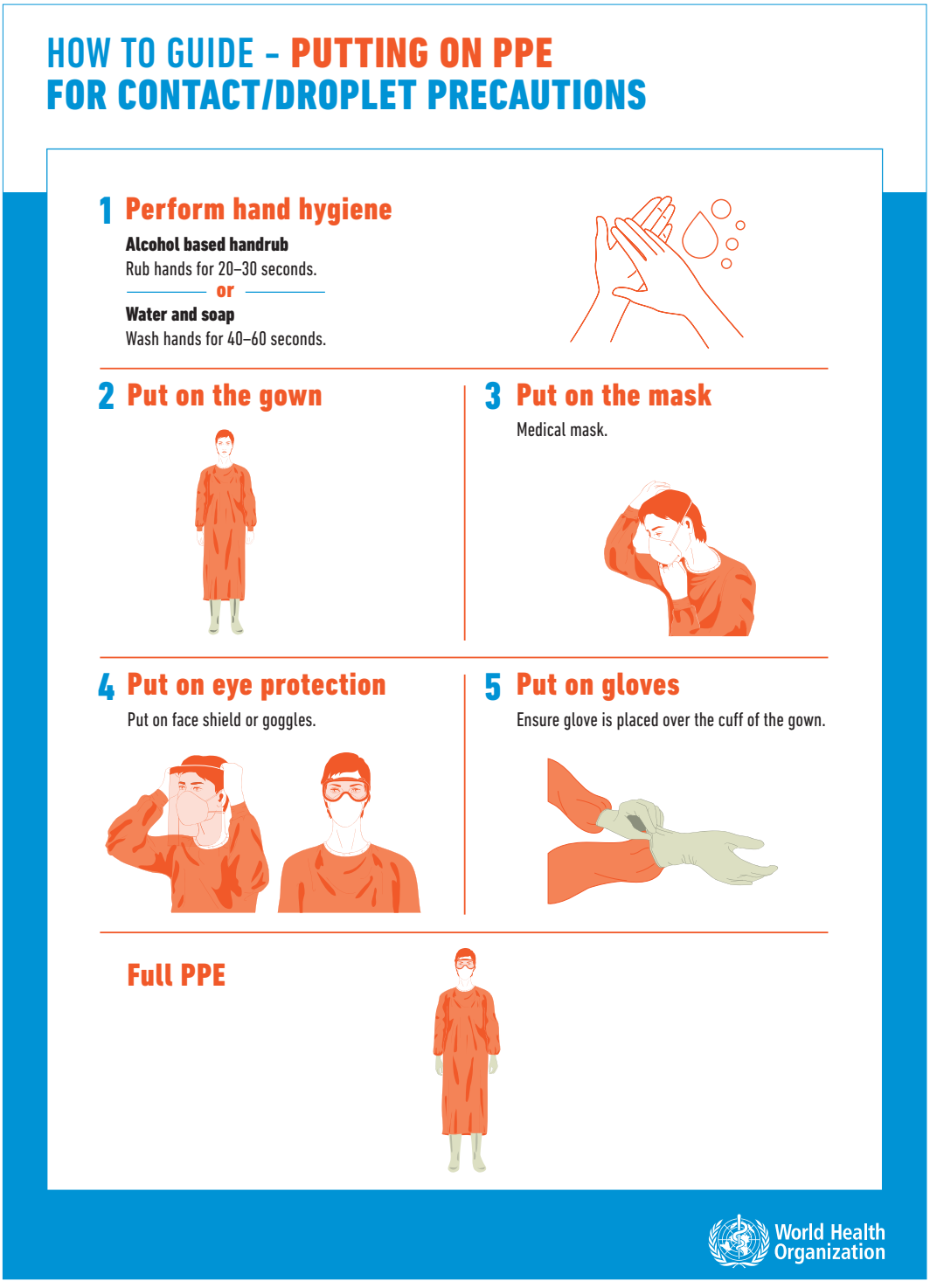
Acute respiratory infections of potential concern include SARS, COVID-19, new influenza viruses causing human infection (e.g. human cases of avian influenza) and novel pathogens causing ARIs that can cause outbreaks with high morbidity and mortality.

Instructions for patients	**Give suspect patient a medical mask and direct the patient to a separate area;** an isolation room if available. If not possible to separate the patient, try to keep at least 1 m distance between suspected patients and other patients in the waiting room. All patients in the waiting room should have a mask and should practise respiratory hygiene (cover their nose and mouth during coughing or sneezing with a tissue or flexed elbow) and perform hand hygiene after contact with respiratory secretions (such as coughing, sneezing or blowing nose).
Apply droplet precautions	**Droplet precautions** prevent transmission of respiratory viruses through respiratory droplets that are expelled when an infected person speaks, coughs, or sneezes. Place patients in single rooms, or group those with the same etiological diagnosis together, maintaining at least 1 m distance between beds. If an etiological diagnosis is not possible, group patients with similar clinical diagnosis and based on epidemiological risk factors, with a spatial separation. Limit patient movement within the institution and ensure that patients wear medical masks when being taken outside their rooms. When providing care in close contact with a patient with respiratory symptoms (e.g. coughing or sneezing), use a medical mask and eye protection (face mask or goggles), because sprays of secretions may occur. *Note:* The risk of COVID-19 spreading is especially high in places where the three Cs overlap: Crowded places, Close-contact settings (especially where people have conversations very near each other) and Confined and enclosed spaces with poor ventilation (see Tool 3.7).
Apply contact precautions	**Contact precautions** prevent direct or indirect transmission from contact with contaminated surfaces or equipment (i.e. contact with contaminated oxygen tubing/interfaces). PPE for contact precautions are a long-sleeved gown and gloves. Hand hygiene followed by putting on PPE for contact and droplet precautions (medical mask and eye protection) should be applied when entering the room. Remove PPE when leaving the room, and practise hand hygiene following PPE removal. If possible, use either disposable or dedicated equipment (e.g. stethoscopes, blood pressure cuffs, pulse oximeters and thermometers). If equipment needs to be shared among patients, clean and disinfect items between each patient use. Ensure that health workers refrain from touching their eyes, nose and mouth with potentially contaminated gloved or ungloved hands. Avoid contaminating environmental surfaces that are not directly related to patient care (e.g. door handles and light switches). Avoid medically unnecessary movement and transport of patients. Practise hand hygiene frequently.
Apply airborne precautions when performing an aerosol-generating procedure	Ensure that health workers performing, or in the room during, **an aerosol-generating procedure** (e.g. open suctioning of respiratory tract, tracheal intubation, non-invasive ventilation, tracheotomy, bronchoscopy, cardiopulmonary resuscitation) use the appropriate PPE, including gloves, long-sleeved gowns, eye protection, and fit-tested particulate respirators (N95 or equivalent, or higher level of protection). A scheduled fit test should not be confused with a user's seal check before each use. Whenever possible, use adequately ventilated single rooms when performing aerosol-generating procedures, meaning negative pressure rooms with a minimum of 6–12 air changes per hour (e.g. equivalent to 40–80 L/s/patient for a $4 \times 2 \times 3$ m^3 room) or at least 160 L/s/patient in facilities with natural ventilation. Avoid the presence of unnecessary individuals in the room. Care for the patient in the same type of room after mechanical ventilation begins.

3.3 Personal protective equipment (PPE)

For specifications for COVID-19 review *Personal protective equipment for COVID-19* and WHO recommendations on mask use by health care workers ( ) ( ).

Remember, PPE use should be guided by risk assessment concerning anticipated contact with blood and other bodily fluids, including respiratory droplets and secretions, during patient care and presence of non-intact skin. For example, if there is a risk of splash to the body and face then use hand hygiene, gloves, gown, medical mask and eyewear. A "how to guide" for putting on and taking off PPE is shown below..



HOW TO GUIDE – TAKING OFF PPE FOR CONTACT/DROPLET PRECAUTIONS

Ensure that infectious waste containers are available for safe disposal of PPE. Separate containers should be available for reusable items.

Order is important

1 Remove gloves

2 Remove the gown

Ensure gown is pulled away from the body during removal and that clothing does not become contaminated and dispose of them safely.

3 Perform hand hygiene

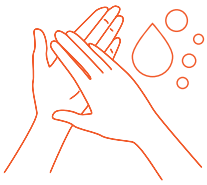
Alcohol based handrub

Rub hands for 20–30 seconds.

or

Water and soap

Wash hands for 40–60 seconds.



4 Remove eye protection

Remove face shield or goggles.

5 Remove the mask

Ensure you are taking the mask off from the straps, avoid touching the mask.

6 Perform hand hygiene

Alcohol based handrub

Rub hands for 20–30 seconds.

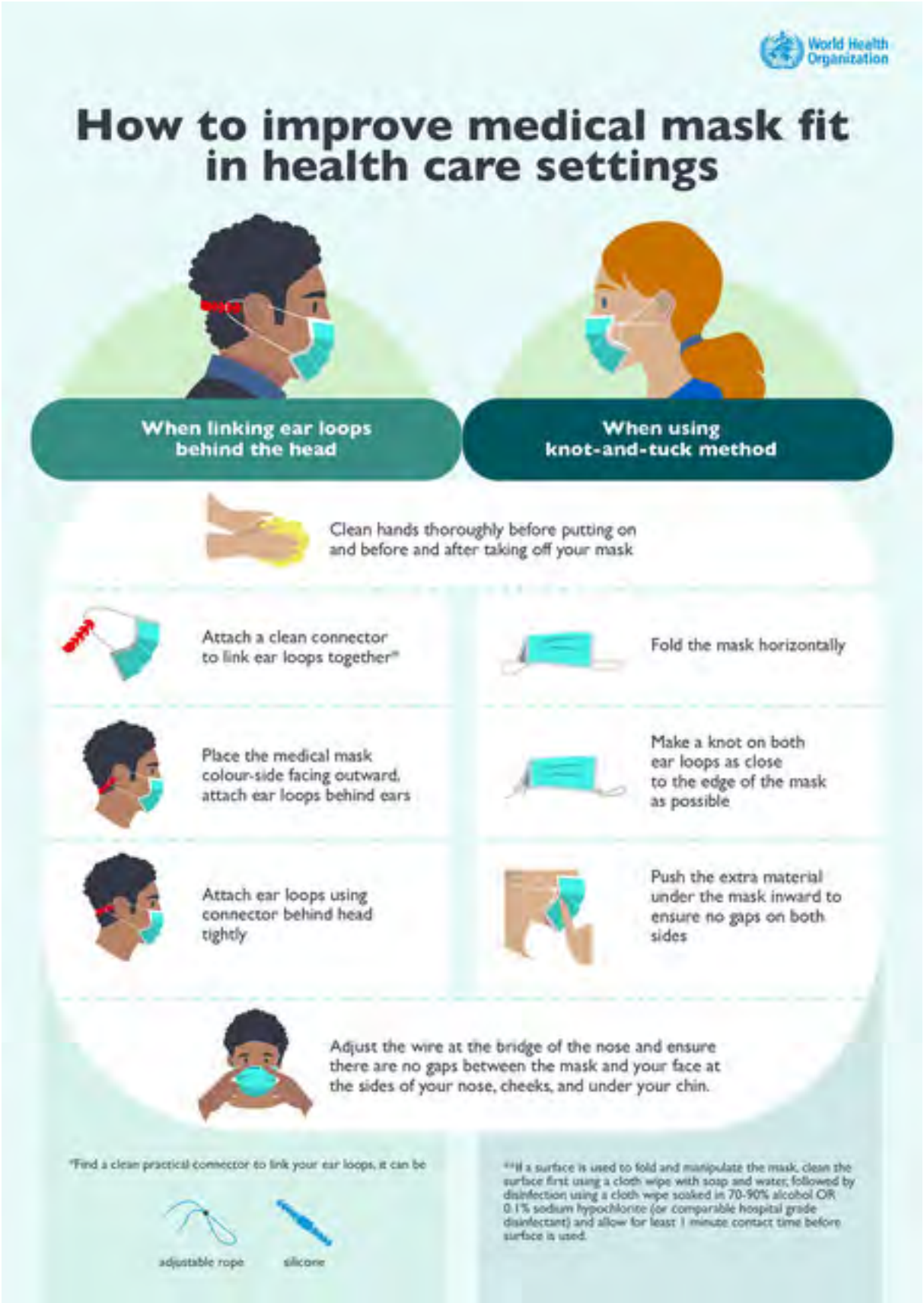
or

Water and soap

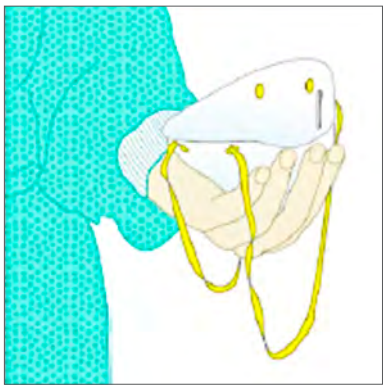
Wash hands for 40–60 seconds.

World Health Organization

3.4 How to improve medical mask fit in health care settings



3.5 Steps to perform a particulate respirator seal check during the putting on of PPE



1 Cup the respirator in your hand with the nosepiece at your fingertips allowing the headbands to hang freely below your hand.

2 Position the respirator under your chin with the nosepiece up.

3 Pull the top strap over your head, resting it high at the back of your head. Pull the bottom strap over your head and position it around the neck below the ears.

4 Place fingertips of both hands at the top of the metal nosepiece.

Mould the nosepiece **(using two fingers of each hand)** to the shape of your nose. (Pinching the nosepiece using one hand may result in less effective respirator performance.)

Cover the front of the respirator with both hands, being careful not to disturb the position of the respirator.

A. Positive seal check

Exhale sharply.

A positive pressure inside the respirator = no leakage.

If leakage, adjust position and/or tension straps.

Reset the seal.

Repeat the steps until respirator is sealed properly.

B. Negative seal check

Inhale deeply. If no leakage, negative pressure will make respirator cling to your face.

Leakage will result in loss of negative pressure in the respirator due to air entering through gaps in the seal.

3.6 Hand hygiene

Hand hygiene must be performed before and after any contact with patients, after contact with contaminated items or surfaces, before and after PPE use and according to the WHO 5 moments (see Tool 3.6).

Use an alcohol-based product if hands are not visibly soiled.

Wash hands with soap and water when they are visibly soiled or contaminated with proteinaceous material.

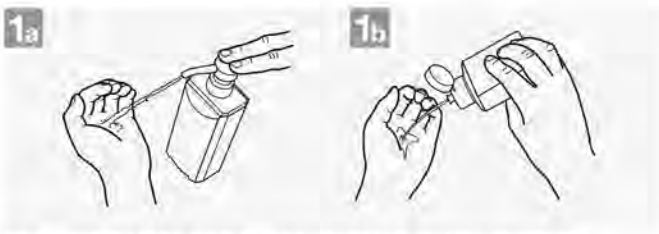
Below is an example of hand washing with soap and water. The same rubbing technique can be used with alcohol-based product.

This entire procedure should take 40–60 seconds for water and soap (or 20–30 seconds for alcohol-based handrub).

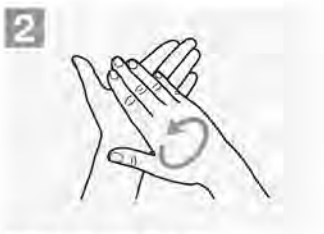
How to Handrub?

RUB HANDS FOR HAND HYGIENE! WASH HANDS WHEN VISIBLY SOILED

Duration of the entire procedure: 20–30 seconds



Apply a palmful of the product in a cupped hand, covering all surfaces;

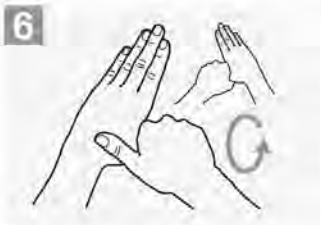


Rub hands palm to palm;

Right palm over left dorsum with interlaced fingers and vice versa;

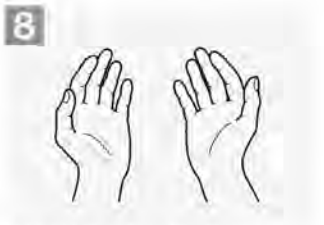
Palm to palm with fingers interlaced;

Backs of fingers to opposing palms with fingers interlocked;



Rotational rubbing of left thumb clasped in right palm and vice versa;

Rotational rubbing, backwards and forwards with clasped fingers of right hand in left palm and vice versa;



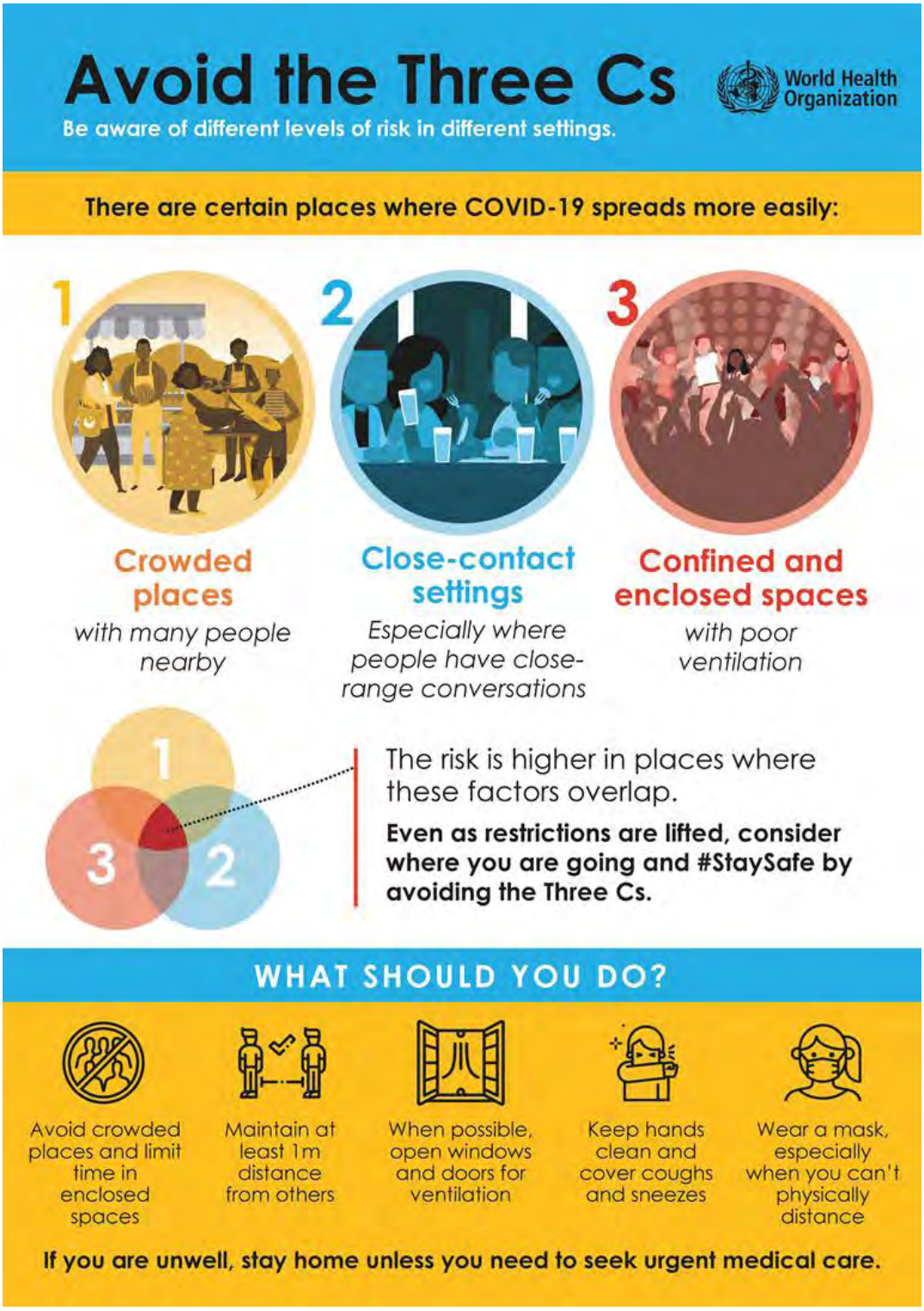
Once dry, your hands are safe.

3.7 The 5 moments for hand hygiene in health care facilities

1	BEFORE TOUCHING A PATIENT	WHEN? Clean your hands before touching a patient when approaching him/her. WHY? To protect the patient against harmful germs carried on your hands.
2	BEFORE CLEAN/ ASEPTIC PROCEDURE	WHEN? Clean your hands immediately before performing a clean/aseptic procedure. WHY? To protect the patient against harmful germs, including the patient's own, from entering his/her body.
3	AFTER BODY FLUID EXPOSURE RISK	WHEN? Clean your hands immediately after an exposure risk to body fluids (and after glove removal). WHY? To protect yourself and the health-care environment from harmful patient germs.
4	AFTER TOUCHING A PATIENT	WHEN? Clean your hands after touching a patient and her/his immediate surroundings, when leaving the patient's side. WHY? To protect yourself and the health-care environment from harmful patient germs.
5	AFTER TOUCHING PATIENT SURROUNDINGS	WHEN? Clean your hands after touching any object or furniture in the patient's immediate surroundings, when leaving – even if the patient has not been touched. WHY? To protect yourself and the health-care environment from harmful patient germs.

3.8 The "Three Cs": settings where transmission of the COVID-19 virus spreads more easily

The risk of COVID-19 spreading is especially high in places where these "3 Cs" overlap.



3.9 Checklist for aerosol-generating procedures

In health facilities where people are receiving treatment for COVID-19, there is an increased risk of infection during medical procedures called aerosol-generating procedures. These can produce very small droplets that can stay suspended in the air for long periods of time and spread beyond conversational distances (typically 1 m). Therefore, health workers performing these procedures or in settings where these procedures are performed should take specific airborne protection measures, including using appropriate PPE such as respirators.

☑ Consider using this checklist when performing aerosol-generating procedures, such as tracheal intubation, non-invasive ventilation, tracheotomy, cardiopulmonary resuscitation and manual ventilation before intubation, bronchoscopy, aspiration, or open suctioning of respiratory tract secretions.

Note: There is limited research available regarding the risk of non-invasive ventilation and high-flow oxygen therapy, but experts suggest using airborne precautions during these procedures.

Checklist for aerosol-generating procedures

☐ **Perform hand hygiene** before and after patient contact and before and after PPE use.

☐ All health workers present should wear the following **PPE:**
- A facial particulate respirator (e.g. European Union FFP2 or United States of America National Institute for Occupational Safety and Health-certified N95). Perform a seal check.
- Eye protection (e.g. goggles or a face shield).
- A clean, non-sterile, long-sleeved gown.
- Gloves (some of these procedures require sterile gloves).

☐ Make sure adequately **ventilated room:**
- **For mechanically ventilated rooms:** Ensure ≥ 6–12 air changes per hour plus control of airflow direction, ideally 12 air changes per hour for new constructions, with a recommended negative pressure differential of ≥ 2.5 Pa (0.01 inch water gauge) to ensure that air flows from the corridor into the patient room.
- **For natural ventilation:** The recommended average natural ventilation rate is 160 L/s/patient.

☐ **Social distancing** – avoid unnecessary individuals in the room.

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WHO IPC posters:

- Contact and droplet precautions – COVID-19 personal protective equipment (PPE): https://www.who.int/docs/default-source/infection-prevention-and-control/contact-droplet-covid-19-precautions.pdf?sfvrsn=74c1a87c_2
- How to guide – Putting on PPE for contact/droplet precautions: https://www.who.int/docs/default-source/infection-prevention-and-control/ppe-en.pdf?sfvrsn=4b45270e_2
- Screening for acute respiratory infection: https://www.who.int/docs/default-source/infection-prevention-and-control/screening-respiratory-infection.pdf?sfvrsn=2c899e42_2

4 Monitoring patients with acute respiratory infection

4 Monitoring patients with acute respiratory infection

Summary

Vital signs, including temperature, heart rate, blood pressure, respiratory rate, oxygen saturation and mental status with AVPU, are standard metrics that can be used when assessing and monitoring patients with ARI in hospital and pre-hospital settings.

Pulse oximetry is used to monitor oxygen saturation (SpO_2). It is an essential tool that should be available at all first access health points, where patients with ARI are assessed to inform triage, clinical assessment and appropriate referral and/or treatment plans. Pulse oximeter is also an essential tool to monitor patients for signs of clinical deterioration or improvement that may require change in clinical management interventions.

In patients with mild or moderate COVID-19 with risk factors for severe disease who do not need hospitalization, monitoring oxygenation with a pulse oximeter at home can be beneficial to identify patients that may develop complications and require urgent referral to health facilities for additional treatments. See *Living guidance for clinical management of COVID-19* Section 10. Management of moderate COVID-19: pneumonia treatment ( ).

Patients with severe or critical COVID-19 should be cared for in a hospital and monitored frequently because of their dynamic clinical condition and need for timely (and titrated) interventions. The acute condition of the patient will dictate the moment when advanced monitors are deployed, as well as the frequency of checks. For example, in an ICU compared with a general ward, haemodynamic and respiratory parameters are monitored more frequently (sometimes continuously), along with a more complete assessment that includes frequent physical examinations, laboratory tests, and intake and output.

All parameters that are monitored should be captured in a standardized charting system (paper based or electronic health record) so that trends can be monitored over time and response to treatments assessed.

There are published **monitoring scoring tools** that can be used to assess and identify deteriorating patients that may be progressing to critical illness. Two examples includes in this toolkit are the National Early Warning Score (NEWS) and the Paediatric Early Warning Score (PEWS). These tools may be useful to identify when patients fail to respond to treatments or deteriorate and should trigger the need for escalation of care and/or new treatment intervention. Regardless of scoring tool used, monitoring vital signs alone must be paired with a systematic approach to interpretation of the data (including clinical history and physical examination) and modification of monitoring and treatment plans accordingly.

Tools

4.1 AVPU scale: a simple tool for assessing level of consciousness

This scale is a simple way to assess a patient's mental status. Each letter corresponds to the patient's level of consciousness.

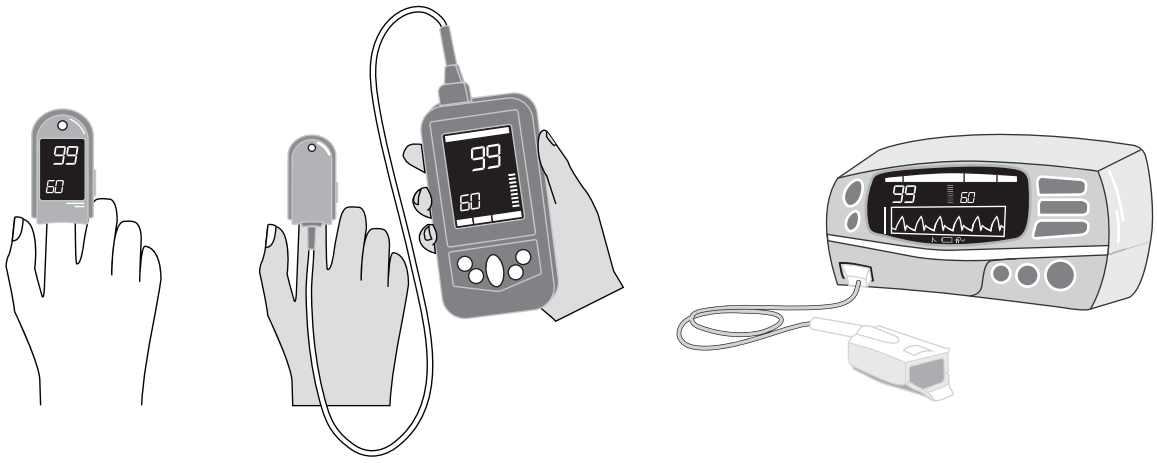
A	**ALERT:** Patient is aware of the examiner, responds to the environment on their own, follows commands, opens eyes spontaneously, and tracks objects.
V	**VERBAL:** Patient does not open eyes spontaneously, but does in response to a verbal stimulus and reacts meaningfully to the verbal stimulus.
P	**PAIN:** Patient does not open eyes spontaneously, but does in response to pain and may move, moan, or cry in response to pain.
U	**UNRESPONSIVE:** Patient does not respond to verbal or painful stimuli.

4.2 Pulse oximetry monitoring

A pulse oximeter measures oxygen saturation of haemoglobin in the blood by comparing the absorbance of light of different wavelengths across a translucent part of the body.

Pulse oximetry is the best non-invasive method available for detecting hypoxaemia and titrating oxygen delivery accordingly. Using clinical signs may mislead the diagnosis of some patients with hypoxaemia (e.g. some COVID-19 patients with "silent hypoxaemia"). Pulse oximetry should be performed on all patients with SARI.

Pulse oximetry may have some limitations and may produce inaccurate results during select clinical conditions (e.g. carbon monoxide poisoning, methaemoglobinaemia, and low perfusion) or when using low-cost oximeters that do not meet the technical specifications for clinical use (see *WHO technical specifications for oxygen concentrators* and *WHO-UNICEF Technical specifications and guidance for oxygen therapy devices*).



Self-contained fingertip | **Portable handheld** | **Table top**

✓ BENEFITS

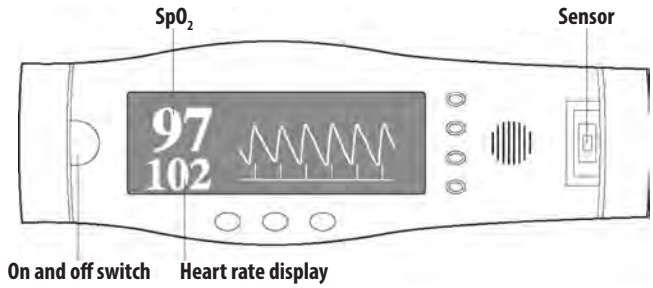
- Accurate
- Fast
- Easy to use
- Non-invasive
- Portable

⚠ LIMITATIONS

- Requires a pulsatile signal – challenging with motion or poor perfusion.
- Does not measure ventilation ($PaCO_2$).
- False readings can be due to many factors including abnormal haemoglobin (Hb), carbon monoxide (CO) poisoning.
- Remember to remove nail polish if present!

Note: Oxygen partial pressures in the atmosphere are lower at higher altitudes. Therefore, patients at facilities in higher altitudes may require higher flow rates for longer duration for adequate therapy compared with patients at sea level. If the altitude is higher than 1000 m, then a correction factor should be calculated to define ARDS: $PaO_2/FiO_2 \times$ barometric pressure/760.

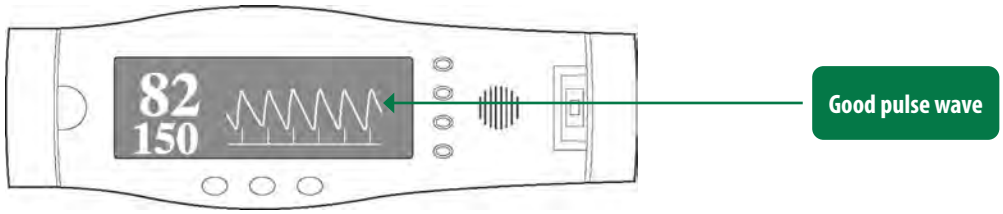
Pulse oximeter displaying normal SpO_2 reading



This image shows a pulse oximeter with a normal oxygen saturation (SpO_2) reading (pulse rate = 102 bpm; SpO_2 = 97%) and a plethysmographic (pulse) wave (i.e. the waveform corresponds with arterial pulsation and rate) indicating a good arterial trace and a valid reading.

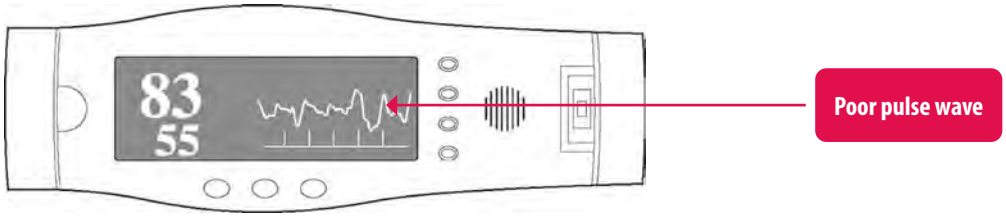
Note: Not all pulse oximeters may display a plethysmograph or signal quality, and without this feature, interpretation of the data must be done cautiously.

Pulse oximeter displaying abnormal SpO_2 reading



In this image (pulse rate = 150 bpm; SpO_2 = 82%), the pulse oximeter has a good plethysmographic wave, indicating a valid arterial trace. Therefore, the SpO_2 reading, which is abnormally low (82%), is likely accurate and indicates that the patient is hypoxaemic. Oxygen should be given. Note the increased heart rate, which is common in seriously ill patients.

Pulse oximeter showing a poor plethysmography (pulse) wave



In this image, the SpO_2 reading is 83% (pulse rate 55 bpm) with a poor pulse wave. The poor pulse wave raises concern that the reading of 83% may not be correct. Multiple factors may cause a poor waveform, including patient movement, poor probe placement, or poor perfusion (shock).

Source: Oxygen therapy for children: a manual for health workers (WHO, 2016); *WHO-UNICEF: Technical specifications and guidance for oxygen therapy devices* (WHO, 2019).

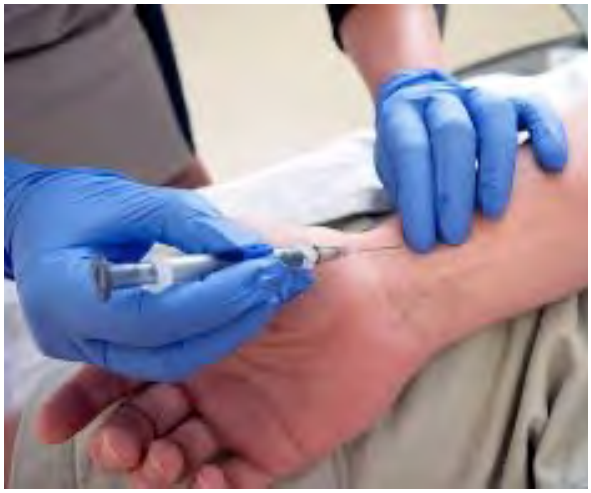
4.3 Blood gas analysis monitoring

Blood gas analysis can be used to measure the pH, partial pressure of oxygen (PaO_2), and partial pressure of carbon dioxide ($PaCO_2$) in arterial, venous or capillary blood.

The pH is a direct indicator of overall acid–base status in arterial, capillary and venous blood. The probable cause of pH disturbances can be inferred only from the $PaCO_2$ and blood bicarbonate (HCO_3) concentration (or the base excess or deficit). In the absence of blood gas analysis, there is no accurate surrogate for assessing acid-base status.

Acidosis is a process that lowers the extracellular fluid pH (pH < 7.35). This can be caused by a fall in the serum bicarbonate concentration (metabolic acidosis with low pH and HCO_3) or an elevation of $PaCO_2$ (respiratory acidosis with low pH and high $PaCO_2$). Acidosis (metabolic or respiratory) is commonly seen when there is major disturbance of the circulation or oxygen delivery, as in severe hypoxaemia due to SARI, ARDS, sepsis and septic shock.

Arterial blood gas analysis can be used for monitoring changes in response to therapy, including ventilator changes. Venous blood and capillary blood may be easier to monitor than arterial blood but should not be used for oxygen level determination. The CO_2 level in arterial, capillary or venous blood helps in assessing and monitoring alveolar ventilation, but peripheral venous values can be inaccurate. While SpO_2 can often be used as a surrogate for PaO_2, end-tidal CO_2 ($EtCO_2$) measurement has limitations when deployed as a surrogate for $PaCO_2$ (see Tool 4.4). Direct measurement of $PaCO_2$ is an important diagnostic tool in patients with SARI and ARDS to help guide protocolized lung protective ventilation.



Source: Oxygen therapy for children: a manual for health workers (WHO, 2016).

Blood gas analysis provides information on oxygenation, ventilation and circulation, but can also inform about electrolyte concentrations (particularly sodium and potassium) which can be measured in the same blood sample by some analysers, such as point of care. Electrolyte abnormalities are common in critically ill patients with SARI and it may be useful for them to be measured for diagnosis and monitoring, besides pH, HCO_3, $PaCO_2$ and PaO_2.

✓ BENEFITS

- Measures pH, HCO_3, $PaCO_2$, PaO_2.
- Informs about ventilation and acidosis.
- May be used to measure lactate, haemoglobin, potassium (e.g. point of care analysers).

⚠ LIMITATIONS

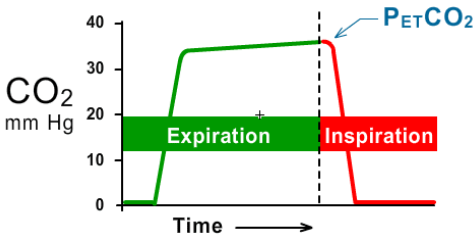
- Invasive arterial puncture.
- Special (heparinized) syringe.
- Rapid transfer (on ice if > 20 minutes) to laboratory.
- Blood gas analyser machine (e.g. I-STAT).
- CO level not detected on all machines.

4.4 Capnometry (capnography)

Capnometry is the non-invasive measurement of $EtCO_2$ partial pressure. This is achieved by shining infrared light through exhaled gas and detecting absorption, from which $EtCO_2$ partial pressure can be derived.

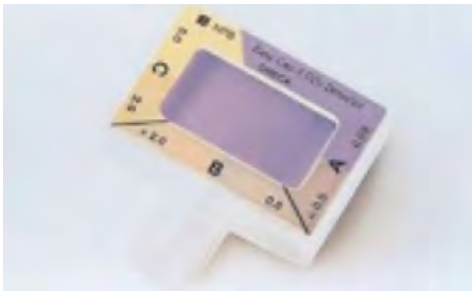
Capnography is the non-invasive measurement of $EtCO_2$ in exhaled breath expressed as the CO_2 concentration over time. The relationship of CO_2 concentration to time is graphically represented by the CO_2 waveform (capnogram).

Normal capnogram

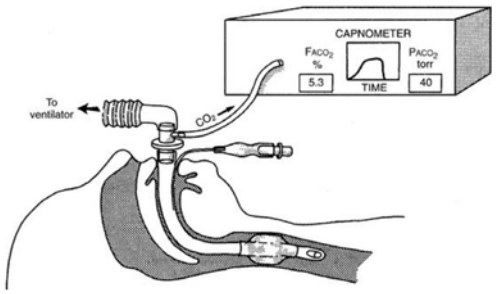


Capnography can be done in line with the breathing circuit, at the hub of the endotracheal tube (i.e. mainstream) or by continuously sampling gas from the exhaled breath of a patient or from a breathing circuit (e.g. nasal, nasal-oral cannula) to a detector (i.e. sidestream). Mainstream systems are configured for intubated patients. Sidestream systems are configured for both intubated and non-intubated patients. Capnography can be used to spot check for correct endotracheal tube placement and continuously monitor for circuit continuity and adequacy of ventilation.[1]

Colorimetric end-tidal CO_2 ($EtCO_2$) detectors



Sidestream capnometry system



Source: Thoracic Key (2021).

CO_2 monitors are either quantitative or qualitative. Quantitative devices measure the precise $EtCO_2$ as a number (capnometry) or a number and a waveform (capnography). Qualitative devices (e.g. colorimetric detectors) report the range in which the $EtCO_2$ falls as opposed to a precise value. For example, the colour in the colorimetric end-tidal CO_2 ($EtCO_2$) detector may change when the endotracheal tube is not correctly placed. $EtCO_2$ measurements can be used to monitor and manage ventilation and circulation.

✓ BENEFITS

- Measures $EtCO_2$ tension in expired air from sampling gas in respiratory circuit.
- In normal lungs, $EtCO_2$ is about 3–5 mmHg less than $PaCO_2$.
- Confirms endotracheal intubation.
- Assess perfusion (during CPR).

⚠ LIMITATIONS

- Inaccurate if there is no discernible plateau: e.g. airflow obstruction.
- Underestimates $PaCO_2$ when there is decreased lung perfusion:
  - pulmonary emboli
  - hypotension
  - high PEEP
  - severe ARDS
  - emphysema.

[1] If there is significant dead space in the circuit (e.g. large filters or heat moisture exchangers) or the patient's lungs (e.g. ARDS), capnography may significantly underestimate $PaCO_2$ and will have limited utility for guiding titration of ventilation.

4.5 National Early Warning Score (NEWS) for adults

The NEWS score was developed by the Royal College of Physicians (United Kingdom of Great Britain and Northern Ireland) to improve the assessment of acute-illness severity of patients in hospital and pre-hospital settings.

For the NEWS update (NEWS 2) in Chart 4 some specific areas were reviewed:

- Determining how the NEWS could be better used to identify patients likely to have sepsis who were at immediate risk of serious clinical deterioration and required urgent clinical intervention.
- Highlighting that a NEWS score of 5 or more is a key threshold for an urgent clinical alert and response.
- NEWS 2:
  - Improves the recording of oxygen use and the NEWS scoring of recommended oxygen saturations in patients with hypercapnic respiratory failure (most often due to COPD).
  - Recognizes the importance of new onset confusion, disorientation, delirium or any acute reduction in the Glasgow Coma Scale (GCS) score as a sign of potentially serious clinical deterioration by including new confusion as part of the AVPU scoring scale (i.e. ACVPU).

Please refer to all materials, including posters and training materials, on their website (). Local adaptation and validation may be necessary.

Chart 1: NEWS scoring system

Physiological parameter	Score						
	3	2	1	0	1	2	3
Respiration rate (per minute)	8		9–11	12–20		21–24	≥ 25
SpO_2 Scale 1 (%)	91	92–93	94–95	≥ 96			
SpO_2 Scale 2 (%)	83	84–85	86–87	88–92 ≥ 93 on air	93–94 on oxygen	95–96 on oxygen	≥ 97 on oxygen
Air or oxygen?		Oxygen		Air			
Systolic blood pressure (mmHg)	90	91–100	101–110	111–219			≥ 220
Pulse (per minute)	40		41–50	51–90	91–110	111–130	≥ 131
Consciousness				Alert			CVPU
Temperature (°C)	35.0		35.1–36.0	36.1–38.0	38.1–39.0	≥ 39.1	

Source: Royal College of Physicians (2017).

Chart 2: NEWS thresholds and triggers

NEW score	Clinical risk	Response
Aggregate score **0–4**	Low	Ward-based response
Red score Score of 3 in any individual parameter	Low–medium	Urgent ward-based response[a]
Aggregate score **5–6**	Medium	Key threshold for urgent response[a]
Aggregate score **7 or more**	High	Urgent or emergency response[b]

[a] Response by a clinician or team with competence in the assessment and treatment of acutely ill patients and in recognizing when the escalation of care to a critical care team is appropriate.

[b] The response team must also include staff with critical care skills, including airway management.

Source: Royal College of Physicians (2017).

Chart 3: Clinical response to NEWS trigger thresholds

NEW score	Monitoring frequency	Clinical response
0	Minimum 12 hourly	• Continue routine NEWS monitoring
Total 1–4	Minimum 4–6 hourly	• Inform registered nurse, who must assess the patient • Registered nurse decides whether increased frequency of monitoring and/or escalation of care is required
3 in single parameter	Minimum 1 hourly	• Registered nurse to immediately inform the medical team caring for the patient • Registered nurse to request urgent assessment by a clinician or team with core competencies in the care of acutely ill patients • Provide clinical care in an environment with monitoring facilities
Total 5 or more **Urgent response threshold**	Minimum 1 hourly	• Registered nurse to inform medical team caring for the patient, who will review and decide whether escalation of care is necessary
Total 7 or more **Emergency response threshold**	Continuous monitoring of vital signs	• Registered nurse to immediately inform the medical team caring for the patient – this should be at least at specialist registrar level • Emergency assessment by a team with critical care competencies, including practitioner(s) with advanced airway management skills • Consider transfer of care to a level 2 or 3 clinical care, i.e. higher dependency unit or ICU • Clinical care in an environment with monitoring facilities

Source: Royal College of Physicians (2017).

Chart 4: NEWS 2 observation chart

NEWS key 0 1 2 3	FULL NAME		DATE OF BIRTH		DATE OF ADMISSION	
	DATE / TIME					DATE / TIME
A+B Respirations Breaths/min	≥25	3				≥25
	21–24	2				21–24
	18–20					18–20
	15–17					15–17
	12–14					12–14
	9–11	1				9–11
	≤8	3				≤8
A+B SpO_2 Scale 1 Oxygen saturation (%)	≥96					≥96
	94–95	1				94–95
	92–93	2				92–93
	≤91	3				≤91
SpO_2 Scale 2† Oxygen saturation (%) Use Scale 2 if target range is 88–92%, eg in hypercapnic respiratory failure †ONLY use Scale 2 under the direction of a qualified clinician	≥97 on O_2	3				≥97 on O_2
	95–96 on O_2	2				95–96 on O_2
	93–94 on O_2	1				93–94 on O_2
	≥93 on air					≥93 on air
	88–92					88–92
	86–87	1				86–87
	84–85	2				84–85
	≤83%	3				≤83%
Air or oxygen?	A=Air					A=Air
	O_2 L/min	2				O_2 L/min
	Device					Device
C Blood pressure mmHg Score uses systolic BP only	≥220	3				≥220
	201–219					201–219
	181–200					181–200
	161–180					161–180
	141–160					141–160
	121–140					121–140
	111–120					111–120
	101–110	1				101–110
	91–100	2				91–100
	81–90	3				81–90
	71–80					71–80
	61–70					61–70
	51–60					51–60
	≤50					≤50
C Pulse Beats/min	≥131	3				≥131
	121–130	2				121–130
	111–120					111–120
	101–110	1				101–110
	91–100					91–100
	81–90					81–90
	71–80					71–80
	61–70					61–70
	51–60					51–60
	41–50	1				41–50
	31–40	3				31–40
	≤30					≤30
D Consciousness Score for NEW onset of confusion (no score if chronic)	Alert					Alert
	Confusion	3				Confusion
	V					V
	P					P
	U					U
E Temperature °C	≥39.1°	2				≥39.1°
	38.1–39.0°	1				38.1–39.0°
	37.1–38.0°					37.1–38.0°
	36.1–37.0°					36.1–37.0°
	35.1–36.0°	1				35.1–36.0°
	≤35.0°	3				≤35.0°
NEWS TOTAL						**TOTAL**
Monitoring frequency						Monitoring
Escalation of care Y/N						Escalation
Initials						Initials

Source: Royal College of Physicians (2017).

4.6 Paediatric Early Warning Score (PEWS)

This score was published in *Critical Care* in 2011 (see Parshuram et al., 2011), has been used in Canada and the United Kingdom of Great Britain and Northern Ireland, and has been shown to be clinically effective in low-resource settings (see Brown et al., 2019).

As in the adult scoring system, it is used to alert staff on general paediatric wards that a child is becoming critically unwell. The scoring system may need calibration or adjustment if used in a different environment to that for which it was developed. A score of 8 or more has a sensitivity of 83% for an impending emergency, including a possible cardiopulmonary arrest, and indicates that the child is critically ill and should be evaluated immediately by a physician and that a higher level of care should be considered. The seven items in the lefthand column should be scored and added together.

		Item sub-score			
Item	**Age group**	**0**	**1**	**2**	**4**
HR (bpm)	0 to < 3 m	> 110 and < 150	≥ 150 or ≤ 110	≥ 180 or ≤ 90	≥ 190 or ≤ 80
	3 to < 12 m	> 100 and < 150	≥ 150 or ≤ 100	≥ 170 or ≤ 80	≥ 180 or ≤ 70
	1–4 yr	> 90 and < 120	≥ 120 or ≤ 90	≥ 150 or ≤ 70	≥ 170 or ≤ 60
	> 4–12 yr	> 70 and < 110	≥ 110 or ≤ 70	≥ 130 or ≤ 60	≥ 150 or ≤ 50
	> 12 yr	> 60 and < 100	≥ 100 or ≤ 60	≥ 120 or ≤ 50	≥ 140 or ≤ 40
SBP (mmHg)	0 to < 3 m	> 60 and < 80	≥ 80 or ≤ 60	≥ 100 or ≤ 50	≥ 130 or ≤ 45
	3 to < 12 m	> 80 and < 100	≥ 100 or ≤ 80	≥ 120 or ≤ 70	≥ 150 or ≤ 60
	1–4 yr	> 90 and < 110	≥ 110 or ≤ 90	≥ 125 or ≤ 75	≥ 160 or ≤ 65
	> 4–12 yr	> 90 and < 120	≥ 120 or ≤ 90	≥ 140 or ≤ 80	≥ 170 or ≤ 70
	> 12 yr	> 100 and < 130	≥ 130 or ≤ 100	≥ 150 or ≤ 85	≥ 190 or ≤ 75
CR time		< 3 seconds			≥ 3 seconds
RR (breaths/min)	0 to < 3 m	> 29 and < 61	≥ 61 or ≤ 29	≥ 81 or ≤ 19	≥ 91 or ≤ 15
	3 to < 12 m	> 24 or < 51	≥ 51 or ≤ 24	≥ 71 or ≤ 19	≥ 81 or ≤ 15
	1–4 yr	> 19 or < 41	≥ 41 or ≤ 19	≥ 61 or ≤ 15	≥ 71 or ≤ 12
	> 4–12 yr	> 19 or < 31	≥ 31 or ≤ 19	≥ 41 or ≤ 14	≥ 51 or ≤ 10
	> 12 yr	> 11 or < 17	≥ 17 or ≤ 11	≥ 23 or ≤ 10	≥ 30 or ≤ 9
Respiratory effort		Normal	Mild increase	Moderate increase	Severe increase/ any apnoea
SpO_2 (%)		> 94%	91% to 94%	≤ 90%	
Oxygen		Room air		< 4 L/min or < 50%	≥ 4 L/min or ≥ 50%

Notes: CR time – capillary refill time; HR – heart rate; RR – respiratory rate; SBP – systolic blood pressure; SpO_2 – peripheral oxygen saturation.

Source: Parshuram et al. (2011).

4.7 Routine monitoring and care framework for COVID-19 patients

To be adapted by context and local care pathway.

Routine monitoring and care framework

SEVERITY OF ILLNESS		MILD		MODERATE			SEVERE	CRITICAL
		Without risk factors	With ≥ 1 risk factors	Without risk factor	With ≥ 1 risk factor			
Patient disposition		Home	Home[a]	Home[b]	Home[c]	Inpatient ward	High dependency, step down or ICU	ICU
Vital signs	Temperature	Self-monitoring (initial assessment, daily and as needed)	Self-monitoring (initial assessment, daily and as needed)	Self-monitoring (initial assessment, daily and as needed)	Every 8–12 h	On admission and every 6–8 h	Intermittent, at least every 4 h	Intermittent, at least every 3 h or continuously
	Oxygen saturation (SpO_2)	No[d]	Self-monitoring (initial assessment, daily and as needed)	No[d]	Every 8–12 h	On admission and every 6–8 h	Continuous or as frequent as possible	Continuously or as frequent as possible
	Respiration rate (RR)	No[d]	Self-monitoring on initial assessment, daily and as needed	No[d]	Every 8–12 h	On admission and every 6–8 h		
	Heart rate (HR) and regularity	No[d]	Self-monitoring (initial assessment, daily and as needed) (if SpO2 is measured)	No[d]	Every 8–12 h (if SpO_2 is measured)	On admission and every 6–8 h		
	Blood pressure (BP)	No[d]	N/A with telemedicine	No[d]	Every 8–12 h	On admission and every 6–8 h	Intermittent, at least every 2–4 h	Continuously if arterial line is in place, or every 5–15 mins during resuscitation, and every 30–60 mins once stabilized
Assessment measures	Symptoms' assessment	Self-monitoring (initial assessment, daily and as needed)	Self-monitoring (initial assessment, daily and as needed)	Self-monitoring (initial assessment, daily and as needed)	Self-monitoring (initial assessment, daily and as needed)	On admission and every 6–8 h	Continuous or as frequent as possible	Continuous or as frequent as possible
	Physical examination	No[d]	No[d]	No[d]	No[d]	On admission and every 6–8 h	Once in shift minimum	Focused examination specific to clinical problems every 30–60 mins during resuscitation. Once stabilized, every 2–4 h
	Mental status (AVPU)	Self-monitoring (on initial assessment, daily and as needed)	Initial assessment, daily and as needed	Self-monitoring (initial assessment, daily and as needed)	Initial assessment, daily and as needed	On admission and every 6–8 h	Intermittent, at least every 2–4 h	Continuous observation at the bedside with the patient or every 1–2 h, intermittently

Routine monitoring and care framework continued

SEVERITY OF ILLNESS		MILD		MODERATE			SEVERE	CRITICAL
		Without risk factors	With ≥ 1 risk factors	Without risk factor	With ≥ 1 risk factor			
Advanced monitoring tools	Intake and output measurements	N/A	N/A	N/A	N/A	Every 6–8 h	Every 4 h	Every 1 h
	3- or 5-lead electrocardiogram (ECG)	N/A	N/A	N/A	N/A	As needed	Continuous cardiac rhythm monitoring if needed	Continuous cardiac rhythm monitoring
	End-tidal CO_2 ($EtCO_2$)	N/A	N/A	N/A	N/A	As needed	Continuously or as frequent as possible in patients at risk of airway obstruction or hypoventilation	Continuous or as frequent as possible
	Arterial blood gases (ABGs)	N/A	N/A	N/A	N/A	As needed	As needed	Daily, after ventilator adjustments, if there are clinical changes or more frequently if available and if SpO_2 reading are unavailable. This can be done as needed to titrate respiratory therapy
	Ventilator parameters	N/A	N/A	N/A	N/A	N/A	N/A	Evaluate peak inspiratory pressure (PIP), plateau pressure (Pplat), set RR and alarms every 2–4 h or within about 1 h of ventilator changes
	Chest X-ray	N/A	N/A	N/A	N/A	As needed	As needed	As needed
	12-lead ECG	N/A	N/A	N/A	N/A	As needed	As needed	As needed

N/A – not applicable/essential, but health care provider in charge of patient follow-up should consider if necessary.

Notes:

[a] **Patients with ≥ 1 risk factor and mild disease** who are not hospitalized should use pulse oximetry monitoring at home as part of a package of care (telemedicine, home hospitalization programmes) including patient and provider education and appropriate follow up and report to health worker on a daily basis. The rest of the vital signs, such as temperature, RR, HR, BP, are recommended to be reported to the health care provider who follows up the patient at home if the equipment is available at home.

[b] **Patients without risk factors and moderate disease** can be initially managed at home with self-monitoring and reporting to a health worker if any complication or emergency signs occur.

[c] **Patients with ≥ 1 risk factor and moderate disease** should, preferably, be referred to a health care facility for monitoring and treatment. If this is not possible, patients can be initially managed at home, preferably monitored by a health worker (telemedicine, home hospitalization programmes) at least once daily; and patients should record vital signs as detailed in the table above and report to the health worker on a daily basis.

[d] **The need for monitoring of vital signs (SpO_2, HR, RR, BP) and physical examination** should be assessed by health care provider who follows up the patient at home with telemedicine or home hospitalization programmes (ensure the equipment is available).

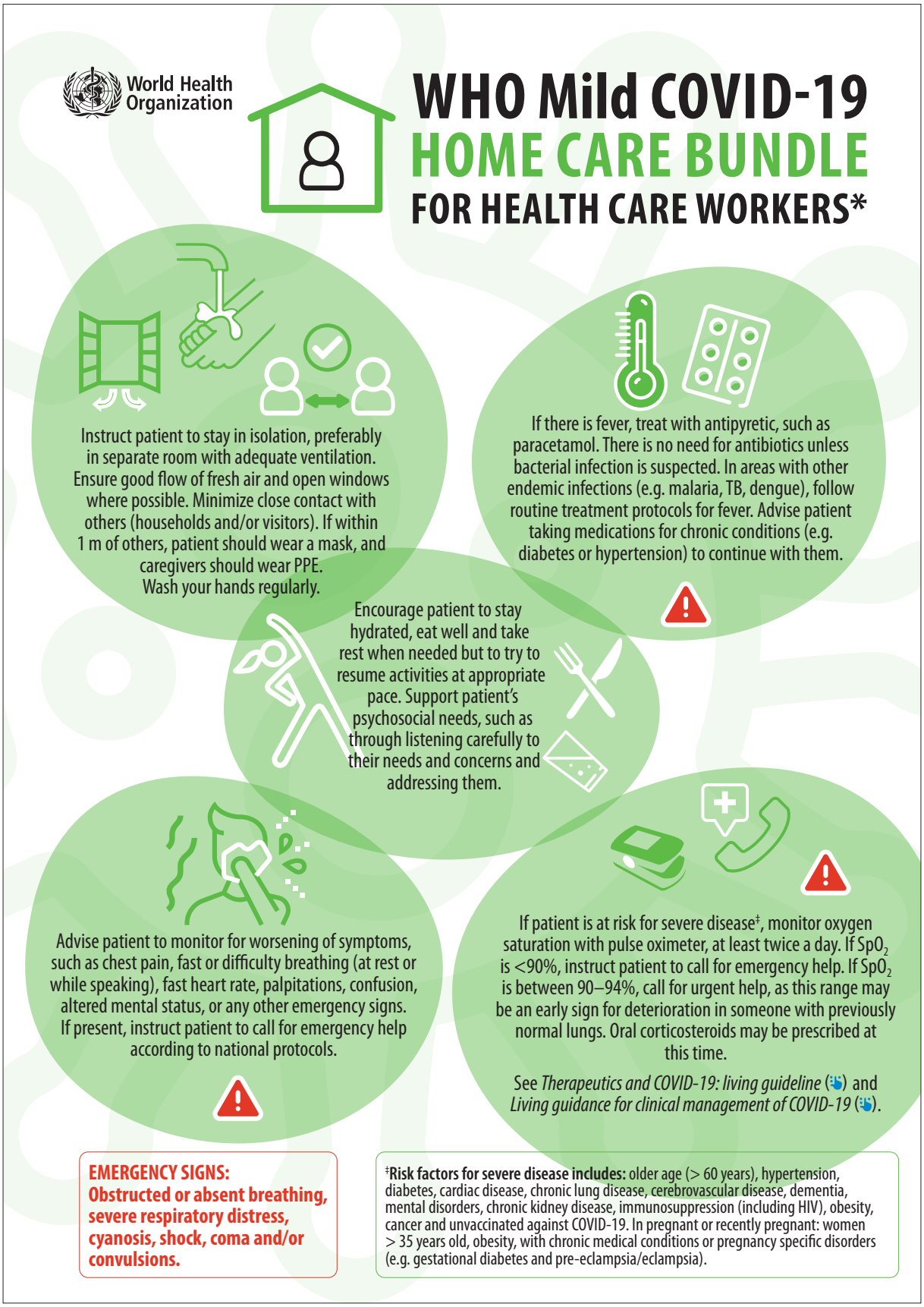
Risk factors for severe disease

Older age (> 60 years), hypertension, diabetes, cardiac disease, chronic lung disease, cerebrovascular disease, dementia, mental disorders, chronic kidney disease, immunosuppression (including HIV), obesity, cancer, pregnancy and post-partum period (up to 6 weeks) and unvaccinated for COVID-19. Risk factors in pregnant or recently pregnant: women > 35 years old, obesity, with chronic medical conditions or pregnancy specific disorders (e.g. gestational diabetes and pre-eclampsia/eclampsia).

Patients with any emergency sign at home, such as obstructed or absent breathing, severe respiratory distress, cyanosis, shock, coma and/or convulsions should seek immediate medical attention and be referred to a health facility.

Source: Modified from WHO Health Emergencies Programme, WHO Academy, 2020.

4.8 WHO Mild COVID-19 home care bundle for health care workers



WHO Mild COVID-19 HOME CARE BUNDLE FOR HEALTH CARE WORKERS*

*This is a derivative product related to the WHO *COVID-19 Clinical management: living guidance, Therapeutics and COVID-19: living guideline*, WHO Home care for patients with suspected or confirmed COVID-19 and OpenWHO.org. Advice for health workers that are caring for COVID-19 patients at home.

Severe disease

Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea) plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO_2 < 90% on room air at rest.

Child with clinical signs of pneumonia (cough or difficulty in breathing) + fast breathing or chest wall indrawing) + at least one of the following:

- SpO_2 < 90%
- Very severe chest wall indrawing, grunting, central cyanosis or presence of any other general danger sign (inability to breastfeed or drink, lethargy or unconsciousness or convulsions).

Critical COVID-19

Patient presenting with acute respiratory distress syndrome, sepsis, septic shock, acute thrombosis or other conditions that normally require life-sustaining therapies.

CAUTION: The oxygen saturation threshold of 90% to define severe COVID-19 and should be interpreted cautiously. For example, clinicians must use their judgment to determine whether a low oxygen saturation is a sign of severity or is normal for a given patient with chronic lung disease. Similarly, a saturation between 90–94% on room air may be abnormal (in patient with normal lungs) and can be an early sign of severe disease, if patient is on a downward trend. Generally, if there is any doubt, err on the side of considering the illness as severe.

Supplemental oxygen and humidification at home should be medically prescribed and supervised by a health worker. Use only concentrators that are approved by the local authorities. Follow the instructions for use and avoid flammable sources close by.

Criteria for discharging patients from isolation (i.e. discontinuing transmission-based precautions) without requiring retesting:

- For symptomatic patients: 10 days after symptom onset, plus at least 3 additional days without symptoms (including without fever and without respiratory symptoms).
- For asymptomatic cases: 10 days after positive test for SARS-CoV-2.

ADDITIONAL REFERENCES

WHO patient leaflet for the self-management of symptoms
https://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/publications-and-technical-guidance/2020/support-for-rehabilitation-self-management-after-covid-19-related-illness-2020-produced-by-whoeurope

WHO Healthy at Home
https://www.who.int/campaigns/connecting-the-world-to-combat-coronavirus/healthyathome

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https://www.who.int/publications/i/item/clinical-management-of-covid-19
https://www.who.int/teams/health-care-readiness-clinical-unit/covid-19

World Health Organization

4.9 Memory aid: key criteria used to assess vital signs in children

	Age				
	< 1 month	1 month – 1 year	1–5 years	5–12 years	> 12 years
Normal RR/min	30–40	30–40	20–30	20–25	12–20
RR/min in severe distress	> 60 or < 20	> 50 or < 10	> 40	> 40	> 40
Normal heart rate (HR)/min	120–180	120–180	100–140	90–140	90–140
Normal SBP (mmHg)	60	80	90 + (2 × age)		120
Lower limit SBP (mmHg)	50	70	70 + (2 × age)		90
Normal urine output	1–2 mL/kg/hr		1 mL/kg/hr		0.5–1 mL/kg/hr

Key tips for assessing a sick child

Blood pressure measurement in children
- Cuff should cover to ¾ of the upper arm, calf or thigh.
- Cuffs that are too small or too large give falsely high readings.
- Child should be at rest and not distressed (this will falsely elevate the reading).

To perform capillary refill (CR) assessment
- Press the nail bed of finger or thumb (peripheral CR) or over the sternum (central CR) for 3 seconds. Release and count in seconds the time taken for the return of colour (perfusion).

Weight estimates in children

It is always best to weigh children rather than estimate their weight.
In an emergency, weight can be estimated in visibly well-nourished children.
- Term infants: 2.5–4.5 kg.
- 6 months of age: 5–7 kg.
- After 1 year of age: (age in years + 4) × 2 kg.

Criteria to define severe malnutrition
- Clinical signs of severe malnutrition: visible ribs and no fat on the buttocks, thighs, arms or shoulders.
- Mid-upper arm circumference < 11.5 cm.
- Severe wasting: < 70% weight-for-length or -3SD on charts.
- Bilateral pedal oedema.

Signs of respiratory distress
- Fast RR.
- Nasal flaring, grunting.
- Intercostal recession and tracheal tug.
- Very severe: indrawing of the lower chest wall; central cyanosis of the lips and tongue; inability to breastfeed or drink; lethargy.

4.10 Memory aid: key physiological aspects to assess in pregnant women

Item sub-score

	Change with pregnancy	
Measurement	**% change**	**Absolute change**
Cardiac output	↑30–50%	(2 L/min)
Heart rate	↑15–20%	(12 bpm)
Stroke volume	↓20–30%	(18 mL)
Mean arterial pressure	↑0–5%	
Central venous pressure	No change	
Systemic vascular resistance	↓20–30%	(320 dynes/cm^5)
Left ventricular stroke work index	No change	
Mean pulmonary artery pressure	No change	
Pulmonary capillary wedge pressure	No change	
Pulmonary vascular resistance	↓30%	(40 dynes/cm^5)

Source: Adapted from Hegewald and Crapo (2011).

Immune system

- May increase susceptibility to intracellular pathogens such as viruses.
- Changes persist following the end of pregnancy.

Cardiovascular

- Blood volume increases by 40–50% causing dilutional anaemia and decreased oncotic pressure.
- Cardiac output increases by 30–50%.
- Heart rate increases by 10–20 bpm.
- Blood pressure decreases by 5–10 mmHg systolic and 10–15 mmHg diastolic. But after 24 weeks' gestation, gradually increases to non-pregnant level by term.
- Systemic vascular resistance decreases by 20%.

Respiratory

- Increased tidal volume (TV) and minute ventilation. Chronic compensated respiratory alkalosis.
- No change in RR, tachypnoea is not a normal variant of pregnancy!
- No change in vital capacity.
- Increased oxygen consumption to 20–40% above non-pregnant levels.
- Decreased oxygen reserve (this makes pregnant patient more susceptible to effects of respiratory compromise).

Maternal–fetal dyad

- Fetus completely dependent on placenta for oxygen, nutrition and waste removal.
- Placenta is dependent on maternal blood cardiac output (500–800 mL of blood or 17% cardiac output goes to uterus every minute).
- With maternal compromise, blood flow will shunt away from uterus and this can occur before discernible maternal haemodynamic changes.
- If maternal oxygen or blood pressure decreases, the placenta will not be able to maintain adequate perfusion or oxygenation and the fetus will become distressed.

Key tips for complications in pregnant women

Tips regarding preterm labour

- Tocolytics may worsen maternal status by decreasing blood pressure, tachycardia, arrhythmias or causing pulmonary oedema.
- Antenatal corticosteroids promote fetal lung maturation if there is need to deliver fetus preterm (weeks 24–34). Can use betamethasone 12 mg IM every 24 hours for two doses or dexamethasone 6 mg IM every 12 hours for four doses.

Tips for managing respiratory distress

- Keep $SpO_2 \geq 92–95\%$.
- Do not delay intubation for worsening respiratory distress. Be prepared for difficult airway!

Tips for managing hypotension

- Ensure adequate resuscitation but avoid fluid overload.
- Do not lay flat. Position with lateral tilt (elevate either hip 10–12 cm) to augment venous return to heart.
- Cautious vasopressor use as risk of reducing uterine perfusion, must monitor fetus.

Tips regarding antimicrobial therapy

- For suspected influenza virus infection, it is **safe** to treat with oseltamivir and give as soon as possible.
- Also give antibiotics – penicillins, cephalosporins and macrolides are appropriate in pregnancy.
- Avoid fluoroquinolones and doxycycline if possible.

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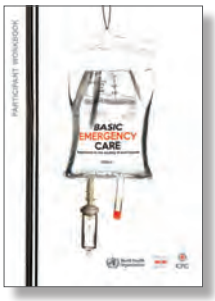
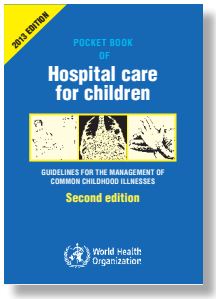
Key resources for supporting the management of SARI



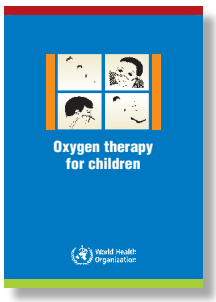
Basic emergency care (BEC): approach to the acutely ill and injured (2018)

Developed by WHO and ICRC, in collaboration with the International Federation for Emergency Medicine, *Basic emergency care (BEC): approach to the acutely ill and injured* is an open-access training course for frontline health care providers who manage acute illness and injury with limited resources. Produced in response to requests from multiple countries and international partners, the BEC package includes a participant workbook and electronic slide decks for each module. Integrating the guidance from WHO *Emergency triage, assessment and treatment (ETAT)* for children and the *Integrated management of adult/adolescent illness (IMAI)*, BEC teaches a systematic approach to the initial assessment and management of time-sensitive conditions where early intervention saves lives.



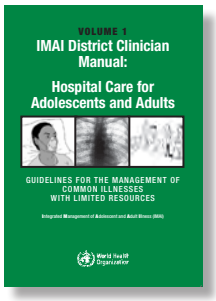
Pocket book of hospital care for children: guidelines for the management of common illnesses with limited resources (second edition) (2013)

This is for use by doctors, nurses and other health workers caring for children at first level referral hospitals with basic laboratory facilities and essential medicines. These guidelines focus on the management of the major causes of childhood mortality in most developing countries including pneumonia, and also cover common procedures, patient monitoring and supportive care on the wards.



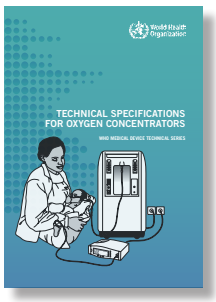
Oxygen therapy for children (2016)

This is a bedside manual for health workers to guide the provision of oxygen therapy for children. The manual focuses on the availability and clinical use of oxygen therapy in children in health facilities to guide health workers, biomedical engineers and administrators. It addresses detection of hypoxaemia, use of pulse oximetry, clinical use of oxygen, delivery systems and monitoring of patients on oxygen therapy. The manual also addresses the practical use of pulse oximetry, and oxygen concentrators and cylinders.



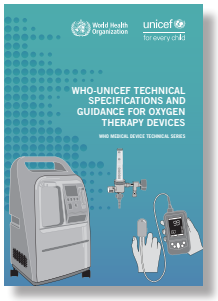
IMAI district clinician manual: hospital care for adolescents and adults. Guidelines for the Management of common illnesses with limited resources (2011)

The manual is written for clinicians working at the district hospital (first-level referral care) who diagnose and manage sick adolescents and adults in resource-constrained settings. It aims to support clinical reasoning, and to provide an effective clinical approach and protocols for the management of common and serious or potentially life-threatening conditions at district hospitals. The target audience thus includes doctors, clinical officers, health officers and senior nurse practitioners. It has been designed to be applicable in both high- and low-HIV prevalence settings.



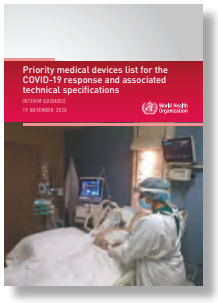
Technical specifications for oxygen concentrators (2015)

This provides an overview of oxygen concentrators and technical specifications to aid in selection, procurement and quality assurance. It highlights the minimum performance requirements and technical characteristics for oxygen concentrators and related equipment that are suitable for the use in health facilities.



WHO-UNICEF technical specifications and guidance for oxygen therapy devices (2019)

The purpose of this document is to increase access to quality products to ensure the supply of oxygen, especially in low- and middle-income countries and low-resource settings within countries from all income groupings. This project is one of many related to improving oxygen supply that other stakeholders are working on. These efforts aim to support ministries of health to ensure oxygen supply is available, as well as raise awareness of the importance of appropriate selection, procurement, maintenance and use of medical devices, both capital equipment and single-use devices.



WHO Priority medical devices list for the COVID-19 response and associated technical specifications (November 2020)

This document describes the medical devices required for the clinical management of COVID-19, selected and prioritized according to the latest available evidence and interim guidelines. It includes: oxygen therapy, pulse oximeters, patient monitors, thermometers, infusion and suction pumps, X-ray, ultrasound and CT scanners as well as PPE. In order to facilitate access to quality assured priority medical devices, the document also includes technical and performance characteristics, related standards, accessories and consumables. It is intended for policy-makers and planning officers in ministries of health, procurement and regulatory agencies, intergovernmental and international agencies as well as the medical device industry.

5 Diagnostic testing for patients with ARI

5 Diagnostic testing for patients with ARI

Summary

The differential diagnoses for SARI include a wide spectrum of community-acquired pathogens, including respiratory viruses, bacteria and other less common micro-organisms. The ranking of differential diagnoses will vary by host factors (e.g. age, presence of chronic conditions, travel history, vaccination), environmental factors (e.g. geographic location, vectors), local epidemiology (e.g. the prevalence of the pathogen in the community, endemic infections) and pathogen factors (e.g. tropism for lungs). See Chapter 1 for more details. **Diagnostic testing should be conducted based on the differential diagnosis and pre-test clinical likelihood of disease.**

In patients presenting with ARI, **the collection of upper respiratory tract samples is recommended** to guide further management. Testing should be done as soon as possible and inform treatment plans. Use appropriate IPC precautions when collecting specimens. See *Infection prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed* ().

Collect specimens from the upper respiratory tract (URT: nasopharyngeal and oropharyngeal) AND, where clinical suspicion remains and URT specimens are negative, collect specimens from the lower respiratory tract when readily available (LRT: expectorated sputum, endotracheal aspirate or bronchoalveolar lavage in ventilated patient) for SARS-CoV-2 testing by RT-PCR or antigen detection rapid diagnostic tests and bacterial stains/cultures.

If patient presents with signs or symptoms that meet criteria for SARI, also collect:

- Samples of blood and sputum for bacterial culture, to diagnose potential bacterial cause of pneumonia and sepsis, ideally before antimicrobial therapy. However, do not delay empiric and appropriate antimicrobial treatment.

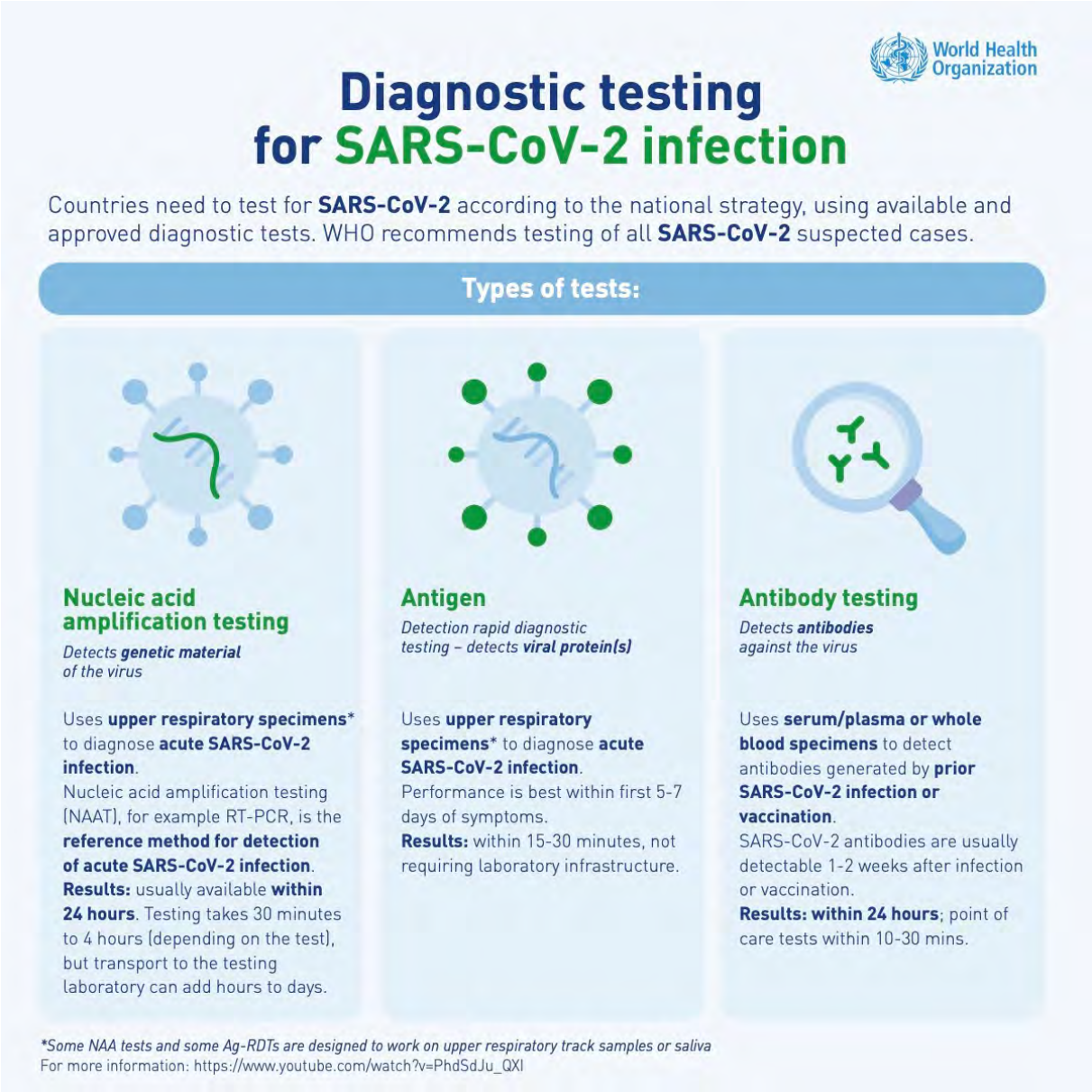
Other considerations for areas with endemic infections should align with local protocols:

- In malaria-endemic areas, patients with fever should be tested for malaria and treated appropriately.
- In areas where arbovirus infection is endemic, then testing for dengue, chikungunya or yellow fever, may be considered in patients with undifferentiated febrile illness, particularly when thrombocytopenia is present.
- In areas where there is high prevalence of TB, TB testing can also be considered.
- Co-infection with SARS-CoV-2 may also occur and a positive diagnostic test for dengue does not exclude the testing for COVID-19.

See WHO *Diagnostic testing for SARS-CoV-2 infection* () ().
See WHO *TB guidelines: recent updates* ().
See WHO *Malaria testing* ().

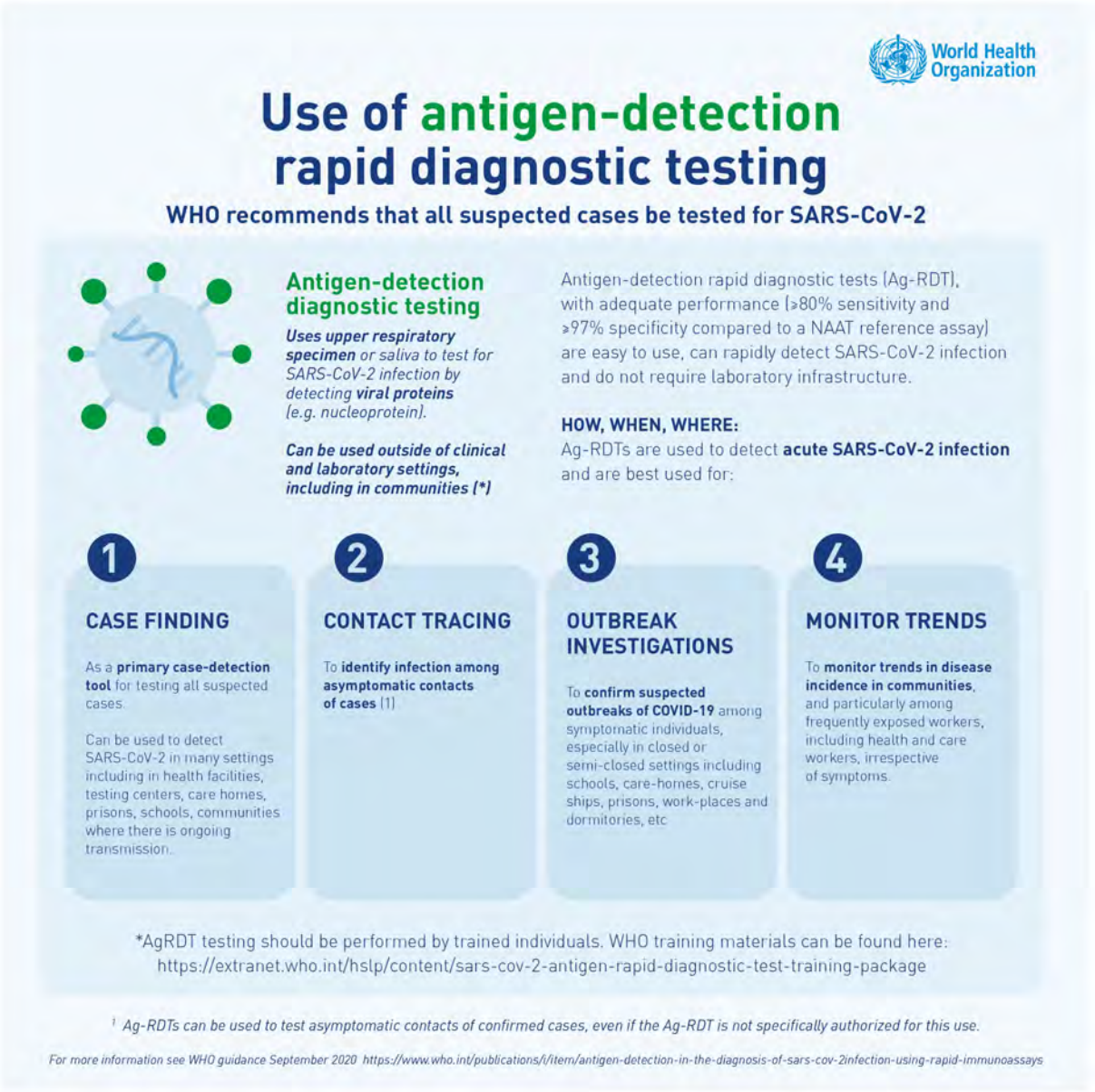
Tools

5.1 Diagnostic testing for SARS-CoV-2 infection



For further information see WHO *Diagnostic testing for SARS-CoV-2 infection* and video on testing for COVID-19 ( ) ( ).

5.2 Use of antigen-detection rapid diagnostic testing for SARS-CoV-2



For further information see WHO *Use of antigen-detection rapid diagnostic testing* and *Antigen-detection in the diagnosis of SARS-CoV-2 infection* ( ) ( ).

5.3 Specimen collection kit for upper respiratory tract specimens

It is best to compile a specimen collection kit before starting to take specimens.

Here is an inventory of all items that should be in the specimen collection kit for URT specimens.

Required items

- PPE (gloves, medical or FFP2/N95 mask, gown, face shield/goggles)
- ice packs/cooler box
- field collection forms
- an alcohol-resistant pen or marker for labelling samples
- sterile Dacron or rayon swabs
- 1–2 mL viral transport medium (VTM)*
- specimen collection containers.

* When antigen rapid diagnostic tests (Ag-RDT) are conducted, sampling/collection material used should follow the manufacturer's instructions. Often VTM is not suitable for RDT. However, having VTM samples is critical for subsequent culture and often for PCR (important for influenza surveillance); thus if Ag-RDT is to be done, an additional sample should be taken.

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Technique

1. Disinfect bottles.
2. Swab with rigid (plastic) shaft for throat and nasal specimens.
3. Use tongue depressors for throat swabs.
4. Use sterile saline (0.9% NS) for nasopharyngeal aspiration.
5. Use sputum or mucus trap for nasopharyngeal aspiration (also require negative pressure).

Swabs

The type of swab used is very important.

Only **sterile Dacron or rayon swabs** with **aluminum or plastic shafts** should be used. This is because calcium alginate or cotton swabs, or swabs with wooden sticks, may contain substances that inactivate some viruses and inhibit PCR testing.

5.3.1 Nasopharyngeal swab technique

Required materials

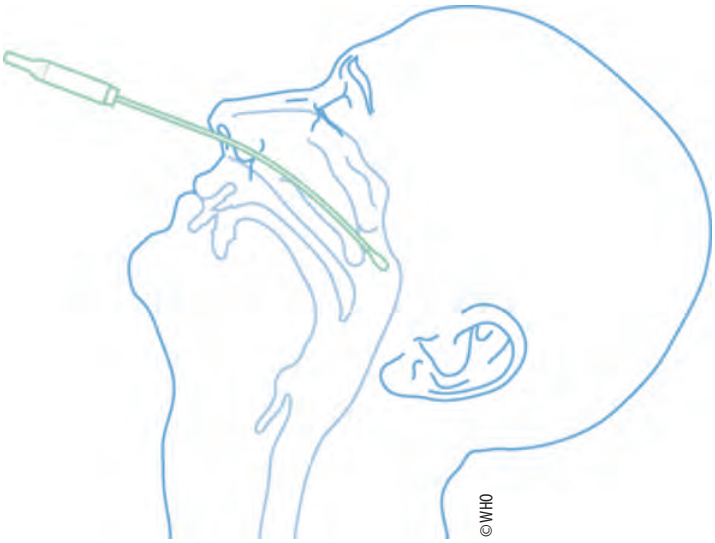
- swab with **flexible** (aluminium or plastic) shaft.

Technique

1. Apply standard, contact and droplet precautions.
2. Insert swab into one nostril and back into the nasopharynx.
3. Leave swab in place for a few seconds.
4. Then slowly remove swab while rotating it over surface of posterior nasopharynx.
5. Withdraw swab from collection site; insert into transport tube or container with VTM.
6. Label specimen container.
7. After collection, immediately transport specimen to the laboratory for viral PCR testing and/or viral antigen detection. If transport to the laboratory is delayed, place specimen on ice or in refrigeration.

In case of nasopharyngeal swab in **infants** and **young children:**

- Use a swab of appropriate size: measure the distance from the nose to the ear (philtrum to the tragus).
- Insert the swab half to full amount of that distance, stopping if you encounter resistance.
- Insert the swab horizontally, below the inferior turbinate, not diagonally up the nose.



How to collect oropharyngeal and nasopharyngeal specimens for the diagnosis of COVID-19 ().

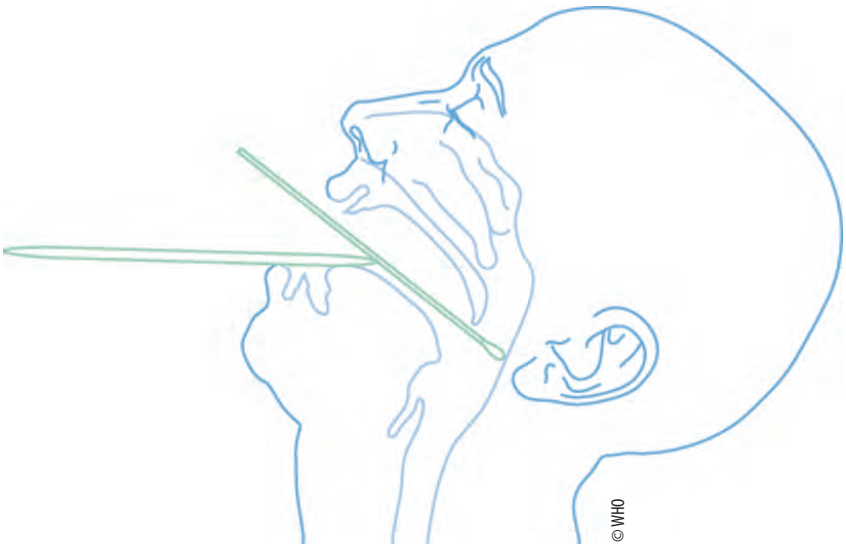
5.3.2 Posterior pharyngeal swab or throat swab technique

Required materials

- swab with rigid (plastic) shaft
- tongue depressor.

Technique

1. Apply standard, contact and droplet precautions.
2. Ask the subject to open his or her mouth and say "ah" to elevate the uvula.
3. Depress the tongue to hold out of way with tongue depressor.
4. Swab the posterior pharynx and do not touch tongue with swab.
5. Insert into transport tube or container with VTM. Break applicator tip to ensure closure of vial.
6. Label specimen container.
7. Immediately transport specimen to the laboratory for viral PCR testing and/or viral antigen detection. If transport to the laboratory is delayed, place specimen on ice or in refrigeration.



For further information see *Optimal insertion depth for nasal mid-turbinate and nasopharyngeal swabs* (Callesan et al., 2021) and video on collecting oropharyngeal and nasopharyngeal specimens for the diagnosis of COVID-19 ( ) ( ).

5.3.3 Tracheal aspirate technique

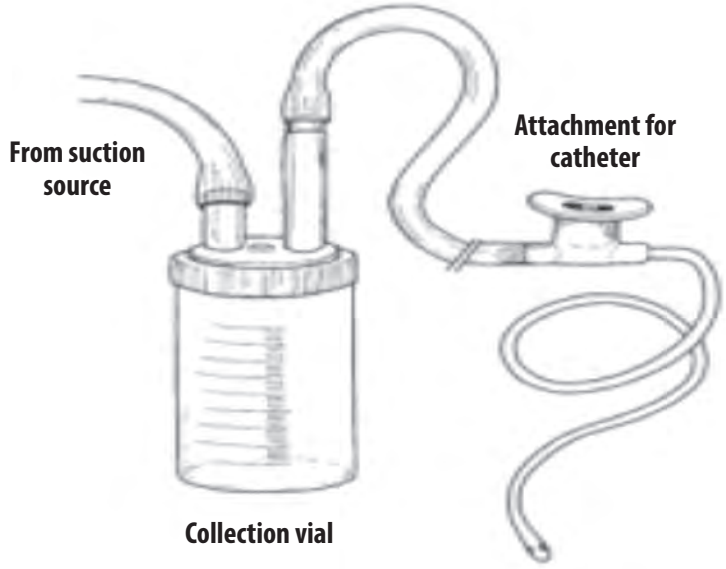
Intended for patients intubated and receiving invasive mechanical ventilation (IMV).

Required materials

- suction outlet (portable or wall)
- sterile suction catheter
- specimen mucus trap (i.e. Lucken's tube)
- sterile saline (0.9% NS)
- IPC for airborne precautions (N-95 particulate mask)
- a sterile suction catheter (not a closed, inline system)
- suction tubing
- airway emergency equipment.

Technique

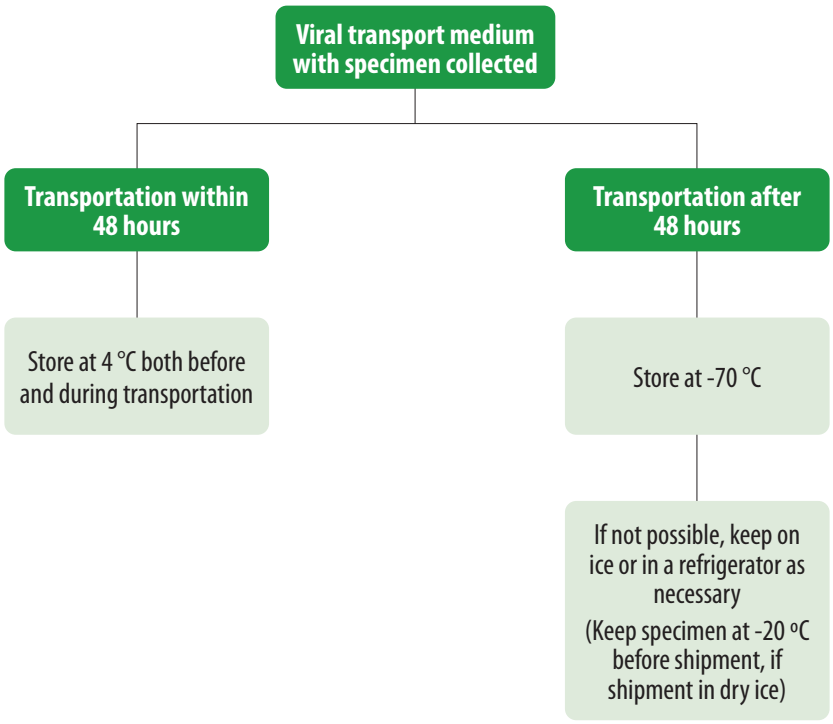
1. Apply standard, contact, droplet and airborne precautions.
2. Prepare patient: pre-oxygenate with 100% fraction of inspired oxygen (FiO_2). Give adequate sedation.
3. Attach mucous trap to catheter and suction outlet. Turn on suction to make sure functioning. Then turn it off.
4. When you are ready, disconnect ventilator tubing from endotracheal tube.
5. Without applying suction, insert sterile suction catheter apparatus into endotracheal tube, about 2–3 cm beyond tip.
6. Apply suction and collect sample into the mucous trap. Hold trap upright to prevent secretions from going into the pump. Slowly withdraw catheter. Replace ventilator tubing.
7. If inadequate sample, instil 3–5 mL of sterile saline, give two insufflations/deep breaths and apply suction.
8. After collection, immediately transport specimen to laboratory for viral testing and bacteriology.
9. Store in refrigerator (2–8 °C) for maximum 24 hours.
10. If delay, store in freezer < -20 °C.



5.4 Guideline for specimen storage

Viral transport medium is used immediately after the collection of samples for viral isolation and testing. It prevents the specimen from drying out and prevents bacterial and fungal growth.

Although you should send specimens in VTM to the laboratory as soon as possible, it is important to properly store them before you send them to a laboratory if there is a delay.



Do not freeze samples in the standard freezer. It is very important to avoid freeze-thaw cycles because this will destroy some types of virus. It is better to keep a sample on ice even for a week, than to allow the sample to freeze and thaw multiple times.

Viral transport medium information

Possible suppliers
Local laboratory and commercial supplier.

Description
It is usually supplied in the form of 1–3 mL of VTM in sterile container.

Stock management
It is important that clinicians liaise with the laboratory to make sure that there is sufficient stock of VTM available at facility, and that it is stored in an area which is accessible to clinicians when needed.

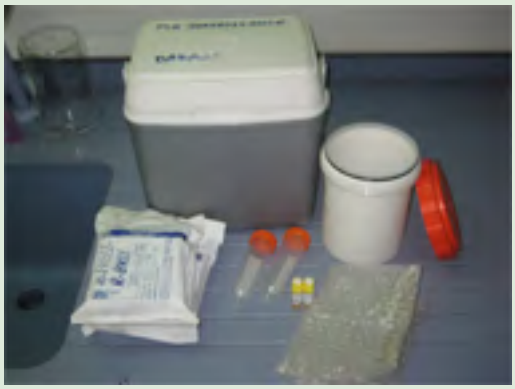
Conservation
If VTM must be stored for long periods, this should be done in a freezer at -20 °C. For short periods of time VTM may be stored in a fridge at 4–6 °C.

5.5 Material for specimen transportation

When you are ready to pack specimens, no more than 500 mL should be in the specimen container. For transportation from the field to the laboratory, you must use three packaging layers. This is done to protect specimens from damage during transportation.

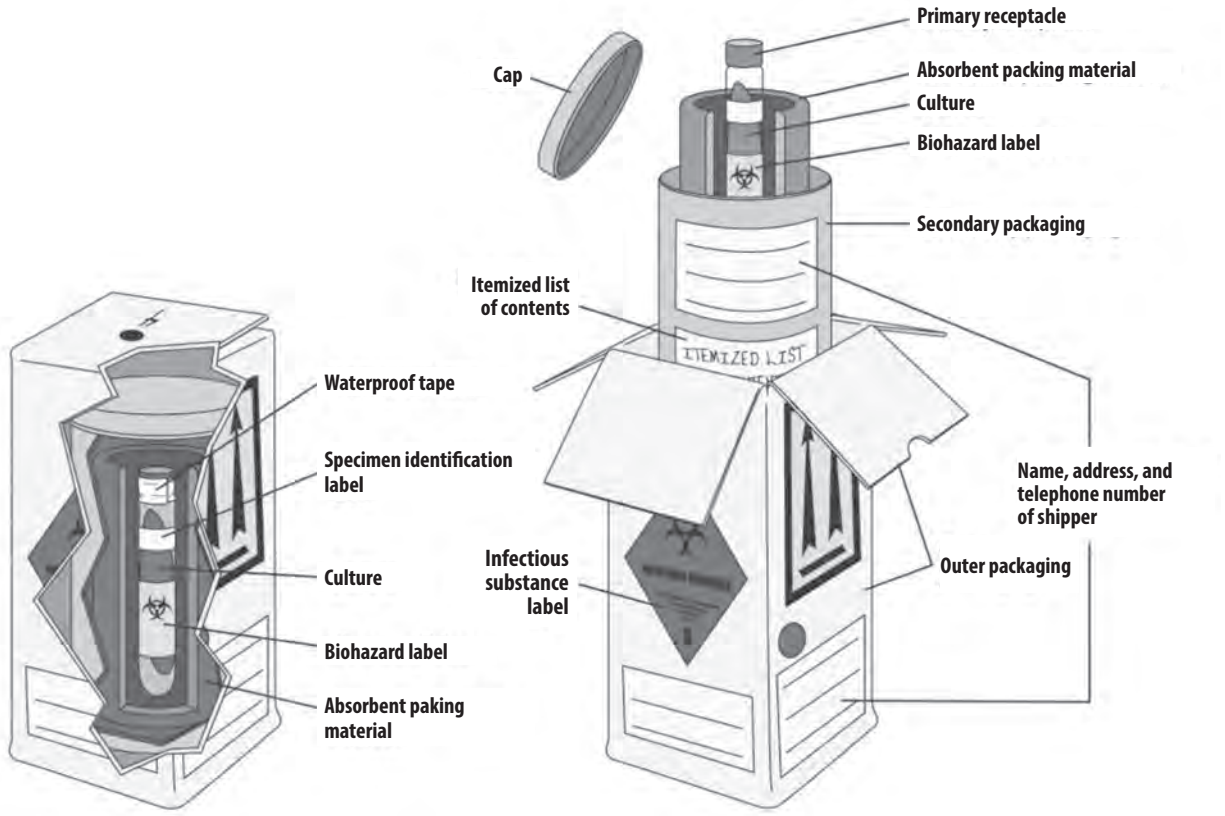
Required materials

- primary waterproof container (e.g. Falcon tube)
- absorbent material:
  - bubble wrap
  - secondary recipient
  - cooler box
  - ice packs
  - sample identification form.



Packing and labelling of infectious substances not refrigerated

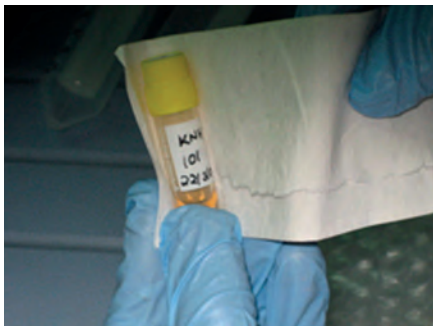
For SARS-CoV-2, specimens should be classified as Category A, UN2814, "infectious substance, affecting humans". Clinical samples will be classified as UN3373, "Biological Substance Category B".



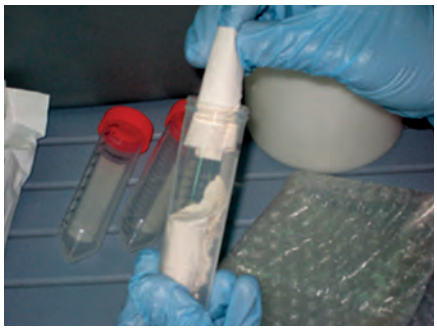
For more details review:

- *Laboratory biosafety guidance related to coronavirus disease (COVID-19)*.
- *Guidance on regulations for the transport of infectious substances 2021–2022*.

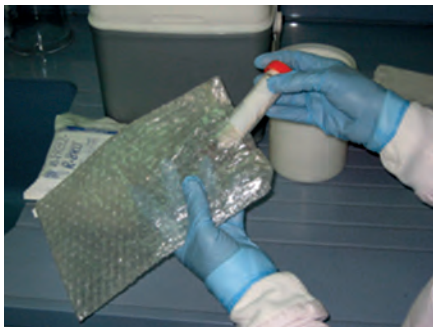
5.6 Guideline for specimen transportation



1 Envelop the cryo-tube with blotting paper.

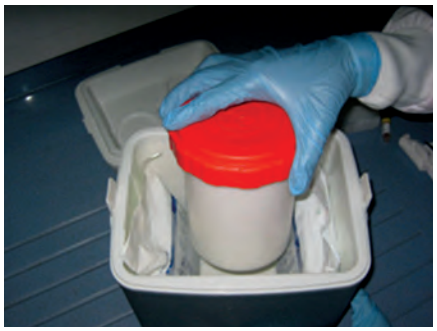


2 Place all components in a waterproof secondary recipient container and close in order to be watertight.

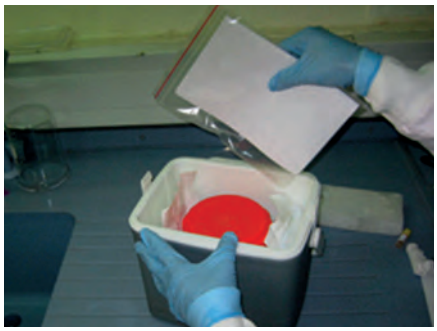


3 Place the primary waterproof container in bubble wrap or a shock-absorbing material.

4 Place all components in a waterproof secondary recipient container and close in order to be watertight.



5 Place ice packs in the cooler box. Put the filled secondary container in the cooler box. The recipient container should be in a vertical position.



6 Insert the sample identification form in a zip bag and place the zip bag in the cooler box, next to the secondary recipient container.

7 Close the cooler box in order to be watertight. Write expeditor and addressee on the external part of the cooler box. Put infectious substance label if necessary.

Source: Adapted from influenza sentinel surveillance training, Institute Pasteur of Madagascar, CDC and WHO.

5.7 Guide for blood culture collection in patients with SARI

Blood cultures should be obtained before starting antimicrobial therapy in all patients with sepsis in the hospital. The Surviving Sepsis Campaign guidelines caution that this should not delay antimicrobial treatment by more than 45 minutes.

This technique is adapted from the United States Centers for Disease Control and Prevention (CDC) website ( ).

Required materials

- PPE (gloves and mask)
- alcohol swabs
- chlorhexidine swabs (associated with less contamination than standard povidone-iodine)
- blood culture bottles (two bottles per set, one anaerobe and one aerobe)
- two sterile needles (adult: 22 gauge; paediatric: 25 gauge)
- two syringes (adult 20 mL; paediatric 5 mL)
- tourniquet
- sterile gauze pad
- adhesive tape
- patient labels
- plastic zip lock bag for transport.

Technique

1. Check patient ID, explain procedure.
2. Hand washing.
3. Disinfect bottle tops with 70% isopropyl alcohol (alcohol pad) in a circular motion, allow to dry.
4. Clean the puncture site with chlorhexidine swab. Using aseptic technique, remove applicator from package. Holding applicator downward, squeeze wings and release solution. Scrub back and forth over the site for 30 seconds on dry skin. Allow to dry.
5. Puncture the vein with clean needle. Use sterile gloves if you plan to palpate vein after cleaning site.
6. For adults, collect 10–20 mL; for children, collect 3–5 mL for each blood culture set.
7. Remove needle from vein, divide blood into two blood culture bottles, by placing same needle perpendicularly into the bottle. Do not overfill bottles. If not enough for both bottles, preferably start filling the aerobic bottle. There are systems with bottles that can tap the blood directly from the vein. If possible, this system is preferred.
8. Gently rotate bottle to mix blood and broth.
9. Two blood cultures (by separate stick) per septic episode is sufficient (except in endocarditis).
10. Place label and put into plastic bag and send to the laboratory.

Contaminated blood culture

If skin is not adequately cleansed before obtaining the culture, or the procedure for taking the culture is not done carefully and cleanly, bacteria from the skin may be injected into the bottle, producing contamination and a false positive blood culture.

This may lead to misdiagnosis and prolonged antimicrobial use.

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6 Oxygen therapy

6 Oxygen therapy

Summary

The administration of supplemental oxygen is necessary when a patient has low blood oxygen levels, termed hypoxaemia. Untreated, acute hypoxaemia can lead to tissue hypoxia (low level of oxygen at the at the cellular level), organ dysfunction and death. Delivery of oxygen to tissues also relies on adequate cardiac output and haemoglobin to carry oxygen to the tissues.

Oxygen delivery (DO_2) = cardiac output (CO) × oxygen content in arterial blood (CaO_2)
- $CaO_2 = 1.34 \times (Hb) \times SpO_2 + (0.003 \times PaO_2)$
- $CO = SV \times HR$

Oxygen therapy improves oxygen delivery to the tissues by increasing oxygen content in the blood. Oxygen content in the blood is frequently measured by pulse oximetry as oxygen saturation (SpO_2).

Oxygen therapy provides patients with an oxygen concentration greater than that in ambient air (> 0.21). While oxygen therapy can be generated from various sources and applied via various delivery mechanisms, the fundamentals of oxygen therapy remain the same.

1. Oxygen concentration (% O_2) from the oxygen source (i.e. liquid oxygen, pressure swing adsorption [PSA], bedside concentrator) is the purity of oxygen produced by the device. It can range widely depending on the quality of the source but generally should range from 0.82–1.0 (82–100%).

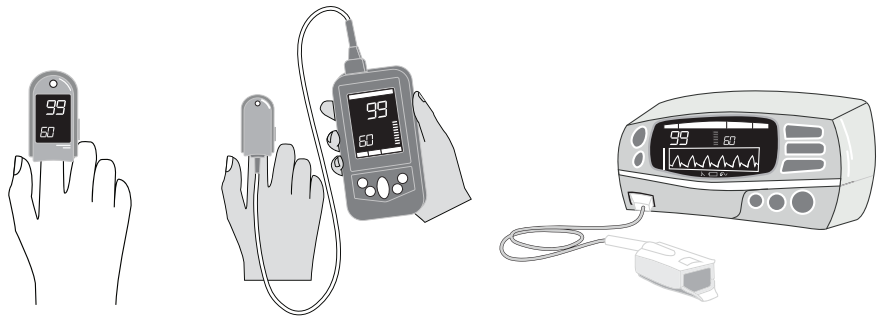
2. Fraction of inspired oxygen (% FiO_2) is the oxygen concentration that is inspired by the patient, usually a result of mixing the oxygen source and ambient air and can range from 0.21–1.0 (21–100%). This varies depending on the delivery device and the patient's respiratory drive.

3. Oxygen saturation (% SpO_2) and oxygen partial pressure (PaO_2) are the measured oxygen levels in blood, the former measured by pulse oximeter and the latter by blood gas analyser.

1 % O_2: oxygen concentration at source
2 % FiO_2: fraction of inspired oxygen
3 % SpO_2: blood oxygen saturation

Source: The clinical use of oxygen in hospitals with limited resources: guidelines for health care workers, hospital engineers and programme managers (WHO, 2009).

Pulse oximeters should be available in all clinical areas where oxygen is delivered. Blood gas analysers and end tidal carbon dioxide ($EtCO_2$) monitors should ideally be available at least in ICU or critical care units to measure ventilatory parameters ($EtCO_2$, pH, $PaCO_2$) (see Chapter 4: Monitoring patients with acute respiratory infection).



Fingertip pulse oximeter | **Portable handheld oximeter** | **Table-top oximeter**

Source: WHO-UNICEF technical specifications and guidance for oxygen therapy devices (2019).

Oxygen delivery devices should be selected based on the oxygen needs of the patient and include nasal cannulas, conventional face masks, Venturi face masks and face masks with reservoir bag. If patients require higher levels of oxygen flow (> 10–15 L/min) to reach SpO_2 targets, and/or have other signs of acute respiratory failure, other respiratory support options, that can deliver higher flows and/or positive pressure support should be considered. These include:

- high-flow nasal oxygen (HFNO);
- non-invasive ventilation devices (CPAP, BiPAP delivered via oronasal mask, full face mask, helmet or nasal interface);
- invasive mechanical ventilation (IMV) delivered via endotracheal tube. Do not delay intubation if there are urgent indications.

Note: Use of HFNO, CPAP, BiPAP and IMV for treatment of severe/critical COVID-19 may consume significant quantities of oxygen.

Rational oxygen use delivers the least amount of oxygen necessary to achieve SpO_2 goals. Although avoiding hypoxaemia is the primary goal of oxygen therapy, it is important to remember that giving a patient more oxygen than they need to meet the SpO_2 goal can be harmful and more rapidly deplete oxygen supplies. Therefore, titration up and down of oxygen therapy and trials of oxygen weaning should be performed on a regular basis (see how to titrate oxygen with different devices: Tools 6.5–6.7). Oxygen sources should routinely be checked for quality, including oxygen concentration and flow or pressure output.

Tools

6.1 Indications for oxygen therapy
6.2 Memory aid: oxygen delivery devices
6.3 Memory aid: oxygen delivery in children
6.4 Algorithm to escalate respiratory support in adults and children with pneumonia
6.5 Flowchart on how to titrate oxygen in neonates
6.6 Flowchart on how to titrate oxygen in children
6.7 Flowchart on how to titrate oxygen in adults
6.8 Key tips on awake prone positioning
6.9 Checklist to troubleshoot warning signs during oxygen therapy delivery
6.10 Oxygen supply calculations
6.11 Memory aids: oxygen supply sources and distribution
6.12 Respiratory care order template for oxygen therapy

6.1 Indications for oxygen therapy

Give oxygen immediately to any patient (adult or child) with:

- **Respiratory distress**
- **Sepsis with hypoperfusion or shock**
- **Alteration of mental status**
- **Hypoxaemia**

- **SpO_2 < 90%** (if patient is haemodynamically stable)
- **SpO_2 < 94%** (if patient with any **emergency signs, with or without respiratory distress**)
- **SpO_2 < 92–95%** (if pregnant)

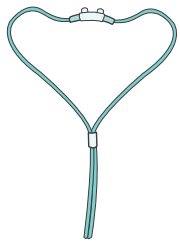
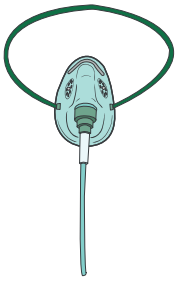
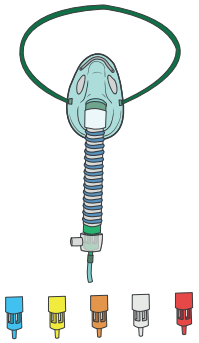
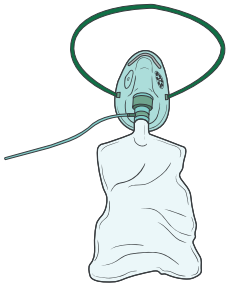
Note: Emergency signs – **obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma and/or convulsions** – may require airway management in addition to oxygen.

Supplemental oxygen therapy should be provided immediately to achieve the following SpO_2 targets:

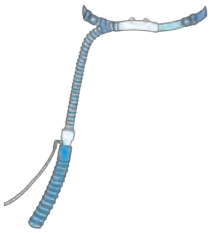
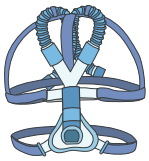
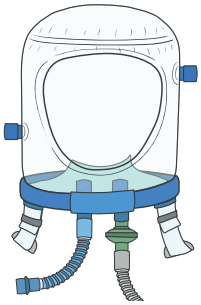
SpO_2 targets
SpO_2 ≥ 90% in adults and children
SpO_2 ≥ 92–95% in pregnant patients
SpO_2 ≥ 94% if child or adult with signs of multi-organ failure, including shock, alteration of mental status, severe anaemia, and/or during resuscitation. Once stabilized, resume target SpO_2 ≥ 90%.

6.2 Memory aid: oxygen delivery devices

Non-invasive O_2 delivery devices

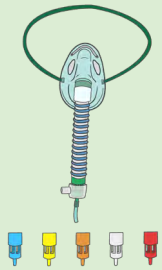
Nasal cannula	Face mask	Venturi face mask	Face mask reservoir bag
			
O_2 flow 1–5 L/min[a]	O_2 flow 5–10 L/min	O_2 flow 2–15 L/min	O_2 flow 10–15 L/min
FiO_2 0.23–0.35[b]	**FiO_2 0.30–0.50[b]**	**FiO_2 0.24–0.6[b]**	**FiO_2 0.5–0.95[b]**

Advanced non-invasive O_2 delivery devices

High-flow nasal oxygen	BiPAP/CPAP			
				
	Oronasal	Nasal	Full face	Helmet
O_2 flow 10–60 L/min[a]	O_2flow ~10–80 L/min[c]			
FiO_2 0.23–1.0[b]	**FiO_2 0.21–1.0[b]**			

[a] O_2 flow ranges differ for neonates, children and adults; see Tool 6.2 for ranges by age.
[b] Delivered O_2 concentration depends on multiple factors including the concentration of the oxygen source and the patient's respiratory pattern (e.g. peak inspiratory flow and minute ventilation).
[c] O_2 consumption for BiPAP/CPAP is widely variable depending on device used and the leak of the system.

Source: USAID-STAR-UCSF OpenCriticalCare.org Project (illustrations Holly Sullivan) ().

Oxygen delivery devices (single use)	Typical flow rate range	FiO_2 delivered	Considerations	Advantages/ disadvantages	Can be used with		
					Oxygen concentrator	Compressed oxygen cylinder	Piped supply oxygen
Nasal cannula, adult and paediatric (single use) 	1–6 L/min	24–44% oxygen Increases by approximately 4% with each litre of oxygen per minute The actual value depends on the patient's inspiratory peak flow	Technically, it is possible to deliver higher flows with this device, however, the oxygen source should deliver the desired flow; it can dry the nasal mucosa and disturb sleeping patterns; humification might be required according to clinical guidance. For paediatric patients with a flow > 4 L/min humidification is necessary (WHO)	**Advantages** Easy to use Patient can eat and talk **Disadvantages** Can be easily dislodged and is not as effective in patients with deviated septum or polyps	**Yes**	**Yes**	**Yes**
Venturi mask; adult, paediatric 	2–15 L/min	24–60% oxygen, according to the type of mask	Allows precise measurement of FiO_2 delivered Utilizes different sized ports to change the FiO_2 delivered (24–50%) Some brands relate a colour to a flow rate and FiO_2 delivered, e.g. blue = 2–4 L/min = 24%; white = 4–6 L/min = 28%; yellow = 8–10 L/min = 35%; red = 10–12 L/min = 40%; green = 12–15 L/min = 60%.	**Advantages** Precise measurement of FiO_2 delivered Does not dry mucous membranes **Disadvantages** Is confining for some patients It interferes with talking and eating	**Yes** with some hesitation, as some studies demonstrate they deliver lower concentrations than expected	**Yes**	**Yes**
Mask with reservoir bag; adult 	> 10 L/min	80–95% oxygen FiO_2 depends on the patient's pattern of breathing	Non-rebreather mask with reservoir bag	**Advantages** Delivers high concentration of oxygen **Disadvantages** Oxygen flow should be > 10 L/min; less can cause the bag to collapse during inspiration	**No**	**Yes**	**Yes**

Disclaimer: This table is intended to provide information from the technical point of view about oxygen delivery devices, including flow rate ranges, achievable FiO_2, and possible oxygen sources that can be used with each device. Clinical decisions should determine the methods of administration of oxygen therapy and device selection.

Source: Priority medical devices list for the COVID-19 response and associated technical specifications (WHO, 2020).

6.3 Memory aid: oxygen delivery in children

Nasal cannula is the preferred method of delivering oxygen to infants and children < 5 years of age with hypoxaemia who require oxygen therapy.

Age of child	Nasal cannula size	Maximal oxygen flow rates
Neonates	Neonatal	0.5–1.0 L/min by nasal cannula
Infants	Infant	1–2 L/min by nasal cannula
Pre-school aged	Child	1–4 L/min by nasal cannula
School-aged	Child to adult	1–5 L/min by nasal cannula

Practical considerations

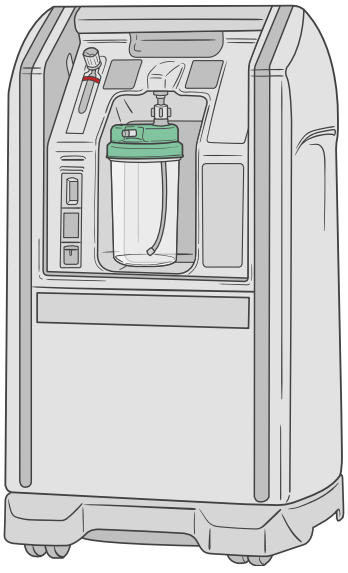
- **Fitting:** The distal prong should fit well into the nostril (premature infants: 1 mm; infants weighing up to 10 kg: 2 mm). The prongs should be secured with a piece of tape on the cheeks near the nose as shown. Care should be taken to keep the nostrils clear of mucus to avoid blockage.

- **Humidification:**

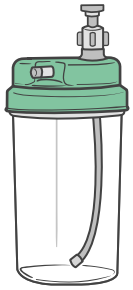
  When oxygen is delivered at standard flow rate (0.5–1 L/min for a neonate, 1–2 L/min for an infant, 1–4 L/min for an older child) through nasal prongs, humidification is not necessary.

  Higher flow rates **without effective humidification** may cause drying of nasal mucosa with associated bleeding, airway obstruction and may cause bronchoconstriction in some conditions (e.g. asthma, COPD).

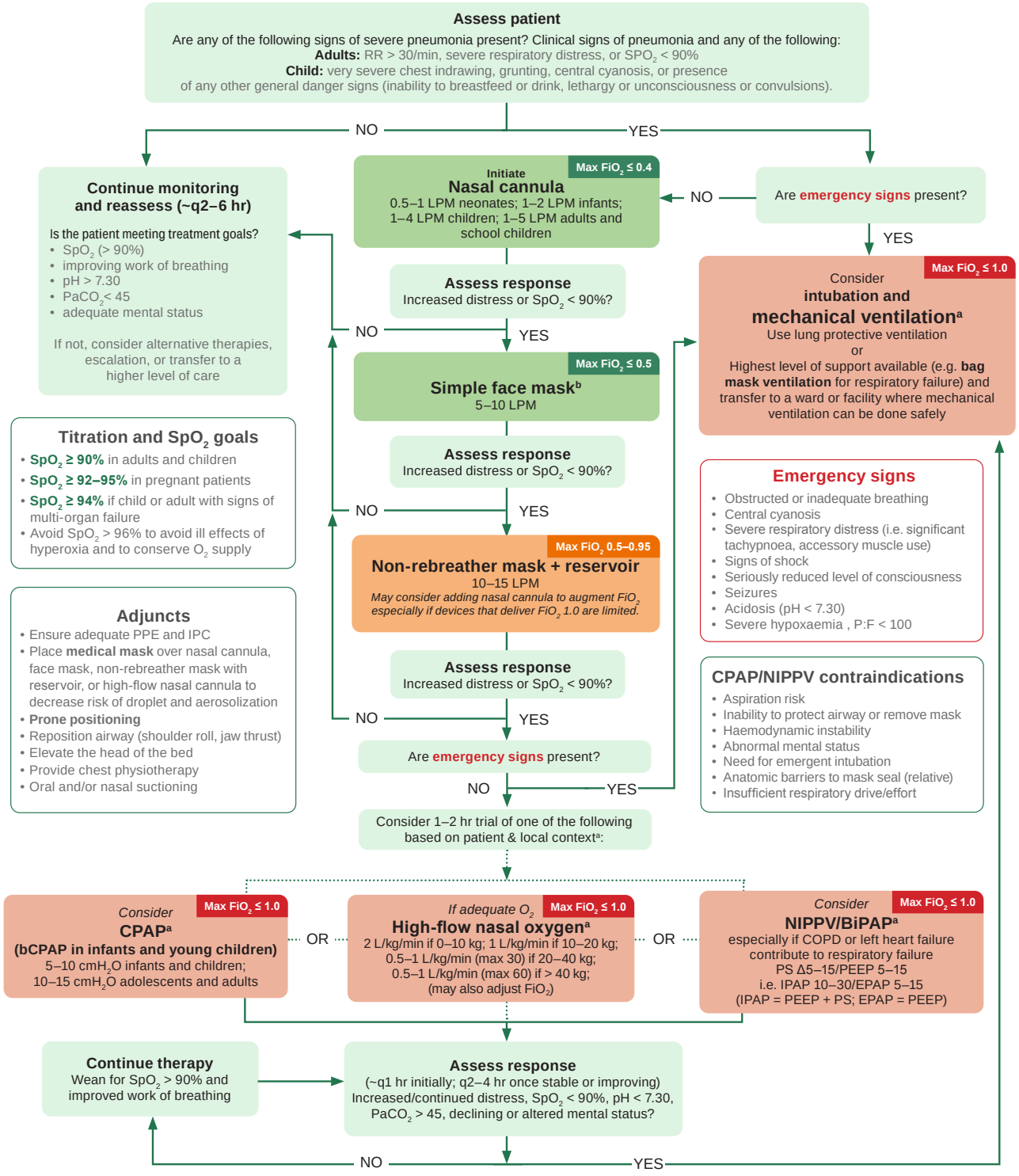
- Humidification is essential when cold oxygen is delivered from a cylinder, compared with concentrators (mainly in tropical countries), as normally concentrators provide oxygen at room temperature.



- Bubble humidifiers reduce the dryness of the oxygen supplied by bubbling the gas through water at room temperature. They must be filled with clean water at least once a day (distilled water or tap water that has been boiled and cooled). The water level in the humidifier should be checked twice daily and topped up as necessary. The humidifier equipment must be washed and disinfected regularly to prevent bacterial colonization.



6.4 Algorithm to escalate respiratory support in adults and children with pneumonia



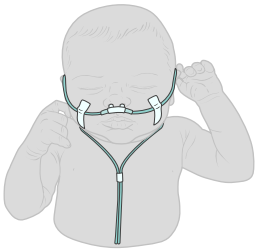
[a] Selection of optimal delivery device should be based on local clinician's judgment and risk-benefit assessment tailored to the individual patient, global and local outcomes data, as well as local resources including O_2 supply, skill of personnel, availability of consumables, monitoring and therapeutic 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.

Source: USAID-STAR-UCSF OpenCriticalCare.org Project and WFSA Intensive & Critical Care Committee.

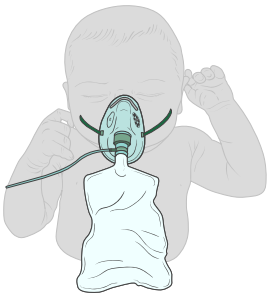
6.5 Flowchart on how to titrate oxygen in neonates



- Start **nasal cannula** oxygen at:
  0.5–1 L/min neonates
  1–2 L/min infants

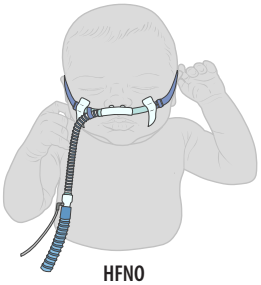
If continued distress or SpO_2 < 90% (or < 94% if emergency signs)

Flow rates higher than 4 L will dry mucous membranes and humidification systems should be used

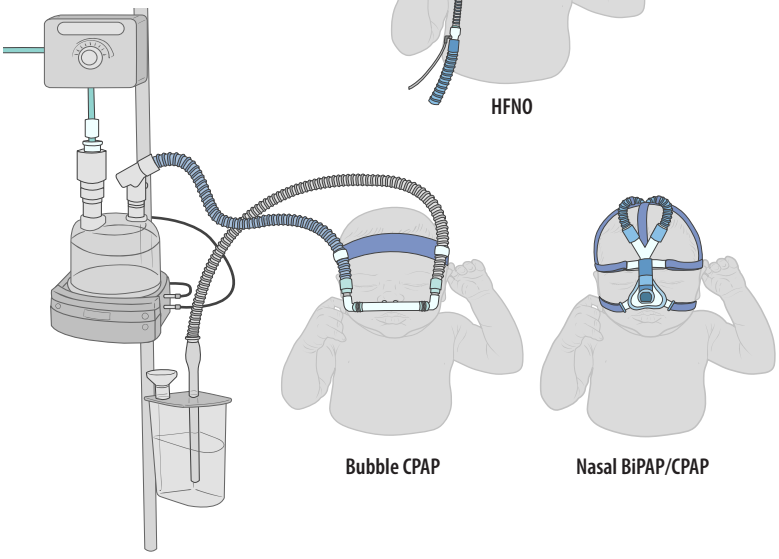


- Consider **face mask with reservoir** only if HFNO, CPAP, bCPAP, BiPAP unavailable
- Start oxygen at **10–15 L/min** and titrate to ensure bag inflates

If continued distress or SpO_2 < 90% (or < 94% if emergency signs)



HFNO



Bubble CPAP

Nasal BiPAP/CPAP

Find higher level of care and consider one of the following if adequate O_2 supply:

HFNO: 0–10 kg 2 L/kg/min
10–20 kg 1 L/kg/min

CPAP: 5–10 cmH_2O

Bubble CPAP: start flow at 5 L/min; immerse expiratory limb (cm depth in H_2O equals CPAP "pressure"; look for bubbles; titrate to 10 L/min if needed to generate bubbles

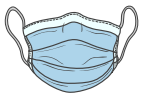
BiPAP: PS Δ5–15/PEEP 5–15
i.e. IPAP 10–30/EPAP 5–15
(IPAP = PEEP + PS; EPAP = PEEP)

If continued respiratory distress or SpO_2 < 90% on 15 L/min, consider intubation and invasive mechanical ventilation (clinical management decisions should be made based on individual patient characteristics, local resources and expertise).

Wean O_2 flow and avoid SpO_2 100% to avoid ill effects of hyperoxia and excess O_2 consumption.

Source: USAID-STAR-UCSF OpenCriticalCare.org Project (illustrations Holly Sullivan).

6.6 Flowchart on how to titrate oxygen in children

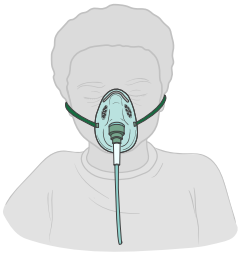


A medical mask should be placed over nasal cannula and HFNO for patients with suspected or confirmed highly infectious respiratory illness (e.g. COVID-19)

- **Start oxygen at 1–5 L/min**
- Use **nasal prongs**
- Assess response

FiO_2 0.23–0.4

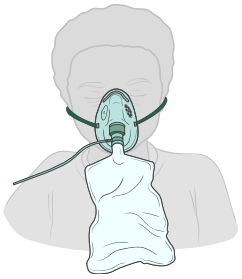
If continued distress or SpO_2 < 90% (or < 94% if emergency signs)



- Use **face mask**
- Increase oxygen to **5–10 L/min**
- Assess response

FiO_2 0.3–0.5

If continued distress or SpO_2 < 90% (or < 94% if emergency signs)

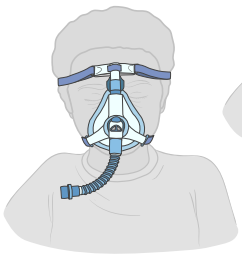


- Use **face mask with reservoir**
- Start oxygen at **10–15 L/min** and titrate to ensure bag inflates

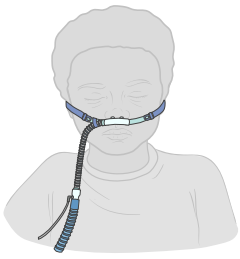
FiO_2 0.5–0.85

If continued distress or SpO_2 < 90% (or < 94% if emergency signs)

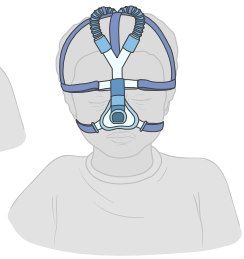
For HFNO, BiPAP, and CPAP, heated humidification should be used



Oronasal BiPAP/CPAP



HFNO



Nasal BiPAP/CPAP

Transfer to higher level care and consider:

HFNO: 10–20 kg 1 L/kg/min
20–40 kg 0.5–1 L/kg/min (max 30)
> 40 kg 0.5–1 L/kg/min (max 60)

CPAP: 5–10 cmH_2O

BiPAP: PS Δ5–15/PEEP 5–15
i.e. IPAP 10–30/EPAP 5–15
(IPAP = PEEP + PS; EPAP = PEEP)

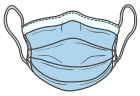
FiO_2 0.21–1.0

If continued respiratory distress or SpO_2 < 90% on 15 L/min, consider intubation and invasive mechanical ventilation (clinical management decisions should be made based on individual patient characteristics, local resources and expertise).

Wean O_2 flow and avoid SpO_2 100% to avoid ill effects of hyperoxia and excess O_2 consumption.

Source: USAID-STAR-UCSF OpenCriticalCare.org Project (illustrations Holly Sullivan) ().

6.7 Flowchart on how to titrate oxygen in adults



A medical mask should be placed over nasal cannulas for patients with suspected or confirmed highly infectious respiratory illness (e.g. COVID-19)

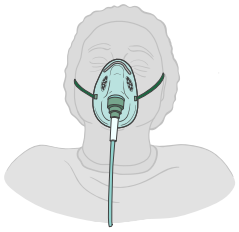
- **Start oxygen at 1–5 L/min**
- Use **nasal prongs**
- Assess response

FiO_2 0.23–0.4

If continued distress or SpO_2 < 90% (or < 94% if pregnant or emergency signs)

- Preferably, if available, use Venturi mask instead of face mask
- Titrate oxygen **2–15 L/min** by colour

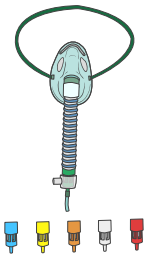
FiO_2 0.24–0.6

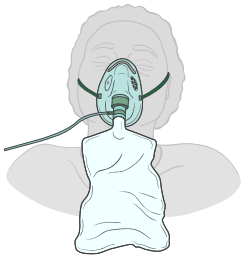


- Use **face mask**
- Increase oxygen to **5–10 L/min**
- Assess response

FiO_2 0.3–0.5

If continued distress or SpO_2 < 90% (or < 94% if pregnant or emergency signs)



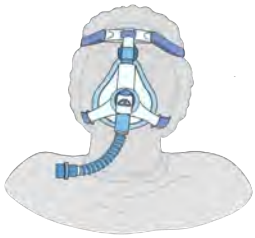


- Use **face mask with reservoir**
- Start oxygen at **10–15 L/min** and titrate to ensure bag inflates

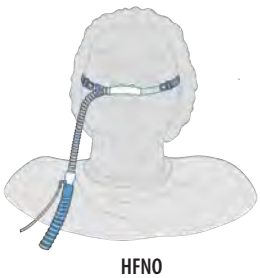
FiO_2 0.5–0.85

If continued distress or SpO_2 < 90% (or < 94% if pregnant or emergency signs)

Heated humidification systems should be used with HFNO and BiPAP/CPAP



Oronasal BiPAP/CPAP



HFNO

Transfer to higher level care and consider:

HFNO: 30–60 L/min (may also adjust FiO_2)

CPAP: 10–15 cmH_2O

BiPAP: PS Δ5–15/PEEP 5–15
i.e. IPAP 10–30/EPAP 5–15
(IPAP = PEEP + PS; EPAP = PEEP)

FiO_2 0.21–1.0

If continued respiratory distress or SpO_2 < 90% on 15 L/min, consider intubation and invasive mechanical ventilation (clinical management decisions should be made based on individual patient characteristics, local resources and expertise).

Wean O_2 flow and avoid SpO_2 100% to avoid ill effects of hyperoxia and excess O_2 consumption.

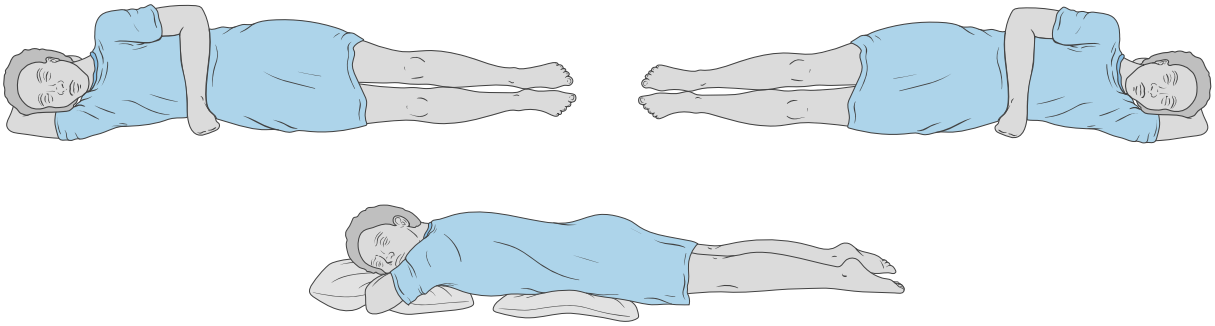
Source: Algorithm modified from *IMAI district clinician manual: hospital care for adolescents and adults* (WHO, 2011). Modification by USAID-STAR-UCSF OpenCriticalCare.org Project (illustrations Holly Sullivan).

6.8 Key tips on awake prone positioning

Prone positioning (lying on their front) in awake spontaneously breathing patients, may improve hypoxaemia. This prone positioning has been often used in patients with moderate-severe ARDS requiring invasive mechanical ventilation and is associated with improved oxygenation and reduced mortality in these patients.

The WHO COVID-19 Clinical Guideline Development Group conditionally recommends:
Awake prone positioning of patients severely ill and hospitalized with COVID-19 requiring supplemental oxygen (including high-flow nasal cannula) or non-invasive ventilation.

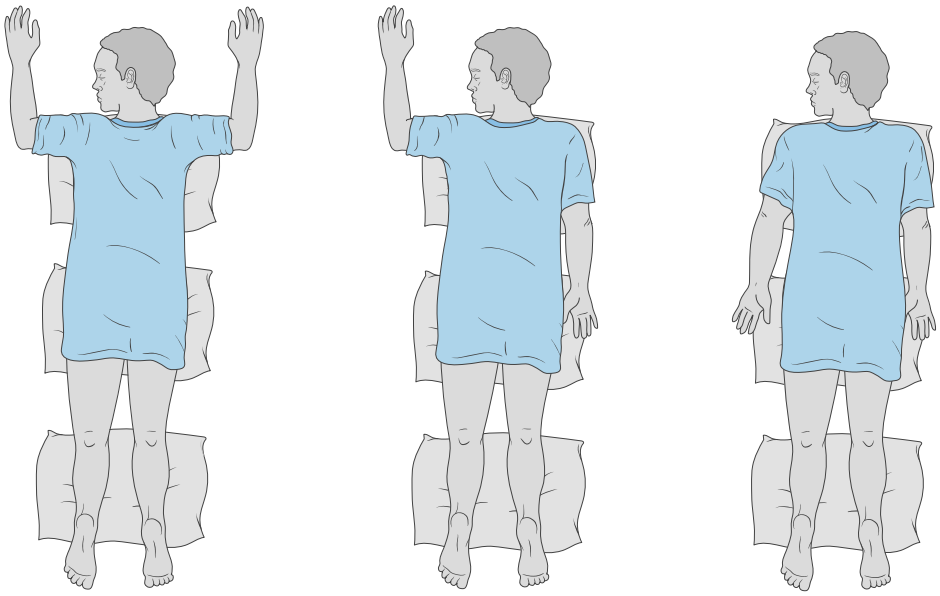
- **Benefits:** observational studies of awake prone patients with severe COVID-19 suggest decreased mortality and need for intubation (very low certainty evidence).
- **Harms:** include possible patient discomfort and pain (very low certainty evidence).



Source: USAID-STAR-UCSF OpenCriticalCare.org Project (illustrations Holly Sullivan) ().

Indications and contraindications for awake prone positioning

Characteristics of patients appropriate for prone position	Contraindications to prone positioning
• Awake and alert. • Capable of communicating and moving independently. • Patient must be able get help if they have discomfort or pain. • Patient must be able to supinate independently, if needed. • Haemodynamically stable. • Able to protect their airway. • Able to be closely monitored by workers with experience with prone positioning.	• Need for immediate intubation. • Haemodynamically unstable (tachycardia, hypotension). • Spinal instability. • Altered mental status or reduced ability to protect the airway. • Unable to readily call for help if needed. • Caution if nausea or vomiting. • Not enough human resources in the unit to monitor.



Source: USAID-STAR-UCSF OpenCriticalCare.org Project (illustrations Holly Sullivan) ().

Proning positioning tips

Characteristics of patients appropriate for prone position

- Patients should attempt to prone on a regular basis (e.g. every 4 hours) and maintain the prone position for as long as possible. (Many patients are unable to maintain the prone position for more than 1–2 hours.)
- Patients should be able to stop proning at any time and return to the supine position as needed.

Rotation and timed position changes

- Regimens vary, and target being in awake prone position 8–12 hours/day, broken into shorter periods over the day.

  For example, some institutional protocols describe rotational protocols, with patients changing position on a regular schedule (e.g. every 1 hour changing position, with positions rotating from prone, to lying on right side, to sitting straight upright, to lying on left side, to prone again, etc.).

Patient comfort: frequent limitations for patients are low back pain, nausea and vomiting

- For nausea or vomiting, immediately assist the patient to an upright position or recovery position. Gently suction or wipe the airway, if the patient cannot clear spontaneously.
- For low back pain, patients may find comfort using padding (i.e. pillows, blankets) under the pelvis.
- If possible, tilt the bed slightly in reverse Trendelenburg position to reduce pressure on the eyes and face.

6.9 Checklist to troubleshoot warning signs during oxygen therapy delivery

☑ If **respiratory distress and hypoxaemia fail to improve** despite increasing oxygen, use a systematic approach to manage your patient. Consider using this checklist. Repeat the quick check BEC with ABCDE approach (see Chapter 2: Screening, triage, clinical assessment and monitoring of SARI).

Checklist to troubleshoot warning signs during oxygen therapy delivery

Equipment

Is the measurement correct?

Repeat measurement:

- ☐ Place pulse oximeter correctly; try another measurement location (e.g. a different finger or the ear or nose if adapter available).
- ☐ Check pulse oximeter plethysmograph or signal quality.
- ☐ Use another pulse oximeter or get an arterial blood gas (if appropriate).

Is there technical difficulty in delivering treatments?

- ☐ Is the mask of the appropriate size for the patient (neonate, infant, child, adult)?
- ☐ Check that the oxygen source is working:

	Yes	No
Cylinder		
Does the cylinder contain oxygen (or another gas)?		
Does the cylinder contain sufficient oxygen?		
Is the pressure above 200 psi?		
Is there any leakage in the circuit? • tubing • connections • masks		
If using the mask with reservoir bag, does it fill up?		
Concentrator		
Is it connected to the electricity source and the power is on?		
Is the oxygen purity measured (or displayed in the screen) above 82%?		
Is there any leakage in the circuit? • tubing • connections • masks		
Are the flows and pressures correct for the type of concentrator used?		

Checklist to troubleshoot warning signs during oxygen therapy delivery

Patient and treatments

Is there an alternate or additional diagnosis?

- ☐ Does the patient have acute heart failure?
- ☐ Does the patient have pleural effusions?
- ☐ Does the patient have pulmonary embolism?

Is the patient getting appropriate therapy for the correct diagnosis?

- ☐ Ensure underlying etiology is being appropriately managed (e.g. antimicrobials given for pneumonia).

Is our treatment causing harm?

- ☐ Consider complications and modify management accordingly (e.g. too much fluid leading to pulmonary oedema? Allergic reaction to medication?).
- ☐ Does the patient have hypoxemia that is refractory to high-flow oxygen (e.g. significant shunt from ARDS)?
- ☐ Consider initiation of mechanical ventilator support for management of respiratory failure.

If the patient's mental status deteriorates despite SpO_2 > 90%, consider the following:

- ☐ Manage airway, assist ventilation if needed – do not wait for arterial blood gas results if the patient requires assisted ventilation on clinical grounds.
- ☐ Check arterial blood gas, if available, to evaluate ventilation. CO_2 retention causing acute respiratory acidosis will not be detected with SpO_2 alone.
- ☐ Consider alternate causes of altered mental status and treat appropriately (e.g. acute central nervous system [CNS] event, electrolyte abnormalities, low glucose).

6.10 Oxygen supply calculations

The ability to administer oxygen to patients with SARI depends on several factors including the supply of oxygen, the device(s) and flow rates being used to deliver oxygen, and the number of patients with SARI who are being treated.

At the facility level, there are many considerations required to estimate oxygen demand, including:

1. Oxygen source type: This may include pressure swing absorption (PSA), vacuum pressure swing adsorption (VPSA) plants, bulk liquid tank, bedside oxygen concentrators, distribution manifolds with high-pressure cylinders, or a combination of sources.

2. Distribution system: Oxygen may travel from the source to the patient's bedside in two main ways: pipe network or bedside high-pressure gas cylinders (or bedside concentrators). Piping networks should be designed to fit in infrastructure; sectioning of the pipes, alarms and monitoring components should be carefully planned. Accessories for monitoring and regulation of the medical gas should be included (e.g. pressure regulators and flowmeters).

3. Delivery equipment and devices: This refers to biomedical equipment connected to the network (e.g. patient ventilators, or direct interfaces such as nasal cannula).

Forecasting oxygen demand can be done using different methodologies and includes considerations like number of beds, hypoxaemia rates per ward, bed occupancy rates, and distance from the main source. Currently, various tools are publicly available to estimate oxygen needs at facility, subnational or national level.

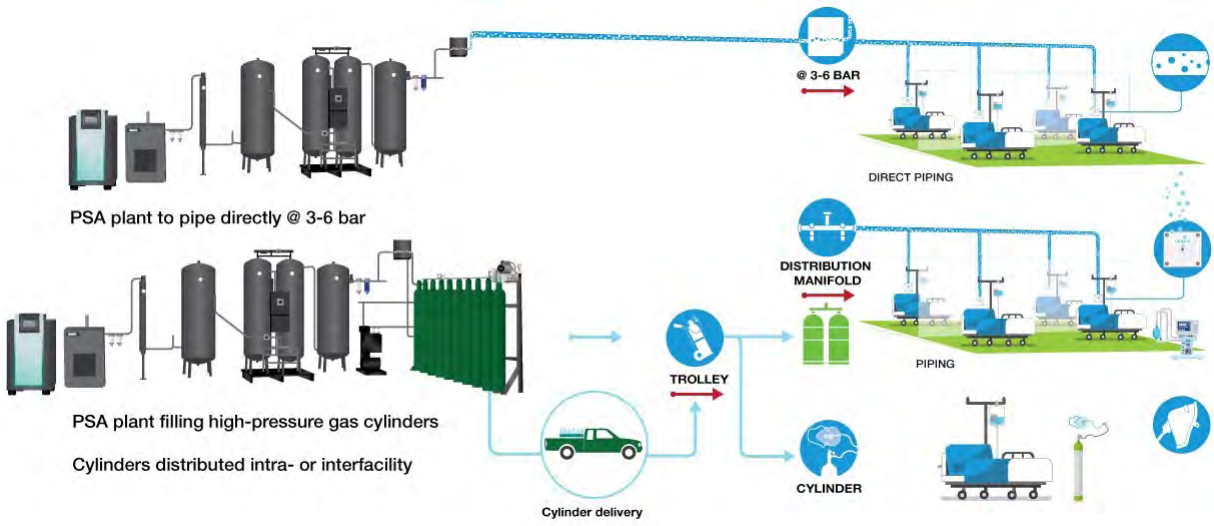
Useful links:
- USAID Open Critical Care.org Project oxygen supply and demand calculator
- UNICEF: Oxygen system planning tool
- PATH: Oxygen delivery toolkit

6.11 Memory aids: oxygen supply sources and distribution

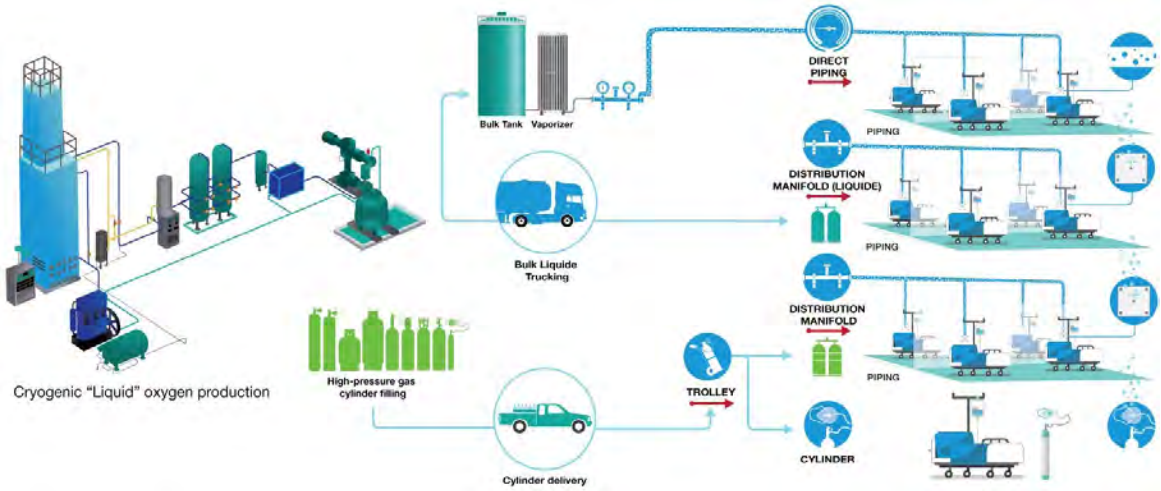
Overview of oxygen supply sources

	PSA bedside concentrators	PSA or VSA O_2 generator plants	Cryogenic liquid
Description	 Different flow rates, typical: 5, 8 or 10 L/min – medical use	 Different sizes and configurations: single and duplex 2–200+ Nm^3/hr	 Produced mainly for heavy industry; serves medical sector where GMP allows
Requirements	• Situated onsite, bedside. • Continuous and reliable electrical source. • Device-specific spares needed. • Timely technical maintenance (preventive every 6 months). • Need for IPC measures as is situated bedside.	• Various own/operate models. • Often situated onsite. • Continuous and reliable electrical source during plant and booster operations. • Detailed technical and financial planning for long-term operations and maintenance (~20 years).	• Third party responsible for production and supply chain. • Plants must be offsite. Bulk liquid tanks with passive vaporization for onsite storage (specialized materials). • *Capital expenditure (CAPEX) and operating expenses (OPEX) are very high; borne by third party.*
Additional considerations	• Difficult to optimize for at-scale needs. • Not suitable for high-flow or higher-pressure needs (e.g. patient ventilators). • Depending on the capacity and oxygen therapy, flow could be split among patients.	• Need > 4 technicians for 24/7 operation. • Continuous supply at all atmospheric pressures. • Supply can be piped bedside and/or plant can fill cylinders to be used bedside or transported elsewhere.	• Goods and service contract. • Product can be used via high-pressure gas cylinders or piped bedside from bulk tank.

Primary system: PSA plan



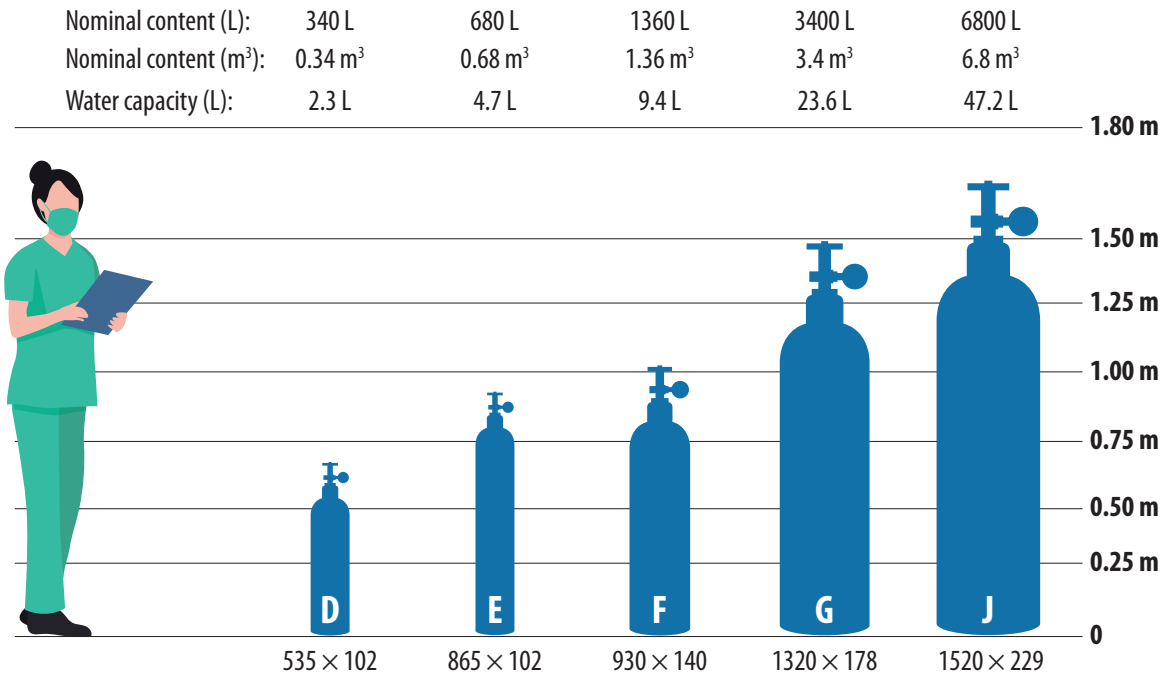
Primary system: cryogenic liquid oxygen



Source: Oxygen access scale up (WHO, 2020).

Cylinders

There is significant variability in terminology (i.e. letter system) and the colour coding systems to label oxygen cylinders. Always check with the cylinder manufacturer and consider the dimensions of the cylinder for accurate capacity information. More information on oxygen cylinder standards can be found in the *WHO-UNICEF technical specifications and guidance for oxygen therapy devices*.



Note: dimensions: height × diameter mm

Source: Adapted from WHO-UNICEF technical specifications and guidance for oxygen therapy devices.

Cylinder size

	D	E	F	G	J
Nominal content/oxygen capacity (L)	340	680	1360	3400	6800
Water capacity (L)	2.3	4.7	9.4	23.6	47.2
Dimensions (height × diameter) (mm)	535 × 102	865 × 102	930 × 140	1320 × 178	1520 × 229
Approximate full weight (kg)	3.9	6.5	17	39	78
Valve outlet connection (and specification)	Pin index (ISO 407)	Pin index (ISO 407)	Bullnose (BS 341)	Bullnose (BS 341)	Pin index side spindle (ISO 407)
Nominal service pressure (kPa/bar/psi)	13 700 kPa (137 bar/1987 psi)	13 700 kPa (137 bar/1987 psi)	13 700 kPa (137 bar/1987 psi)	13 700 kPa (137 bar/1987 psi)	13 700 kPa (137 bar/1987 psi)
Health facility use	Emergency and ambulance transport	Emergency and ambulance transport	Stand-alone	Stand-alone	Manifold connection and stand-alone

Notes: BS – British Standard; ISO – International Organization for Standardization; psi – pounds per square inch absolute.

Source: BOC Healthcare (https://www.bochealthcare.co.uk/en/images/cylinder_data_med309965_2011_tcm409-54065.pdf, accessed 12 June 2019).

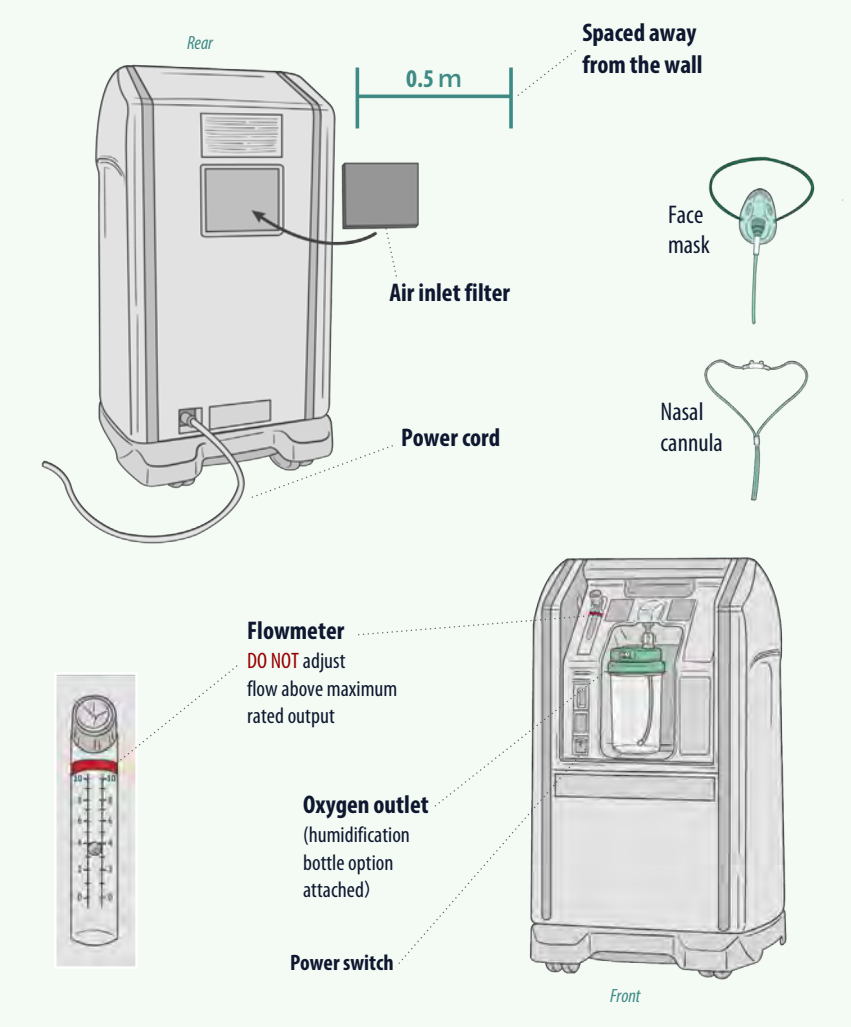
Duration of cylinders

Rate of oxygen administration for one patient	Cylinder size				
	D 340 L	E 680 L	F 1360 L	G 3400 L	J 6800 L
2 L/min	2 hr 50 min	5 hr 40 min	11 hr 20 min	28 hr 20 min	56 hr
	8.5 tanks	4 tanks	2 tanks	1 tanks	0.5 tanks
5 L/min	1 hr 8 min	2 hr 16 min	4 hr 30 min	11 hr 20 min	23 hr
	21 tanks	10 tanks	2 tanks	1 tanks	1 tanks
8 L/min	42 min	1 hr 24 min	2 hr 50 min	7 hr	14 hr
	34 tanks	17 tanks	8 tanks	4 tanks	2 tanks
10 L/min	34 min	1 hr 8 min	2 hr 16 min	5 hr 50 min	11 hr
	42 tanks	21 tanks	10 tanks	4 tanks	2.2 tanks

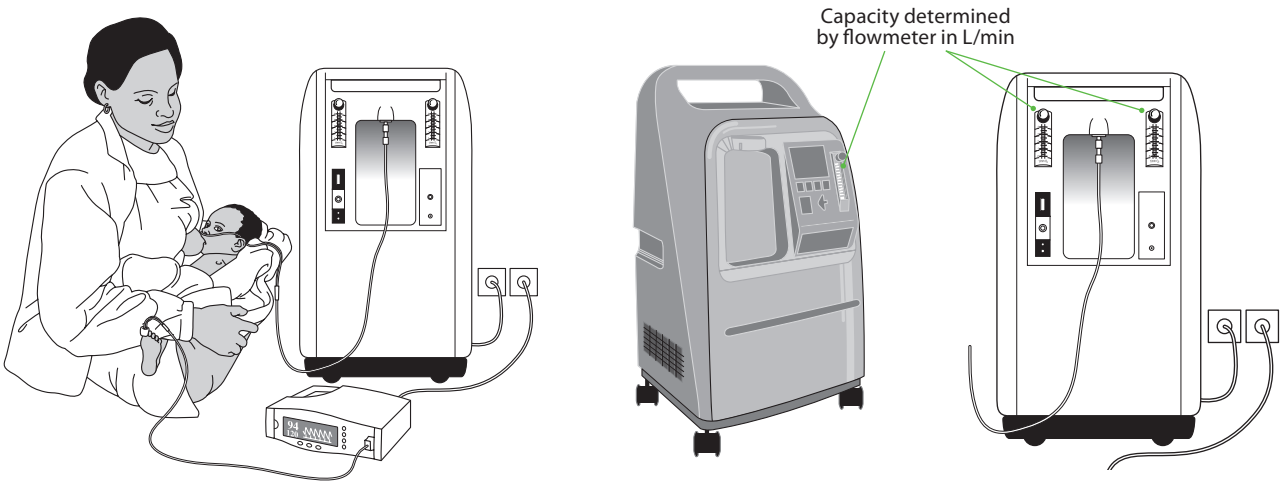
Top row: duration of cylinder

Bottom row: number of cylinders required/24 hr

Concentrators



Source: USAID-STAR-UCSF OpenCriticalCare.org Project. ()



Source: *WHO technical specifications for oxygen concentrators* (WHO, 2015).

There are multiple devices available and approved, with different power efficiencies and a range of minimum and maximum oxygen output between a minimum of 0.125 L/min to a maximum of 10 L/min. Few portable oxygen concentrators can deliver more than 10 L/min, and many oxygen concentrators may claim a wide range of flows but only with low oxygen concentrations. Always check manufacturers' specifications and *WHO technical specifications for oxygen concentrators* ().

Oxygen concentrators are easily movable by an individual and can be located some distance from the flowmeter assembly. This is useful in situation where different patients must share the same oxygen source using a flowmeter stand (mainly for children).

Source: WHO technical specifications for oxygen concentrators (WHO, 2015).

6.12 Respiratory care order template for oxygen therapy

Last updated 27 May 2021

Hospital name/Logo	**Oxygen therapy order set** v1.2				
Surname/Family name	Name	Attending/Team			
Date / /	ID number	Age	Sex	Weight (kg)	Height (cm)

CHOOSE A DELIVERY DEVICE

☐	**Nasal cannula**	☐ **Titrate flow rate** _____ litres per minute (0.5–1 LPM neonates; 1–2 LPM infants; 1–4 LPM children; 1–5 LPM adults) to maintain **oxygen saturation (SpO_2)** by pulse oximeter to goal > _____ (consider 90–94% for most patients)* or ☐ Set flow rate at: _____ litres per minute (typical range 0.5–5 LPM) ☐ Attach room temperature bubble humidifier and change sterile/distilled H_2O: [per protocol every] or [q _____ hours] (consider if > 4 LPM, especially in paediatrics, though evidence of benefit is lacking)
☐	**Simple face mask**	☐ Titrate flow rate from 5–10 litres per minute to maintain **oxygen saturation (SpO_2)** by pulse oximeter to goal > _____ (consider 90–94% for most patients)* or ☐ Set flow rate at: _____ litres per minute (typical range 5–10 LPM) ☐ Attach room temperature bubble humidifier and change sterile/distilled H_2O: [per protocol every] or [q _____ hours] (consider especially in paediatrics, though evidence of benefit is lacking)
☐	**Face mask with reservoir bag**	☐ Titrate flow rate from 10–15 litres per minute to maintain **oxygen saturation (SpO_2)** by pulse oximeter to goal > _____ (consider SpO_2 goal 90–94% for most patients) or ☐ Set flow rate at: _____ litres per minute (typical range 10–15 LPM) Attach room temperature bubble humidifier and change sterile/distilled H_2O: [per protocol every] or [q _____ hours]
☐	**Venturi mask**	☐ Select Venturi device adapter (or setting) (FiO_2 24–60%) to maintain **oxygen saturation (SpO_2)** by pulse oximeter to goal > _____ (consider 90–94% for most patients) or ☐ Set flow rate at _____ litres per minute for FiO_2 adapter: _____ (O_2 input flow rate determined by specific adapter used. Always refer to manufacturer's insert) 24% 2–4 LPM; 28% 4–5 LPM; 35% 8–10 LPM; 40% 10–12 LPM; 60% 12–15 LPM (colour may vary by manufacturer) Note: Do not use humidifiers with Venturi masks as moisture may affect accuracy of FiO_2
☐	**High-flow nasal cannula (HFNO)**	☐ Set flow rate: _____ litres per minute and titrate FiO_2 (typical range 0.40–1.0) to **maintain oxygen saturation (SpO_2)** goal > _____ (consider SpO_2 goal 90–94% for most patients) If patient trajectory is improving and tolerating < _____ LPM flow (typical < 20 LPM for adults or < 4 LPM for children) and < _____ FiO_2 (typical 0.40), then consider trial on standard nasal cannula or ☐ Titrate flow rate with 1.0 FiO_2 oxygen to maintain **oxygen saturation (SpO_2)** by pulse oximeter to goal > _____ (consider SpO_2 goal 90–94% for most patients) Typical flow rates by patient weight: as tolerated by patient; can titrate for work of breathing up to max. above: 0–10 kg = 2 L/kg/min; 10–20 kg = 1 L/kg/min; 20–40 kg = 0.5–1 L/kg/min (max. 30 LPM); > 40 kg = 0.5–1 L/kg/min if > 40 kg (max. 60 LPM) (Mandatory) Attach active heat and humidification system and change with sterile/distilled water. [Change every _____ hours]

Pulse oximetry	In addition to routine monitors, check oxygen saturation (SpO_2):	☐	Continuously	☐	Every _____ [hours] [minutes]

* SpO_2 goal ≥ 90% in adults and children; SpO_2 goal ≥ 92–95% in pregnant patients; SpO_2 goal ≥ 94% if child or adult with signs of multi-organ failure, including shock, alteration of mental status, severe anaemia and/or ongoing resuscitation. (Once stabilized, resume target SpO_2 ≥ 90%.)

Date (time): _____ **Name:** _____ **Signature:** _____ **Contact #:** _____

TO PRINT MORE
forms scan here

TO LEARN MORE
on calculating oxygen consumption needs scan or click here

Source: USAID-STAR-UCSF OpenCriticalCare.org Project.

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7 Therapies for SARI (COVID-19, influenza, bacterial pneumonia): antimicrobials and immunomodulators

7 Therapies for SARI (COVID-19, influenza, bacterial pneumonia): antimicrobials and immunomodulators

Summary

Patients with SARI should receive optimized supportive care, as soon as possible, and this includes oxygen therapy. In addition, based on the differential diagnosis and results of diagnostic tests (when available) appropriate antimicrobial and/or immunomodulator therapy should be given.

In patients with mild confirmed COVID-19, empirical antibiotic or antifungal therapy or prophylaxis is not recommended. In general, the use of empiric antibiotics or antifungals should be discouraged in COVID-19 cases, as their use may lead to higher bacterial or fungal resistance rates, which will impact the burden of disease and deaths in a population during the pandemic and beyond. **If patient is at high risk for severe COVID-19,** see WHO *Therapeutics and COVID-19: living guideline* for current recommendations.

In patients with moderate COVID-19 with non-severe pneumonia, antibiotics or antifungal should also not be prescribed unless there is clinical suspicion of a bacterial or fungal infection. A recent systematic review of critical patients hospitalized with COVID-19 reported only 8% of patients experiencing bacterial/fungal co-infection during hospital admission. **If patient is at high risk for severe COVID-19,** see WHO *Therapeutics and COVID-19: living guideline* for current recommendations.

In patients with severe and critical COVID-19 (severe pneumonia, ARDS, sepsis, septic shock), the following treatments should be administered immediately (within 1 hour): empiric antimicrobial therapy if suspect bacterial co-infection, initiation of fluid bolus and/or vasopressors for hypotension (see Chapter 8 for details) AND COVID-19 therapeutics: see WHO *Therapeutics and COVID-19: living guideline* for most recent recommendations; in addition to treatment with corticosteroids and either IL-6 receptor blockers or baricitinib.

When **seasonal influenza A or B viruses** are confirmed or suspected to be circulating in the community, treat patients at risk and those with SARI and patients as soon as possible with oseltamivir AND antimicrobials for all likely pathogens (if bacteria are considered) as soon as possible (within 1 hour). Patients with suspected or confirmed avian influenza should also be treated. Oseltamivir is a neuraminidase inhibitor antiviral drug and is active against all currently circulating influenza viruses that infect humans. See *Guidelines for the clinical management of severe illness from influenza virus infections*.

In settings endemic for other infections, such as TB and malaria, patients should be screened as per usual local protocols, and if screened positive, appropriate PPE should be donned and appropriate treatment started. For example, in areas where TB is prevalent and a patient is suspected to have COVID-19 and/or TB, appropriate PPE should be donned for possible COVID-19 and TB immediately. In malaria-endemic areas, patients with fever should be tested for the presence of malaria and treated as appropriate.

A positive test for another pathogen does not rule out a SARS-CoV-2 infection and a positive test for SARS-CoV-2 does not rule out co-infection with another pathogen or other etiology for the patient's symptoms.

Tools

7.1 Memory aid: treatment for acute respiratory infections according to severity (when COVID-19 and influenza are circulating)

7.2 COVID-19 and therapeutics

- 7.2.1 Corticosteroids for COVID-19
- 7.2.2 Interleukin-6 receptor blockers for COVID-19: tocilizumab, sarilumab
- 7.2.3 Monoclonal antibodies for COVID-19: casirivimab and imdevimab

7.3 Memory aid: invasive fungal infections in patients with COVID-19

7.4 Treatment for influenza infection fact sheet

7.1 Memory aid: treatment for acute respiratory infections according to severity (when COVID-19 and influenza are circulating)

Testing for different pathogens causing SARI should follow the national protocols.

	Mild disease	Pneumonia	Severe pneumonia
Adults	**Patients with uncomplicated upper respiratory tract viral infection** may have *non-specific symptoms* such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnoea, nasal congestion or headache. Rarely, patients may also present with diarrhoea, nausea and vomiting. The elderly, immunosuppressed and pregnant women may present with atypical symptoms (mainly COVID-19).	Fever, cough, dyspnoea, fast breathing, **but no signs of severe pneumonia, including SpO_2 ≥ 90% on room air.**	Clinical signs of pneumonia (fever, cough, dyspnoea) **plus one of the following:** • **respiratory rate > 30 breaths/min** • **severe respiratory distress** • **SpO_2 < 90% on room air.**
Children	**Patients with uncomplicated upper respiratory tract viral infection** may have *non-specific symptoms* such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnoea, nasal congestion or headache. Rarely, patients may also present with diarrhoea, nausea and vomiting.	Cough or difficulty breathing, plus fast breathing[a] and/or chest indrawing but **no signs of severe pneumonia.**	Pneumonia plus at least one of the following **signs of severe pneumonia:** • **SpO_2 < 90%** • **Very severe chest wall indrawing, grunting, central cyanosis, or presence of any other general danger sign (inability to breastfeed or drink, lethargy or unconsciousness, or convulsions).**
Treatment	• Isolation in hospital, community facility or home care (if required for highly infectious pathogen). • Give antipyretics for fever. Monitor and refer immediately if signs of decompensation. If COVID-19 and risk factors: consider if therapies are required (see *Therapeutics and COVID-19: living guideline*). If influenza circulating and risk factors for severe disease: consider if oseltamivir should be prescribed (see *Guidelines for the clinical management of severe illness from influenza virus infections*).	• Isolation in hospital, community facility or home care depending on risk factors (if required for highly infectious pathogen). • Give antipyretics for fever. • Give appropriate antibiotic if required if suspicion of bacterial source or co-infection. Monitor (including saturation of oxygen with pulse oximeter twice daily for patients of high risk of severity) and refer immediately if signs of decompensation. If COVID-19 and risk factors: consider if therapies are required (see *Therapeutics and COVID-19: living guideline*). If influenza circulating and risk factors for severe disease: consider if oseltamivir should be prescribed (see *Guidelines for the clinical management of severe illness from influenza virus infections*).	• Isolation and treatment in a hospital (if required for highly infectious pathogen), consider intensive care. • Give antipyretics for fever. • Give recommended antibiotic. • Manage airway as appropriate. • Give oxygen if: – SpO_2 < 90% and haemodynamically stable – SpO_2 < 94% and with any emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma or convulsions) with or without respiratory distress – SpO_2 < 92–95% if pregnant. • If COVID-19 suspected, give steroids and IL-6 RB and/or other medications (see *Therapeutics and COVID-19: living guideline*). • *If influenza circulating* treat (oseltamivir) (see *Guidelines for the clinical management of severe illness from influenza virus infections*). Monitor for signs of decompensation.

Note:
[a] Fast breathing is defined by age: < 2 months: ≥ 60 breaths/min; 2–11 months: ≥ 50 breaths/min; 1–5 years: ≥ 40 breaths/min.

Sources: Pocket book of hospital care for children (WHO, 2013); Paediatric emergency triage, assessment and treatment: care of critically ill children (WHO, 2016); *WHO Clinical management of COVID-19*.

Empiric antibiotics for severe pneumonia and sepsis in adults

For severe pneumonia, and sepsis in adults, give empirical broad-spectrum IV antimicrobials within the first hour for suspected pathogens. This is crucially important. Refer to national or institutional recommendations. Common choices include:

Empiric antibiotic treatment for community-acquired bacterial pneumonia in adults

	Adults	Total treatment duration
Mild to moderate cases	***FIRST CHOICE*** Amoxicillin (oral): 1 g given every 8 hours *or* Phenoxymethylpenicillin (oral): 500 mg given every 6 hours (500 mg = 800 000 IU ***SECOND CHOICE*** Amoxicillin+clavulanic acid (oral): 875 mg + 125 mg given every 8 hours *or* Doxycycline[a] (oral): 100 mg given every 12 hours	5 days
Severe cases	***FIRST CHOICE*** Ceftriaxone (IV/IM): 2 g given once a day (IV), 1 g given once a day (IM) *or* Cefotaxime (IV/IM): 2 g given every 8 hours **if CURB-65 ≥ 2** CONSIDER ADDING Clarithromycin [b] (oral or IV): 500 mg given every 12 hours ***SECOND CHOICE*** Amoxicillin+clavulanic acid (IV): 1 g + 200 mg given every 8 hours **if CURB-65 ≥ 2** CONSIDER ADDING Clarithromycin [b] (oral or IV): 500 mg given every 12 hours	5 days (consider longer treatment and/or investigate for complications if the patient is not clinically stable at Day 5)

Notes:

IM: intramuscular; IV: intravenous; IU: international units.

[a] Doxycycline is contraindicated in pregnant women.

[b] The rationale of adding clarithromycin to beta-lactam is to cover for possible atypical bacteria. Azithromycin could be used as an alternative when clarithromycin is not available but there are increasing concerns about its potential for the emergence and spread of antibiotic resistance because of its long half-life. Erythromycin could also be considered but it is associated with higher toxicity (diarrhoea is frequently associated with its use).

All dosages are for normal renal function.

ACCESS antibiotics are indicated in green, WATCH antibiotics in yellow and RESERVE antibiotics in red.

Empiric antibiotic treatment for community-acquired sepsis of bacterial origin in adults

Most probable source of infection	Empiric antibiotic treatment	Total treatment duration
Clinical sepsis of unknown origin[a]	Ceftriaxone [b] (IV): 2 g given once a day *or* Cefotaxime [b] (IV): 2 g given every 8 hours *and* Gentamicin [c] (IV): 5 mg/kg given once a day *or* Amikacin [c]: 15 mg/kg given once a day	7 days (but duration depends on the patient's underlying disease and clinical progression)

Notes:

IV: intravenous.

[a] If the source of the infection is determined please follow infection-specific guidance.
[b] Ceftriaxone or cefotaxime are alternative options. The choice can be made based on local availabilities.
[b] Gentamicin and amikacin are alternative options. The choice can be made based on local availabilities. In addition, amikacin is still effective against isolates producing extended-spectrum β-lactamases (ESBL) and is considered an appropriate carbapenem-sparing option in settings where ESBL-producing isolates are very prevalent.

All dosages are for normal renal function.

ACCESS antibiotics are indicated in green, WATCH antibiotics in yellow and RESERVE antibiotics in red.

Empiric antibiotics for SARI and severe bacterial pneumonia in children

	Children
Severe pneumonia (pneumonia with any danger sign, which requires referral to facility/hospital, admission and injectable therapy)	Ampicillin (IV/IM): 50 mg/kg dose given every 12 hours (1st week of life) 50 mg/kg dose given every 8 hours (> 1st week of life) ***and*** Gentamicin (IV/IM): • Neonates: 5 mg/kg dose given once a day • Children: 7.5 mg/kg dose given once a day **Ampicillin can be replaced by** Amoxicillin (IV/IM): 50 mg/kg dose given every 12 hours *or* Benzylpenicillin (IV/IM): 30 mg (50.000 IU)/kg given every 6 hours **If no clinical response to ampicillin *and* gentamicin change to second line:** Cefotaxime (IV/IM): 50mg/kg dose given every 8 hours *or* Ceftriaxone (IV/IM): 80 mg/kg dose given once a day

Note:

ACCESS antibiotics are indicated in green, WATCH antibiotics in yellow and RESERVE antibiotics in red.

Empiric antibiotics for hospital-acquired bacterial pneumonia (non VAP)

Adults	Children	Total treatment duration
FIRST CHOICE Amoxicillin+clavulanic acid [a] (IV): 1 g + 200 mg given every 8 hours *or* Ceftriaxone (IV/IM): 2 g given once a day (IV), 1 g given once a day (IM) *or* Cefotaxime (IV/IM): 2 g given every 8 hours *or* Piperacillin+tazobactam [b] (IV): 4 g + 500 mg given every 6 hours	Amoxicillin+clavulanic acid (IV/oral) 40–50 mg/kg/dose of amoxicillin component, given every 12 hours *or* 30 mg/kg dose given every 8 hours Oral weight bands[c] 3–< 6 kg: 250 mg given every 12 hours 6–< 10 kg: 375 mg given every 12 hours 10–< 15 kg: 500 mg given every 12 hours 15–< 20 kg: 750 mg given every 12 hours 20–< 30 kg: 1000 mg given every 12 hours *or* Ceftriaxone (IV/IM): 80 mg/kg dose given once a day *or* Cefotaxime (IV/IM): 50 mg/kg dose given every 8 hours *or* Piperacillin+tazobactam (IV): 100 mg/kg/dose of piperacillin component, given every 8 hours	7 days[d]

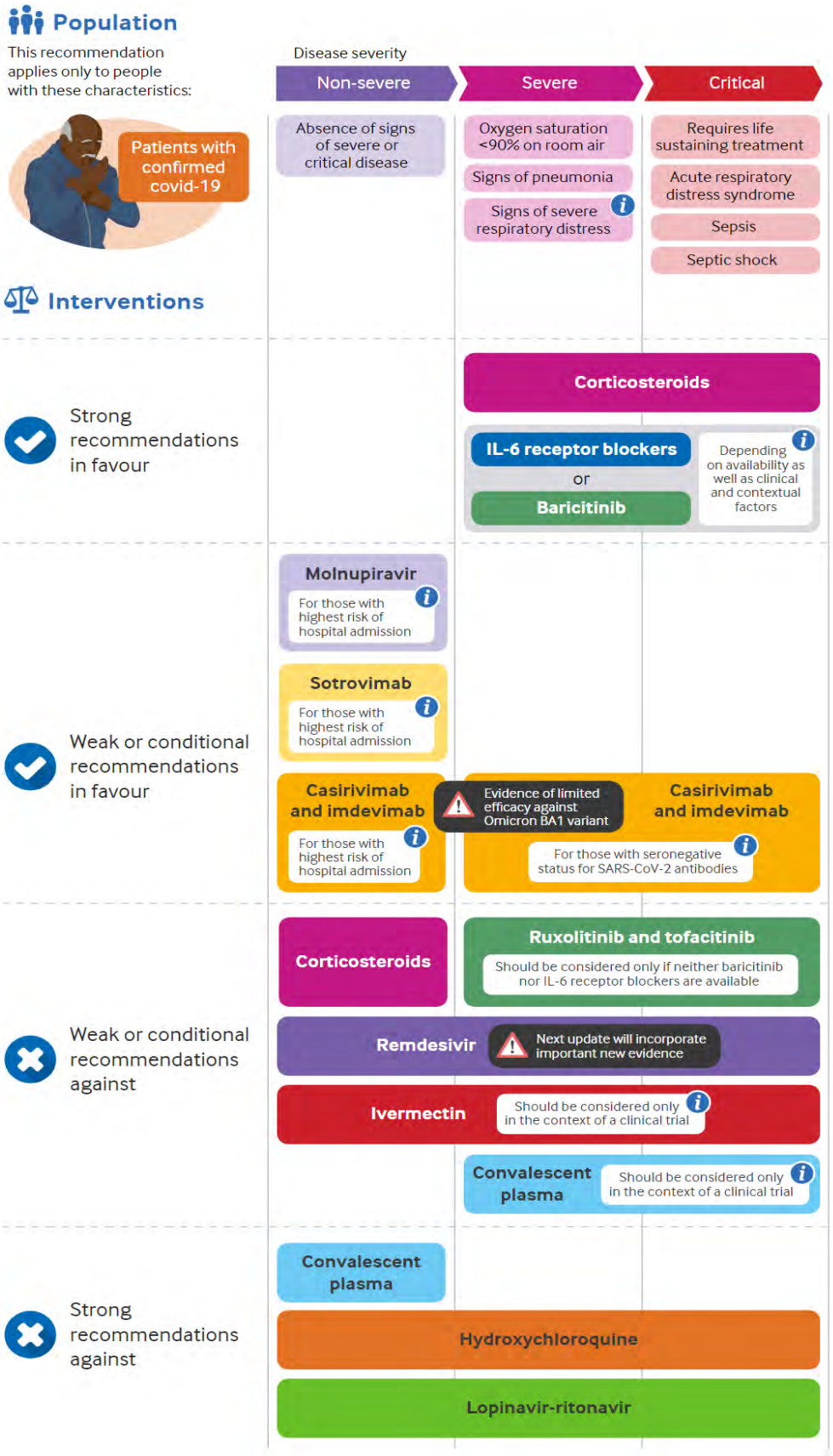
Notes:

VAP: ventilator-associated pneumonia.

[a] Amoxicillin+clavulanic acid can be used within 5 days of hospital admission and if no prior antibiotic exposure or risk for resistance.
[b] Piperacillin+tazobactam offers anti-pseudomonal coverage (which the other options do not). Risk of *Pseudomonas aeruginosa* is higher in patients with recent antibiotic exposure and especially in patients with known previous respiratory colonization and underlying lung diseases.
[c] Where possible use dispersible tablets. Oral syrup must be refrigerated as clavulanic acid is rapidly metabolized in high ambient temperatures.
[d] Reassess the diagnosis and consider longer treatment if the patient is not clinically stable at Day 7.

ACCESS antibiotics are indicated in green, WATCH antibiotics in yellow and RESERVE antibiotics in red.

7.2 COVID-19 and therapeutics



Source: A living WHO guideline on drugs for COVID-19 (BMJ, 2020) ().

The WHO *Therapeutics and COVID-19: living guideline* currently includes recommendations of therapeutics for COVID-19 and is constantly updated as new evidence emerges. See *WHO Living guideline: drugs to prevent COVID-19*. Guidelines on the clinical management of COVID-19 patients are included in *Living guidance for clinical management of COVID-19*.

7.2.1 Corticosteroids for COVID-19

In patients with severe or critical COVID-19 WHO makes a strong recommendation to use systemic corticosteroids rather than no corticosteroids. See updated recommendations on therapeutics for patients with COVID-19: *Therapeutics and COVID-19: living guideline* ().

The following recommendations on the use of corticosteroids are based on clinical trials in which the benefit was observed in patients who were mechanically ventilated or required supplemental oxygen at enrolment. *No benefit was seen in patients who did not require supplemental oxygen at enrolment.*

Indication: severe or critical COVID-19

Route[a]	Systemic corticosteroids may be administered orally or intravenously.
Type[b]	Daily regimen of **dexamethasone 6 mg once daily** is equivalent to: • **150 mg of hydrocortisone daily** (e.g. 50 mg every 8 hours) *or* • **40 mg of prednisone daily** *or* • **32 mg of methylprednisolone daily** (e.g. 8 mg every 6 hours or 16 mg every 12 hours).
Duration	Up to 5–14 days or until hospital discharge.
General monitoring	Monitor glucose levels (even if no diabetes diagnosed previously).
Special populations to monitor closely for complications	• Patients receiving other immunosuppressants/immunomodulators. • Patients with these conditions: – diabetes (specially with diabetic ketoacidosis) – severe immunodeficiency disorders – haematological and other malignancies – low number of white blood cells – organ transplantations – iron overload states – severe burns – injection drug use – malnutrition – open wound following trauma.
Examples of possible complications	• Hyperglycaemia or decompensated diabetes • Immunosuppression • Superinfections: bacterial, fungal, viral, parasites • Poor wound healing.

Notes:

[a] If intestinal dysfunction is suspected, clinicians must consider administering systemic corticosteroids intravenously rather than orally.
[b] Different corticosteroid preparations have different potencies and doses vary for different steroids. Care should be taken not to confuse doses for different products.

7.2.2 Interleukin-6 receptor blockers for COVID-19: tocilizumab, sarilumab

In patients with severe or critical COVID-19 WHO makes a strong recommendation for treatment with IL-6 receptor blockers (tocilizumab or sarilumab) in combination with other corticosteroids. See updated recommendations on therapeutics for patients with COVID-19: *Therapeutics and COVID-19: living guideline* (👆).

IL-6 receptor blockers should be prescribed and supervised by doctors who are experienced in the use of biologics and who have fully familiarized themselves with the efficacy and safety profile of these products.

Tocilizumab

Indication (patient criteria)

Patients with severe or critical COVID-19 requiring supplemental oxygen and/or mechanical ventilation AND corticosteroid treatment (see *Therapeutics and COVID-19: living guideline* (👆)).

Treatment should be started as early as possible in the patient's critical illness.

Dose and route

Tocilizumab 8 mg/kg (maximum dose of 800 mg) intravenous infusion administered over 60 minutes as a single dose.

- Avoid IV push or bolus.
- If clinical response is determined to be inadequate after 12–48 hours, a second dose may be considered.
- Renal dose adjustment is not warranted.
- **Do not exceed maximum dose of 800 mg.**

Dose of tocilizumab (mg) to be given:

Patient body weight	Band dose
< 30 kg	12 mg/kg
31–45 kg	8 mg/kg
46–55 kg	400 mg
56–65 kg	480 mg
66–80 kg	600 mg
81–90 kg	680 mg
> 91 kg	800 mg

Available formulations

Volume tocilizumab 20 mg/mL:
80 mg in 4-mL vial
200 mg in 10-mL vial
400 mg in 20-mL vial.

Tocilizumab *continued*

Preparation of infusion and administration	1. Ensure area of preparation is well ventilated, clear and clean. 2. Ensure appropriate PPE is worn: gloves, mask and goggles. 3. Collect the appropriate numbers of tocilizumab vials from the fridge (between 2–8 °C) and a 100-mL bag of 0.9% sodium chloride for IV infusion. 4. Tocilizumab solution should be clear to opalescent, colourless to pale yellow and free of visible particles for administration. 5. Withdraw the volume of sodium chloride 0.9% from the 100-mL IV infusion bag equivalent to that which you will be injecting of tocilizumab, calculated as required for the patient dose (see table above). * *For patients < 30 kg, dilute to 50 mL in 0.9% or 0.45% sodium chloride Injection for intravenous infusion.* 6. Discard the withdrawn sodium chloride 0.9% inside the syringe and needle into a sharp bin. 7. Using an appropriate volume IV syringe, draw up the calculated mL of tocilizumab 20 mg/mL solution required from the vial(s) (see table above). 8. Slowly add the tocilizumab solution to the sodium chloride 0.9% IV infusion to make a final volume of 100 mL. 9. Dispose the tocilizumab needle and syringe in a sharp bin. 10. Mix the tocilizumab solution by gently inverting several times. Do not shake the solution. 11. Complete and apply an IV infusion label to the tocilizumab infusion. 12. Obtain second check for the IV tocilizumab infusion from a colleague and sign for preparation and administration. 13. Record baseline vital signs before, and saturation of oxygen (SpO_2) during and after administration: heart rate, blood pressure, temperature, respiratory rate. 14. Connect the tocilizumab IV infusion to the patient IV line and administer over 1 hour via volumetric infusion pump. Do not use the same IV line for other medications while the tocilizumab is being administered. 15. Complete patient observations again and monitor the patient for signs of hypersensitivity to tocilizumab during and after the administration. 16. Acute infusion reactions can occur during the administration of tocilizumab or within 24 hours of infusion. 17. For mild reactions (such as flushing or chills), the infusion rate can be slowed down and the patient continually monitored. 18. For severe reactions (such as hives, difficulty breathing, chest pain, high or low blood pressure, swelling of hand and face, fever, chills or anaphylaxis) or when mild reactions that do not disappear despite slowing infusion, stop the infusion and inform the doctor immediately for additional treatment. 19. Once tocilizumab infusion is complete, take down the infusion and flush the giving set with 20 mL of sodium chloride 0.9% over 15 minutes to ensure all the tocilizumab has been given. 20. Dispose of the infusion and giving set in a sharp bin.

Tocilizumab *continued*

Monitoring for potential serious adverse events	Please refer to USPI, SmPC or local labelling for important safety issues and warnings. • Monitor the patient for signs of hypersensitivity to tocilizumab during and after administration: 15 minutes after starting the infusion, then every 30 minutes during the infusion and for 1 hour after the end of the infusion (15 min, 45 min, 1 hr, 1 hr 15 min, 1 hr 45 min). • Laboratory monitoring is recommended due to potential consequences of treatment-related changes, at baseline, 72 hours, and after infusion of IL-6 RB: – **Neutrophil count** (it is not recommended to initiate treatment in patients with neutropenia). – **Platelets count** (it is not recommended to initiate treatment in patients with < 50 000/mL). – **Transaminases** (it is not recommended to initiate treatment in patients with elevated transaminases ALT or AST above 1.5× ULN. Discontinue infusion or do not give second dose in patients who develop persistent elevated ALT or AST above 3× ULN or who develop ALT or AST above 5× ULN). – **Lipid profile** (LDL, HDL cholesterol, triglycerides) (possibility of elevated lipid profile after treatment). • At baseline: – **Screening for HIV, Hep B (HBsAg, HBcAb) and C (HC Ab)*** (Discuss the results with microbiology or infectious diseases physicians if unsure how to interpret.) Individual clinical assessment of these patients is needed. * *Delays in the result of these tests should not restrain clinicians from starting treatment when indicated.* • Before, during and after IL-6 receptor blockers infusion: patients should be regularly clinically assessed for bacterial infection. Monitor the appearance of sepsis produced by other pathogens different from COVID-19 (caution is recommended when considering the use in patients with a history of recurring or chronic infections or underlying conditions which may predispose patients to infections). • In areas of high prevalence of TB or immunosupressed patients, monitoring and assessment for presumptive TB is important before and after administration. • Observe for hypersensitivity reactions during and after administration as mentioned in preparation and infusion section.
Safety profile/adverse effects	• The most common side-effects (occurring in up to 1 patient in 10) with tocilizumab are upper respiratory tract infections (nose and throat infection), nasopharyngitis (inflammation of the nose and throat), headache, hypertension (high blood pressure) and abnormal liver function tests. The most serious side-effects are serious infections, complications of diverticulitis and hypersensitivity (allergic) reactions.
High-risk groups that require special precautions for use	• Age > 70 years. • Patients with recurring chronic infections or underlying conditions that predispose to infections, e.g. interstitial lung disease, diabetes, diverticulitis or patients taking steroids. Additionally there appears to be an increase risk of serious infections with increased body weight. • Patients receiving IL-6 RB on long-term regimens for conditions other than COVID-19 (risk of fatal infections such as active TB, bacterial, viral and other opportunistic infections). • Women of childbearing potential must use effective contraception during and up to 3 months after treatment. • Pregnant women – only use in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Tocilizumab *continued*

Examples of possible complications	• Acute severe infections: TB, bacterial, invasive fungal, viral and other opportunistic superinfections. • Immunosuppression. • Elevated liver function tests and lipid profile. • Gastrointestinal perforation. • Hypersensitive reactions, anaphylaxis. • Important risks include: – Serious infection – Complications of diverticulitis – Serious hypersensitivity reactions – Neutropenia – Hepatotoxicity – Thrombocytopenia and the potential risk of bleeding – Elevated lipid levels and the potential risk of cardiovascular and cerebrovascular events – Malignancies – Demyelinating disorders – Immunogenicity.
Not recommended	• On immunosuppressive therapy (excluding steroids) • HIV with CD4 < 200. • ANC < 200. • Suspected active severe bacterial, viral, fungal or TB infection (other than COVID-19). • Patients who may be at increased risk of gastrointestinal (GI) perforations: history of diverticulitis or bowel perforation. • Patients with elevated ALT or AST above 10 times the upper limit of the reference range. • Paediatric population < 2 years old.
Contraindications	• Tocilizumab is contraindicated in those with prior hypersensitivity to the medication or any known ingredient in it.

Notes:
Avoid concurrent use of live vaccines during treatment as clinical safety has not been established.
Further guidance for use can be obtained from the product information and training packages provided by the license holder.
Report all adverse events to the national pharmacovigilance centre or the manufacturer.

ALT – alanine aminotransferase; AST – aspartate aminotransferase; SmPC – Summary of Product Characteristics (European Union); ULN – upper limit of normal; USPI– United States Prescribing Information.

Sarilumab

Indication (patient criteria)	**Patients with severe or critical COVID-19 requiring** supplemental oxygen and/or mechanical ventilation AND corticosteroid treatment (see *Therapeutics and COVID-19: living guideline*). Treatment should be started as early as possible in the patient's critical illness.
Dose and route	**Sarilumab will be administered as an IV infusion at a dose of 400 mg over at least 60 minutes using a dedicated IV line.** • Avoid IV push or IV bolus. (Subcutaneous administration has not been studied for COVID-19.) • If a clinical response is determined to be inadequate after 12–48 hours, a second dose may be considered. • Renal dose adjustment is not warranted.
Available formulations	**Single dose 200 mg pre-filled syringe 200 mg/1.14 mL.** • Do not use sarilumab with autoinjector directly for SC injection, follow instructions to dilute them for IV infusion (see below).
Preparation of infusion and administration **Infusion instructions**	1. Ensure area of preparation is well-ventilated, clear and clean. 2. Ensure appropriate PPE is worn: gloves, mask and goggles. 3. Collect the contents of 2 prefilled syringes (200 mg/1.14 mL) of sarilumab, which should be diluted in 100 mL of 0.9% sodium chloride to prepare 400 mg of sarilumab IV bag. Note: The needle attached to the sarilumab syringe is approx. 12.5 mm long (half of normal). Take care to ensure it fully penetrates the port and reaches the fluid. 4. After mixing it is best practice to ensure the drug is not trapped in the injection port. A flush of 25 mL of normal saline can be given. 5. Invert bag 10 times to mix, do not shake. 6. Ensure the product solution is clear and free from any precipitation. Label as local policy. 7. The infusion should be started within 4 hours of preparation and can be given via central line or peripheral line. 8. Do not infuse concomitantly in the same IV line with other medications. 9. The inline filter and the IV infusion pump must be able to deliver as little as 0.17 mL/min (10 mL/hr). 10. Infusion speed must be set at 10 mL/h for 15 minutes, then increased to 130 mL/hr for the next 45 minutes. Infuse over 60 minutes. 11. After completion of the infusion, 25 mL of 0.9% saline should be used to flush the drug through the giving set. 12. IV infusion sets that have been evaluated in sarilumab compatibility include:

Infusion set	Examples
Standard infusion set with PVC tubing containing DEHP (PVS+DEHP) with 0.2 um PES inline filter	Baxter, product code 2C6571 or similar Alaris, product no. 2430-0500 or similar
DEHP-free infusion set made from polyethylene lined PVC tubing (PE-line PVC) with 0.2 um PES inline filter	Alaris, product no. 11532269 or similar Hospira, product no. 14255-28 or similar
DEHP-free PVC infusion set made from PVC tubing containing TOTAM (PVC-TOTM) with 0.2 um PES inline filter	Baxter, product code 2H6480 or similar Hospira, product no. 12336-05 or similar
Infusion set made from polyurethane (PU) with 0.2 um PES inline filter	B Braun, product 870009SP or similar

Sarilumab *continued*

Preparation of infusion and administration **Infusion instructions**	13. Monitor for infusion-related reactions: chills, nausea, headache, wheezing, itching, flushing, pyrexia, dizziness. If infusion-related reactions are mild, stop infusion and treat symptoms. Reduce infusion rate by at least 50% when re-starting infusion. 14. For severe infusion-related reactions, stop the infusion and inform the doctor immediately. 15. Once the sarilumab infusion is complete, take down the infusion and flush the giving set with 20 mL of sodium chloride 0.9% at same rate as infusion. 16. Document the administration. 17. Dispose the infusion and giving set in a sharp bin.
Monitoring for potential serious adverse events	Please refer to USPI, SmPC or local labelling for important safety issues and warnings. • Monitor the patient for signs of hypersensitivity to sarilumab during and after administration: 15 minutes after starting the infusion, then every 30 minutes during the infusion and for 1 hour after the end of the infusion (15 min, 45 min, 1 hr, 1 hr 15 min, 1 hr 45 min). • Laboratory monitoring is recommended due to potential consequences of treatment-related changes, at baseline, 72 hours, and after infusion of IL-6 RB: – **Neutrophil count** (it is not recommended to initiate treatment in patients with neutropenia). – **Platelets count** (it is not recommended to initiate treatment in patients with < 50 000/mL). – **Transaminases** (it is not recommended to initiate treatment in patients with elevated transaminases ALT or AST above 1.5x ULN. Discontinue infusion or do not give second dose in patients who develop persistent elevated ALT or AST above 3x ULN or who develop ALT or AST above 5x ULN. – SmPC recommends dose to be modified if ALT > 1–3 upper limit. – Lipid profile (LDL, HDL cholesterol, triglycerides) (possibility of elevated lipid profile after treatment). • At baseline: – **Screening for HIV, Hep B (HBsAg, HBcAb) and C (HC Ab)*** (Discuss the results with microbiology or infectious diseases physicians if unsure how to interpret.) * *Delays in the result of these tests should not restrain clinicians from starting treatment when indicated.* • Before, during and after IL-6 receptor blockers infusion: patients should be regularly clinically assessed for bacterial infection. Monitor the appearance of sepsis produced by other pathogens different from COVID-19 (caution is recommended when considering the use in patients with a history of recurring or chronic infections or underlying conditions which may predispose patients to infections). • In areas of high prevalence of TB or immunosupressed patients, monitoring and assessment for presumptive TB is important before and after administration.
Safety profile/adverse effects	• Transient and/or reversible elevations in liver enzyme levels that appear to be dose dependent and rare occurrences of neutropenia and thrombocytopenia. Additional adverse effects, such as serious infections (e.g. TB, bacterial or fungal infections), and bowel perforation, have been reported, but only with long-term use of sarilumab.
High-risk groups that require special precautions for use	• Age > 70 years. • Patients with recurring chronic infections or underlying conditions that predispose to infections. • Patients receiving IL-6 RB on long-term regimens for conditions other than COVID-19 (risk of fatal infections such as active TB, bacterial, viral and other opportunistic infections). • Women of childbearing potential must use effective contraception during and up to 3 months after treatment. • Pregnant women – only use in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Sarilumab *continued*

Examples of possible complications	• Acute severe infections: TB, bacterial, invasive fungal, viral and other opportunistic superinfections. • Immunosuppression • Elevated liver function tests and lipid profile. • Gastrointestinal perforation. • Hypersensitive reactions, anaphylaxis.
Not recommended	• On immunosuppressive therapy (excluding steroids). • HIV with CD4 < 200. • ANC < 200. • Suspected active severe bacterial, viral, fungal or TB infection (other than COVID-19). • Patients who may be at increased risk of gastrointestinal (GI) perforations: history of diverticulitis or bowel perforation. • Patients with elevated ALT or AST above 10 times the upper limit of the reference range. • Paediatric population < 2 years old.
Contraindications	• Sarilumab is contraindicated in those with prior hypersensitivity to the medication or any known ingredient in it.

Notes:
Avoid concurrent use of live vaccines during treatment as clinical safety has not been established.
Further guidance for use can be obtained from the product information and training packages provided by the license holder.
Report all adverse events to the national pharmacovigilance centre or the manufacturer.

ALT – alanine aminotransferase; AST – aspartate aminotransferase; SmPC – Summary of Product Characteristics (European Union); ULN – upper limit of normal; USPI– United States Prescribing Information.

7.2.3 Monoclonal antibodies for COVID–19: casirivimab and imdevimab

For patients with non-severe COVID-19 (who do not meet the criteria for severe or critical infection) at the highest risk of developing severe disease there is a conditional recommendation to use a combination of neutralizing monoclonal antibodies (casirivimab and imdevimab).

For patients with severe and critical COVID-19 with seronegative status there is a conditional recommendation to use a combination of neutralizing monoclonal antibodies (casirivimab and imdevimab). See updated recommendations on therapeutics for patients with COVID-19: *Therapeutics and COVID-19: living guideline* ().

See the following posters/clinical tools regarding administration of casirimab and imdevimab:

- Preparation of intravenous casirimab and imdevimab for COVID-19 ().
- Preparation and administration of subcutaneous casirimab and imdevimab for COVID-19 ().
- Safety and monitoring in patents receiving casirimab and imdevimab for COVID-19 ().

WHO has noted that there is a predicted lack of efficacy for casirivimab and imdevimab with the Omicron variant; updated recommendations may be warranted when sufficient evidence addressing this is available.

Casirivimab and imdevimab

Indication (patient criteria)

1. Patients with confirmed non-severe COVID-19 at highest risk for infection:

- Those with risk beyond 10% for being hospitalized with COVID-19. Those at highest risk for progression of infection:
  - Older age.
  - Risk factors: hypertension, diabetes, cardiac disease, chronic lung disease, cerebrovascular disease, dementia, mental disorders, chronic kidney disease, immunosuppression, obesity, cancer.
  - Not vaccinated.

2. Severe or critical COVID-19:

- Seronegative for SARS-CoV-2.
- Serologic testing should be conducted with tests that detect the presence of the SARS-CoV-2 spike protein antibodies and have performance characteristics similar to the reference standard test used to characterize seronegative patients in the RECOVERY trial (i.e. Oxford fluorescent-based ELISA assay for serum IgG against the SARS-CoV-2 spike protein), with an arbitrary cut-off determined by a panel of positive controls.
- Some lateral flow assay may be suitable and can usually be performed in several minutes.

3. No medical contraindication:

- No allergy to casirivimab and imdevimab or components: L-histidine, L-histidine monohydrochloride monohydrage, polysorbate 80, sucrose.

(See *Therapeutics and COVID-19: living guideline* ( )).

Dose and route

Casirivimab and imdevimab can be administered as 1200–8000 mg (600–4000 mg each antibody) demonstrating efficacy at all doses. (Adults and paediatic patients ≥ 12 years of age and weighing ≥ 40 kg.)

Table 1. Dose of casirivimab and imdevimab

Drug	**Dose** (non-severe disease)	**Dose** (severe and critical disease)
Casirivimab	600 mg IV/SC *or* 1200 mg IV	1200–4000 mg IV
Imdevimab	600 mg IV/SC *or* 1200 mg IV	1200–4000 mg IV
Total dose	**1200-2400 mg IV** *or* **1200 mg SC***	**2400–8000 mg IV**

Casirivimab and imdevimab *continued*

Dose and route	*Notes:* *** If administered subcutaneously (SC), maximum total dose is 1200 mg.** IV – intravenous infusion is preferred. SC – subcutaneous is an alternative route of administration. It can be given when intravenous infusion is not feasible and would lead to a delay in treatment. **Preferred: Casirivimab and imdevimab intravenous** single infusion using a dedicated IV line with a sterile low protein binding inline or add-on 0.2 micron filter via pump (preferred) or gravity + 1 hour post-infusion close monitoring (covered below in more detail). **Alternative:** Casirivimab and imdevimab by consecutive subcutaneous injections (syringes) + 1 hour post-injection close monitoring (covered below in more detail). *Renal or hepatic dose adjustment is not currently warranted for either drug.*
Storage conditions	• Store in a refrigerator at 2–8 °C in the original carton to protect from light. • Do not freeze. • Do not shake.
Available formulations	The vials of casirivimab and imdevimab come in two different sizes (20 mL or 6 mL). a) **Each 20-mL vial contains 11.1 mL of product** Concentration: 1332 mg per 11.1 mL (120 mg/mL). b) **Each 6-mL vial contains 2.5 mL of product** Concentration: 300 mg per 2.5 mL (120 mg/mL).
Preparation of intravenous perfusion	1. Wear PPE: gloves, gown, protective eyewear and respiratory mask. 2. Remove casirivimab and imdevimab vials from refrigerated storage. 3. Prepare in a well-ventilated area in clean room. 4. Allow to equilibrate to room temperature for approximately 20 minutes before preparation. **Do not shake the vials or expose to direct heat.** 5. Inspect the casirivimab and imdevimab vials to ensure there is no discolouration or particulate matter prior to administration. If either is observed, the vials should be discarded. **The solution in each vial should be clear to slightly opalescent (colourless to pale yellow).** 6. Obtain a prefilled intravenous infusion bag containing 50 mL, 100 mL, 150 mL or 250 mL of 0.9% of sodium chloride injection or 5% dextrose injection. 7. To allow for space in the infusion bag for the addition of the casirivimab and imdevimab, use a syringe and aseptic non-touch technique to withdraw the total volume dose equivalent from the infusion bag and discard. **For example, if preparing a total dose of casirivimab and imdevimab of 1200 mg infusion, remove 10 mL of fluid from the infusion bag prior to injecting the monoclonal antibody (see Table 2 below).** 8. Using a separate syringe for each vial, withdraw the appropriate amount of casirivimab and imdevimab from each respective vial and inject into a prefilled intravenous infusion bag containing either 0.9% of sodium chloride injection or 5% dextrose injection. **If using one vial to prepare more than one bag, then prepare all bags at the same time.** 9. Gently invert infusion bag by hand ten times to mix. **Do not shake.** 10. The product is preservative free, so the diluted infusion solution should be administrered immediately. *If not possible to immediately administer, the diluted casirivimab and imdevimab infusion solution can be stored in the refrigerator at 2–8 °C for up to **36 hours** or at room temperature up to 25 °C for no more than **4 hours**. If refrigerated, remove approximately **30 minutes** prior to patient infusion to allow for equilibration to room temperature.*

Casirivimab and imdevimab *continued*

Preparation of intravenous perfusion

Table 2. Recommended dilution instructions for 600 mg of casirivimab and 600 mg of imdevimab for intravenous infusion (total dose: 1200 mg)

Size of prefilled 0.9% sodium chloride or 5% dextrose infusion bag	Preparing casirivimab and imdevimab using individual vials
50 mL 100 mL 150 mL 250 mL	Add: • **5 mL of casirivimab** (use two 6-mL vials of casirivimab *or* 5-mL of one 20-mL vial) ***and*** • **5 mL of imdevimab** (use two 6-mL vials of imdevimab *or* 5-mL of one 20-mL vial) Inject 5 mL of casirivimab + 5 mL of imdevimab into a prefilled 0.9% sodium chloride or 5% dextrose infusion bag and administer as instructed.

Table 3. Recommended dilution instructions for 1200 mg of casirivimab and 1200 mg of imdevimab for intravenous infusion (total dose: 2400 mg)

Size of prefilled 0.9% sodium chloride or 5% dextrose infusion bag	Preparing casirivimab and imdevimab using individual vials
50 mL 100 mL 150 mL 250 mL	Add: • **10 mL of casirivimab** (use four 6-mL vials of casirivimab *or* 10-mL from a 20-mL vial) ***and*** • **10 mL of imdevimab** (use four 6-mL vials of imdevimab *or* 10-mL from a 20-mL vial) Inject 10 mL of casirivimab + 10 mL of imdevimab into a prefilled infusion bag of 0.9% sodium chloride or 5% dextrose and administer as instructed.

Table 4. Recommended dilution instructions for 4000 mg of casirivimab and 4000 mg of imdevimab for intravenous infusion (total dose: 8000 mg)

Size of prefilled 0.9% sodium chloride or 5% dextrose infusion bag	Preparing casirivimab and imdevimab using individual vials
150 mL 250 mL 500 mL	Add: • **33.3 mL of casirivimab** (use three 20-mL vials of casirivimab) ***and*** • **33.3 mL of imdevimab** (use three 20-mL vials of imdevimab) Inject 33.3 mL of casirivmab + 33.3 mL of imdevimab into a prefilled infusion bag of 0.9% sodium chloride or 5% dextrose and administer as instructed.

Casirivimab and imdevimab *continued*

Preparation of subcutaneous injections

1. Wear PPE: gloves, gown, protective eyewear and respiratory mask.
2. Remove casirivimab and imdevimab vials from refrigerated storage.
3. Prepare in a well-ventilated area in clean room.
4. Allow to equilibrate to room temperature for approximately 20 minutes before preparation.
   Do not shake the vials or expose to direct heat.
5. Inspect the casirivimab and imdevimab vials to ensure there is no discolouration or particulate matter prior to administration. If either is observed, the vials should be discarded.
   The solution in each vial should be clear to slightly opalescent (colourless to pale yellow).
6. Casirivimab and imdevimab should be administered consecutively by subcutaneous injection using the appropriate number of syringes.
   Obtain 3-mL or 5-mL polypropylene luer lock syringes with luer connection and 21-gauge 1½ inch transfer needles.
7. Withdraw appropriate dose of casirivimab and imdevimab into each syringe.
   Replace the transfer needle with a 25–27 gauge needle for subcutaneous injection.
8. The product is preservative free, so should be administrered immediately.
   *If not possible to immediately administer, store the prepared syringes of casirivimab and imdevimab at room temperature up to 25 °C for no more than **4 hours**.*

Administration of intravenous infusion

Casirivimab and imdevimab infusion should be administered by a qualified health care professional using aseptic non-touch technique.

1. Materials needed:
   a) Polyvinyl chloride (PVC), polyethylene (PE)-lined PVC or polyurethane (PU) infusion set;
   b) In-line or add-on low protein binding 0.2 micron polyethersulfone (PES) filter.
2. Attach the infusion set to the intravenous bag.
3. Prime the infusion set.
4. Administer the entire infusion solution in the bag via pump (preferred) or gravity through an intravenous line containing a sterile inline or add-on low protein binding 0.2 micron filter.
5. Do not administer the infusion solution with another medication.
6. After infusion is complete, flush tubing with either 0.9% sodium chloride injection or 5% dextrose injection.
7. Discard the completed infusion bag.
8. Clinically monitor patient during administration of medication and observe patient for 1 hour after infusion is complete.

Table 5. Administration rate for 600 mg casirivimab and 600 mg imdevimab for intravenous infusion (total 1200 mg)

Size of prefilled 0.9% sodium chloride or 5% dextrose infusion bag	Maximum infusion rate	Minimum infusion time
50 mL	150	20 minutes
100 mL	300	20 minutes
150 mL	500	20 minutes
250 mL	500	30 minutes

Note: Infusion should not be administered > 4 hours.

Casirivimab and imdevimab *continued*

Administration of intravenous infusion

Table 6. Administration rate for 1200 mg casirivimab and 1200 mg imdevimab for intravenous infusion (total 2400 mg)

Size of prefilled 0.9% sodium chloride or 5% dextrose infusion bag	Maximum infusion rate	Minimum infusion time
50 mL	150	20 minutes
100 mL	300	20 minutes
150 mL	450	20 minutes
250 mL	500	30 minutes

Note: Infusion should not be administered > 4 hours.

Table 7. Administration rate for 4000 mg casirivimab and 4000 mg imdevimab for intravenous infusion (total 8000 mg)

Size of prefilled 0.9% sodium chloride or 5% dextrose infusion bag	Maximum infusion rate	Minimum infusion time
150 mL	350	60 minutes
250 mL	250	60 minutes
500 mL	500	60 minutes

Note: Infusion should not be administered > 4 hours.

Administration of subcutaneous injection

1. Administer the subcutaneous injection of casirivimab and imdevimab consecutively, each at a different injection site into the upper thigh, back of the upper arm or abdomen to space apart each injection. **Avoid the waistline and 2 inches (5 cm) around the navel.** Do **NOT** inject into skin that is tender, damaged, bruised or scarred.
2. Clinically monitor patient after the injections and observe for 1 hour.

General monitoring

- Casirivimab and imdevimab can be administered as an intravenous infusion or subcutaneous injection.
- It should only be administered in health care settings by a qualified health care provider who has access to immediate emergency medical services that can treat severe infusion reactions.
- Patient should be clinically monitored during dose administration.
- Patient should be observed for 1 hour after intravenous or subcutaneous dosing is complete, with vital signs (blood pressure, heart rate, respiratory rate, temperature and oxygen saturation) checked at 15 minutes, 30 minutes and 1 hour post infusion.

Special populations to monitor closely for complications

- There are limited data regarding the use of casirivimab and imdevimab in pregnant patients with COVID-19.
- Casirivimab and imdevimab should be used in pregnancy only if the potential benefit justifies the potential risk to the mother and fetus.
- There are no available data on the presence of casirivimab and imdevimab in human milk or animal milk, the effects on breastfed infants, or the effects of the drug on milk production.

Contraindications

- Casirivimab and imdevimab is contraindicated in those with prior hypersensitivity to the medication or any known ingredient in casirivimab and imdevimab.

Casirivimab and imdevimab *continued*

Examples of possible complications	• Hypersensitivity reactions including anaphylaxis have been observed with casirivimab and imdevimab. • Infusion-related reactions (IV). • Injection site related reactions (SQ/SC). • *Hypersensitivity reactions occurring more than 24 hours after the infusion of casirivimab and imdevimab have been reported. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration, and initiate appropriate medications and/or supportive therapy.* • *Infusion-related reactions occurring during infusion and up to 24 hours post infusion have been observed and may be severe or life threatening.* ***These reactions may include:*** *fever, difficulty breathing, reduced oxygenation, chills, fatigue, irregular heart beat, chest pain or discomfort, weakness, nausea, headache, angioedema, throat irritation, bronchospasm, hypertension, hypotension, throat irritation, rash, pruritis, muscle aches, pre-syncope, syncope, dizziness and diaphoresis.* • *If an infusion-related reaction occurs consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.*
Reporting of adverse events	Report all adverse events to WHO and the manufacturer (): www.roche.com/products/local_safety_reporting.htm

Notes:

As a precautionary measure, vaccination for SARS-CoV-2 should be deferred for ≥ 90 days in people who have received casirivimab and imdevimab. The antibody treatment may interfere with vaccine-induced immune responses.

If using the 20-mL multidose vial of casirivimab or imdevimab and there is remaining product, it can be returned to the refrigerator and stored for a maximum for 48 hours per the open vial policy.

7.3 Memory aid: invasive fungal infections in patients with COVID-19

Secondary invasive fungal infections such as mucormycosis, candidemia, aspergillosis or cryptococcosis with life-threatening outcomes are increasingly being observed in settings where corticosteroids are being used inappropriately (higher than recommended doses, for longer than recommended duration or in non-severe COVID-19 patients).

Mucormycosis

Risk factors	• diabetes mellitus *(poorly controlled or complicated)* with or without diabetic ketoacidosis (DKA) • prolonged corticosteroid use • haematological malignancies • haematopoietic stem cell transplant • solid organ transplantation • iron chelation therapy • iron overload states • burns • other immunosuppressive conditions or medications (e.g. TNF- inhibitors or other immunosuppressive medication, cancer – chemotherapy, chronic immunosuppression – HIV).
Prevention	Use the recommended dose and duration of corticosteroids based on WHO recommendations and clinical practice guidelines for the indication. See WHO *Therapeutics and COVID-19: living guideline* (). Follow strict adherence to protocol of low-dose steroid and strict glycaemic control. Follow strict adherence to quality of oxygen humidification protocol and biosafety: • Appropriate hygiene should be followed when oxygen is being administered. • Use of sterile water for humidifiers during the oxygen therapy is recommended. • Disposable items should not be reused and where this avoidable they should be properly sterilized. • Use of medical masks. • Educate patients on early signs and symptoms of some of the most important secondary fungal infections in COVID-19 recovering patients (e.g. facial pain or orbital pain-diplopia, nasal blockage or excessive discharge of blood or brown/black discharge, loosening of teeth, etc. all could be signs of rhino-orbito-cerebral mucormycosis [ROCM]). • Include ENT surgeon and ophthalmologist in the post-COVID-19 clinic to pick up the cases early. • Environmental control in hospital. Restrict antibiotics only when bacterial infection is suspected/proven, as the use of antibiotics also increases likelihood of fungal infection.
Signs and symptoms	• facial swelling (pain and numbness can be present) • nasal or sinus congestion • black lesions on nasal bridge or upper inside of mouth • blackish and foul-smelling nasal discharge • loosening of a tooth or a TMJ-like symptoms • eye pain-diplopia • headache or cranial nerve palsy • fever • for respiratory or gastrointestinal mucormycosis, there is no specific symptom or sign; however, suspect the disease if there is chest pain, shortness of breath, cough haemoptysis, blackish discolouration in the skin with necrosis, abdominal pain, nausea and vomiting, gastrointestinal bleeding, mental status changes or coma.
Diagnosis	• early diagnosis is key! • imaging (CT or MRI) • endoscopic or bronchoscopic sample collection • histopathology or culture PLUS patient risk factors and clinical presentation.

Treatment	*Primary regimen:* **Liposomal (lipid) amphotericin B 5–10 mg/kg IV daily for 3–6 weeks:** • early administration is key – delay of 6 days was associated with two-fold increase in mortality in 12 weeks; • monitor renal function regularly. **Surgical debridement:** • early aggressive surgical resection and debridement is key for local control of disease and can reduce morbidity and mortality. Control underlying disease/risk (e.g. DM-DKA – discontinue corticosteroids, etc.). *Alternative regimens:* • amphotericin B deoxycholate 1–1.5 mg/kg IV daily (administered in at least 1000 mL of 5% dextrose over 2 hrs for 3–6 weeks): – during amphotericin B deoxycholate infusion, pre or peri-infusion normal saline and other symptomatic therapy may minimize the infusion related toxicity; monitor renal function regularly. • posaconazole: – posaconazole IV 300 mg IV over 90 mins every 12h Day 1, then 300 mg IV daily; – delayed-release tablet 300 mg PO/12h on Day 1, then 300 mg PO daily; – suspension 200 mg QID, then 400 mg PO/12h after stabilization of disease; • isavuconazonium sulfate (prodrug of isavuconazole) 372 mg PO/IV q8h x 6 doses, later 372 mg PO/IV daily. Step-down or salvage therapy: • if the patient is stable, posaconazole or isavuconazole tablet for 3–6 months after 3–6 weeks amphotericin B therapy; • if there is disease progression while the patient is on amphotericin B therapy, liposomal amphotericin B dose may be increased to 10 g/kg/d or replace with posaconazole or isavuconazole; • if the patient has renal compromise, start with isavuconazole or posaconazole.

NOTE 1: High doses of liposomal and deoxycholate amphotericin B need careful administration and monitoring and management – and reference detailed guidance. It should be given with saline fluid loading to reduce renal toxicity, and potassium and magnesium monitoring and supplements.

NOTE 2: As alternative regimen – posaconazole or isavuconazole injection is preferred.

NOTE 3: Step-down or salvage therapy:
- if the patient is stable, posaconazole or isavuconazole tablet for 3–6 months after 3–6 weeks amphotericin B therapy;
- if there is disease progression while the patient is on amphotericin B therapy, liposomal amphotericin B dose may be increased to 10 mg/kg/d or replace with posaconazole or isavuconazole;
- if the patient has renal compromise, start with isavuconazole or posaconazole.

Candidemia

Risk factors	• diabetes mellitus *(poorly controlled or complicated)* • prolonged corticosteroid use • haematological malignancies • active solid malignancy • recent chemotherapy • HIV infection • haemodialysis • long ICU stays • use of broad-spectrum antibiotics or antifungal agents • central venous catheters • parenteral nutrition • immunosuppressive agents • neutropenia • severe pancreatitis • *Candida* spp. colonization • recent abdominal surgery • extensive burns • COVID-19 infection.
Prevention	Control of risk factors (above) mainly in nosocomial transmission. Use the recommended dose and duration of corticosteroids based on WHO recommendations and clinical practice guidelines. See WHO *Therapeutics and COVID-19: living guideline* (). Consider gradual withdrawal practices with corticosteroid regimens: • if a patient has received more than 3 weeks' treatment; • has recently received repeated courses of steroids; • has taken a short course within 1 year of stopping long-term therapy; • has other possible causes of adrenal suppression. Follow strict adherence to protocol of low-dose steroid and strict glycaemic control.
Clinical presentations	• Sepsis. • Candidemia: one or more positive blood cultures for *Candida* spp. • Less frequent: infective endocarditis; endophthalmitis.
Diagnosis	• One or more positive blood cultures for *Candida* spp. (they could be negative in 50% cases). • Beta-D-glucan (poor specificity). • Candida mannan and anti-mannan detection. • Clinical signs: suspected dissemination (e.g. fever, multiple colonized or infected sites, even if negative blood cultures).
Treatment	*First-line: echinocandins:* • caspofungin: 70 mg IV × 1, then 50 mg/day IV; • micafungin: 100 mg/day IV; • anidulafungin: 100 mg/day IV; Duration: 14 days timed from clearance of bloodstream and resolution of symptoms. *Alternative regimens: amphotericin B, voriconazole, isavunoconazole.* • amphotericin B (lipid formulation): 3–5 mg/kg/day IV (especially if azole and echinocandin resistance or intolerance is of concern); • voriconazole, 6 mg/kg IV/PO × 2 doses on Day 1, then 3 mg/kg twice daily isavuconazole.

NOTE 1: The clinical presentation of candidemia is indistinguishable from most bacterial bloodstream infections – and the blood cultures can be falsely negative – this could lead to delays in appropriate therapy. Empiric treatment should be considered after consultation with infectious disease specialist if the patient is critically ill with unexplained sepsis and has some of the clinical risk factors, and/or colonized in none-sterile sites – or elevated markers (e.g. serum beta glucans levels, etc.).

NOTE 2: Fluconazole resistance is common depending on strain and varies with geographic location.

Aspergillosis

Risk factors	• prolonged neutropenia (acute leukaemia, myelodysplastic syndromes) • prolonged high-dose corticosteroids • allogenic stem cell transplant • solid organ transplant • haematologic malignancy • immunosuppressive medications • chronic granulomatous disease, e.g. TB, sarcoidosis • chronic lung diseases, e.g. asthma, cystic fibrosis • antimicrobial drug exposure • inherited immunodeficiencies • ICU care and mechanical ventilation • COVID-19 infection, especially those treated in ICU.
Prevention	Use the recommended dose and duration of corticosteroids based on WHO recommendations and clinical practice guidelines. See WHO *Therapeutics and COVID-19: living guideline* ( ). Control of risk factors. Consider gradual withdrawal practices with corticosteroid regimens: • if a patient has received more than 3 weeks' treatment; • has recently received repeated courses of steroids; • has taken a short course within 1 year of stopping long-term therapy; • has other possible causes of adrenal suppression. Follow strict adherence to protocol of low-dose steroid and strict glycaemic control. Follow strict adherence to quality of oxygen humidification protocol and biosafety: • appropriate hygiene should be followed when oxygen is being administered; • use of sterile water for humidifiers during the oxygen therapy is recommended; • disposable items should not be reused and where this avoidable it should be properly sterilized. Restrict antibiotics only when bacterial infection is suspected/proven, as the use of antibiotics also increases likelihood of fungal infection.
Signs and symptoms	• Chest pain, fever, cough, shortness of breath, haemoptysis. • Invasive pulmonary infection – coronavirus disease-associated pulmonary aspergillosis (CAPA). • Dissemination can occur: CNS, skin, GI tract, etc. • Pulmonary deterioration – worsening respiratory status and need for increased respiratory support, hemoptysis, chest pain, sepsis (fever, tachycardia, tachypnoea, hypotension, change in mental status).
Diagnosis	• Imaging – multiple nodule, thick-walled cavities; in immunosuppressed patients halo sigh or air-crescent sign. • Histopathology or culture PLUS patient risk factors and clinical presentation. • Galactomannan antigen: serum, BAL fluid more sensitivity but reduced specificity for invasive disease. • Beta-D-glucan assay in serum.
Treatment	*Primary regimen*: • voriconazole 6 mg/kg IV/PO every 12 hrs on Day 1, then 4 mg/kg IV/PO every 12 hrs. *Alternative regimens:* • liposomal amphotericin B 3–5mg/kg IV daily. • posaconazole: – delayed-release tablets 300 mg PO/12h on Day 1, then 300 mg PO daily; – suspension 200 mg QID, then 400 mg PO/12h after stabilization of disease; – posaconazole IV 300 mg IV over 90 mins every 12h Day 1, then 300 mg IV daily. • isavuconazonium sulfate (prodrug of isavuconazole) 372 mg PO/IV q8h × 6 doses, later 372 mg PO/IV daily.

NOTE 1: High doses of liposomal and deoxycholate amphotericin B need careful administration and monitoring and management – and reference detailed guidance. It should be given with saline fluid loading to reduce renal toxicity, and potassium and magnesium monitoring.

NOTE 2: Posaconazole suspension should be taken with food. Not FDA approved treatment, but clinically used.

NOTE 3: As alternative regimen – posaconazole or isavuconazole injection is preferred.

NOTE 4: Step-down or salvage therapy:
- if the patient is stable, posaconazole or isavuconazole tablet for 3–6 months after 3–6 weeks amphotericin B therapy;
- if there is disease progression while the patient is on amphotericin B therapy, liposomal amphotericin B dose may be increased to 10 mg/kg/d or replace with posaconazole or isavuconazole;
- if the patient has renal compromise, start with isavuconazole or posaconazole.

Cryptococcosis

Risk factors	• conditions associated with reduced cell mediated immunity (e.g. lymphoma) • chronic corticosteroid use • HIV infection (CD4 cell count < 200) • allogenic stem cell transplant • solid organ transplantation.
Prevention	Control of risk factors.
Signs and symptoms	• Meningoencephalitis (common presentation) with symptoms (fever, malaise, headache, meningism) but could be asymptomatic. – Encephalopathic presentation: lethargy, seizure, dementia, personality changes or altered mental status. – Meningitis (fever, malaise, headache, meningism is seen in 25% of patients). • Less frequent: pulmonary (pneumonia presentation) or disseminated disease.
Diagnosis	• Direct microscopy, culture, serology (CrAg, LAT, EIA, LFA), molecular identification (PCR). • Lumbar puncture: analysis of CSF: CrAg, India staining, culture.
Treatment	*Primary regimen:* • *induction phase:* liposomal amphotericin B 3–4 mg/kg IV daily (or amphotericin B or amphotericin B lipid complex) AND fluconazole 800–1200 mg/day IV/PO for 2 weeks; or Duration > 2 weeks or until CSF sterilization achieved (if takes more than 2 weeks). • *consolidation phase:* fluconazole 800 mg/daily for 10 weeks. *Alternative regimens:* • amphotericin B deoxycholate AND flucytosine followed by fluconazole • fluconazole AND flucytosine • amphotericin B deoxycholate AND fluconazole • flucytosine (5-FC) 25 mg/kg PO four times daily if no renal impairment.

7.4 Treatment for influenza infection fact sheet

- See *Guidelines for the clinical management of severe illness from influenza virus infections*, March 2022 ( ).
- Oseltamivir is recommended to be used when influenza is suspected or known to be circulating.
- If testing for influenza is not possible, empiric treatment is indicated.
- Oseltamivir is not proven to be effective for COVID-19.

Treatment dosing

Populations	Dosing[a]
Adults	
Mild illness	75 mg orally, twice daily for 5 days
With severe illness or severe immunocompromising conditions	75 mg orally, twice daily for 5 days Consider higher dose: 150 mg orally, twice daily
Children ≥ 1 year old	
< 15 kg	30 mg orally, twice daily for 5 days
15 to < 23 kg	45 mg orally, twice daily for 5 days
23 to < 40 kg	60 mg orally, twice daily for 5 days
≥ 40 kg	75 mg orally, twice daily for 5 days
Children < 1 year old	
14 days to 1 year	3 mg/kg orally, twice daily for 5 days

Note:
[a] The route of administration can be either via NG or OG tube if the patient cannot take medication orally (see safety profile). Where the clinical course remains severe or progressive, despite ≥ 5 days of antiviral treatment, treatment should be continued without a break until virus infection is resolved or there is satisfactory clinical improvement.

Safety considerations and side-effects

Safety profile: oseltamivir has not been associated with increased adverse effects in adult outpatients. However, oseltamivir has not been evaluated in severely ill patients, pregnancy or paediatric populations. Oseltamivir should be used with caution:

- In patients with kidney disease: reduce dose to 75 mg daily if creatinine clearance is 10–30 mL/min.
- In patients with liver disease the safety and efficacy has not been evaluated, so dose reduction is not recommended now.
- For pregnant or nursing mothers, oseltamivir is recommended as therapy in pandemic influenza (H1N1) virus as there is a high risk of severe illness in pregnant women and there is no evidence of adverse effects or birth defects.

Side-effects: side-effects are generally minor:

- Gastrointestinal tract: nausea (mitigated by taking with food), vomiting.
- Rare neuropsychiatric adverse events – association seen primarily in one country, causality has not been established.

Oral formulations

Formulations	Description
Capsules	30 mg, 45 mg, 75 mg each Store at room temperature (15–30 °C)
Liquid suspension	White powder mixed with 23 mL of drinking water fruit flavoured Refrigeration required Use within 10 days Oral dispenser included (must confirm dosage and volume when administering)
Oral suspension	If commercial suspension unavailable a suspension may be prepared from oseltamivir capsules[a]

Note:
[a] Preparation of oral oseltamivir suspension:
- The inhouse suspension should be made at 15 mg/mL for patients > 1 year; and 10 mg/mL for ≤ 1 year.
- The suspension can be made from oseltamivir phosphate capsules using sterile water at the bedside.

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https://www.cdc.gov/fungal/diseases/mucormycosis/diagnosis.html
https://www.cdc.gov/fungal/diseases/mucormycosis/symptoms.html
https://www.cdc.gov/fungal/diseases/mucormycosis/health-professionals.html

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8 Sepsis and septic shock

8 Sepsis and septic shock

Summary

Early identification of patients with sepsis and implementation of early, evidence-based therapies improves outcomes and reduces mortality: implementing the *Surviving Sepsis Campaign International Guidelines for Management of Sepsis and Septic Shock* (2021) saves lives.

Antimicrobial therapy within 1 hour
Early, targeted resuscitation for septic shock
Early application of lung protective ventilation for ARDS

To treat patients with **septic shock**, it is crucial to deliver early, targeted resuscitation using crystalloid fluid, vasopressors and, in some cases, inotropes and/or blood transfusion. **Fluid resuscitation with crystalloid fluids** remains the most common intervention for septic shock; it should be given as a challenge to improve targets of perfusion, and promptly stopped when no longer responsive, to avoid harms of excess fluid. Resuscitation strategies for children with septic shock should be modified if the child has severe malaria with anaemia or severe malnutrition or is being cared for in settings without ICU capacity, specifically invasive mechanical ventilation. Resuscitation targets for adults and children include improved blood pressure and other markers of tissue perfusion.

Markers of tissue perfusion in adults and children
Capillary refill < 2 sec
Absence of skin mottling
Strong peripheral pulses
Warm and dry extremities
Regular urine output
Normal mental status
Normalization of lactate
In children: improved heart rate *(tachycardia is an early sign of septic shock and low blood pressure is a late finding)*

Refer to the shock quick cards for initial approach and management of patients with septic shock; from the *WHO-ICRC Basic emergency care (BEC): approach to the acutely ill and injured*.

Tools

8.1 Sepsis and septic shock definitions

For further information see: Surviving Sepsis Campaign (October 2021) ().

Sepsis adults

Life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection
Signs of organ dysfunction include:
Altered mental status
Difficulty or fast breathing
Low oxygen saturation
Reduced urinary output
Fast heart rate
Weak pulse
Cold extremities
Low blood pressure
Skin mottling
Laboratory evidence of: • coagulopathy • thrombocytopenia • acidosis • high lactate • hyperbilirubinaemia

Sepsis children

Suspected or proven infection and ≥ two age-based systemic inflammatory response syndrome (SIRS) criteria, of which one must be abnormal temperature or white blood cell count
SIRS criteria include:
Abnormal temperature < 36 °C or > 38.5 °C
Heart rate > 2 SD above normal for age or bradycardia if < 1 year of age
Respiratory rate > 2 SD above normal for age
Abnormal white blood cell count or > 10% immature neutrophils

Septic shock adults

Sepsis with circulatory and cellular/metabolic abnormalities profound enough to substantially increase mortality
Criteria:
Persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥ 65 mmHg *or* Serum lactate level > 2 mmol/L (18 mg/dL)

Septic shock children

Sepsis with circulatory and cellular/metabolic abnormalities profound enough to substantially increase mortality
Criteria: two or three of the following
Altered mental status
Tachycardia or bradycardia HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children
Prolonged capillary refill (> 2 sec) or feeble pulse
Tachypnoea
Mottled or cool skin or petechial or purpuric rash
High lactate
Oliguria
Hyperthermia or hypothermia
or
Any hypotension (SBP < 5th centile or 2 SD below normal for age)

WHO paediatric emergency, triage, assessment and treatment (ETAT): definition of shock for children

Shock is the presence of all three clinical criteria:
Delayed capillary refill ≥ 3 sec
Cold extremities
Weak and fast pulse
or
Frank hypotension for age:

	Age			
	< 1 m	1–12 m	1–12 yr	> 12 yr
SBP	< 50	< 70	70+ (2 × age)	< 90

For more information see: WHO *Paediatric emergency triage, assessment and treatment* (ETAT) ().

8.2 Sequential Organ Failure Assessment (SOFA) score

The SOFA score is commonly used to describe and quantify organ failure and can also be used to predict outcome. The SOFA score has been proposed for use in triage strategies because it helps to quantify the principle of utility.

The SOFA score ranges from 0 to 24 and includes points related to six organ systems:

- respiratory (hypoxaemia defined by low PaO_2/FiO_2);
- coagulation (low platelets);
- liver (high bilirubin);
- cardiovascular (hypotension);
- central nervous system (low level of consciousness defined by Glasgow Coma Scale [GCS]);
- renal (low urine output or high creatinine).

Sepsis is defined by an increase in the sepsis-related SOFA score of ≥ 2 points. (Assume the baseline score is 0 if data are not available.) To use the SOFA scoring system for triage, add the points for each clinical characteristic at presentation and then at 48 hours. Both the initial and 48-hour scores are predictive of mortality. The maximum score is 24.

Variables	0	1	2	3	4
Respiratory PaO_2/FiO_2, mmHg	> 400	≤ 400	≤ 300	≤ 200[a]	≤ 100[a]
Coagulation Platelets × $10^3/\mu L$[b]	> 150	≤ 150	≤ 100	≤ 50	≤ 20
Liver Bilirubin, mg/dL[b]	< 1.2	1.2–1.9	2.0–5.9	6.0–11.9	> 12.0
Cardiovascular Hypotension	No hypotension	Mean arterial pressure < 70 mmHg	Dopamine ≤ 5 *or* Dobutamine (any dose)	Dopamine > 5, Epinephrine ≤ 0.1, *or* Norepinephrine ≤ 0.1[c]	Dopamine > 15, Epinephrine > 0.1, *or* Norepinephrine > 0.1[c]
Central nervous system GCS	15	13–14	10–12	6–9	< 6
Renal Creatinine, mg/dL[d] or urine output, mL/day	< 1.2	1.2–1.9	2.0–3.4	3.5–4.9 or < 500 mL/day	> 5.0 or < 200 mL/day

Notes:

bpm – beats per minute; FiO_2 – fraction of inspired oxygen; MAP – mean arterial pressure; PaO_2 – partial pressure of oxygen; SBP – systolic blood pressure; SOFA – sequential organ failure assessment.

[a] Values are with respiratory support.
[b] To convert bilirubin from mg/dL to µmol/L, multiply by 17.1.
[c] Adrenergic agents administered for at least 1 hour (doses given are in µg/kg per minute).
[d] To convert creatinine from mg/dL to µmol/L, multiply by 88.4.

8.3 Quick Sequential Organ Failure Assessment (qSOFA)

The qSOFA score (also known as quickSOFA) is a bedside prompt that may identify adult patients with suspected infection who may be at greater risk for a poor outcome outside the ICU. In a patient with suspected infection, the presence of ≥ two of the following qSOFA criteria may be associated with an increased risk of death:

Note: **Although the presence of a positive qSOFA should alert clinicians to the possibility of sepsis in all resource settings, given the poor sensitivity of the qSOFA, there is a strong recommendation by the Surviving Sepsis Campaign (October 2021) against its use as a single screening tool.**

For further information see the latest Surviving Sepsis Campaign guidelines (October 2021) ().

Altered mental status
(Glasgow coma scale [GCS] < 15, AVPU scale: alert, verbal, pain, unresponsive – not alert)
Respiratory rate (RR)
≥ 22 breaths per minute
Systolic blood pressure (SBP)
≤ 100 mmHg

ALTERED MENTAL STATUS | FAST RESPIRATORY RATE | LOW BLOOD PRESSURE

qSOFA Calculator		
Is the patient in the ICU	Yes	No
Altered mentation	Yes	No
Respiratory rate (breaths per minute)		(0 to 60)
Systolic blood pressure (mmHg)		(0 to 300)

Source: Adapted from www.qsofa.org

8.4 Paediatric Logistic Organ Dysfunction (PELOD-2) score

Multiple organ dysfunction syndrome is a frequent cause of death in adult and paediatric ICUs. The PELOD-2 score was developed to describe the severity of age-specific organ dysfunction in children and has since been validated in many settings. This descriptive score relies on **10 variables that correspond to five different organ dysfunctions**. Any increased organ dysfunction in the PELOD-2 score is closely related to an increased risk of mortality, but neurologic and respiratory dysfunctions are the most critical.

In the population in which the PELOD-2 was developed, a score of 10 was associated with ~10% probability of mortality, while a score of 20 was associated with > 90% probability of mortality. However, the predicted risk of death is population specific and varies with resource availability.

All variables must be collected, but measurements can be done only if justified by the patient's clinical status. If a variable is not measured, it should be considered normal. If a variable is measured more than once in 24 hours, the worst value is used in calculating the score.

Organ dysfunctions and variables	Points by severity levels						
	0	1	2	3	4	5	6
Neurologic[a]							
GCS	≥ 11	5–10			3–4		
Pupil reaction	Both reactive					Both fixed	
Cardiovascular[b]							
Lactate (mmol/L)	< 5.0	5.0–10.9			≥ 11.0		
Cardiovascular[b]							
Mean arterial pressure (mmHg)							
0 to < 1 months	≥ 46		31–45	17–30			≤16
1–11 months	≥ 55		39–54	25–38			≤ 24
12–23 months	≥ 60		44–59	31–43			≤ 30
24–59 months	≥ 62		46–61	32–44			≤ 31
60–143 months	≥ 65		49–64	36–48			≤ 35
>144 months	≥ 67		52–66	38–51			≤ 37
Renal							
Cr (µmol/L)							
0 to < 1 months	≤ 69		≥ 70				
1–11 months	≤ 22		≥ 23				
12–23 months	≤ 34		≥ 35				
24–59 months	≤ 50		≥ 51				
60–143 months	≤ 58		≥ 59				
>144 months	≤ 92		≥ 93				
Respiratory[c]							
$PaCO_2$ (mmHg) FiO_2	≥ 61		≤ 60				
$PaCO_2$ (mmHg)	≤ 58	59–94		≥ 95			
Invasive ventilation	No			Yes			
Haematologic							
WBC ($\times 10^9$/L)							
Platelets ($\times 10^9$/L)	≥ 142	77–141	≤ 76				

Notes:

[a] Neurologic dysfunction: Glasgow Coma Score: use the lowest value. If the patient is sedated, record the estimated Glasgow Coma Score before sedation. Assess only patients with known or suspected acute central nervous system disease. Pupillary reactions: nonreactive pupils must be > 3 mm. Do not assess after iatrogenic pupillary dilation.

[b] Cardiovascular dysfunction: heart rate and mean arterial pressure: do not assess during crying or iatrogenic agitation.

[c] Respiratory dysfunction: PaO_2 used: use arterial measurement only. PaO_2/FiO_2 ratio is considered normal in children with cyanotic heart disease. $PaCO_2$ can be measured from arterial, capillary or venous samples. Invasive ventilation; the use of mask ventilation is not considered invasive ventilation. FiO_2: fraction of inspired oxygen.

8.5 Algorithm on targeted resuscitation in adults with shock

Shock features in adults:
- SBP < 100 mmHg, HR > 90/min
- Signs of hypoperfusion:
  – Delayed capillary refill > 3 sec
  – Cold extremities
  – RR > 22/min
  – Decreased urinary output (< 0.5 mL/kg/hr)
  – Altered mental status
  – Elevated lactate

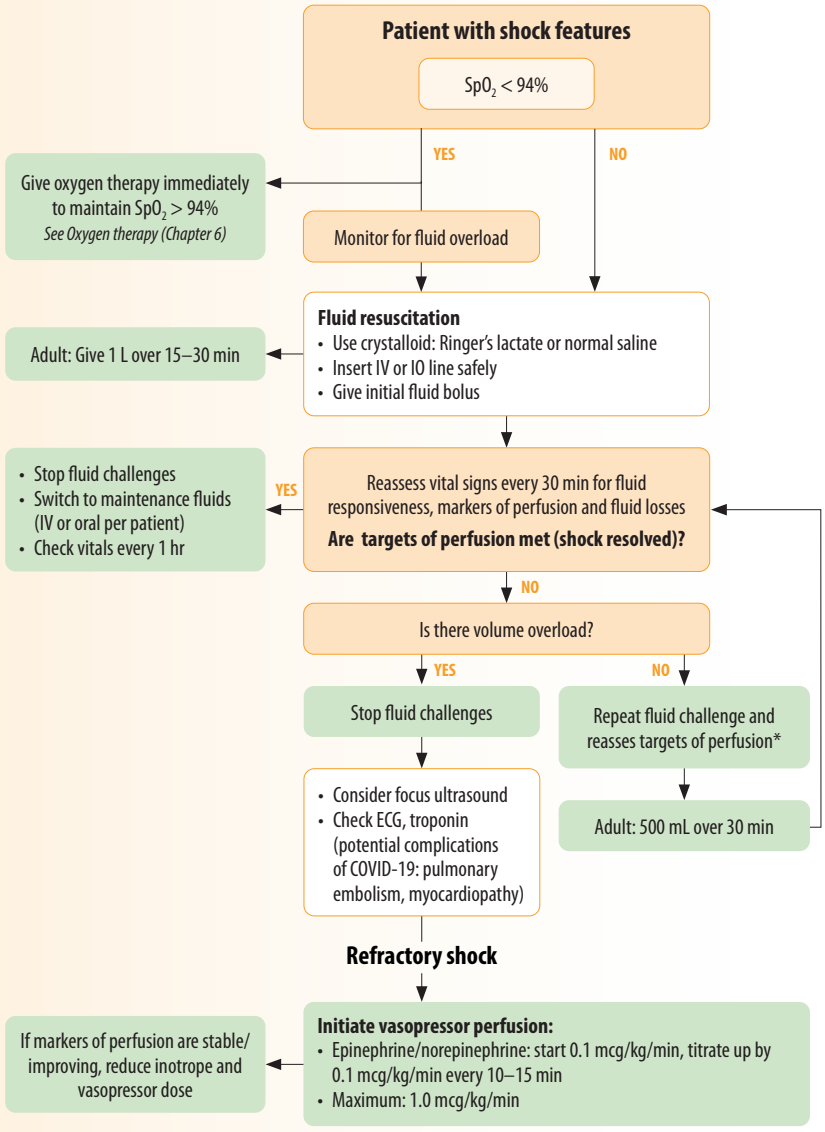
General clinical management:
1. Immediately obtain body fluid cultures
2. Give empiric antimicrobials (within 1 hr)
3. Check laboratory: CBC, biochemistry, lactate, CRP
4. Check serum glucose, replete as needed
5. Monitor and replete electrolytes as needed
6. Treat severe acidemia (pH < 7.2) with bicarbonate
7. Monitor fluid balance
8. Provide symptom relief (paracetamol)
9. Begin early nutrition (if tolerating oral)
10. Counsel patient and family

Fluid responsiveness:

When fluid therapy improves blood pressure or markers of perfusion (i.e. test blood pressure after fluid bolus or passive leg raise)

Markers of good perfusion:
- SBP > 90–100 mmHg or age appropriate for child
- Strong pulse
- Normal RR
- Normal mental status (AVPU)
- Urine output > 0.5 mL/kg/hr for adult or > 1 mL/kg/hr for child
- Brisk capillary refill
- Normalization of lactate

Fluid overload:
- Dyspnoea, drop in SpO_2, increase RR
- Elevated JPV > 12 cm
- Peripheral oedema
- Hepatomegaly in children



*If despite fluid challenge x 2 targets of perfusion are not met.

Notes:

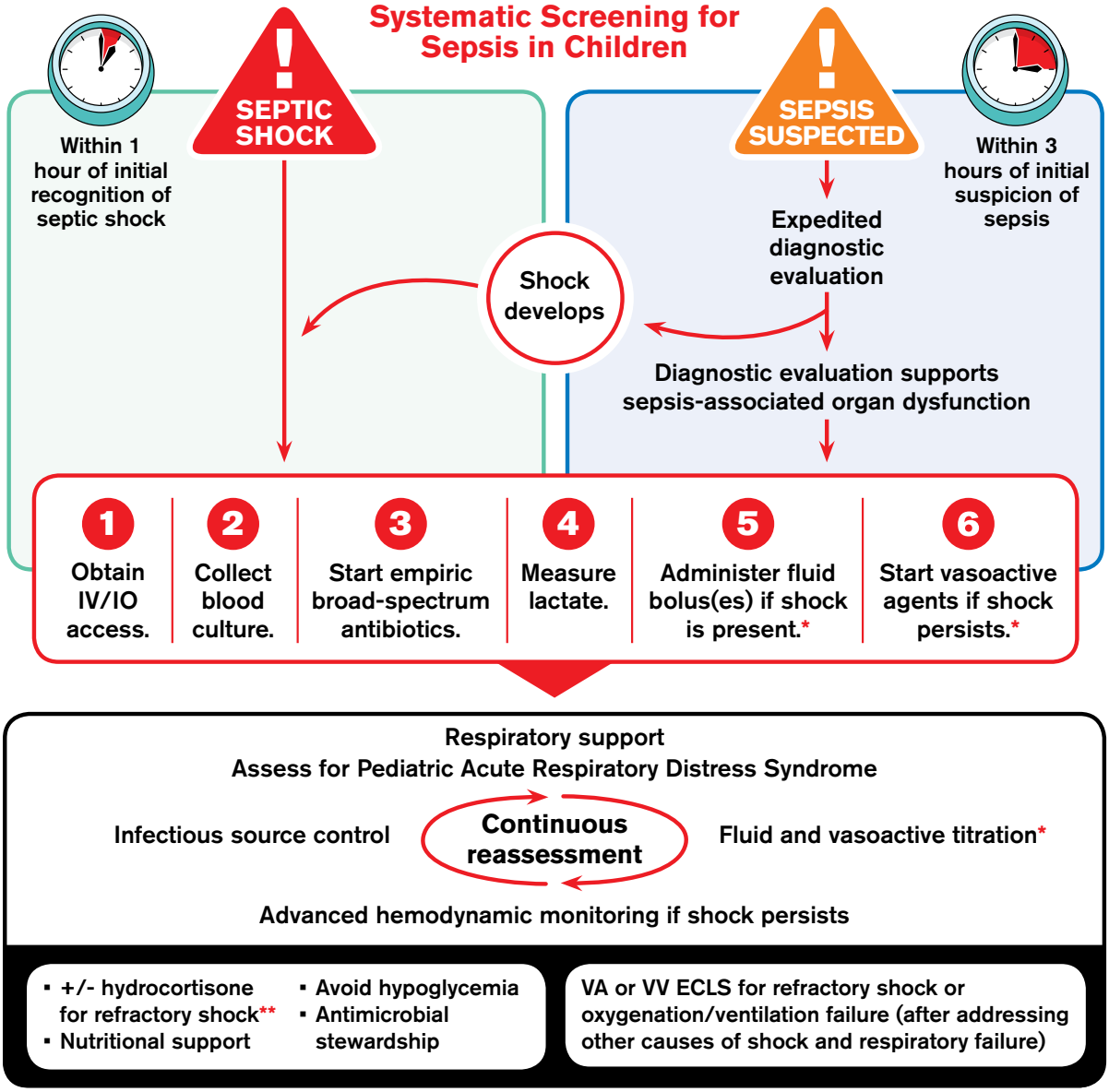
AVPU – alert, verbal, pain, unresponsive; HR – heart rate; JVP – jugular venous pressure; RR – respiratory rate; SBP – systolic blood pressure; SpO_2 – oxygen saturation.

Source: Modified from *Optimized supportive care for Ebola virus disease (WHO, 2019)*

8.6 Algorithms on initial resuscitation, and on fluid and vasoactive–inotrope management for children with septic shock

This initial resuscitation algorithm for children (👆) from the Surviving Sepsis Campaign, is based on recently published paediatric sepsis and septic shock guidelines and has been adapted for use in health care systems with and without intensive care.

8.6.1 Initial resuscitation algorithm for children

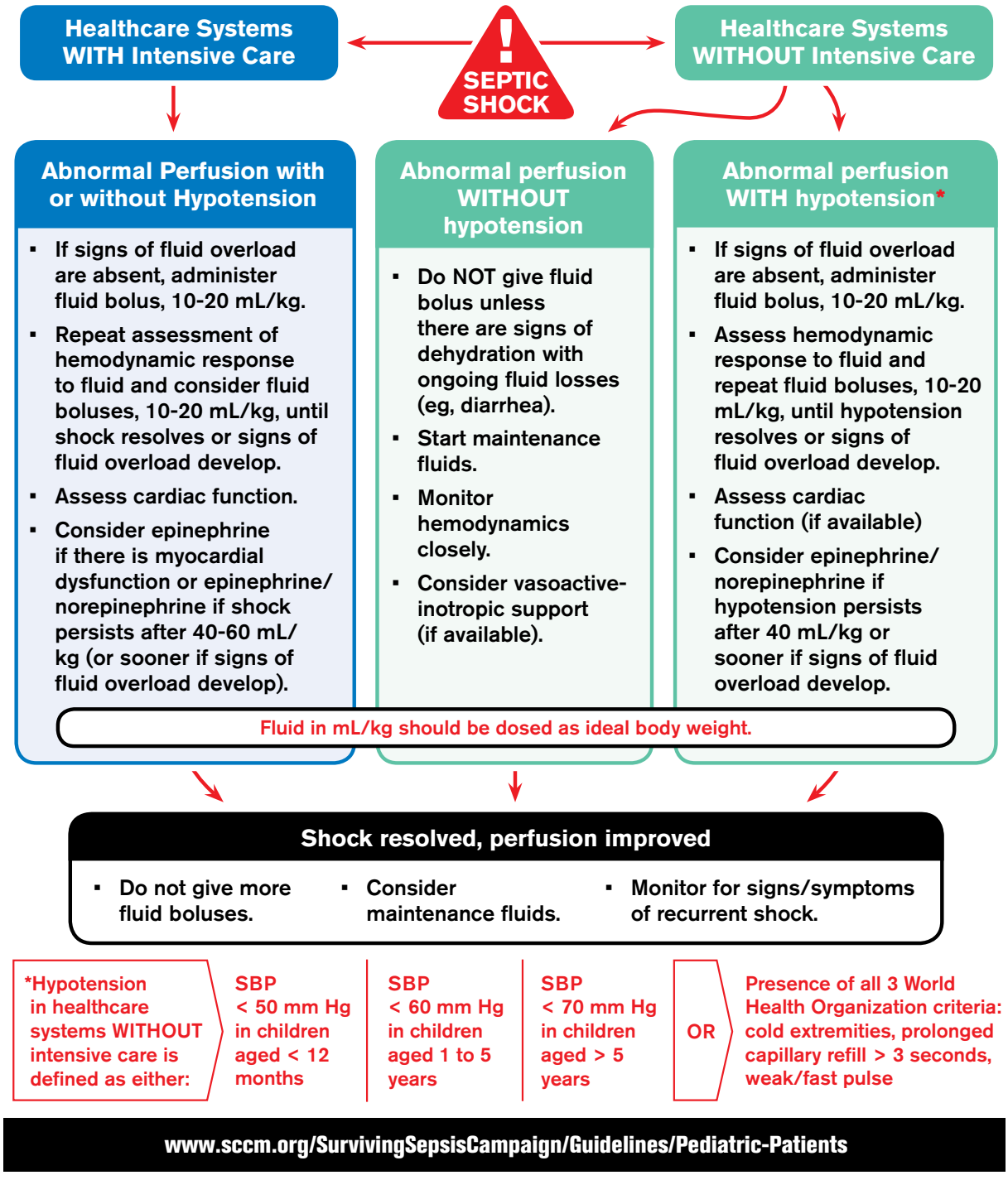


*See fluid and vasoactive algorithm. Note: Fluid bolus should be omitted from bundle if a) fluid overload is present or b) it is a low-resource setting without hypotension. Fluid in mL/kg should be dosed as ideal body weight.

**Hydrocortisone may produce benefit or harm.

Notes: ECLS – extracorporeal life support; VA – veno-arterial; VV – veno-venous.
Source: Surviving Sepsis Campaign paediatric patients (👆)

8.6.2 Fluid and vasoactive-inotrope management algorithm for children



Source: Rhodes et al. (2020); Surviving Sepsis Campaign paediatric patients (); Weiss et al. (2020).

8.7 Guide to the use of vasopressors in septic shock for adults and children

In adults, the Surviving Sepsis Campaign guidelines recommend vasopressors to be started if MAP < 65 mmHg. Administer vasopressors at a strictly controlled rate, titrate to maintain MAP 65 mmHg, reduce as the MAP improves and discontinue promptly when no longer needed. Dose initiation and titration should be individualized. The MAP goal can be individualized based on other clinical history (i.e. consider higher MAP target > 80 mmHg in patients with chronic hypertension).

Also, target other markers of perfusion such as:

Markers of tissue perfusion in adults and children
Capillary refill < 2 sec
Absence of skin mottling
Strong peripheral pulses
Warm and dry extremities
Regular urine output
Normal mental status
Normalization of lactate
In children: improved heart rate *(tachycardia is an early sign of septic shock and low blood pressure is a late finding)*

Vasopressors: norepinephrine is recommended as the first-line agent; however, **epinephrine** can be used as an alternative. **Dopamine** is not recommended because of the risk of tachyarrhythmias and concern of worse outcome.

Inotropes: dobutamine when there are persistent signs of hypoperfusion and clinical evidence of myocardial dysfunction (i.e. by ECHO, $ScvO_2$ < 70%) after adequate MAP and fluid status achieved.

Vasopressin is recommended as a second-line agent for refactory distributive shock.

Note: Vasopressor and inotrope selection should be informed by the patient's physiology including heart rate and assessment of cardiac function.

In children, the Surviving Sepsis Campaign guidelines recommend vasopressors if clinical signs of shock persist after fluid resuscitation and should not be delayed. These agents should be administered at a strictly controlled rate and titrated to achieve targets of adequate tissue perfusion.

Recommendation of **epinephrine or norepinephrine** as the first-line vasoactive infusion guided by clinician preference, individual patient physiology, and local system factors. If shock persists, add a second agent, and **vasopressin** can be added in children requiring high-dose vasopressors.

Note: Children can move between various shock states and vasopressors should be adjusted accordingly.

Dosing of vasopressors in adults and children

Route	Norepinephrine	Dobutamine	Epinephrine	Vasopressin
Central vein preferred	Initial: **0.05 µg/kg/min** Range: increase by 0.1 µg/kg/min increments; consider refractory if > 1 µg/kg/min	Initial: **2–5 µg/kg/min** Range: increase by 2.5 µg/kg/min increments; maximum 20 µg/kg/min	Initial: **0.05 µg/kg/min** Range: increase by 0.1 µg/kg/min increments; consider refractory if > 1 µg/kg/min	Initial: **0.01–0.04 units/min** Fixed dose No titration necessary
Peripheral vein if necessary[a]	Same dosing	Same dosing	Same dosing	Same dosing

Note: Thus, in septic shock, inotropes should be used in combination with vasopressors to maintain MAP at goal in adults, and children with low systemic vascular resistance.

[a] Requires close nursing care to check infusion site. If necrosis, stop infusion and consider injection of 1 mL phentolamine (vasodilator) solution subcutaneously. Phentolamine dose (adults): 5–10 mg in 10 mL of NS.

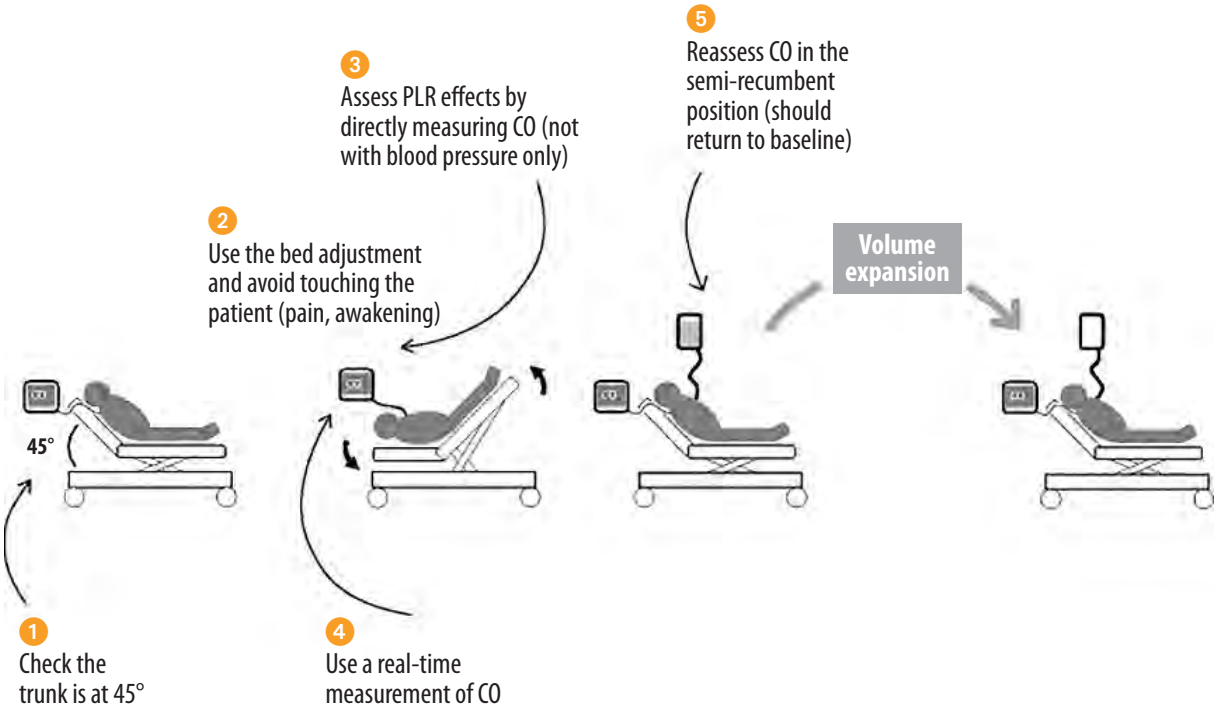
Side-effects of vasopressors and inotropes

Side-effects of vasopressors
Tachyarrhythmias
Ischaemia to organs
Cool and cyanotic extremities
Soft tissue necrosis (with peripheral administration if the vasopressor is extravasated)
Side-effects of inotropes
Tachyarrhythmias
Hypotension (due to peripheral vasodilation)

8.8 The five rules for passive leg raise (PLR)

In acute circulatory failure, passive leg raising (PLR) is a test that predicts whether cardiac output (CO) will increase with volume expansion. By transferring a volume of around 300 mL of venous blood from the lower body towards the right heart, PLR mimics a fluid challenge. However, no fluid is infused and the haemodynamic effects are rapidly reversible.

Best method for passive leg raising – the five rules to be followed



Notes: CO – cardiac output; PLR – passive leg raise.
Source: Monnet and Teboul (2015).

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9 Acute respiratory distress syndrome (ARDS)

9 Acute respiratory distress syndrome (ARDS)

Summary

When to suspect ARDS

- signs of severe or worsening respiratory distress
- hypoxaemia (SpO_2 < 90%) despite escalating oxygen therapy or SpO_2/FiO_2 < 315
- new bilateral opacities on chest images
- pulmonary oedema, cardiac failure or fluid overload not the primary cause.

Intubation and invasive mechanical ventilation may be indicated for many patients with ARDS (particularly those with moderate or severe ARDS) and hypoxaemic respiratory failure.

Lung protective ventilation (LPV) reduces mortality in patients with ARDS. A lung protective ventilation strategy includes:

- low tidal volumes (TV) (target 6 mL/kg predicted body weight or less);
- low plateau airway pressure (Pplat) (target Pplat ≤ 30 cmH_2O);
- moderate positive end-expiratory pressure (PEEP) (8–14 cmH_2O needed in most ARDS cases);
- driving pressure (Pplat-PEEP) ≤15 cmH_2O to titrate TV when PEEP≥15 *and* Pplat ≥30.

In ARDS patients who do not require intubation, i.e. mild ARDS, use of **high-nasal flow oxygen (HNFO)** or non-invasive ventilation (NIV) using CPAP or BiPAP may be safe when: significant hypercapnia is absent, mental status is normal, and haemodynamics are stable. These therapies require a monitored setting, with experienced personnel and capacity for performing emergent endotracheal intubation. A time-limited trial (~1 hr) of **CPAP or BiPAP** may be appropriate for select patients.

Do not delay the decision to intubate and start invasive mechanical ventilation when indications are present, including:

- severe hypoxaemia refractory to supplemental oxygen use
- severe hypercapnia refractory to non-invasive ventilation (if available)
- haemodynamic instability
- need for airway protection
- presence of emergency signs.

HFNO, BiPAP and CPAP may consume significant quantities of oxygen. See *Oxygen sources and distribution for COVID-19 treatment centres* ( ).

Use airborne precautions when conducting aerosol-generating procedures. See *Transmission of SARS-CoV-2: implications for infection prevention precautions* ( ).

Tools

9.1 Memory aid: diagnosis and classification of ARDS in adults
9.2 Memory aid: diagnosis and classification of pARDS in children
9.3 Advanced non-invasive mechanical ventilation in ARDS: algorithm to escalate supportive respiratory therapy
9.4 Checklist for rapid sequence intubation procedure in adults and children
9.5 Considerations for intubation and mechanical ventilation in children
9.6 List of commonly used medicines and dosage in ICU with ventilated patients (adults, children)
9.7 Choice of induction agent in adults
9.8 Choice of induction agent in children
9.9 Protocol to deliver lung protective ventilation (LPV)
  9.10.1 ARDS-net PEEP FiO_2 grid to guide PEEP
  9.10.2 Goals of Pplat and pH in lung protective ventilation
9.10 Memory aid: comparison of normal waveforms during volume and pressure-limited ventilation
9.11 Memory aid: recognizing and interpreting abnormal pressure and flow waveforms during volume control ventilation
9.12 Guide to distinguishing between causes of high peak airway pressures: resistance versus compliance
9.13 Troubleshooting high peak airway pressures, low tidal volumes, desaturation or haemodynamic instability in ventilated patients
9.14 Respiratory care pocket card reference
9.15 Adult ventilation order set (ARDS)
9.16 Checklist for proning in severe ARDS
9.17 Ventilation circuit types, filter and humidifier locations for SARI

9.1 Memory aid: diagnosis and classification of ARDS in adults

Berlin definition of acute respiratory distress syndrome (ARDS), 2012
ARDS Definition Task Force et al. (2012).

Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging[a]	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[b]	
Mild	$200 < PaO_2/FiO_2 \leq 300$ with PEEP or CPAP ≥ 5 cm H_2O[c]
Moderate	$100 < PaO_2/FiO_2 \leq 200$ with PEEP ≥ 5 cm H_2O
Severe	$PaO_2/FiO_2 \leq 100$ with PEEP ≥ 5 cm H_2O

Notes:
[a] Chest radiograph or computed tomography scan;
[b] If altitude is higher than 1000 m, the correction factor should be calculated as follows: [$PaO_2/FiO_2 \times$ (barometric pressure/760)];
[c] This may be delivered non-invasively in the mild ARDS group;
CPAP – continuous positive airway pressure; FiO_2 – fraction of inspired oxygen; PaO_2 – partial pressure arterial oxygen; PEEP – positive end-expiratory pressure.

A recent publication suggests a modified definition for resource-constrained environments, that excludes the need for CPAP or PEEP, arterial blood analysis and chest radiograph (Kigali modifications).

Kigali modifications of Berlin definition, 2016
Riviello et al. (2016).

Chest imaging	1. Bilateral opacities – not fully explained by effusions, lobar/lung collapse or nodules by chest radiograph or ultrasound 2. Ultrasound findings defined as presence of B-lines or consolidations without associated effusions found in at least one area on each side of the chest *The protocol requires six areas of each side of chest (two anterior, two lateral, two posterolateral) to be examined.*
Oxygenation	**$SpO_2/FiO_2 \leq 315$,** no PEEP or CPAP requirement

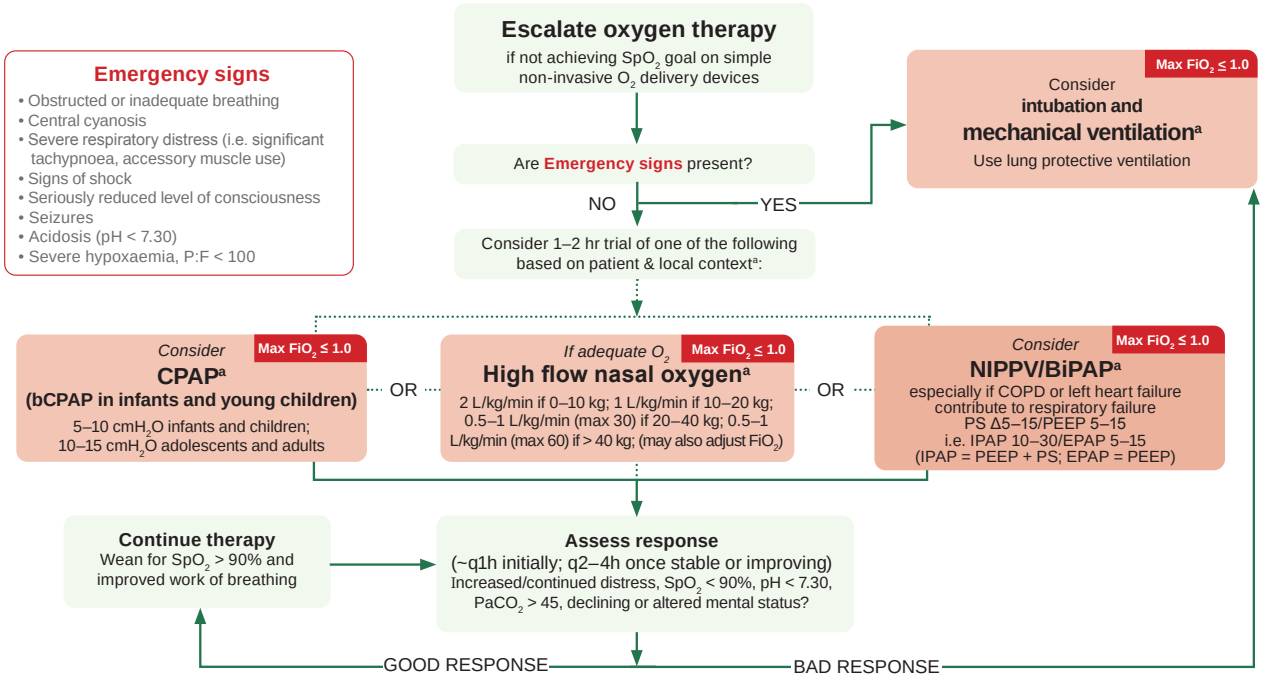
9.2 Memory aid: diagnosis and classification of pARDS in children

Paediatric acute respiratory distress syndrome (pARDS) definition
Pediatric Acute Lung Injury Consensus Conference Group (2015).

Age	Exclude patients with perinatal 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	Chest imaging findings of new infiltrates(s) consistent with acute pulmonary parenchymal disease			
Oxygenation	**Non-invasive mechanical ventilation**	**Invasive mechanical ventilation**		
	pARDS (no severity stratification)	**Mild**	**Moderate**	**Severe**
	Full face mask bilevel ventilation of CPAP ≥ 5 cm H_2O **PF ratio** ≤ 300, **SF ratio** ≤ 264	4 ≤ **OI** < 8 5 ≤ **OSI** < 7.5	8 ≤ **OI** < 16 7.5 ≤ **OSI** < 12.3	**OI** ≥ 16 **OSI** ≥ 12.3

Notes: CPAP – continuous positive airway pressure; OI – Oxygenation Index ([FiO_2 × mean airway pressure × 100]/PaO_2); OSI – oxygen saturation index ([FiO_2 × mean airway pressure × 100]/SpO_2); PF ratio – PaO_2/FiO_2 ratio; SF ratio – SpO_2/FiO_2 ratio.

9.3 Advanced non-invasive oxygen delivery in ARDS: algorithm to escalate supportive respiratory therapy



[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.

Do not delay the decision to intubate and start invasive mechanical ventilation when indications are present, including:

- severe hypoxaemia refractory to supplemental oxygen use
- severe hypercapnia refractory to non-invasive ventilation (if available)
- haemodynamic instability
- need for airway protection
- presence of emergency signs.

✓ Predictive factors of success with non-invasive ventilation

- Absence of multiorgan failure
- Younger age
- Initial PaO_2/FiO_2 > 150 mmHg

✓ Early signs of success with non-invasive ventilation

- Improved oxygenation
- Decreased respiratory rate
- Stable PaO_2/FiO_2 > 150 mmHg

Notes: See Antonelli et al., 2001; Bellani et al., 2021; Bellani et al., 2017; Carteaux et al., 2016; Seghal et al., 2015; Suttapanit et al., 2020; Thille et al., 2013.

9.4 Checklist for rapid sequence intubation procedure in adults and children

☑ This tool can be used before performing endotracheal intubation.

Intubation and IMV can be indicated, for adults and children, in case of hypoxaemia refractory to supplemental oxygen, depressed level of consciousness (AVPU) and severe shock.

1. Appropriate infection prevention precautions

- ☐ If suspect COVID-19 or any other droplet/airborne infection, use airborne precautions.
- ☐ Minimize personnel in patient's room during aerosol-generating procedures.
- ☐ Mask ventilation should be avoided if possible to minimize aerosolization.
  Note: If mask ventilation is necessary, then an inline bacterial viral filter should be utilized and for adults a two-handed, two-person technique should be used.

2. Equipment needed

- ☐ Suction: working Yankauer sucker under right side of pillow.
- ☐ Self-inflating resuscitation bag, 15 L/min oxygen, PEEP valve (pre-oxygenation and post-intubation) endotracheal tube (ETT): correct size, cuff checked and lubricated +/- stylet two working laryngoscopes with blades (direct laryngoscopes or videolaryngoscope).
- ☐ 10 mL syringe. Tube tie or tape.
- ☐ Gum elastic bougie on trolley top. Oropharyngeal airway on trolley top.
- ☐ Confirm laryngeal mask airway and surgical airway are available.
- ☐ Capnometry or capnography set up.
- ☐ Stethoscope.
- ☐ Ventilator checks complete.
- ☐ Ensure appropriate bacterial viral filter placement and in-line/closed suction setup in place.
- ☐ Alternate oxygen source (cylinder/flowmeter).

3. Drugs needed

- ☐ IV access patent and accessible.
- ☐ Induction agents: hypnotic/analgesic/neuromuscular blockers bolus and maintenance infusions prepared.
- ☐ Vasopressor and atropine prepared.

4. Team role description

- ☐ Lead provider 1: airway management and drug administration. Provider 2: assistance and drug administration.
- ☐ Provider 3: cricoid pressure (controversial).
- ☐ Provider 4 (respiratory therapist): airway management and ventilation assistance.
- ☐ Team members available immediately outside patient room.
- ☐ Team members available to provide spotting for correct PPE donning and doffing.

Note: See Gelb et al., 2018.

Rapid sequence intubation (RSI)

Definition: RSI is a protocol designed for the quick intubation of the trachea.

Target: Patients suspected of having an increased risk of aspirating stomach contents into the lungs.

T**echnique:** Quicker form of the process normally used to "induce" a state of general anaesthesia.

It uses drugs to rapidly allow an ETT to be placed between the vocal cords, by blocking the patient's involuntary reflexes and muscle tone in the oropharynx and larynx. Once the ETT has been passed between the vocal cords, a cuff is inflated around the tube in the trachea and the patient can then be artificially ventilated. Correct ETT position can be verified by direct visualization through the vocal cords; capnography (persistent CO_2 return; may show CO_2 transiently if in esophagus); high SpO_2, bilateral breath sounds on chest auscultation; and correct position on X-ray.

5. Protocol

☐ **Pre-oxygenate for 5 minutes with 100% FiO_2**
Ideally this is done with a device capable of reliably delivering 100% FiO_2 (HNFO, CPAP or BiPAP).

Note: Children, infants and obese patients have reduced functional residual capacity; they can desaturate quickly on induction.
Note: If the mask's seal is broken, or for example the mask is removed so that the patient can speak clearly, the process must start again for an additional 5 minutes.

☐ **Anticipate shock**
Benzodiazepines, thiopental, inhalational agents and propofol cause myocardial depression and vasodilation; this can unmask or worsen shock. Induction agents such as etomidate, ketamine or opiates can also cause haemodynamic instability in patients with high pre-induction sympathetic tone.

- ☐ Anticipate instability and consider use ketamine for induction if available.
- ☐ Anticipate instability by pre-loading with volume (10–20 mL/kg 0.9% isotonic crystalloid) and/or starting/increasing inotropic support.

Ensure a blood pressure raising agent that can be given as a bolus is immediately available in a syringe bedside (e.g. ephedrine, phenylephrine, diluted epinephrine). Check the blood pressure as often as possible – if an automatic blood pressure machine is used, set at frequent intervals (e.g. every 1 minute) during induction and intubation.

☐ **Use induction agent ± opiate and neuromuscular relaxant in all patients** to optimize the view and make intubation easier.

☐ **Confirm correct ETT placement with end-tidal CO_2 as the gold standard.** When end-tidal CO_2 measurement is not available, several additional signs and techniques are frequently used to assess endotracheal tube placement, including:

- direct visualization of cords
- improving SpO_2
- bilateral equal air on auscultation
- condensation in the endotracheal with exhalation
- external palpation of the endotracheal tube balloon in the trachea
- ultrasound of the endotracheal tube in the trachea
- chest X-ray position of ETT tip 1–2 cm above the carina (in adults), or T3 posterior.

9.5 Considerations for intubation and mechanical ventilation in children

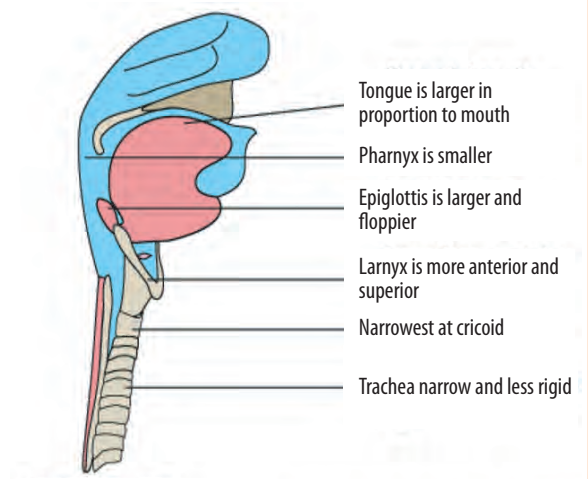
Specifications for children

Decompress the stomach to prevent diaphragmatic splinting:
- use airway adjuncts to reduce stomach inflation;
- in bag-mask ventilation, place NG tube early and regularly aspirate with large bore syringe to decompress stomach.

Consider atropine in neonates and children to prevent bradycardia caused by vagal stimulation during laryngoscopy or with the use of succinylcholine.

Anatomical differences between children and adults

Anatomical differences between children and adults can make ventilation more difficult.
- **Lower chest wall rigidity** of children implies an earlier respiratory failure in infants in any pathology that causes ↓ compliance of lung, e.g. viral pneumonitis.
- **Smaller airway diameter** of children implies an upper airway resistance.
- **Larger abdomen** of children implies a ↓ functional residual capacity → ↑ atelectasis at end expiration and atelectrauma.
- **Larger tongue**, anterior **larynx, narrow cricoid ring, larger occiput** require positioning of the airway (e.g. use of neck rolls) to optimize visualization on laryngoscopy:
  - neonates and infants in neutral position
  - older children in "sniffing morning air" position.



Child's upper airway

Tips: Anticipate a difficult airway, particularly if stridor or a small posteriorly placed jaw are present. Pre-oxygenate, have a range of ETT and blades and the most experienced operator available.

Choice of endotracheal tubes size for paediatric patients

	Term infant	Estimate at 6 months	Children ≥ 1 year (kg)
Diameter (size) of ETT (cuffed preferred)	3–3.5	3.5–4	(Age/4) + 4 (uncuffed); (Age/4) + 3.5 (cuffed)
Length oral ETT at lips (confirm on X-ray)	8–9	10	(Age/2) + 12 cm
Length nasal ETT at nose (confirm on X-ray)	10–11	12	(Age/2) +15 cm
Suction catheter size	2 × ETT = 6	2 × ETT = 8	2 × ETT

Normal physiologic parameters and equipment							
Age	**kg**	**HR**	**MAP**	**RR**	**Blade**	**ETT mm**	**ETT@Lips**
0–1 m	<1	140	30	< 60	Miller 0	2.5	7 cm
0–1 m	1–2	140	30	< 60	Miller 0	3.0	8 cm
0–1 m	2–3	130–140	30	< 60	Mil0/Mil1	3.5	9 cm
0–1 m	> 3	130–140	40	< 60	Mil0/Mil1	3.5–4.0	10 cm
1–6 m	4–6	130	50	24–30	Mil1/Mil1.5	3.5–4.0	12 cm
6 m–1 yr	6–10	130	60	22–26	Wis 1.5	4.0	13 cm
1–2 yr	10–12	120	60	20–24	Wis 1.5	4.5	14 cm
2–4 yr	12–16	110	60	18–22	Wis 1.5/Mac 2	5.0	15 cm
4–6 yr	16–20	90–110	70	16–20	Mil 2/Mac 2	5.5	16 cm
6–8 yr	20–30	90	70	16–20	Mil 2/Mac 2	6.0	17 cm
9–12 yr	30–45	80	70–80	12–18	Mil/Mac 2–3	6.5–7.0	18 cm
>12 yr	> 50	75	70–80	10–16	Mil/Mac 2–3	7.0	20–22 cm

Neonatal and paediatric general estimates	
Neonatal "1-2-3(kg)/7-8-9 (ETT@Lips) rule" For preterm and term newborns: MAP equals the number of weeks post conceptual age (PCA) By day of life 5, MAP = number of weeks PCA + 5	ETT size: (Age/4) + 4, or 5th finger size ETT depth: [(height in cm)/10] + 5 or 3 × ETT size Age +11 cm at lip

Notes: ETT – endotracheal tube; HR – heart rate; LMA – laryngeal mask airway; MAP – median arterial pressure; RR – respiratory rate.

9.6 List of commonly used medicines and dosage in ICU with ventilated patients (adults, children)

INDUCTION AGENT
NEUROMUSCULAR BLOCKING AGENT
SEDATIVE/HYPNOTIC
CARDIOVASCULAR SUPPORT AGENT
ANALGESIC

Medications

ACETAMINOPHEN	See Paracetamol
ADENOSINE	*Adult:* 6 mg IV push; then 12 mg IV q1min × 2 prn *Peds:* 0.1 mg/kg IV push (max 6 mg/dose), may repeat 0.2 mg/kg IV (max 12 mg/dose)
ADRENALINE (EPINEPHRINE)	*Adult:* Arrest: 1 mg q3–5min IV prn; ETT 2–2.5 mg q3–5min prn (dilute in 5–10 mL NS or sterile water) Anaphylaxis/hypotension: 0.05–0.1 mg IV q5min prn; 0.2–0.5 mg IM q5min prn; Infusion: 0.5–20 mcg/min IV Racemic 2.25% solut 0.5 mL via neb *Peds:* Arrest: 10 mcg/kg IV (max 1 mg) q3–5min prn; 100 mcg/kg ETT q3–5 min prn Anaphylaxis: Children > 6 mo < 30 kg: 10 mcg/kg IM; > 30 kg 300 mcg IM Severe Hypotension: 0.5–10 mcg/kg IV Infusion: 0.02–1 mcg/kg/min IV Racemic 2.25% solut 0.25–0.5 mL via neb
ALBUTEROL	*Adult & Peds:* (bronchodilation) Nebulized: 2.5 mg in 3 mL every 20 min or continuous (5–20 mg/hr)
AMIODARONE	*Adult:* 150–300 mg IV (dependent on rhythm) then 1 mg/min × 6hr, then 0.5 mg/min x18hr *Peds:* 5 mg/kg IV (max 300 mg) over 30 min, may repeat × 2; Infusion: 5–15 mcg/kg/min IV
ATRACURIUM	*Adult & Peds:* 0.4–0.5 mg/kg IV (t½ = ~20 min)
ATROPINE	*Adult:* Arrest/bradycardia: 0.5 mg IV q3–5min max 3 mg; ETT 1–2 mg q3–5min prn *Peds:* Arrest/brady: 0.02 mg/kg (max 0.5 mg) IV, repeat x 1 q5min prn; ETT 0.04–0.06 mg/kg; repeat × 1 prn
CALCIUM CHLORIDE	*Adult:* Arrest, CCB toxicity: 1–2 gm IV slowly; repeat q10min prn *Peds:* Arrest, CCB toxicity: 20 mg/kg IV (max 2 g); repeat q10min prn
CARBOPROST (HEMABATE)	*Adult:* 250 mcg IM, repeat q15min prn. Max 2 mg (see PPH for full details)
CISATRACURIUM	*Adult:* 0.1–0.2 mg/kg IV (t½ = ~ 25 min); Infusion 0.5–10 mcg/kg/min IV *Peds:* 0.1–0.15 mg/kg IV; Infusion 0.5–4 mcg/kg/min IV
CODEINE	*Adult:* 15–60 mg PO/IM/SQ; repeat q4h prn *Peds:* not recommended in children < 12 yr
DANTROLENE	*Adult & Peds:* 2.5 mg/kg IV, repeat 1 mg/kg prn (max of 10 mg/kg)
DEXMEDETOMIDINE	*Adult & Peds:* Load: 0.5–1 mcg/kg IV (over 10 min), Infusion: 0.2–1.5 mcg/kg/hr IV
DEXAMETHASONE	*Adult & Peds:* Airway oedema: 0.5 mg/kg IV q6hr PONV: Adults 4–8 mg IV; Peds 0.1 mg/kg IV
DIAZEPAM	*Adult:* 5–10 mg IV *Peds:* 0.2–0.3 mg/kg IV

DICLOFENAC	*Adult:* 50–100 mg PO *Peds:* 0.5 mg/kg IV/IM; 1 mg/kg PO/PR
DIPHENHYDRAMINE	*Adult:* 25–50 mg IV/IM/PO q4–6hr *Peds:* 0.5–1 mg/kg IV q4–6 hours; max 50 mg
DOBUTAMINE	*Adult & Peds:* 0.5–20 mcg/kg/min IV infusion
DOPAMINE	*Adult & Peds:* 0.5–20 mcg/kg/min IV infusion
EPINEPHRINE	See Adrenaline
EPHEDRINE	*Adult:* 5–10 mg IV prn *Peds:* 0.1–0.2 mg/kg (max 25 g/dose) IV prn
ERGOMETRINE	*Adult:* 0.5 mg IV/IM slow
ESMOLOL	*Adult & Peds:* Bolus: 0.5 mg/kg IV prn; Infusion: 50–300 mcg/kg/min IV
ETOMIDATE	*Adult & Peds:* 0.2–0.3 mg/kg IV
FENTANYL	*Adult:* Analgesia: 25–100 mcg IV prn; Infusion 25–200 mcg/hr (or higher) *Peds:* Analgesia: 0.5–1 mcg/kg IV prn; 1–2 mcg/kg intranasal prn; Infusion: 0.5–5 mcg/kg/hr IV
GLYCOPYRROLATE	*Adult:* Reversal: 0.1–0.2 mg IV *Peds:* Reversal: 0.015 mg/kg IV; Antisialagogue: 4 mcg/kg IM
HYDRALAZINE	*Adult:* 10–20 mg IV *Peds:* 0.1–0.2 mg/kg IV
HYDROCODONE	*Adult:* 20–40 mg PO *Peds:* 0.2 mg/kg PO
HYDROCORTISONE	*Adult:* 100 mg IV; stress dose 50 mg IV q6hr *Peds:* (stress dose) 1–2 mg/kg IV
HYDROMORPHONE	*Adult:* 0.5–2 mg IV prn *Peds:* IV: 5–10 mcg/kg IV prn PO/PR: 50–80 mcg/kg q3–6h prn
INTRALIPID	*Adult & Peds:* LAST: 1.5 mL/kg followed by infusion 0.25 mL/kg/min up to 0.5 mL/kg/min ; use ideal body weight; 12 mL/kg in peds
KETAMINE	*Adult:* Induction: 0.5–2 mg/kg IV, 4–10 mg/kg IM; Analgesia: 0.2–0.8 mg/kg IV, 2–4 mg/kg IM; Infusion 2–15 mcg/kg/min IV *Peds:* Induction: 1–3 mg/kg IV, 5–8 mg/kg IM, 5–10 mg/kg PR; Analgesia: 0.2–0.5 mg/kg IV, 2–4 mg/kg IM; Infusion: 2–10 mcg/kg/min IV
KETOROLAC	*Adult:* 30–60 mg IV/IM, then 15–30 mg IV/IM q6h prn *Peds:* 0.5 mg/kg (max 30 mg) IV q6h prn; 1 mg/kg IM
LABETALOL	*Adult:* 10–20 mg IV, double dose q15min prn to max 300 mg; Infusion 0.5–2 mg/min (or higher) *Peds:* 0.1 mg/kg IV q5–10min
LIDOCAINE	*Adult:* Arrest: 1–1.5 mg/kg IV, 0.5–0.75 mg/kg q5–10min prn (max 3 mg/kg), ETT 2–3.75 mg/kg, infusion 1–4 mg/min; analgesia: 1–2 mg/kg IV, infusion: 0.5–3 mg/kg/hr IV *Peds:* Arrest: 1 mg/kg IV, repeat x1 prn, ETT 2–3 mg/kg infusion 20–50 mcg/kg/min IV; Analgesia: 1 mg/kg IV; infusion: 1.5–2 mg/kg/hr IV
LORAZEPAM	*Adult:* 1–4 mg IV prn *Peds:* 0.1 mg/kg IV prn (max 4 mg/dose)

MAGNESIUM SULFATE	*Adult:* Asthma: 2 gm IV over 20 min; eclampsia/pre-eclampsia: load 4–6 gm IV, infusion 1–2 gm/hr IV; torsade de pointes: 1–2 gm IV, infusion 0.5–1 gm/hr IV *Peds:* Asthma: 25–75 mg/kg (max 2 gm) IV over 20 min; torsade de pointes: 25–50 mg/kg/dose (max 2 gm) IV
MEPERIDINE	See Pethidine
METARAMINOL	*Adult & Peds:* 0.5 mg IV bolus, repeat q2–3min prn (avoid in children < 12)
METHADONE	*Adult:* Analgesia: 2.5–10 mg PO/IM/IV/SQ (based on opioid tolerance), repeat q8–12h prn *Peds:* Analgesia: 0.05–0.1 mg/kg PO/IM/IV/SQ; (t½ = 18–24 hrs)
METHOHEXITAL	*Adult:* Induction: 1–1.5 mg/kg IV *Peds:* Induction: 1–3 mg/kg IV, 20–30 mg/kg PR
METHYLER-GONOVINE/ METHERGINE	*Adult:* 0.2 mg IM; repeat q5–10min max 2 doses
METHYLPREDNISOLONE	*Adult:* Asthma: 40–80 mg IV; anaphylaxis: 125 mg IV *Peds:* Asthma: 1 mg/kg IV; anaphylaxis: 1–2 mg/kg IV
METOCLOPRAMIDE	Adult: 10–20 mg IV/PO, repeat 5–10 mg q6h prn *Peds:* 0.1–0.15 mg/kg IV/PO q6h prn
MIDAZOLAM	*Adult:* 0.5–4 mg IV *Peds:* 0.1–0.2 mg/kg IV, 0.5 mg/kg PO/PR
MISOPROSTOL	*Adult:* 1 mg PR
MORPHINE SULFATE	*Adult:* 2.5–10 mg IV/IM *Peds:* 0.05–0.1 mg/kg IV/IM
NALOXONE	*Adult:* Excessive sedation: 0.02–0.2 mg q4–8; opioid overdose: 0.1–2 mg IV/IM q2–3min prn, 2 mg nebulized, 4 mg intranasal *Peds:* Excessive sedation: 0.5–1 mcg/kg IV q2–3min prn; opioid overdose: 10 mcg/kg IV/IM q2–3min prn; 4 mg intranasal
NEOSTIGMINE	*Adult & Peds:* 0.03–0.07 mg/kg IV (max 5 mg) Add atropine IV 0.5–1 mg (adults), 20 mcg/kg (peds) or glycopyrrolate (see "glycopyrrolate")
NITROGLYCERIN	*Adult:* Infusion: 10–200 mcg/min IV *Peds:* 0.5–20 mcg/kg/min IV infusion IV
NOREPINEPHRINE	*Adult:* Infusion: 0.05–2 mcg/kg/min or 0.5–20 mcg/min IV *Peds:* Infusion: 0.05–2 mcg/kg/min IV
ONDANSETRON	*Adult:* 4–8 mg IV, repeat q4–8h prn *Peds:* 0.15 mg/kg IV; repeat q6-8h prn
OXYCODONE	*Adult:* 5–15 mg (or higher depending on opioid tolerance), repeat q3–4h prn *Peds:* 0.1 mg/kg PO; repeat q3–4h prn
OXYTOCIN (PITOCIN)	*Adult:* 3 U stat IV over 30 sec, consider repeat dosing and infusion
PANCURONIUM	*Adult:* 0.04–0.1 mg/kg IV *Peds:* 0.05–0.15 mg/kg IV (t½ = ~110 min)
PARACETAMOL (ACETAMINOPHEN)	*Adult:* 500–1000 mg IV/PO, repeat q4–6 prn (max 2–4 gm/day) *Peds:* PO/IV: 10–15 mg/kg, repeat q6h prn, PR: 40 mg/kg × 1, max: 75 mg/kg/24 hr
PETHIDINE (MEPERIDINE)	*Adult:* Shivering/analgesia: 12.5–50 mg IV *Peds:* 0.5–1 mg/kg IV, max 400 mg daily
PHENOBARBITAL/ PHENOBARBITONE	*Adult & Peds:* Status epilepticus: 15–20 mg/kg IV, may repeat 5–10 mg/kg in 10 min prn x 1

PHENYLEPHRINE	*Adult:* 40–100 mcg IV q1–2min prn; infusion 10–200 mcg/min
PITOCIN	See Oxytocin
PROCHLORPERAZINE	*Adult:* 5–10 mg IV/IM/PO q3–6h prn (max 40 mg/day) *Peds:* 0.1–0.15 mg/kg PO/IM/IV q6–8h prn (max 10 mg/dose)
PROMETHAZINE	*Adult:* 12.5–25 mg PO/PR q4–6h prn *Peds:* 0.2–0.5 mg/kg PO/PR q6–8h Max 25 mg/dose (do not give if < 2 yr)
PROPOFOL	Induction: Dose variable, Adults: 1–2.5 mg/kg; Children 2–4 mg/kg Infusion: 10–250 mcg/kg/min
RANITIDINE	*Adult:* 50 mg IV; 150–300 mg PO *Peds:* 1 mg/kg IV; 2.5 mg/kg PO
REMIFENTANIL	*Adult & Peds:* Bolus: 0.5–1 mcg/kg IV; Infusion: 0.05–0.5 mcg/kg/min IV
ROCURONIUM	*Adult:* 0.6–1.2 mg/kg IV (t½ = ~60 min) *Peds:* 0.9–1.2 mg/kg IV
SCOPOLAMINE	*Adult & Adolescents:* 1 patch q72h *Peds:* 6 mcg/kg IV (max 0.3 mg)
SODIUM CITRATE (Bicitra)	*Adult:* 15–30 mL PO q6h prn *Peds* ≥ 2 yr: 1–1.5 mL/kg q6–8h prn (max 30 mL/dose)
SODIUM BICARBONATE	*Adult:* 50–100 mEq IV prn (1 "amp" of 50 mL 8.4% = 50 mEq) *Peds:* 1–2 mEq/kg IV
SUCCINYLCHOLINE/ SUXAMETHONIUM	*Adult:* (induction) 0.6–2 mg/kg IV (high end for RSI) IM: 3–4 mg/kg; max 5 mL at injection site (t½ = ~6–8 min) *Peds:* 1–2 mg/kg IV; 3–4 mg/kg IM
SUFENTANIL	*Adult:* Analgesia: 0.5–2 mcg/kg IV Infusion: 0.05–2 mcg/kg/hr
SUGAMMADEX	*Adult:* 2 TOF twitches: 2 mg/kg; 0 TOF, 1–2 PTC: 4 mg/kg; Immediate emergent reversal: 16 mg/kg
TERBUTALINE	*Adult:* (tocolysis) 5–10 mcg/kg IV q15min (max 250 mcg)
THIOPENTAL/ THIOPENTONE	*Adult:* (induction) 3–6 mg/kg
TRAMADOL	*Adult:* 25–100 mg PO q4–6h prn *Peds:* not recommended in children < 12 yr
TRANEXAMIC ACID	*Adult:* 1 g IV over 10 min, repeat × 1 after 30 min prn
VASOPRESSIN	*Adult:* (shock) 0.03–0.05 units/minute drip *Peds:* (shock) Infusion: 0.0002–0.002 units/kg/min IV
VECURONIUM	*Adult & Peds:* (induction) 0.1 mg/kg IV (t½ = ~65 min) 0.8–1.7 mcg/kg/min drip

Notes: CCB – calcium channel blocker; ETT– endotracheal tube; IV– intravenous; IM – intramuscular; min – minute; PO – per os/oral; PONV – post-operative nausea and vomiting; PR – per rectal; prn – pro re nata; PTC – post-tetanic count; SQ – subcutaneous; TOF – train of four.

Source: Adapted from USAID-STAR-UCSF Project ().

9.7 Choice of induction agents in adults

Choice of induction agents in adult patients

		Intravenous dose	Notes
Opiates	**Fentanyl**	50–250 mcg	Can cause ↓ blood pressure May cause chest stiffness
	Morphine	2.5–10 mg	Takes long time to be effective ~10 mins
Sedative/hypnotic	**Midazolam**	0.5–4 mg	Can cause delirium Accumulates in liver failure
	Lorazepam	1–4 mg	Can cause delirium Accumulates in liver failure
	Diazepam	5–10 mg	Can cause delirium Accumulates in renal failure
Induction agent	**Ketamine**	0.5–2 mg/kg	Can cause ↑ intracranial pressure
	Etomidate	0.2–0.3 mg/kg	Can cause adrenal suppression with multiple doses
	Propofol 1%	1–2.5 mg/kg[a]	Can cause ↓ blood pressure
	Thiopental	3–6 mg/kg	
Neuromuscular blockers	**Suxamethonium**	0.6–2 mg/kg	Avoid if hyperkalaemia, neuromuscular patients, recent burn or renal failure
	Rocuronium	0.6–1.2 mg/kg	First-line RSI paralytic
	Vecuronium	0.1 mg/kg	
	Atracurium	0.4–0.5 mg/kg	
	Pancuronium	0.04–0.1 mg/kg	Prolonged block if renal failure

Note:
[a] Consider dose reduction for critically ill patients or selecting alternate agents if haemodynamically unstable.

9.8 Choice of induction agents in children

Choice of induction agents in paediatric patients

		Intravenous dose	Notes
Opiates	**Atropine**	20 mcg/kg (min. dose 100 mcg); > 12 years 300–600 mcg	
	Fentanyl	2–5 mcg/kg	Can cause ↓ blood pressure
	Morphine	0.1–0.2 mg/kg	Relatively prolonged onset: ~10 mins
Sedative/hypnotic	**Midazolam**	0.1–0.2 mg/kg	Can cause delirium Accumulates in liver failure
	Lorazepam	0.1 mg/kg	Can cause delirium Accumulates in liver failure
	Diazepam	0.2–0.3 mg/kg	Can cause delirium Accumulates in renal failure
Induction agent	**Ketamine**	1–3 mg/kg	Can cause ↑ intracranial pressure
	Etomidate	0.2–0.3 mg/kg	Can cause adrenal suppression with multiple doses
	Propofol 1% (induction only)	2–4 mg/kg[a] (> 3 years)	Can cause ↓ blood pressure
Neuromuscular blockers	**Suxamethonium**	3 mg/kg/dose (neonate); 1–2 mg/kg all other ages	Avoid if hyperkalaemia, neuromuscular patients, recent burn or renal failure
	Rocuronium	0.9–1.2 mg/kg	First-line RSI paralytic
	Vecuronium	0.1 mg/kg	
	Atracurium	0.4–0.5 mg/kg	
	Pancuronium	0.05–0.15 mg/kg	Vastly prolonged block in renal failure

Note:
[a] Consider dose reduction for critically ill patients or selecting alternate agents if haemodynamically unstable.

9.9 Protocol to deliver lung protective ventilation (LPV)

This protocol to deliver lung protective ventilation (LPV) was used in the low tidal volume (TV) trial published in 2000 (ARDS Network et al., 2000).

Ventilator set up and adjustment

- Calculate predicted body weight (PBW):
  Males = 50 + 1.1 [height (cm) – 152]
  Females = 45.5 + 1.1 [height (cm) – 152].
- Select any ventilator mode.
- Set ventilator settings to achieve initial tidal volume (TV) = 6 mL/kg PBW (range 4–8 mL/kg).
- Reduce TV by 1 mL/kg at intervals ≤ 2 hrs until achieve pressure goals.
- Set initial rate to approximate baseline minute ventilation (MV) (not > 35 breaths/min in adults).
  MV = Tidal volume (TV) x Respiratory rate (RR)
- Set I:E ratio (ratio of the duration of inspiration and expiration phases):
  – set high inspiratory flow rates
  – monitor for intrinsic PEEP
  – in severe ARDS I:E ratios of 1:1 or inverse ratios may be needed.
- Set inspiratory flow rate above patient demand (commonly > 60 L/min).
- Set FiO_2 at 1.0 and titrate down.
- Set PEEP 5–10 cmH_2O or higher for severe ARDS.
- Adjust TV and RR to achieve pH and Pplat goals below.

Note: Principles are the same for children except that children younger than 8 years require a lower maximum PEEP – 15 cmH_2O and the peak Pplat should be < 28 cmH_2O.

9.9.1 ARDS-net PEEP FiO_2 grid to guide PEEP

See ( ).

Set PEEP corresponding to severity of oxygen impairment:

Oxygenation goal: PaO_2 55–80 mmHg or SpO_2 88–95%

- Use a minimum PEEP of 5 cmH_2O
- Consider incremental PEEP/FiO_2 combinations such as shown below to achieve goal
- PEEP levels > 15 should not be used in children < 8 years

There are two PEEP/FiO_2 grids – the second one can be used for more severe hypoxaemia.

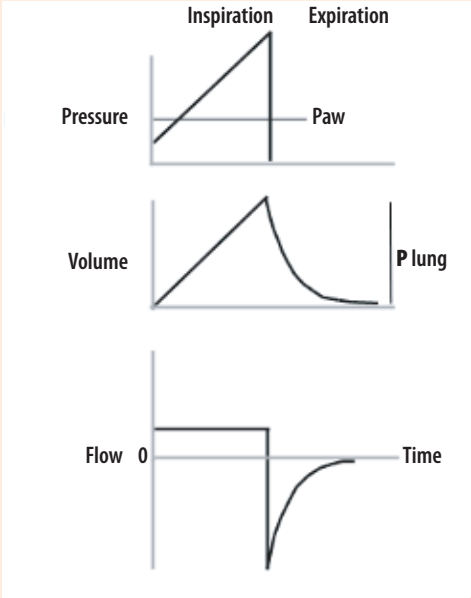
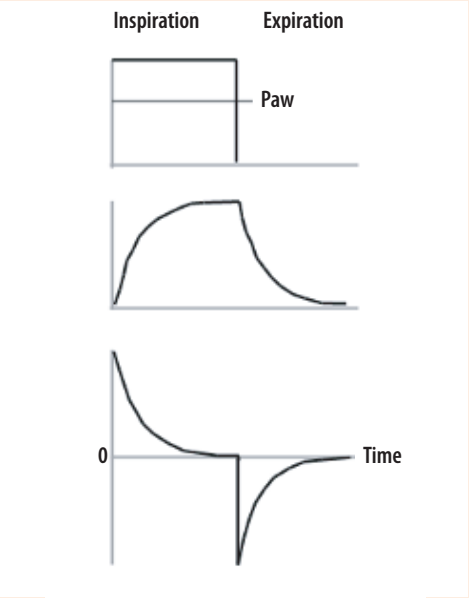
Lower PEEP/higher FiO_2														
FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18–24
Higher PEEP/lower FiO_2 for more severe hypoxaemia														
FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5–0.8	0.8	0.9	1.0	1.0
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22	18–24

9.9.2 Goals of Pplat and pH in lung protective ventilation

Pplat goal: ≤ 30 cmH_2O	Check Pplat using 0.5 second inspiratory pause, at least every 4 hours and after each change in PEEP or TV • **If Pplat > 30 cmH_2O or > 28 cmH_2O in children:** decrease TV by 1 mL/kg steps (minimum = 4 mL/kg). • **If Pplat < 25 cmH_2O and TV < 6 mL/kg:** increase TV by 1 mL/kg until Pplat > 25 cmH_2O or TV = 6 mL/kg. • **If Pplat < 30 cmH_2O and breath stacking or asynchrony occurs:** may increase TV in 1 mL/kg increments to 7–8 mL/kg if Pplat remains ≤ 30 cmH_2O.
pH goal: 7.30–7.45	Acidosis management: (pH < 7.30) • **If pH 7.15–7.30:** increase RR until pH > 7.30 or $PaCO_2$ < 25 (maximum set RR = 35). • **If pH < 7.15:** increase RR to 35. • **If pH remains < 7.15,** TV may be increased in 1 mL/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded). • May give $NaHCO_3$ to act as a transient buffer.
Alkalosis management: pH > 7.45	Decrease ventilator rate if possible.
Inspiration to expiration ratio goal	Recommend that duration of inspiration be less than duration of expiration.

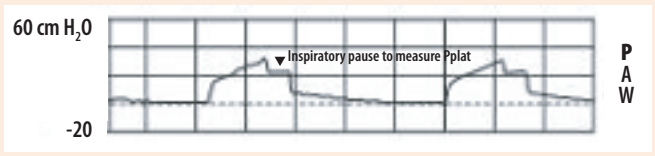
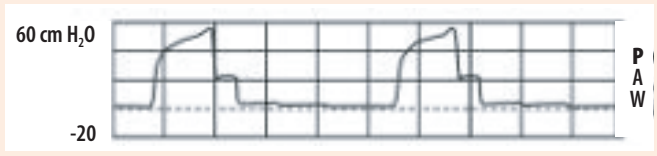
Notes: Paw – airway pressure; PEEP – positive end-expiratory pressure; Pplat – plateau airway pressure.

9.10 Memory aid: comparison of normal waveforms during volume and pressure-limited ventilation

Volume control	Pressure control
	
• Volume cycled ventilation • Flow is fixed (shown) or decelerating • Volume is set and the airway pressures are variable • Inspiration cycles to expiration after fixed time or volume delivered • To measure Pplat you need to perform an inspiratory pause, which means briefly stopping gas flow at the end of pressure + PEEP inspiration • Patient can trigger a breath	• Pressure limited ventilation • Flow is variable • Pressure is set (see square wave form) and the volumes are variable • Inspiration cycles to expiration after fixed time • Pplat is the set inspiratory pressure (Pinsp), equal to driving pressure + PEEP • Patient can trigger a breath

Notes: Paw – airway pressure; PEEP – positive end-expiratory pressure; Pplat – plateau airway pressure.

9.11 Memory aid: recognizing and interpreting abnormal pressure and flow waveforms during volume control ventilation

Pressure curves	Characteristics	Interpretation
	Normal pressure curve	Normal
	Increased peak airway pressure Increased Pplat	Reduced compliance
	Increased peak airway pressure Normal Pplat Intrinsic PEEP	Increased resistance

Flow curves	Characteristics	Interpretation
	Normal flow pattern	Normal
	High expiratory peak flow rate expiratory flow is shorter	Reduced compliance
	Prolonged expiratory flow Intrinsic PEEP	Increased resistance

Source: Hess DR (2005).

9.12 Guide to distinguishing between the causes of high peak airway pressures: resistance versus compliance

Abnormal airway pressure(s)	High peak with high plateau airway pressure	High peak with normal plateau airway pressure
Main physiologic problem	Reduced respiratory system compliance (Crs)	High resistance (R)
Formula	$C_{rs} = \frac{\text{Tidal volume}}{P_{plat} - PEEP}$	$R = \frac{P_{peak} - P_{plat}}{\text{Flow}}$
Normal	60–100 mL/cm H_2O	5–10 cm H_2O/L/sec for intubated adult
Problems that can be treated quickly	• mainstem bronchus intubation • tension pneumothorax • pleural effusion • abdominal distension • congestive heart failure • atelectasis • hyperinflation	**Patient problems:** • patient biting, coughing, fighting ventilator • secretions • bronchospasm **Ventilator problems:** • tube kinked • circuit filled with water • small endotracheal tube
Other problems that may improve over the time	• ARDS • consolidation • fibrosis • chest wall oedema • thoracic deformity	• asthma • chronic obstructive pulmonary disease (COPD)

Factors influencing peak airway pressure

P airway = **P** resistance + **P** compliance

Airflow resistance	Respiratory system compliance	Chest wall compliance
• size of airway • lower airway obstruction • mechanical obstruction	• chest wall • tidal volume • lung elasticity	• chest wall • patient position • external compression of chest from abdomen

9.13 Troubleshooting high peak airway pressures, low tidal volumes, desaturation or haemodynamic instability in ventilated patients

☑

☐ **Is the endotracheal tube in the trachea?**
- Large cuff leak or no chest rise with inspiration suggest that ETT is dislodged: assess with direct laryngoscopy and re-intubate.

☐ **Is there a problem with the ventilator circuit or oxygen supply?**
- Take the patient off the ventilator and hand ventilate with 100% oxygen while checking equipment.

☐ **Can you pass a suction catheter through the endotracheal tube?**
- If no, ETT may be kinked: straighten or insert bite block to prevent patient from biting.
- If no, ETT may be blocked with secretions: reintubate with new ETT.
- If yes, suction ETT to remove sputum/mucus plugs.

☐ **Are there breath sounds bilaterally?**
- Unilaterally absent breath sounds: evaluate for mainstem intubation/lobar collapse versus pneumothorax by assessing mediastinal shift and by chest X-ray or ultrasound if patient not in extremis.
- Suspicion of tension pneumothorax mandates immediate needle decompression followed by chest tube placement, without a chest X-ray.
- Mainstem intubation may be suspected clinically if ETT further in patient than previously. Withdraw to previous position; can confirm with bronchoscopy if available.
- Lobar collapse or atelectasis may respond to aggressive suctioning and can be confirmed with chest X-ray.
- Bilateral wheezing: consider bronchospasm; give bronchodilators.
- Bilateral crackles: consider pulmonary oedema; give diuretic or more PEEP depending on full clinical evaluation of volume status.

☐ **Are there other problems causing low compliance?**
- Abdominal distension: drain stomach with NG tube.
- Auto-PEEP: diagnose by examining ventilator waveforms. Treat with bronchodilators, sedation; may require temporary disconnection from positive pressure.

☐ **Is there haemodyamic instability?**
- Restore haemodyamic stability with fluid or vasopressors while determining and treating primary cause.
- If severe hypotension, evaluate for tension pneumothorax or severe auto-PEEP (often in patients with asthma or COPD).
- Other causes include high airway pressures reducing venous return, vasodilation due to sedative and analgesic medications or a new problem (sepsis, bleeding, pulmonary embolism, myocardial infarction).

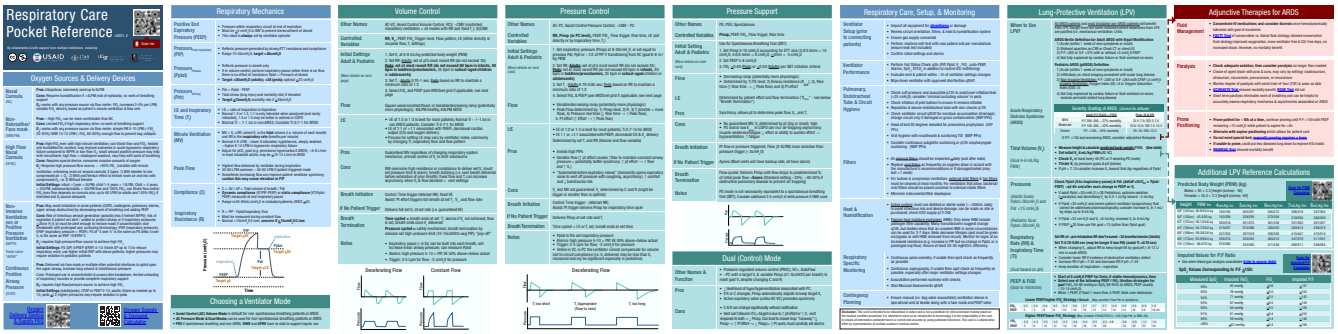
☐ **Is the patient agitated and asynchronous with the ventilator?**
- May be secondary to any other problem or may be primary problem and causing asynchrony: treat cautiously with sedation.

9.14 Respiratory care pocket card reference

The following respiratory care pocket card reference is intended to serve as a tool to learn about the fundamentals of oxygen delivery, including mechanical ventilation, ARDS management and ventilator liberation ().

The card, which can be printed or saved to your mobile device, is available in:

- English
- French
- Portuguese
- Spanish.



Source: USAID-STAR-UCSF Open Critical Care Project ().

Respiratory Care Pocket Reference v2022.2

Scan me

By collaborators & with support from multiple institutions, including:

Open Critical Care.org | USAID | STAR | UCSF CHESA | Association of Anesthesiologists of Uganda

Oxygen Sources & Delivery Devices

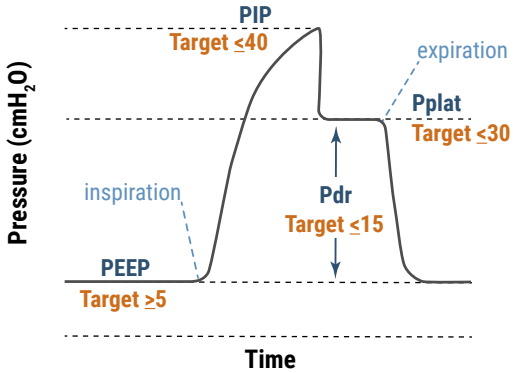
Nasal Cannula (NC)	**Pros:** Ubiquitous; commonly used up to 6LPM **Cons:** Requires humidification if >4LPM (risk of epistaxis); no work of breathing support **O_2:** works with any pressure source via flow meter; FiO_2 increases 2-4% per LPM; variable FiO_2 delivery based on patient's minute ventilation & flow rate
Non-Rebreather/ Face mask (NRB/FM)	**Pros:** ~High FiO_2 **Cons:** Limited FiO_2 if high respiratory drive; no work of breathing support **O_2:** works with any pressure source via flow meter; simple FM 5-10 LPM (~FiO_2 35-50%); NRB 10-15 LPM (~FiO_2 60-95%); enough flow to prevent bag collapse
High Flow Nasal Cannula (HFNC)	**Pros:** High FiO_2 even with high minute ventilation; can titrate flow and FiO_2; heated and humidified for comfort; may improve outcomes in acute hypoxemic respiratory failure compared to NIPPV or low-flow O_2; small amount positive pressure may help with recruitment; high flow = deadspace washout, may help with work of breathing **Cons:** Requires special device; consumes massive amounts of oxygen **O_2:** Requires high pressure/flow source; ~ >90% FiO_2 (variable with minute ventilation, entraining room air around cannula) 3 types: 1) With blender to mix compressed air + O_2; 2) With port/Venturi effect to entrain room air and mix with compressed O_2; or 3) Without blender. **Initial Settings:** infant <1year = 8LPM; child 1-4 years = 10LPM; Child > 4 years = 20LPM; adolescents/adults = 40LPM flow and 100% FiO_2; can titrate flow and/or FiO_2 (max flow depends on cannula size; up to 60 LPM for adults and 100% FiO_2) if tolerated and O_2 source adequate.
Non-invasive Ventilation (NIV) **or Positive Pressure Ventilation** (NIPPV) Trade name "BiPAP"	**Pros:** May avoid intubation in some patients (COPD, cardiogenic pulmonary edema, upper airway obstruction) by decreasing work of breathing and adding PEEP **Cons:** Risk of infectious aerosol generation (possibly less if helmet NIPPV); risk of aspiration if patient not alert / unable to protect airway or if inspiratory pressures ≥20cm H_2O; pt must be alert enough to remove mask if uncomfortable; skin breakdown with prolonged use; confusing terminology: IPAP (inspiratory pressure) = PS + PEEP; EPAP (expiratory pressure) = PEEP; PS of "5 over 5" is the same as PS Δ 5 over 5, is the same as IPAP 10/EPAP 5 **O_2:** requires high pressure/flow source to achieve high FiO_2 **Initial Settings:** PS Δ5-8/PEEP (EPAP) 5-10; titrate ΔP up to 15 to reduce inspiratory work; use higher initial IPAP with obese patients; higher pressures may require sedation in pediatric patients
Continuous Positive Airway Pressure (CPAP)	**Pros:** Delivered via face mask or multiple other potential interfaces to splint open the upper airway, increase lung volume & intrathoracic pressure Cons: Prolonged use is uncomfortable & causes skin breakdown; limited unloading of inspiratory muscles or provide complete respiratory support **O_2:** requires high flow/pressure source to achieve high FiO_2 **Initial Settings** (adults/peds): CPAP or PEEP 5-10; adults: titrate as needed up to 15; peds ≤12; higher pressures may require sedation in peds

Oxygen Delivery Device & Supply FAQ

Oxygen Supply & Demand Calculator

Respiratory Mechanics

Positive End Expiratory Pressure (PEEP)	• Pressure within respiratory circuit at end of expiration • Must be ≥5 cmH_2O in IMV to prevent derecruitment of alveoli • This value is **always** set by ventilator operator
$Pressure_{Peak\ Inspiratory}$ (PIP)	• Reflects pressure generated by airway/ETT resistance and compliance • Range 10-40cmH_2O; **target <40cmH_2O**
$Pressure_{Plateau}$ (Pplat)	• Reflects pressure in alveoli only • If in volume control, perform inspiratory pause (when there is no flow, there is no effect of resistance; Pplat = Pressure at alveoli • **Target <30cmH_2O (adults); <28 (peds);** optimal ≤25 cmH_2O
$Pressure_{Driving}$ (Pdr)	• Pdr = Pplat - PEEP • Tidal stress (lung injury and mortality risk) if elevated • **Target ≤15cmH_2O;** mortality risk if ≥20cmH_2O
I:E and Inspiratory Time (T_i)	• I:E = ratio of Inspiration to Expiration • Normal 1:2 or 1:3, 1:1 is only tolerated when paralyzed (and rarely indicated), 1:4 or 1:5 may be better in asthma or COPD • Normal Ti ~ 1-1.5s in non ARDS; Consider Ti 0.7-1 for ARDS
Minute Ventilation (MV)	• MV = V_T x RR; where V_T is the **tidal** volume (i.e. volume of each breath) and RR is the **respiratory rate** (breaths per minute) • Normal 4-6 LPM; ~lower if obtunded, hypothermic, deeply sedated; ~higher 8-14 LPM in hypoxemic respiratory failure • Adjust for pCO_2 goal (e.g. permissive hypercarbia if ARDS); ~6-8 L/min in most intubated adults, may be ≥10-15 L/min in ARDS
Peak Flow	• Highest flow delivered by ventilator during inspiration • 40-60 LPM common; ~50-80 LPM if patient triggered mode • Sometimes increasing flow can improve patient-ventilator synchrony; **caution this may cause elevation in PIP**
Compliance (C)	• C = ΔV / ΔP = Tidal volume of breath / Pdr • **Dynamic compliance** (VT/PIP-PEEP) or **static compliance** (VT/Pplat-PEEP) measured at end inspiratory pause • Range is 60-80mL/cmH_2O in intubated patients; ARDS ≤40
Inspiratory Resistance (R)	• R = PIP - Pplat/inspiratory flow • Must be measured during constant flow • Normal <10cmH_2O/L/sec; **concern if ≥15cmH_2O/L/sec**

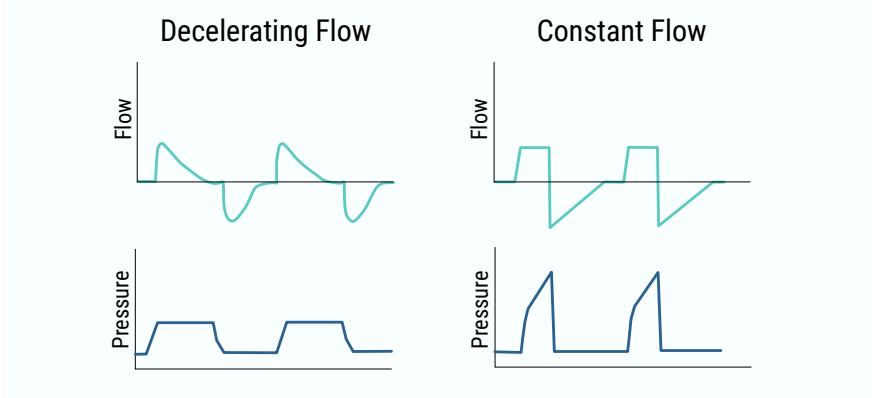


Choosing a Ventilator Mode

- **Assist Control (AC) Volume Mode** is default for non-spontaneous breathing patients or ARDS
- **AC Pressure Mode & Dual Modes** can be used for non-spontaneous breathing patients or ARDS
- **PSV** if spontaneous breathing and non-ARDS; **SIMV** and **APRV** have no data to support regular use

Volume Control

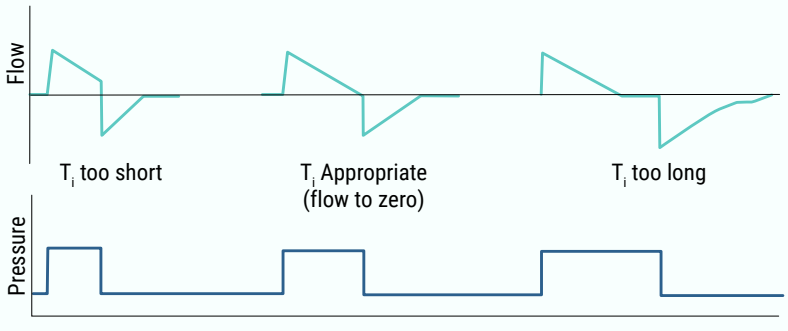
Other Names	AC-VC; Assist Control Volume Control; VCV; ~CMV (controlled mandatory ventilation = all modes with RR and fixed T_i); (S)CMV
Controlled Variables	**RR, V_T,** PEEP, FiO_2,Trigger level, Flow pattern, I:E (either directly or via peak flow, T_i settings)
Initial Settings Adult & Pediatric (More details on next page)	1. Set V_T at 6-8 mL/kg predicted body weight (PBW) 2. Set RR: Adults: set at pt's most recent RR (do not exceed 35); **Peds: set at most recent RR (do not exceed 60 bpm in infants, 40 bpm in toddlers/preschoolers,** 35 bpm in **school-aged children** or **adolescents)** 3. Set T_i : Adults 0.70-1 sec; Peds based on RR to maintain a minimum ratio of 1:2 4. Select FiO_2 and PEEP (use ARDSnet grid if applicable; see next page
Flow	Square wave/constant/fixed; or Variable/decreasing ramp (potentially more physiologic); 40LPM healthy, 60LPM ARDS
I:E	• I:E of 1:2 or 1:3 is best for most patients; Normal Ti ~ 1-1.5s in non ARDS patients; Consider Ti 0.7-1 for ARDS • I:E of 1:1 or >1:1 associated with PEEPi, decreased cardiac output (CO) and oxygen delivery • Process for setting I:E may vary by ventilator make; commonly by changing Ti, inspiratory flow and flow pattern
Pros	Guaranteed MV regardless of changing respiratory system mechanics; precise control of V_T to limit volutrauma
Cons	Will overcome high resistance or compliance to deliver set V_T (must set pressure limit & alarm); breath stacking (i.e. next breath delivered before exhalation of prior breath); fixed flow and T_i can increase asynchrony when V_T & flow demand > vent settings
Breath Initiation	Control: Time trigger (60s/set RR): fixed VE Assist: Pt effort triggers full breath at set T_i, V_T, and flow rate
If No Patient Trigger	Delivers full set V_T at set rate (i.e. guaranteed VE)
Breath Termination	**Time cycled =** breath ends at set T_i; alarms if V_T not achieved; flow is set, breath ends once V_T delivered **Pressure cycled =** safety mechanism; breath termination by clinician set high-pressure limit (10-15cmH20>avg PIP); "pop-off"
Notes	• Inspiratory pause (~0.3s) can be built into each breath, will increase mean airway pressure; can measure Pplat • Alarms: high pressure 5-10 > PIP, VE 50% above+below actual • Trigger: 2-5 Lpm for flow; -2 cmH_20 for pressure



Pressure Control

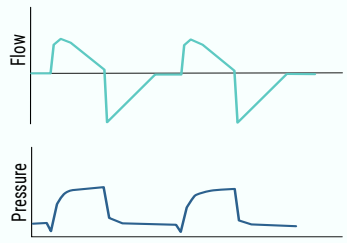
Other Names	AC-PC; Assist Control Pressure Control; ~CMV - PC
Controlled Variables	**RR, Pinsp (or PC level),** PEEP, FiO_2, Flow trigger, Rise time, I:E (set directly or by Inspiratory time, T_i)
Initial Settings Adult & Pediatric (More details on next card)	1. Set inspiratory pressure (Pinsp) at 8-20cmH_2O, or set equal to previous Pdr, Pplt or ~1/2 of PIP if transitioning from VC (goal 6-8 m:/Kg PBW 2. Set RR: **Adults:** set at pt's most recent RR (do not exceed 35); **Peds:** set at most recent RR (do not exceed 60 bpm in **infants,** 40 bpm in **toddlers/preschoolers,** 35 bpm in **school-aged** children or **adolescents)** 3. Set T_i : Adults 0.70-0.85 sec; Peds based on RR to maintain a minimum ratio of 1:2 4. Select FiO_2 & PEEP (use ARDSnet grid if applicable; see next page
Flow	• Variable/decreasing ramp (potentially more physiologic) • Peak Flow determined by: 1) Pinsp level, 2) R, 3) T_i (shorter = more flow), 4) Pressure rise time (↓ Rise time → ↑ Peak flow), 5. Pt effort (↑ Effort → ↑ Peak flow)
I:E	• I:E of 1:2 or 1:3 is best for most patients; Ti 0.7-1s for ARDS • I:E 1:1 or >1:1 associated with PEEPi, decreased CO & O_2 delivery Determined by set T_i and RR (Volume and flow variable)
Pros	• Avoids high PIPs • Variable flow (↑ pt effort causes ↑flow to maintain constant airway pressure = potentially better synchrony: ↑ pt effort → ↑ flow and ↑ V_T) • "Automated/active expiratory valves" (transiently opens expiratory valve to vent off pressure with coughing, asynchrony); ↑ comfort and ↓ barotrauma risk
Cons	V_T and MV not guaranteed; V_T determined by C and R (might be bigger or smaller than is optimal)
Breath Initiation	Control: Time trigger - (60s/set RR) Assist: Pt trigger delivers Pinsp for inspiratory time cycle
If No Patient Trigger	Delivers Pinsp at set rate and T_i
Breath Termination	Time cycled = I:E or T_i set, breath ends at set time
Notes	• Pplat is the set inspiratory pressure • Alarms: high pressure 5-10 > PIP, VE 50% above+below actual • Trigger: 2-5 Lpm for flow; -2 cmH_2O for pressure • Unlike in VC, in PC the ventilator cannot compensate for volume lost to circuit compliance (i.e. V_T delivered may be less than V_T measured and my be significant especially in pediatrics)

Decelerating Flow



Pressure Support

Other Names	PS; PSV; Spontaneous
Controlled Variables	**Pinsp** (PS), PEEP, FiO_2, Flow trigger, Rise time
Initial Setting Adult & Pediatric (More details on next card)	Use for Spontaneous Breathing Trial (SBT): 1. Set Pinsp Δ5-10 cmH_2O accounting for ETT size (3.0/3.5mm = 10 cmH_2O; 4.0/4.5mm = Δ8 cmH_2O; ≥5mm = Δ5 cmH_2O 2. Set PEEP 5-8 cmH_2O 3. FiO_2 ≤0.40 (Peds) or ≤0.50 (Adults) per SBT initiation criteria
Flow	• Decreasing ramp (potentially more physiologic) • Determined by 1) PS level; 2) Airway resistance (R_{aw}); 3), Rise time (↑ Rise time --> ↓ Peak flow) and 4) Pt effort
I:E	Determined by patient effort and flow termination ("E_{sens}" - see below "Breath Termination")
Pros	Synchrony: allows pt to determine peak flow, V_T, and T_i
Cons	• No guaranteed MV; V_T determined by pt (big or small); high • PS and/or low E_{sens} in COPD can incr air-trapping asynchrony; muscle weakness/fatigue: ↓ effort or ability to sustain effort --> hypoventilation, ↑ fatigue
Breath Initiation	Pt flow or pressure triggered; Flow (3-5LPM) more sensitive than pressure trigger (~2cmH_2O)
If No Patient Trigger	Apnea (Most vents will have backup rate; all have alarm)
Breath Termination	Flow cycled: Delivers Pinsp until flow drops to predetermined % of initial peak flow **~Esens** (Standard setting ~25%; ~40-50% if obstructive pulmonary disease to prevent air trapping)
Notes	PS mode is not necessarily equivalent to a spontaneous breathing trial (SBT); must know if PS is relative to PEEP or ambient



Dual (Control) Mode

Other Names & Function	• Pressure regulated volume control (PRVC); VC+, AutoFlow • ~PC with a target V_T & variable Pinsp (Δ1-3cmH2O per breath) to meet goal V_T despite changing C and R;
Pros	• ↓ likelihood of hypo/hyperventilation associated with PC. • If R or C changes, Pinsp automatically adjusts to keep target V_T • Active expiratory valve (unlike AC-VC) promotes synchrony
Cons	• C & R can change significantly without notification • Vent can't discern if V_T>target is due to ↑ pt effort or ↑ C; vent response to both = ↓ Pinsp; Can lead to closed-loop "runaway" (↓ Pinsp--> ↑ Pt Effort--> ↓ Pinsp)= ↑ Pt work; must carefully set alarms

Respiratory Care, Setup, & Monitoring

Ventilator Setup (prior to connecting patients)	• Inspect all equipment for **cleanliness** or damage • Review circuit orientation, filters, & heat & humidification system • Ensure gas supply connected • Perform machine self-test with new patient and per manufacture (ensure leak test included) • Confirm initial settings and alarms
Ventilator Performance	• Perform Full Status Check q4h: (PIP, Pplat, V_T, FiO_2, auto-PEEP, Alarms, SpO_2, $ETCO_2$ in addition to routine ICU monitoring) • Evaluate vent & patient within ~1h of ventilator settings changes • Wipe down ventilator with approved disinfection qShift
Pulmonary, Endotracheal Tube & Circuit Hygiene	• Check cuff pressure and auscultate q12h to avoid over-inflation/leak (<25 cmH_20); consider 'minimal occluding volume' in peds • Check inflation of pilot balloon to ensure it remains inflated • Reposition & secure endotracheal tube with skin checks q12h • Check ventilator circuit qShift for moisture accumulation (drainage); change circuit only if damaged or gross contamination **(Ventilator Associated Pneumonia Prophylaxis -VAP PPx)** • Head of bed 30 degrees elevated for pneumonia prophylaxis (VAP PPx) • Oral hygiene with mouthwash & suctioning TID **(VAP PPx)** • Consider continuous subglottic suctioning or q12h oropharyngeal suctioning **(VAP PPx)**
Filters	• All external filters should be inspected ≥daily (and after nebs) • Replace viral filters as frequently as supplies allow in accord with the manufacturer's recommendations or if damaged/soiled (may last >1 week) • For turbine & compressor ventilators, external inlet filters & fan filters must be cleaned at least monthly. For ventilators that allow, bacterial/viral filters should be placed proximal to external intake filters • Minimize instrumental/filter deadspace
Heat & Humidification	• Active system: must use distilled or sterile water (~>500mL daily) to avoid infectious risk and device damage; can be made on site or purchased; check H2O supply q12-24h • Passive heat moisture exchanger (HME): Only some HME include pathogen filter capability; Many manufacturers suggest change q24h, but studies show that an unsoiled HME in some circumstances can be used for 3-7 days. Nebs decrease lifespan (and must be given via bypass or with HME removed from circuit). Monitor for signs of an increased resistance (e.g. increase in PIP but no change in Pplat, or a prolonged exp flow). Ensure at least 28-30 mgH2O/L efficiency
Respiratory Specific Monitoring	• Continuous pulse oximetry, if unable then spot check as frequently as possible • Continuous capnography, if unable then spot check as frequently as possible, especially after major ventilator settings changes • Auscultation performed routinely with checks • Skin/Mucosal Assessments qShift
Contingency Planning	• Ensure manual (i.e. bag valve resuscitator) ventilation device is operational and at beside along with a face mask and PEEP valve

Disclaimer: This card is intended to be educational in nature and is not a substitute for clinical decision making based on the medical condition presented. It is intended to serve as an introduction to terminology. It is the responsibility of the user to ensure all information contained herein is current and accurate by using published references. This card is a collaborative effort by representatives of multiple academic medical centers.

Lung-Protective Ventilation (LPV)

When to Use LPV?

Acute Respiratory Distress Syndrome (ARDS)

All ARDS patients and most intubated non-ARDS patients will benefit from LPV, though there are some instances where departures from LPV are justified.

ARDS Berlin Definition for Adult ARDS with Kigali Modification

1) Acute (within 1 week of new symptoms or insult)
2) Bilateral opacities on CXR or Chest CT or chest US
3) P:F ≤300 or S:F <315 with or without ≥5 cmH_2O PEEP
4) Not fully explained by cardiac failure or fluid overload on exam

Pediatric ARDS (pARDS) Definition

1) Acute (within 1 week of new symptoms or insult)
2) Infiltrate(s) on chest imaging consistent with acute lung disease
3) Non-Invasive Ventilation: P:F ≤300 or S:F ≤264 with CPAP ≤5 cmH_2O
   Invasive Ventilation: Oxygen Index (OI) ≥4 or Oxygen Saturation Index (OSI) ≥5
4) Not fully explained by cardiac failure or fluid overload on exam; exclude perinatal related lung disease

Severity Grading of ARDS *(Correct for altitude)*

	Adult; P:F (PaO2 ÷ FiO2)	Peds; OI & OSI
Mild	P:F 200-300, ~27% mortality	OI 4-7.9; OSI 5-7.4
Moderate	P:F 100-200, ~32% mortality	OI 8-15.9; OSI 7.5-12.2
Severe	PF: <100, ~45% mortality	OI>16; OSI>12.3

If P:F <150 and worsening ARDS, consider adjunctive therapies

Tidal Volume (V_T)

(Goal 4-6 mL/Kg PBW)

- **Measure height & calculate predicted body weight** (PBW) **(See table)**
- **Set initial V_T 6 mL/kg PBW**v(AC-VC)
- **Check V_T** at least every 4h (PC or if weaning PS mode)
- **Titrate V_T** by pressure goals & pH (below)
- If pH < 7.15 consider increase V_T toward 8mL/kg regardless of Pplat

Pressures

(Adults Goals: Pplat<30cmH_2O and Pdr <15 cmH_2O)

(Pediatric Goal: Pplat<28cmH_2O)

Check Pplat (0.5s inspiratory pause) & Pdr (deltaP=Vt/C_{RS} = Pplat-PEEP) ~q4-6h and after each change in PEEP or V_T

- If adult Pplat >30 cmH_2O (>28 Pediatrics), optimize sedation (±paralysis) and decreasing V_T by 0.5-1 cc/kg toward ~4 mL/kg
- If Pplat <30 cmH_2O and severe patient-ventilator dyssynchrony that cannot be addressed pharmacologically, consider increase V_T in 1 mL/kg steps up to 8 mL/kg
- If Pplat <25 cm H_2O and V_T <6 mL/kg, increase V_T to 6 mL/kg
- If PEEP ≥20 then use Pdr goal <15 (rather than Pplat goal)

Respiratory Rate (RR) & Inspiratory Time (Ti)

(Goal based on pH)

Set RR at ~pre-intubation RR don't exceed ~35 breaths/minute (Adults)

Set Ti 0.70-0.85 sec (may be longer if low RR) (avoid Ti <0.70 sec)

- When changing V_T, adjust RR to keep target VE by goal pH (~8-12 L/min in acute ARDS)
- Consider lower RR if evidence of obstructive ventilatory defect
- Increase RR if pH <7.30 and decrease RR if pH >7.45
- Keep duration of inspiration ≤ expiration

PEEP & FiO2

(Goal to minimize)

- **Start at 5 cmH_2O PEEP for 2min, if stable hemodynamics, then**
- **Select one of the following PEEP / FiO_2 titration strategies for goal** PaO_2 55-80 mmHg or SpO_2 88-95% (In ARDS, PEEP usually ~10-14 cmH_2O).
- When ↑ PEEP, if Pplat ↑ more than Δ PEEP, think over-distension

Lower PEEP/higher FiO_2 Strategy (***Default** - May consider if low Pdr or pediatrics)

FiO_2	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18-24

Higher PEEP/lower FiO_2 Strategy (May consider if PaO2/FiO2 is <100, high Pdr, or BMI>40)

FiO_2	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5 - 0.8	0.8	0.9	1.0	1.0
PEEP	5	8	10	12	14	16	16	18	20	22	22	22	24

Adjunctive Therapies for ARDS Hypoxemia

Fluid Management	• **Concentrate IV medications and consider diuresis** once hemodynamically tolerated with goal of euvolemia • **FACTT Trial** of conservative vs. liberal fluid strategy showed conservative fluid strategy improved oxygenation, more ventilator-free & ICU-free days, no increased shock. However, no mortality benefit.
Paralysis	• **May be considered in severe ARDS if high PEEP and FiO2, especially if asynchrony present;** requires adequate sedation and train of four monitoring • Choice of agent (each with pros & cons, may vary by setting): cisatracurium, atracurium, rocuronium, pancuronium, or vecuronium • **ACURASYS Trial** showed mortality benefit; **PETAL Trial** did not • Short term paralysis eliminates work of breathing and can be helpful to accurately assess respiratory mechanics & asynchronies associated w/ ARDS
Prone Positioning	• **Prone patient for ~12-16h at a time,** continue proning until P:F >150 with PEEP remaining <10 cmH_2O while patient is supine for >4h • **Alternate with supine positioning** which allows for patient care • **Do not need special bed; manually proning requires a team** • **If unable to prone,** could put less diseased lung down to improve V/Q match • **PROSEVA Trial** showed mortality benefit

Additional LPV Reference Calculations

Predicted Body Weight (PBW) (kg)

Males = 50 + 2.3 [height (inches) - 60]
Females = 45.5 + 2.3 [height (inches) -60]

Scan for PBW Calculator

Height	PBW f/m	4mL/Kg f/m	5mL/Kg f/m	6mL/Kg f/m	7mL/Kg f/m	8mL/Kg f/m
58" (147cm)	40.9/45.4 kg	164/182	205/227	245/272	286/318	327/363
60" (152cm)	45.5/50 kg	182/200	228/250	273/300	319/350	364/400
62" (157cm)	50.1/54.6 kg	200/218	251/273	301/328	351/382	401/437
64" (163cm)	54.7/59.2 kg	219/237	274/296	328/355	383/414	438/474
66" (168cm)	59.3/63.8 kg	237/255	297/319	356/383	415/447	474/510
68" (173cm)	63.9/68.4 kg	256/274	320/342	383/410	447/479	511/547
70" (178cm)	68.5/73 kg	274/292	343/365	411/438	480/511	548/584

Imputed Values for P:F Ratio

- Use when blood gas analysis unavailable **(Link to source data)**

Scan for Imputed P:F Calculator

SpO_2 Values Corresponding to P:F ≤150:

Measured SpO_2	Imputed PaO_2	FiO_2	Imputed P:F
96%	82 mmHg	≥0.6	≤137
95%	76 mmHg	≥0.5	≤152
94%	71 mmHg	≥0.5	≤142
93%	67 mmHg	≥0.5	≤134
92%	64 mmHg	≥0.5	≤128
91%	61 mmHg	≥0.4	≤153
90%	59 mmHg	≥0.4	≤148
<89%	≤57 mmHg	≥0.4	≤150

9.15 Adult ventilation order set (ARDS)

Last updated March 10, 2021

Hospital Name/Logo	**Adult Ventilator (ARDS) Order Set**				
Surname/Family Name	Name	Attending/Team			
Today's Date / /	Patient MRN/Registration #	Age	Sex	Predicted Weight (kg):	Height(cm)

Mode: ☐ AC-VC ☐ AC-PC ☐ PRVC ☐ _____

Tidal Volume:
1. Initiate at 6-8 mL/kg predicted body weight (PBW). Titrate down in 0.5-1 mL/kg steps Q 1-2hrs if needed to prevent acute acidosis.
2. If **EIP > 30 cm H2O**, ↓ VT to as low as 4 mL/kg.
3. **pH < 7.15**, ↑ VT 1 mL/kg steps to 8 mL/kg regardless of EIP until pH = 7.20.
4. When **severe asynchrony** occurs and sedation cannot be increased, then ↑VT 1 mL/kg to upper limit of 8mL/kg.
5. If **EIP<25** and VT<6mL/kg, ↑ VT to 6mL/kg.
6. When using AC-PC adjust PIP for VT=6mL/kg

Plateau Pressure:
1. 25-30 cm H2O.
2. EIP > 30 cm H2O allowed if PEEP > 20 cm H2O or pH < 7.20

Respiratory Rate:
1. Set Rate 6-35 (Typical starting rate 20, consider >25 if profound acidosis or markedly increased preintubation RR; consider lower if signs of obstructive pulmonary physiology)
2. Adjust RR to target Minute Ventilation (prior to intubation), though be cautious for possible air trapping if set too fast and/or too large of tidal volumes. (Typical minute ventilation requirements for adult ARDS ~8-12 LPM, 130-190 mL/kg PBW)
3. ↑RR when pH < 7.30 (Max ~35)
4. ↓ RR when pH > 7.45.

Inspiratory Time: 0.70-0.85 sec. Avoid Tinsp < 0.70. Upper I:E Limit of 1:1 (Tinsp of 0.85 @ RR of 35)

Peak Flow Rate: 60-75 L/min for comfort. Avoid peak flow rate < 50 L/min

Arterial pH:
1. Target: **7.30-7.45**
2. **pH < 7.25** and PaCO2 < 25: Consider Buffer Rx
3. **pH < 7.15**: Modify VT/EIP goals to achieve pH = 7.20. Buffer Rx indicated to maintain lung-protective ventilation.

PEEP FiO2 Titration: Maintain PaO2 of 55-80 mm Hg (SpO2 88-95%). Select one of the PEEP FiO2 Tables below:

☐ **ARDS Net ARMA Trial Low PEEP Table** (Default for most patients)

FiO2	**0.3**	**0.4**	**0.5**	**0.6**	**0.7**	**0.8**	**0.9**	**1.0**
PEEP	5	5-8	8-10	10	10-14	14	14-18	18-26

☐ **ARDS Net Modified from ALVEOLI Trial High PEEP Table** (May consider if PaO2/FiO2 is <100, or BMI>40)

FiO2	**0.3**	**0.4**	**0.5**	**0.60 - 0.70**	**0.8**	**0.9**	**1.0**
PEEP	5-14	14-16	16-18	16-20	20-22	22	22-24

Free Form PEEP: Maintain PEEP at _____cm H2O and Titrate FiO2 for Protocol PaO2/SpO2 range.

Alternative Arterial: For patients concurrently managed on the traumatic brain injury protocols, or patients with/at risk for myocardial or gastrointestinal ischemia:
PaO2 range: _____ PaCO2 Range: _____ pH Range: _____

Arterial Blood Gas:
1. Protocol initiation and/or immediately after intubation
2. Every day, first 7 days of protocol
3. Severe acidosis (pH < 7.15) after VT ↑ to 7 and 8 mL/Kg
4. Every PEEP ↑ > 10 cm H2O
5. Check SpO2 at least Q4h and < 30 min after adjustments in PEEP/FiO2

VD/VT (deadspace): When volumetric capnography available (or by crude estimation with time-based capnography - i.e., PaCO2-end tidal CO2/PaCO2), check on protocol initiation, after PEEP titrations and daily.

Routine Care:
- ☐ Head of bed 30 degrees
- ☐ Mouthwash oral solution (15 mL) swish and suction orally q12h white intubated
- ☐ Oropharyngeal suctioning q 12h
- ☐ Perform full status check ~q4h (PIP, Pplat, VT, FiO2, RR)

Date (time): _____ **Name:** _____ **Signature:** _____ **Contact #:** _____

TO PRINT MORE
forms scan here

TO LEARN MORE
on calculating PBW and for lung protective ventilation
scan or click here

Source: Adapted with permission from San Francisco General Hospital, San Francisco (CA) and USAID-STAR-UCSF Open Critical Care Project ( ).

9.16 Checklist for proning in severe ARDS

This checklist is adapted from Messerole et al. (2002) and the most recent randomized control trial by Guérin et al. (2013). These studies found an improved mortality in patients treated with LPV plus prone position.

Prone ventilation should be carried out by four to five team members using a protocol rehearsed in advance. It is easier to perform in children. See the following article and video ( ).

Timing and duration of prone position

The most recent clinical trial (Guérin et al., 2013) observed mortality benefit in patients with severe ARDS. Patients were turned prone within 24 hours of recognition and kept prone for at least 12–16 consecutive hours a day.

Contraindications

- Elevated intracranial pressure > 30 mmHg or cerebral perfusion pressure < 60 mmHg
- Massive haemoptysis
- Recent tracheal surgery or sternotomy
- Serious facial trauma or facial surgery
- Deep venous thrombosis treated for less than 2 days
- Cardiac pacemaker inserted in the last 2 days
- Unstable spine, femur or pelvic fractures
- MAP < 65 mmHg
- Pregnancy
- Single anterior chest tube with air leaks.

Preparation of the patient for proning while IMV

1	Check for contraindications.
2	Consider possible adverse effects of prone positioning (e.g. if on chest tube drainage).
3	Whenever possible, explain the manoeuvre to the patient or their family.
4	Confirm from a recent chest X-ray that the tip of the endotracheal tube is located 2–4 cm above the main carina.
5	Inspect and confirm that the endotracheal tube and all central and large bore peripheral catheters are firmly secured.
6	Consider exactly how the patient's head, neck and shoulder girdle will be supported after they are turned prone. Assemble all needed pillows, foam pads or other supports that might be needed.
7	Stop tube feeding, check for residual, fully evacuate the stomach, and cap or clamp the feeding and gastric tubes.
8	Prepare endotracheal suctioning equipment, and review what the process will be if copious airway secretions abruptly interfere with ventilation.
9	Decide whether the turn will be rightward or leftward.
10	Prepare all IV tubing and other catheters and tubing for connection when the patient is prone: • Assure sufficient tubing length. • If chest drainage: relocate all drainage bags on the opposite side of the bed, move chest tube drains between the legs. • Reposition IV tubing toward the patient's head, on the opposite side of the bed.

Turning procedure

1	Place one (or more) people on both sides of the bed (to be responsible for the turning processes) and another at the head of the bed (to assure the central lines and the endotracheal tube do not become dislodged or kinked).
2	Increase the FiO_2 to 1.0 and note the mode of ventilation, the tidal volume, the minute ventilation, and the peak and plateau airway pressures.
3	Pull the patient to the edge of the bed furthest from whichever lateral decubitus position will be used while turning.
4	Place a new draw sheet on the side of the bed that the patient will face when in this lateral decubitus position. Leave most of the sheet hanging.
5	Turn the patient to the lateral decubitus position with the dependent arm tucked slightly under the thorax. As the turning progresses the nondependent arm can be raised in a cocked position over the patient's head. Alternatively, the turn can progress using a log-rolling procedure.
6	Remove ECG leads and patches. Suction the airway, mouth and nasal passages if necessary.
7	Continue turning to the prone position.
8	Reposition in the centre of the bed using the new draw sheet.
9	If the patient is on a standard hospital bed, turn their face toward the ventilator. Assure that the airway is not kinked and has not migrated during the turning process. Suction the airway if necessary.
10	Support the face and shoulders appropriately avoiding any contact of the supporting padding with the orbits or the eyes.
11	Position the arms for patient comfort. If the patient cannot communicate avoid any type of arm extension that might result in a brachial plexus injury.
12	Auscultate the chest to check for right mainstem intubation. Reassess the tidal volume and minute ventilation.
13	Adjust all tubing and reassess connections and functions.
14	Reattach ECG patches and leads to the back.
15	Tilt the patient into reverse Trendelenburg. Slight, intermittent lateral repositioning (20–30°) should also be used, changing sides at least every 2 hours.
16	Document a skin assessment every shift, specifically inspecting weight bearing, ventral surfaces.

Criteria for stopping proning in severe ARDS:

- Oxygenation improvement defined as **$PaO_2/FiO_2 \geq 150$ mmHg with PEEP ≤ 10 cmH_2O and $FiO_2 \leq 0.6$**; in the prone group, these criteria had to be met in supine at least 4 hours after the end of the last prone session.
- **PaO_2/FiO_2 ratio deterioration by more than 20%** relative to supine before two consecutive prone sessions.
- **Complications occurring during a prone session** such as:
  - non-scheduled extubation
  - mainstem bronchus intubation
  - endotracheal tube obstruction
  - haemoptysis, $SpO_2 < 85\%$
  - $PaO_2 < 55$ mmHg for more than 5 minutes under FiO_2 1.0
  - cardiac arrest
  - HR < 30 beats per minute for more than 1 minute
  - SBP < 60 mmHg for more than 5 minutes
  - or any other life-threatening reason for which the clinician decided to stop.

9.17 Ventilator circuit types, filter and humidifier locations for SARI

When managing a patient with infectious SARI, careful consideration must be given to the placement of adequate bacterial-viral (BV) filters to protect health care workers and patients from potential exposure to infectious particles.

Filters may be placed at the air intake, inspiratory limb, patient wye, expiratory limb and/or exhaust port; however, placement at each of these sites does not provide equivalent function.
Ideally a two-filter setup should be used:

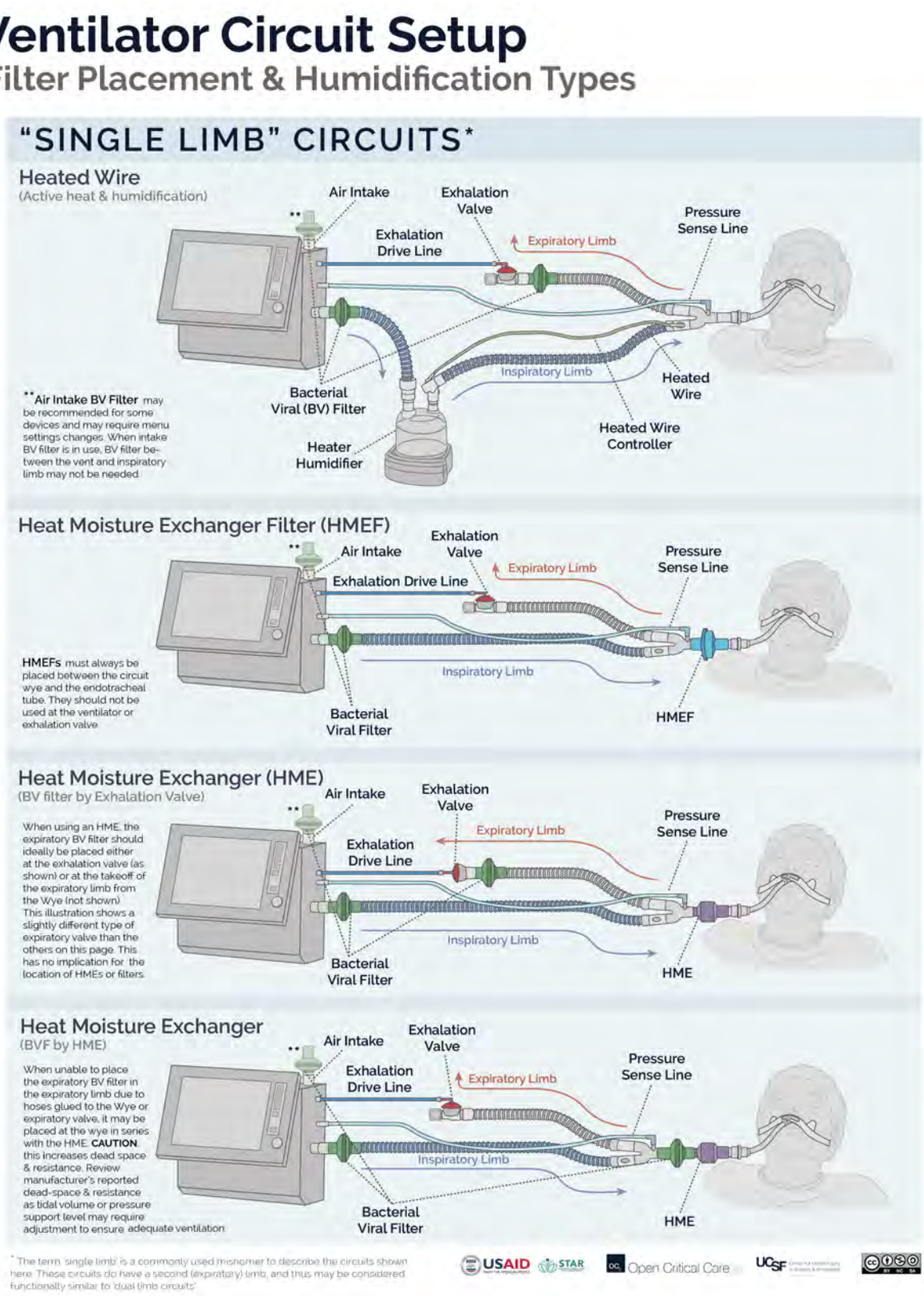
- **Inspiratory/patient filter:** The first BV filter should be placed between the patient and the inspiratory limb take off from the ventilator. This filter is often placed between the inspiratory limb and the ventilator or between the circuit wye connector and the patient. The inspiratory/patient filter has two purposes: 1) to protect the ventilator from exhaled gases from an infected patient; and 2) to protect a non-infected patient from a possibly contaminated ventilator.

- **Expiratory filter:** A second BV filter should be placed between the patient and the exhalation valve on the expiratory limb of the circuit. This filter is intended to protect the room environment and health care staff from aerosolized particles, and to protect the device in a dual limb circuit setup.

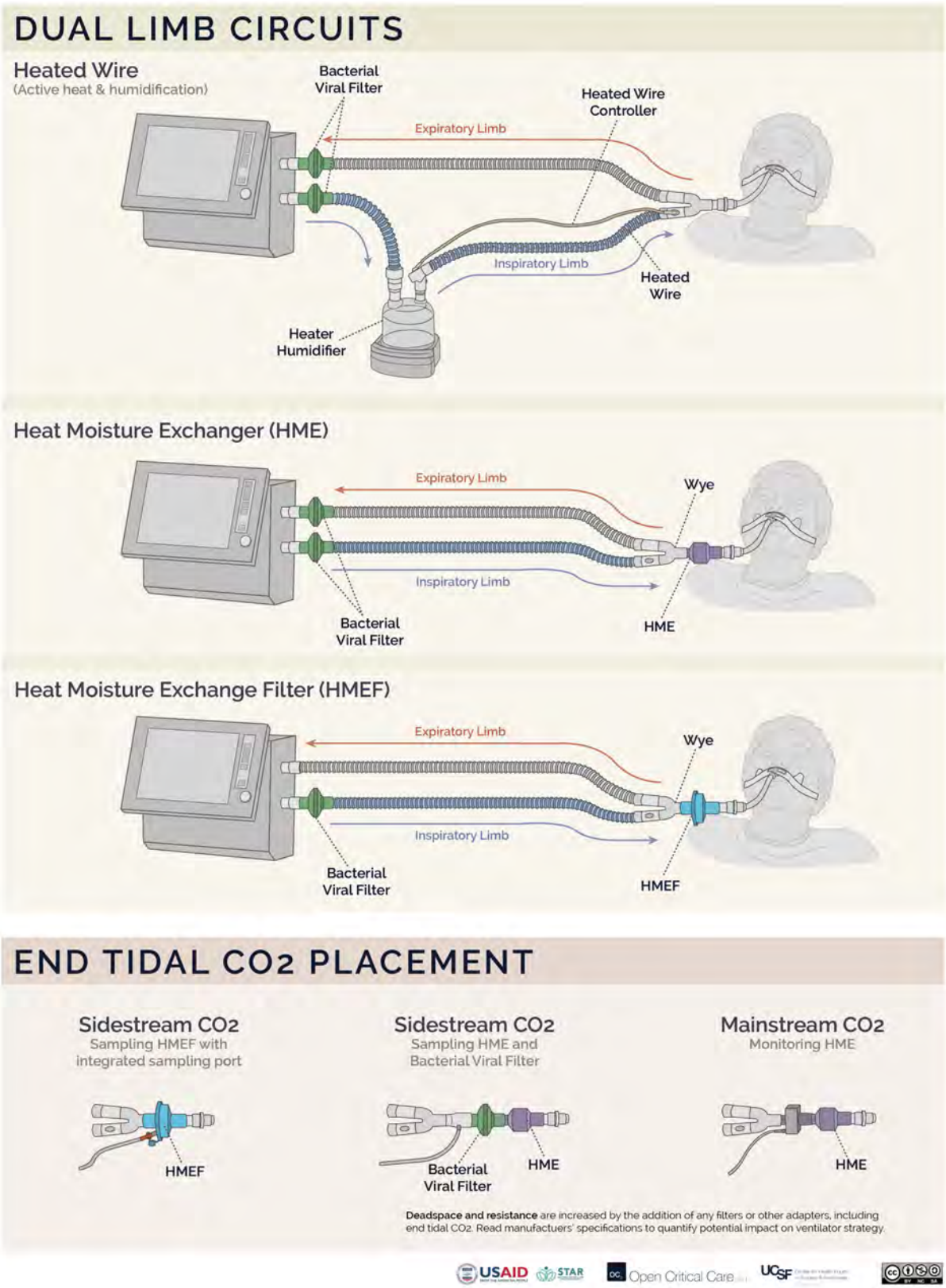
If using an active heat and humidification system, then the inspiratory filter should be a BV filter, without heat-moisture exchange (HME) function. If not using an active heat and humidification system, then the circuit must include either: 1) an HME with BV filter function (also known as an HMEF) between the wye and patient; or 2) an HME without BV filter function placed at the wye, in addition to an inspiratory and expiratory BV filter.

Placement of HME, BV or HMEF filters between the circuit wye and the patient's endotracheal tube can add significant dead space to the circuit, especially for paediatric patients, and must always be accounted for when using this setup.

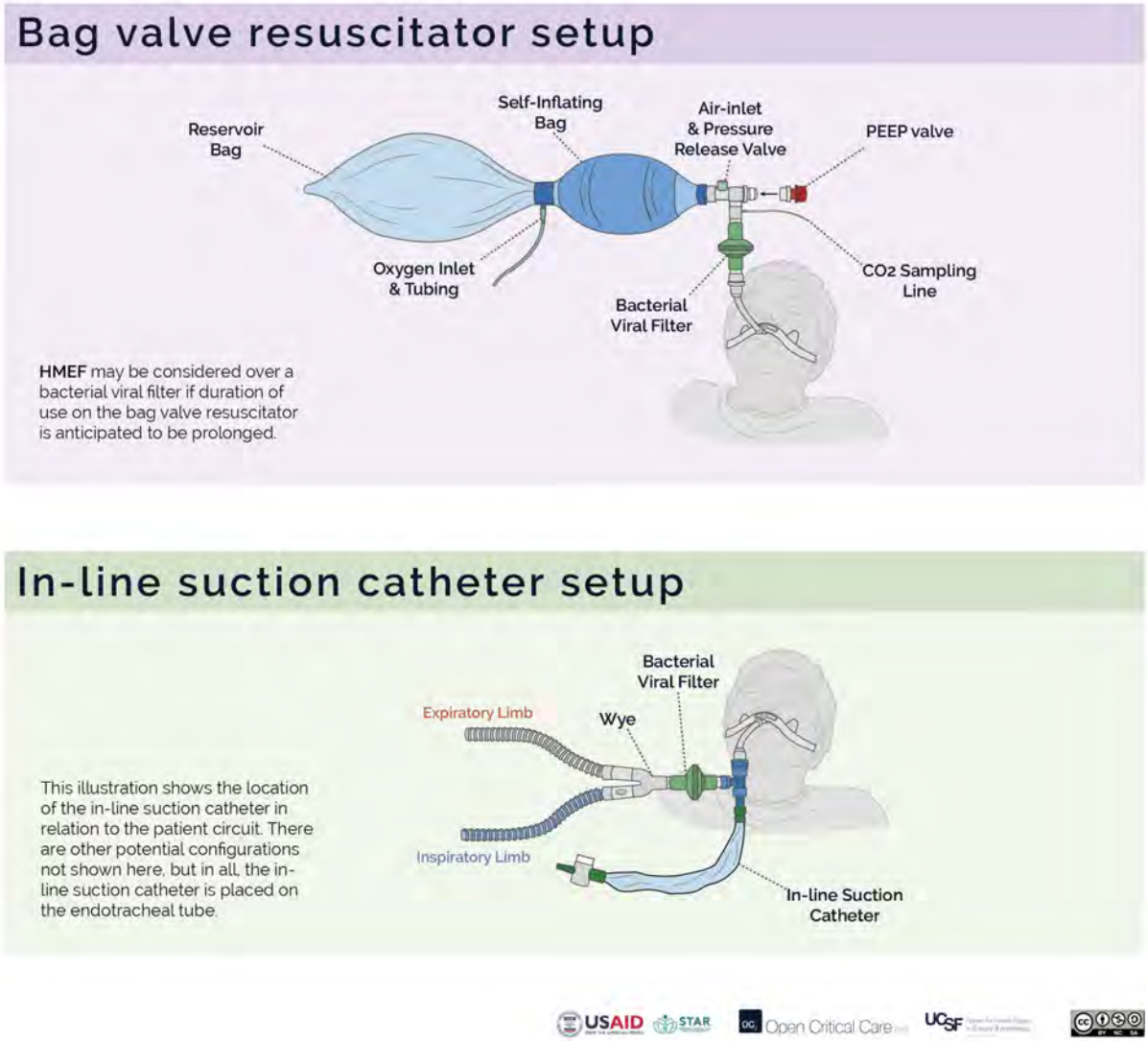
Invasive mechanical ventilation devices



Source: USAID-STAR-UCSF Open Critical Care Project ().



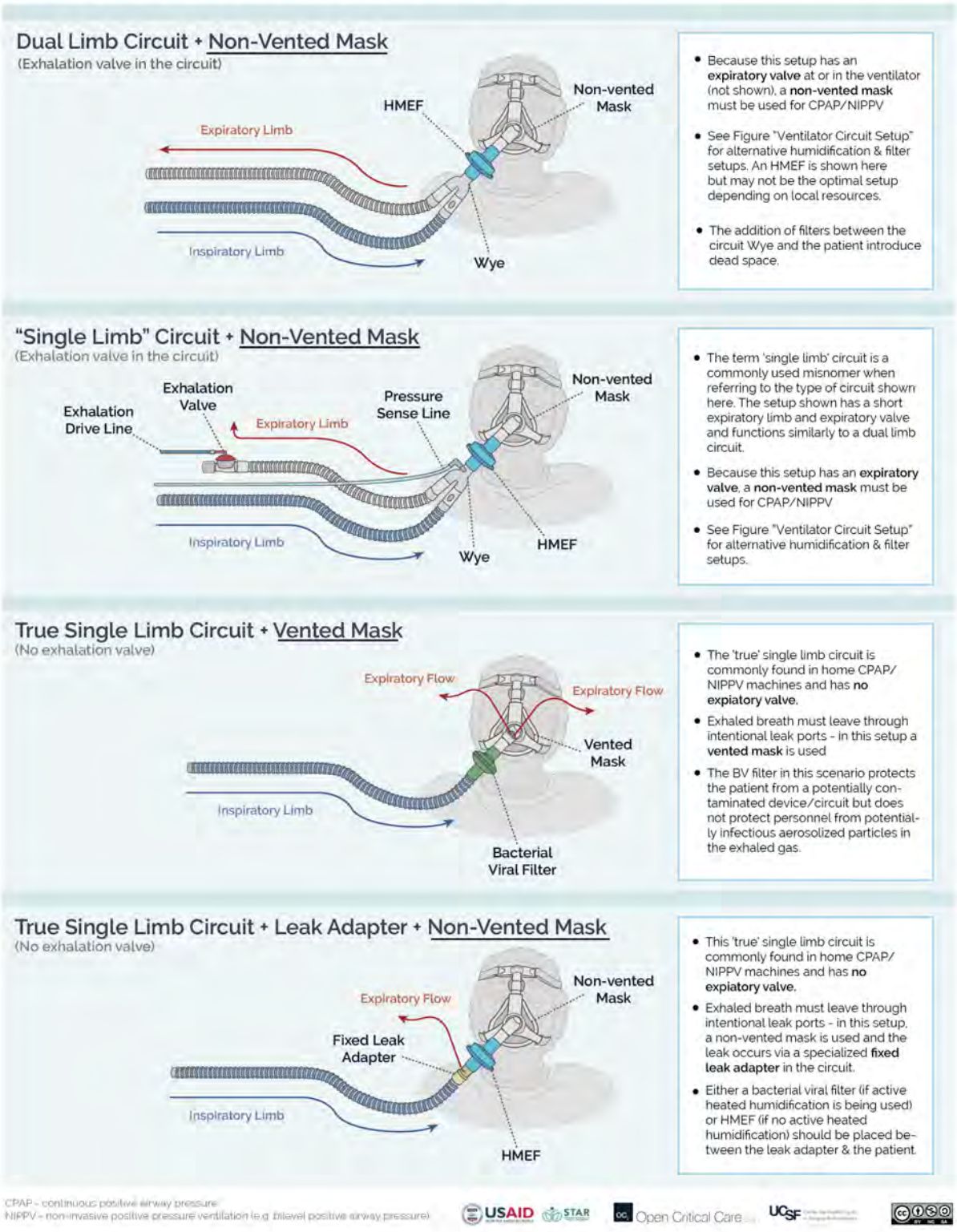
Source: USAID-STAR-UCSF Open Critical Care Project ().



Source: USAID-STAR-UCSF Open Critical Care Project ().

CPAP/NIPPV Circuit Setup

Mask types, filter and humidification placement



Source: USAID-STAR-UCSF Open Critical Care Project ( ).

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10 Manage pain, sedation and delirium

10 Manage pain, sedation and delirium

Summary

In critically ill patients, comfort and safety should be the goals when managing pain control, anxiolysis and prevention and treatment of delirium.

Implementation of a protocolized management approach to pain, agitation and delirium **(PAD protocol)** improves patient outcomes

Short-term outcomes	Long-term outcomes
• Fewer days of delirium • Fewer days of IMV (quicker time to extubation) • Fewer days in ICU • Lower hospital costs • More mobilization during ICU stay • Increased survival	• Better cognitive function • Better physical mobility • Fewer psychiatric conditions (e.g. PTSD, depression, anxiety) • Increased survival

Steps to develop a PAD protocol adapted to the health facility

Step 1	**Assess and recognize pain, agitation and delirium** using standardized and reproducible scales (i.e. VAS, RASS, CAM-ICU).
Step 2	**Manage pain first:** prevention and treatment (treat pain with a multimodal approach using opioids and non-opioids to minimize the harmful effects of sedatives).
Step 3	**Manage agitation:** choice of targeted sedation (treat anxiety using non-benzodiazepines sedatives and target light sedation). Evaluate patients daily for potential reductions of sedation, anxiolytics, and analgesics as well as for sedation interruptions in intubated patients when criteria are met.
Step 4	**Manage delirium:** prevention and treatment (prioritize non-pharmacologic interventions to prevent or treat delirium, over pharmacologic treatments).
Step 5	**Special situations** that may need deep sedation and neuromuscular blockade (i.e. severe ARDS).
Step 6	**Monitor-record-interpret-respond.**
Step 7	**Deliver quality care:** implementation as part of ABCDEF bundle.

Tools

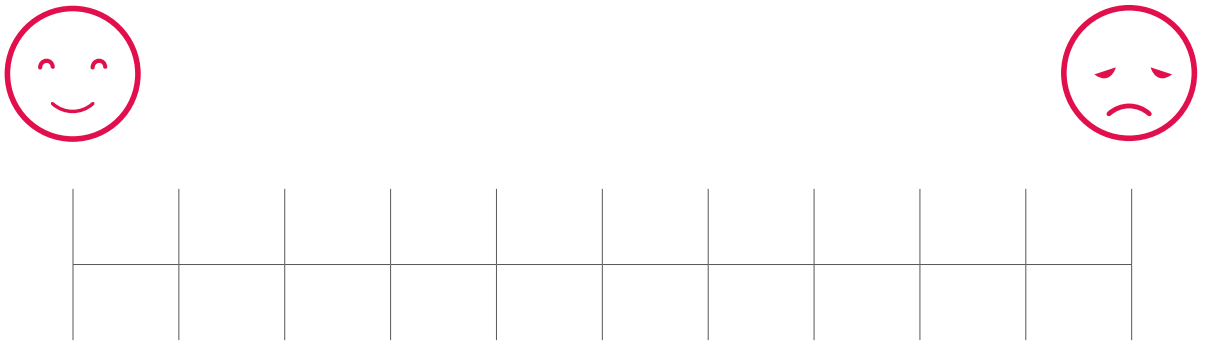
10.1 Numerical pain assessment scales

Visual analogue scale

The visual analogue scale (VAS) for pain assessment in adults and adolescents is a validated and widely used method of monitoring the subjective level of pain experienced by patients. It is a 10 cm long scale, which ranges from 0 (no pain) to 10 (the worst pain that one can imagine). It is flexible, in that patients can make verbal or visual responses (i.e. if verbal communication is not possible, the patient can be shown a 10 cm scale and can point to the region which corresponds to their pain).

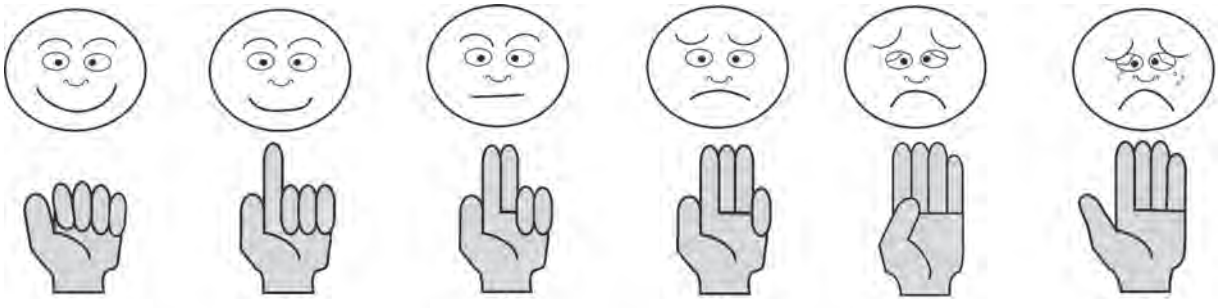
A major limitation of the VAS is that it requires an awake patient who grasps the concept of a scale. These conditions are frequently not satisfied in ICU patients.

The lower the VAS score, the higher the quality of the analgesia. However, a low VAS score with excessive sedation must be avoided, if possible. The level of sedation must be also closely monitored (see the Richmond Agitation-Sedation Scale tool).



Wong–Baker Faces Scale

The Wong-Baker Faces Scale can be used in younger children – they are asked to point to the face that reflects their pain level.



Source: Wong and Hockenberry (2001).

10.2 Behavioural pain assessment scales

There are two validated behavioural pain assessment scales that can be used to assess pain in non-communicative or sedated patients (e.g. mechanical ventilation); these are recommended to use instead of physiological indicators alone. The sedation and pain levels of children in intensive care should be assessed at least 4 hourly in intensive care.

- **BPS:** Behavioural Pain Scale
- **CPOT:** Critical-Care Pain Observation Tool
- In children: **Comfort-B Scale** and **FLACC** Behavioural Pain Assessment Scale

10.2.1 Behavioural Pain Scale (BPS)

BPS score ranges from 3 (no pain) to 12 (maximum pain).

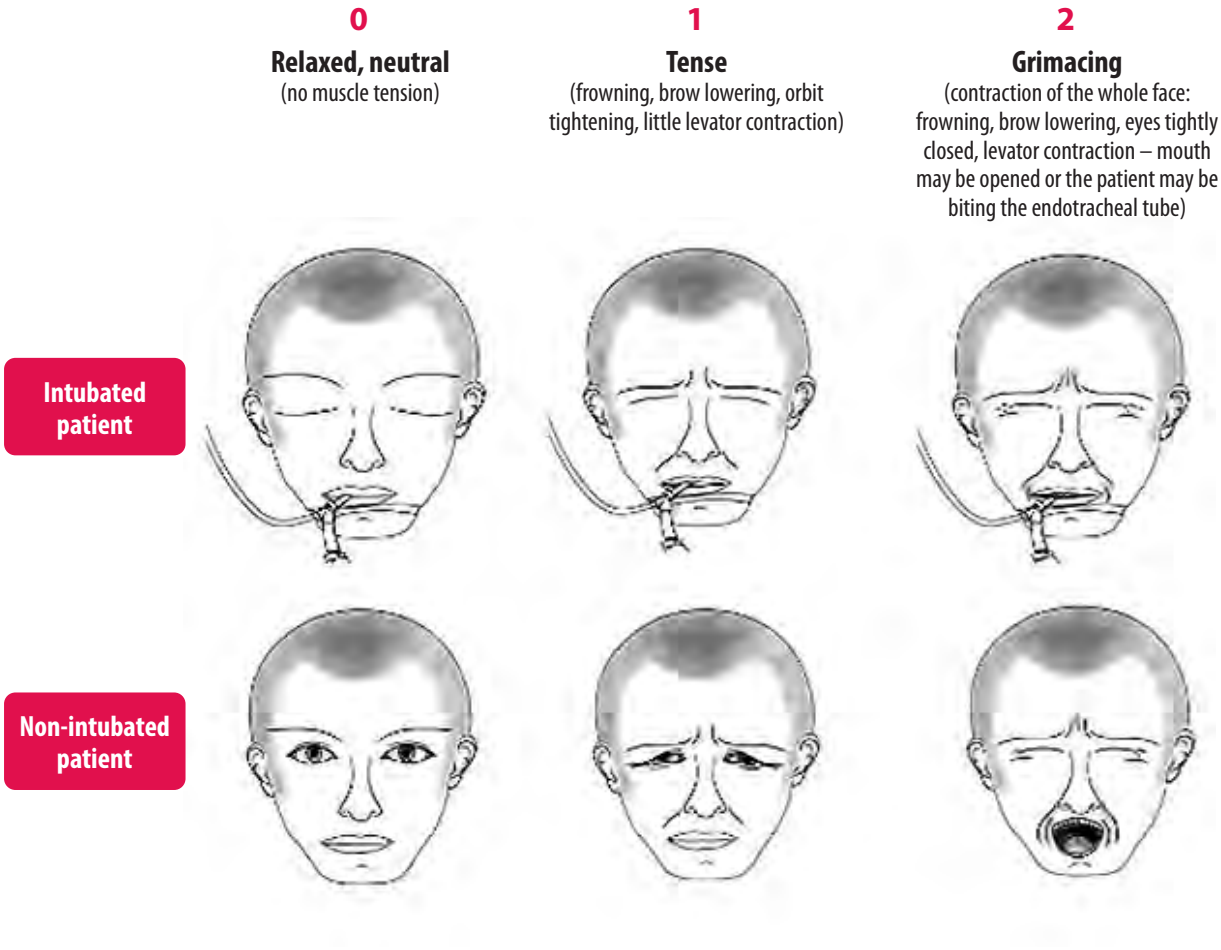
Item	Description	Score
Facial expression	Relaxed	1
	Partially tightened (e.g. brow lowering)	2
	Fully tightened (e.g. eyelid closing)	3
	Grimacing	4
Upper limb movements	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with mechanical ventilation	Tolerating movement	1
	Coughing but tolerating ventilation most of the time	2
	Fighting ventilator	3
	Unable to control ventilation	4

10.2.2 Critical-Care Pain Observation Tool (CPOT)

Indicator	Score		Description
Facial expressions	Relaxed, neutral	0	No muscle tension
	Tense	1	Presence of frowning, brow lowering, orbit tightening and levator contraction or any other change (e.g. opening eyes or tearing during nociceptive procedures)
	Grimacing	2	All previous facial movements plus eyelid tightly closed (the patient may present with mouth open or biting endotracheal tube)
Body movements	Absence of movements or normal position	0	Does not move at all (doesn't necessarily mean absence of pain) or normal position (movements not aimed toward the pain site or not made for the purpose of protection)
	Protection	1	Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements
	Restlessness/agitation	2	Pulling tube, attempting to sit up, moving limbs/thrashing, not following commands, striking at staff, trying to climb out of bed
Compliance with the ventilator (intubated patients) *or* **Vocalization (extubated patient)**	Tolerating ventilator or movement	0	Alarms not activated, easy ventilation
	Coughing but tolerating	1	Coughing, alarms may be activated but stop spontaneously
	Fighting ventilator	2	Asynchrony; blocking ventilation, alarms frequently activated
	Talking in normal tone or no sound	0	Talking in normal tone or no sound
	Sighing, moaning	1	Sighing, moaning
	Crying out, sobbing	2	Crying out, sobbing
Muscle tension Evaluation by passive flexion and extension of upper limbs when patient is at rest or evaluation when patient is being turned	Relaxed	0	No resistance to passive movements
	Tense, rigid	1	Resistance to passive movements
	Very tense or rigid	2	Strong resistance to passive movements or incapacity to complete them
	Total	(_ /8)	

Source: Adapted from Gélinas et al (2006).

Facial expressions



Source: Adapted from Payen et al (2001).

Note: A score of 1 may be attributed when a change in the patient's facial expression is observed compared with rest (e.g. opening or weeping).

How to use the Critical-Care Pain Observation Tool

1. The patient must be observed at rest for 1 minute to obtain a baseline vaue of the CPOT.
2. Then, the patient should be observed during nociceptive procedures known to be painful (e.g. turning, wound care) to detect any changes in the patient's behaviours to pain.
3. The patient should be evaluated before and at the peak effect of an analgesic agent to assess whether the treatment was effective or not in relieving pain.
4. For the rating of the CPOT, the patient should be attributed the highest score observed for each item during the observation period.
5. The patient should be attributed a score for each behaviour included in the CPOT and muscle tension should be evaluated last, especially when the patient is at rest because the stimulation of touch alone (when performing passive flexion and extension of the arm) may lead to behavioural reactions.

Free teaching CPOT video available from the Society of Critical Care Medicine ().

Observation of patient at rest (baseline)

The nurse looks at the patient's face and body to note any visible reaction for an observation period of 1 minute. She/he gives a score for all items except for muscle tension. At the end of the 1-minute period, the nurse holds the patient's arm in both hands – one at the elbow, and one to hold the patient's hand. Then she/he performs and passive flexion and extension of the upper limb, and feels any resistance the patient may exhibit. If the movements are performed easily, the patient is found to be relaxed with no resistance (score 0). If the movements can still be performed but with more strength, then it is concluded that the patient is showing resistance to movement (score 1). Finally, if the nurse cannot perform the movement, strong resistance is felt (score 2). This can be observed in patients who are spastic.

Observation of patient during turning

Even during the turning procedure, the nurse can still assess the patient's pain. While she/he is turning the patient on one side, she/he looks at the patient's face to note any reactions such as frowning or grimacing. These reactions may be brief or can last longer. The nurse also looks out for body movements. For instance, she/he looks for protective movements like the patient trying to reach or touching the pain site (e.g. surgical incision, injury site). In the mechanically ventilated patient the nurse pays attention to alarms and if they stop spontaneously or require that she/he intervenes (reassurance, administering medication). According to muscle tension, the nurse can feel if the patient is resisting to the movement or not. A score of 2 is given when the patient is resisting against the movement and attempts to get on his/her back.

10.2.3 COMFORT-B Scale

It cannot be used in children who are receiving muscle relaxant drugs or children with severe neurological impairment. The child should be observed for 2 minutes and six behaviours are scored as below (score either respiratory response or crying, depending on the child's intubation status).

Children scoring 11–22 are in the optimal range of sedation; children scoring < 10 may be oversedated (consider weaning); and children > 23 are undersedated.

COMFORT-B Scale

Item	Description	Score
Alertness	1. Deeply asleep	
	2. Lightly asleep	
	3. Drowsy	
	4. Fully awake and alert	
	5. Hyperalert	
Calmness/agitation	1. Calm	
	2. Slightly anxious	
	3. Anxious	
	4. Very anxious	
	5. Panicky	

COMFORT-B Scale

Item	Description	Score
Respiratory response (ventilated children)	1. No coughing and no spontaneous respiration	
	2. Spontaneous respiration with little or no response to ventilation	
	3. Occasional cough or resistance to ventilator	
	4. Actively breathes against ventilator or coughs regularly	
	5. Fights ventilator, cough or choking	
Cry (non-ventilated children)	1. Quiet breathing, no crying	
	2. Sobbing or gasping	
	3. Moaning	
	4. Crying	
	5. Screaming	
Physical movement	1. No movement	
	2. Occasional, slight movements	
	3. Frequent, slight movements	
	4. Vigorous movement limited to extremities	
	5. Vigorous movements including torso and head	
Muscle tone	1. Muscles totally relaxed, no muscle tone	
	2. Reduced muscle tone	
	3. Normal muscle tone	
	4. Increased muscle tone and flexion of fingers and toes	
	5. Extreme muscle rigidity and flexion of fingers and toes	
Facial tension	1. Facial muscle totally relaxed	
	2. Facial muscle tone normal; no facial muscle tension evident	
	3. Tension evident in some facial muscles	
	4. Tension evident throughout facial muscles	
	5. Facial muscles contorted and grimacing	
	Total score	

Source: Adapted from Ambuel et al (1992).

10.2.4 FLACC Behavioural Pain Assessment Scale

The FLACC scale is a measurement used to assess pain for children between 2 months and 7 years or for individuals who are unable to communicate their pain.

FLACC Behavioural Pain Assessment Scale

Categories	Scoring		
	0	1	2
Face	No particular expression or smile	Occasional grimace or frown; withdrawn, disinterested	Frequent to constant frown, clenched jaw, quivering chin
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arches, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

Source: Merkel et al (1997).

How to use the FLACC

In patients who are awake: observe for 1 to 5 minutes or longer. Observe legs and body uncovered. Reposition patient or observe activity. Observe body for tenseness and tone. Initiate consoling interventions if needed.

In patients who are asleep: observe for 5 minutes or longer. Observe legs and body uncovered. If possible, reposition the patient. Touch the body and observe for tenseness and tone.

Face

- Score 0 if the patient has a relaxed face, makes eye contact, shows interest in surroundings.
- Score 1 if the patient has a worried facial expression, with eyebrows lowered, eyes partially closed, cheeks raised, mouth pursed.
- Score 2 if the patient has deep furrows in the forehead, closed eyes, an open mouth, deep lines around nose and lips.

Legs

- Score 0 if the muscle tone and motion in the limbs are normal.
- Score 1 if the patient has increased tone, rigidity, or tension; if there is intermittent flexion or extension of the limbs.
- Score 2 if the patient has hypertonicity, the legs are pulled tight, there is exaggerated flexion or extension of the limbs, tremors.

Activity

- Score 0 if the patient moves easily and freely, normal activity or restrictions.
- Score 1 if the patient shifts positions, appears hesitant to move, demonstrates guarding, a tense torso, pressure on a body part.
- Score 2 if the patient is in a fixed position, rocking; demonstrates side-to-side head movement or rubbing of body part.

Cry

- Score 0 if the patient has no cry or moan, awake or asleep.
- Score 1 if the patient has occasional moans, awake or asleep.
- Score 2 if the patient has frequent or continuous moans, cries, grunts.

Consolability

- Score 0 if the patient is clam and does not require consoling.
- Score 1 if the patient responds to comfort by touching or talking in 30 seconds to 1 minute.
- Score 0 if the patient requires constant comforting or is inconsolable.

Interpreting the **Behavioural Score**

Each category is scored on the 0–2 scale, which results in a total score of 0–10; 0 = Relaxed and comfortable; 1–3 = Mild discomfort; 4–6 = Moderate pain; 7–10 = Severe discomfort or pain or both.

10.3 Richmond Agitation–Sedation Scale (RASS)

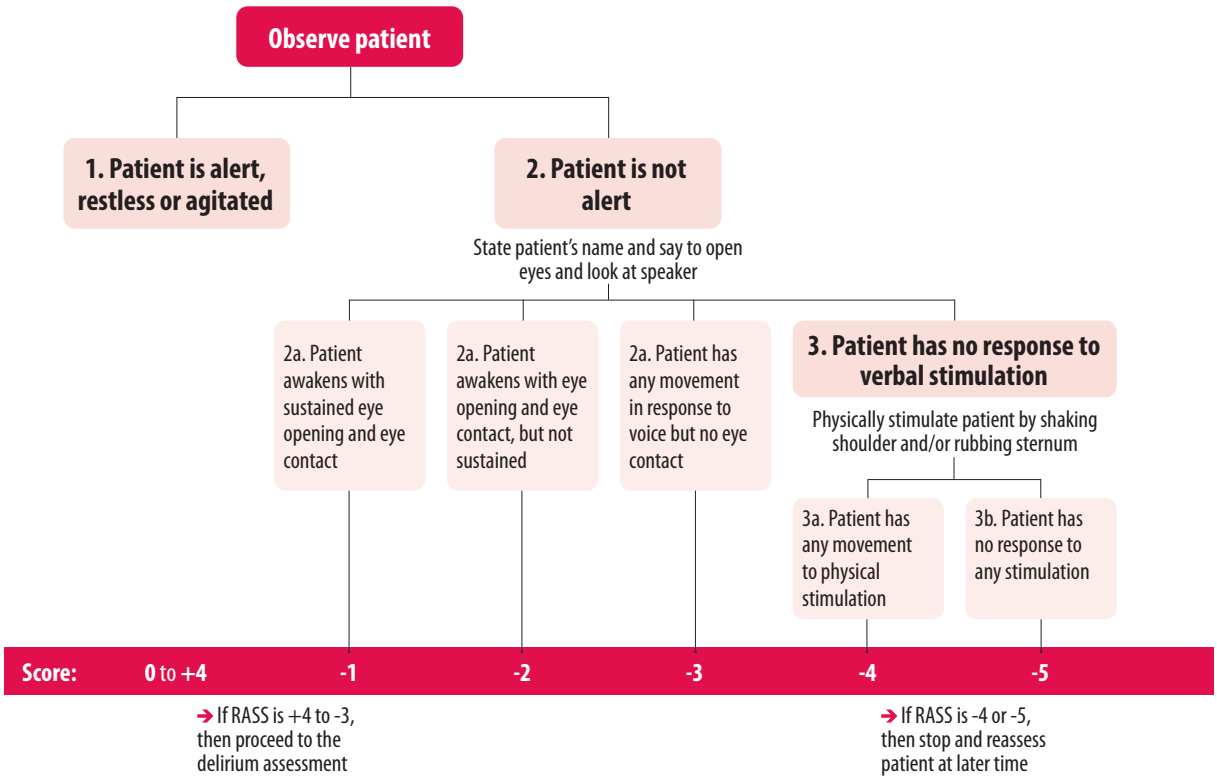
Assess agitation, anxiety and sedation levels on a regular basis using a standardized scale and set a daily sedation target based on clinical condition and management plans for the day. Consider the use of the Richmond Agitation-Sedation Scale (RASS). This has been validated in many clinical trials and can be easily taught to staff.

Score	Term	Description	
+4	Combative	Overtly combative, violent, immediate danger to staff	
+3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive	
+2	Agitated	Frequent non-purposeful movement, fights ventilator	
+1	Restless	Anxious but movements not aggressive vigorous	
0	Alert and calm		
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to voice (> 10 seconds)	Verbal stimulation
-2	Light sedation	Briefly awakens with eye contact to voice (< 10 seconds)	
-3	Moderate sedation	Movement or eye opening to voice (but no eye contact)	
-4	Deep sedation	No response to voice, but movement or eye opening to physical stimulation	Physical stimulation
-5	Unarousable	No response to voice or physical stimulation	

Source: Adapted from Sessler et al (2002).

Algorithm for RASS assessment

In most patients, this assessment is very quick and takes only 30 seconds (only 10% take a few minutes).



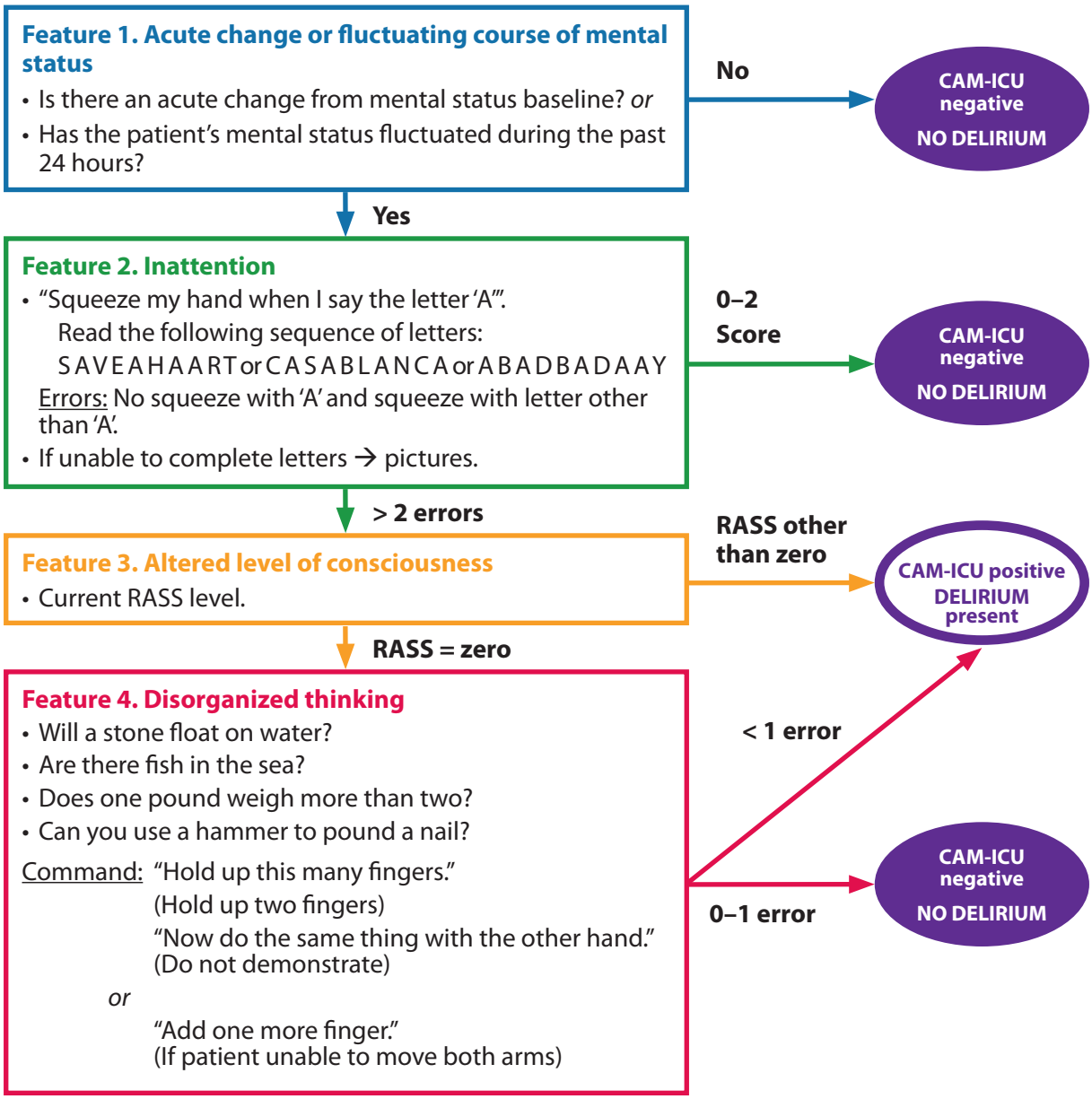
Source: Adapted from Sessler et al (2002).

10.4 Flowchart and worksheet for the Confusion Assessment Method of the ICU for adults (CAM-ICU)

Use the CAM-ICU flowsheets and worksheet (☝) reproduced below, to assess delirium in conjunction with the RASS scale. Additional training materials on how to do the CAM-ICU and train staff can also be found at the same link.

CAM-ICU flowchart

The flowchart can be used as a pocket card or wall poster to easily reference the procedure to assess for the presence of delirium.



Source: Ely et al (2001).

CAM-ICU worksheet

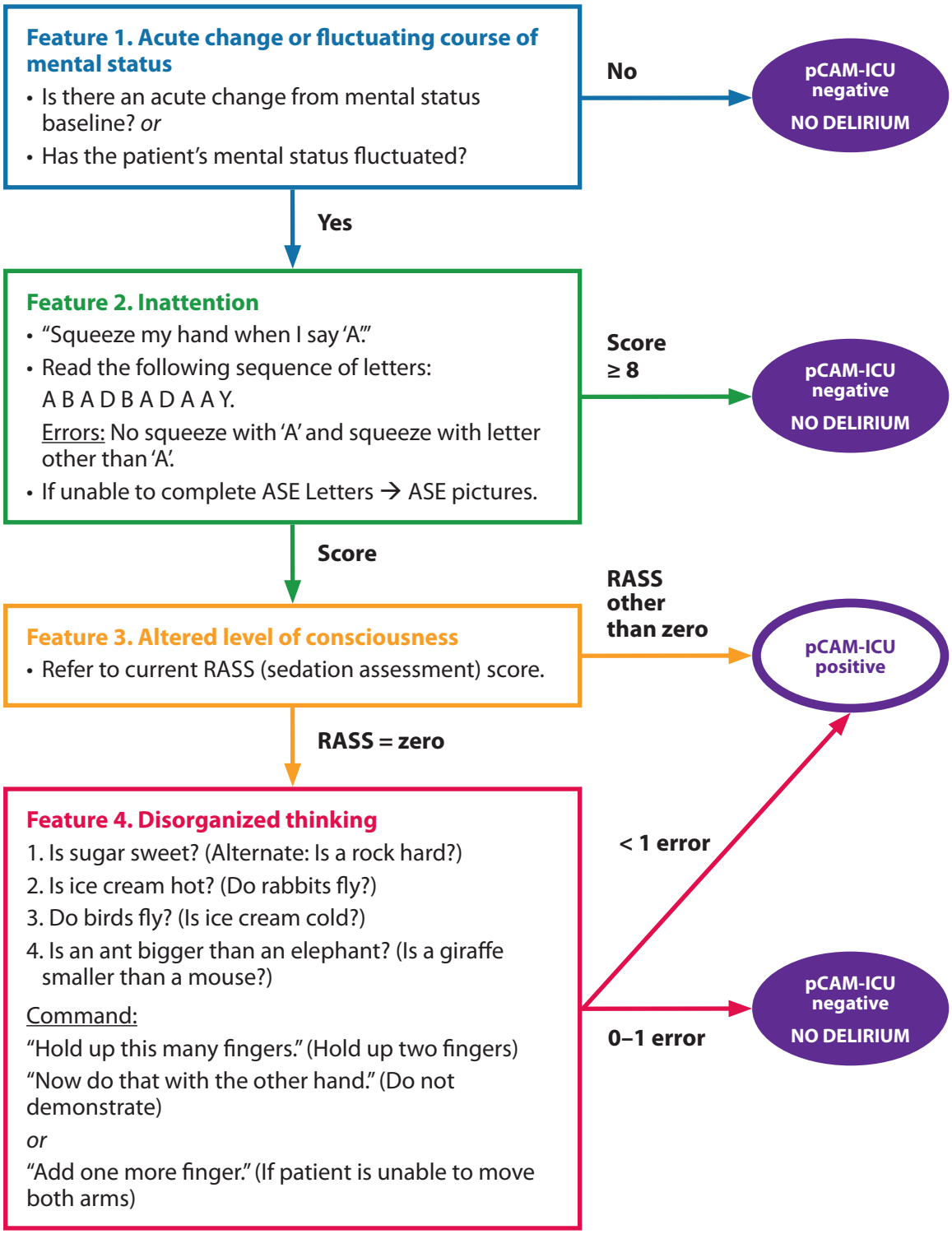
	Score	Check here if present
Feature 1: Acute onset or fluctuating course		
Is the patient different than his/her baseline mental status? *or* Has the patient had any fluctuation in mental status in the past 24 hours as evidenced by fluctuation on a sedation/level of consciousness scale (i.e. RASS/SAS, GCS or previous delirium assessment)?	Either question Yes →	☐
Feature 2: Inattention		
Letters attention test: Directions: Say to the patient, "I am going to read you a series of 10 letters. Whenever you hear the letter 'A', indicate by squeezing my hand." Read the letters from the following list in a normal tone 3 seconds apart. S A V E A H A A R T *or* C A S A B L A N C A *or* A B A D B A D A A Y Errors are counted when patient fails to squeeze on the letter "A" and when the patient squeezes on any letter other than "A". If unable to complete letters attention test → use pictures (see Tool 10.6)	Number of errors > 2 →	☐
Feature 3: Altered level of consciousness		
Present if actual RASS score is anything other than alert and calm (zero)	RASS anything other than zero →	☐
Feature 4: Disorganized thinking		
Yes/No questions: Will a stone float on water? Are there fish in the sea? Does one pound weigh more than two? Can you use a hammer to pound a nail? **Errors are counted when the patient incorrectly answers a question.** Command: Say to the patient, "Hold up this many fingers." (Hold up two fingers in front of the patient) "Now do the same thing with the other hand." (Do not repeat the number of fingers) *Note:* If patient is unable to move both arms, for second part of command ask patient to "Add one more finger". **An error is counted if patient unable to complete entire command.**	Combined number of errors > 1 →	☐
Overall CAM-ICU **CAM-ICU positive =** **Feature 1** _____ + **Feature 2** _____ + *either* **Feature 3** _____ *or* **Feature 4** _____	Criteria met →	☐ CAM-ICU positive (DELIRIUM present)
	Criteria not met →	☐ CAM-ICU negative (NO DELIRIUM)

Source: Ely et al (2001).

10.5 Flowchart and worksheet for the Confusion Assessment Method of the ICU for children (pCAM-ICU)

This tool is adapted from Smith et al (2011) (see References and resources).

pCAM-ICU flowchart



pCAM-ICU worksheet

Feature 1: Acute change or fluctuating course of mental status		
A. Is there an acute change from mental status baseline? Yes or No B. Has my patient's mental status fluctuated during the past 24 hours? Yes or No Evidenced by fluctuation on a sedation scale (RASS), SAS, GCS or previous delirium assessment.	If either answer YES then circle ⊕ →	+ / –
Feature 2: Inattention → FEATURE POSITIVE if SCORE 0–7 on Vigilance "A" test *or* ASE picture test		
Vigilance "A" test: I want my patient to squeeze my hand when I say ONLY the letter "A". I will read the 10-letter sequence in the same order every day, with my normal voice, saying each letter once every second. Directions to patient: "Squeeze my hand when I say the letter 'A'. Let's practise, 'A'". To score: When I say the letter "A" and the patient does not squeeze my hand, I subtract 1 point. When I say the other letters and the patient squeezes my hand, I subtract 1 point. A___B___A___D___B___A___D___A___A___Y___	If the SCORE is 0–7 then circle ⊕ →	+ / –
or		
ASE picture test: I will show the patient **"5 memory pictures"**. I want the patient to remember the 5 **"memory pictures"** when shown a larger **"deck"** of 10 pictures. Directions to patient: "I am going to show you 5 pictures that I want you to remember". (Show 1 **picture** every **3 seconds** and state object's name.) Directions if patient can verbalize: "Say yes when you see **1 of those 5 pictures** again". (Show all pictures from **deck** and state object's name.) Directions to intubated patient: "Nod your head yes when you see **1 of those 5 pictures** again". To score: If the patient nods or says "yes" to ONLY the **5 memory pictures** they have completed the task successfully – SCORE 10/10. If patient does not nod or say "yes" to 1 of the 5 memory pictures, I will subtract 1 point. If the patient nods or says "yes" to the other pictures in the deck, I will subtract 1 point. Memory picture: _____ / 5 Deck pictures: _____ / 5	If the SCORE is 0–7 then circle ⊕ →	+ / –
Feature 3: Altered level of consciousness → FEATURE POSITIVE if the current RASS score is anything other than 0		
At the time of sedation assessment the RASS score was _____		+ / –

Feature 4: Disorganized thinking		
Directions if patient can verbalize: "I am going to ask you 4 questions, say 'yes' or 'no' to answer". Directions to intubated patient: "I am going to ask you 4 questions, nod your head yes or no to answer". **Set A:** 1. Is sugar sweet? 2. Is ice cream hot? 3. Do birds fly? 4. Is an ant bigger than an elephant? **Set B:** 1. Is a rock hard? 2. Do rabbits fly? 3. Is ice cream cold? 4. Is a giraffe smaller than a mouse? 5. Directions to patient: "Hold up this many fingers." (Examiner hold up two fingers for patient to see) Directions to patient: "Now do the same thing with the other hand." (Do not show fingers again to patient) Directions to patient if unable to move **both** arms: "Now, add one more finger." (Do not show fingers again to patient) To score: If the patient answers a question incorrectly, I will subtract 1 point. If the patient is not able to complete the command no. 5, I will subtract 1 point.	If the SCORE is 0–3 then circle ⊕ →	+ / –
Paediatric delirium = Feature 1 _____ **+ Feature 2** _____ *+ either* **Feature 3** _____ *or* **Feature 4** _____		

10.6 Procedure for assessing attention: attention screening exam (ASE) for adults

This procedure is to be used to assess for feature 2 (**inattention** – a cardinal feature of delirium), when the patient is unable to complete the letters attention test (SAVEAHAART). This happens in only about 10% of patients.

Step 1

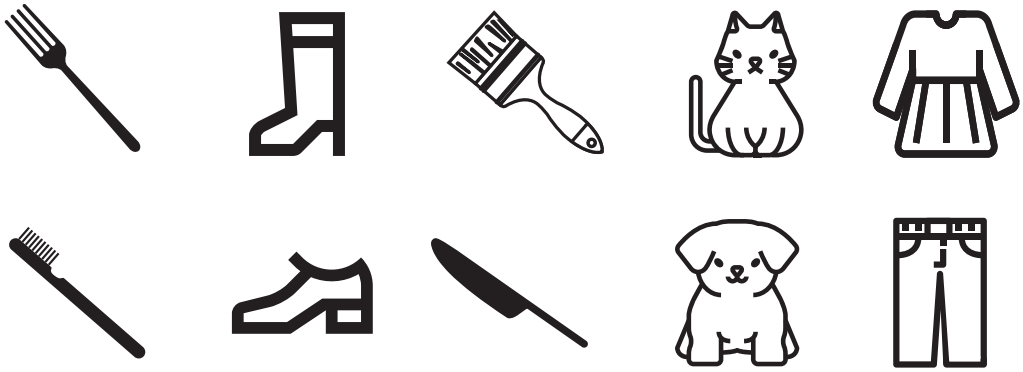
- Say to the patient: *"Mr or Mrs …, I am going to show you pictures of some common objects. Watch carefully and try to remember each picture because I will ask what pictures you have seen."*

- Present five pictures: naming them and showing them each for 3 seconds.

Step 2

- Say to the patient: *"Now I am going to show you some more pictures. Some of these you have already seen and some are new. Let me know whether or not you saw the picture before by nodding your head yes (demonstrate) or no (demonstrate)."*

- Present ten pictures (five new, five repeated): naming them and showing them each for 3 seconds.



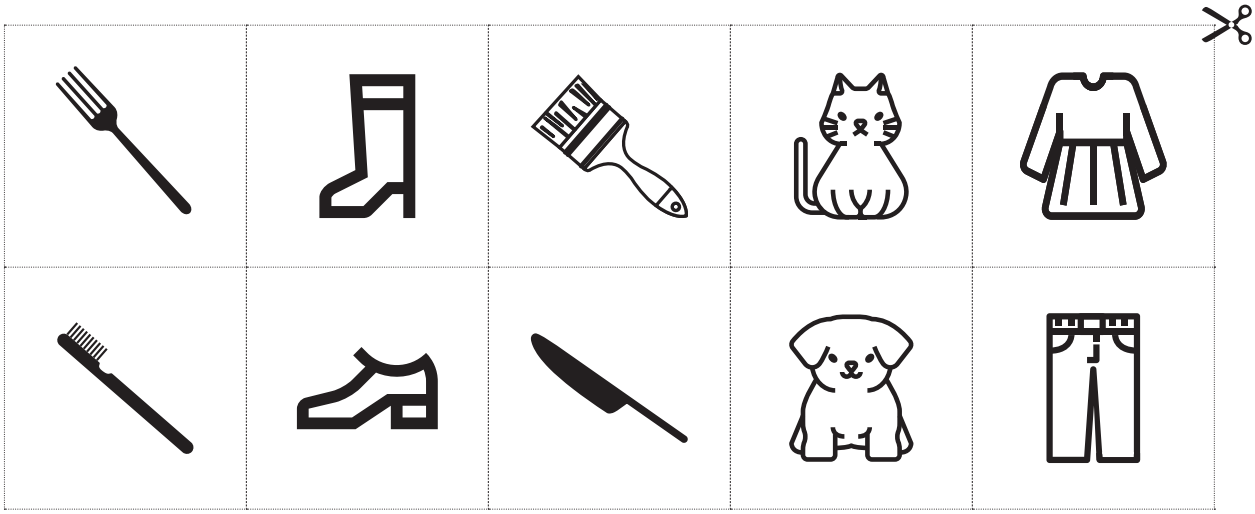
Scoring

This test is scored by the number of correct "yes" or "no" answers during Step 2 (out of a possible 10).

Important: Alternate daily between Forms A and B (see next tool) if repeat measures are taken. If a patient wears glasses make sure they have them on when attempting the ASE.

Source: Adapted from Ely and Vanderbilt University (2002).

Form A



Source: Adapted from Ely and Vanderbilt University (2002).

Form B

Source: Adapted from Ely and Vanderbilt University (2002).

10.7 Guide to commonly used sedatives in adults

There are many sedative medications available to treat agitation and anxiety. You will need to see which medications your hospital currently has and consider which medications you may want to use in the future. It is important to familiarize yourself with the basic pharmacokinetics and side-effects of any drug you use. The goal is to reach the sedation target with the lowest possible sedative medication to minimize toxicity. The doses provided below are intended to be used for adult patients who are intubated and receiving mechanical ventilation. Continuous infusions of benzodiazepines should be avoided in adult patient if safe alternatives are to reduce the risks of oversedation, prolonged days of IMV and delirium.

	Propofol	Midazolam	Lorazepam	Diazepam	Dexmedetomidine[a]	Ketamine
Onset	< 1 minute	1–5 minutes	5–20 minutes	2–5 minutes	1–3 minutes	< 1 minute
Infusion	10–80 µg/kg/min	0.04–0.2 mg/kg/hr	0.01–0.1 mg/kg/hr	Not used	0.2–1.5 µg/kg/hr	0.2–0.5 mg/kg/hr
Time to arousal	10–15 minutes	1–2 hours	2–6 hours	2–4 hours	6–10 minutes	1–2 hours
Risks	Respiratory depression Hypotension Idiosyncratic rhabdomyolysis and acidosis and cardiovascular collapse (Propofol Infusion Syndrome, PRIS) Raised triglycerides	Respiratory depression Hypotension Prolonged sedation with infusions due to active metabolite Reduce dose in renal and liver failure Delirium	Respiratory depression Hypotension Propylene glycol carrier may irritate veins and cause metabolic acidosis with prolonged administration Delirium	Respiratory depression Hypotension Oversedation with repeated boluses with accumulation of drug and active metabolite Delirium	Hypotension Bradycardia More pronounced in elderly	Laryngospasm Emergence delirium Respiratory depression (especially in neonates or when used concurrently with opiates) Porphyria Genitourinary symptoms

Note:
[a] Less commonly available.

Early in severe ARDS, however, deep sedation targets may be needed to safely achieve LPV targets and reduce asynchrony. In cases when NMB are administered, remember to also give a continuous sedative for amnesia and analgesic for pain.

10.8 Guide to commonly used opioid analgesics in adults

There are several opioids available to treat pain. You will need to see which medications your hospital currently has and consider which medications you may want to use in the future. Familiarize yourself with the basic pharmacokinetics and side-effects of any drug you use. Be sure to set a therapeutic analgesia plan and communicate to all caregivers for a consistent approach.

These considerations are adapted from the *Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult* (Jacobi et al., 2002) (see References and resources).

The doses provided below are suggestions and will need adjustment based on the amount of pain and whether the patient is receiving mechanical ventilation.

	Morphine	Hydromorphone	Fentanyl
Intermittent dose IV	0.01–0.15 mg/kg every 1–2 hr	10–30 µg/kg every 1–2 hr	0.35–1.5 µg/kg every 0.5–1 hr
Infusion	0.07–0.5 mg/kg/hr	7–15 µg/kg/hr	0.7–10 µg/kg/hr
Half-life	3–7 hr	2–3 hr	1.5–6 hr
Equianalgesic IV dose[a]	10 mg	1.5 mg	200 µg
Situations where drug is preferred	Intermittent dosing	Intermittent dosing Haemodynamic instability Renal failure	Rapid onset in acutely distressed patients Haemodynamic instability Renal failure
Risks[b]	Histamine release causing hypotension Prolonged effect in renal failure due to metabolite		Rigidity with high doses Repeated dosing may cause accumulation and prolonged effects

Notes:
[a] These doses produce approximately the same analgesic effects;
[b] Side-effects common to all agents include respiratory depression, coma and delirium, hypotension (especially with morphine) and ileus.

Meperidine (pethidine), tramadol and codeine may be available at many hospitals; however, each drug has noteworthy limitations and thus are not optimal for critically ill patients. Meperidine has variable efficacy for analgesia, has an active metabolite that causes neuroexcitation (apprehension, tremors, delirium and seizures) and may interact with antidepressants (contraindicated with monoamine oxidase inhibitors and best avoided with selective serotonin-reuptake inhibitors), so it is not recommended for repetitive use. Tramadol is generally considered inferior to many other analgesics and can cause adverse reactions when used with other serotonin re-uptake inhibiting medications. Codeine has markedly different pharmacodynamics across different patients due to variability in drug metabolizing rates.

10.9 Guide to using neuromuscular blockers in adults

WHO suggests that in moderate-severe ARDS (PaO_2/FiO_2 < 150), neuromuscular blockade by continuous infusion should not be routinely used.

A trial found that neuromuscular blockade improved survival in adult patients with severe ARDS without causing significant weakness (Papazian et al., 2010), but results of a recent larger trial found that use of neuromuscular blockade with high PEEP strategy was not associated with a survival benefit when compared with a light sedation strategy without neuromuscular blockade (NHLBI PCTN et al., 2019). Continuous neuromuscular blockade may still be considered in patients with ARDS, both adults and children, in certain situations: ventilator dyssynchrony despite sedation, such that tidal volume limitation cannot be reliably achieved; or refractory hypoxaemia or hypercapnia. Neuromuscular blockade may also be useful to ascertain accurate pulmonary mechanics (e.g. plateau pressure measurements), but this alone is not an indication for neuromuscular blockade infusion.

Suxamethonium (ie succinylcholine) is a depolarizing muscle relaxant used most commonly for rapid sequence induction for intubation. This medication can cause bradycardia (especially in infants or children < 5 years of age) and life-threatening hyperkalaemia. Because of this latter concern, suxamethonium is contraindicated in chronic skeletal muscle disease, denervating events or neuromuscular disease, recent burns, rhabdomyolysis, history of malignant hyperthermia or concurrent hyperkalaemia.

	Pancuronium	Vecuronium	Cisatracurium	Rocuronium
IV dose	Intermittent: 0.08–0.1 mg/kg Infusion: 0.2–0.6 µg/kg/min (usually 1–2.5 mg/hr)	Intermittent: 0.08–0.1 mg/kg Infusion: 0.2–0.8 µg/kg/min (usually 1–4 mg/hr)	Intermittent: 0.15–0.20 mg/kg Infusion: 3 mcg/kg/min for first 20 minutes then reduce to 1–2 mcg/kg/min (range: 0.5–10 mcg/kg/min)	Intermittent: 0.6–1.2 mg/kg Infusion: 0.5–0.7 mg/kg/hr
Common points on dosing	Tailor intermittent dose to patient response. Titrate infusion dose clinically or to achieve one or two twitches with train of four stimulation on peripheral nerve stimulator, if available			
Onset	< 4 minutes	2–3 minutes	2–3 minutes	2–3 minutes
Specific risks	Long duration of activity: ~90–160 minutes Accumulation in hepatic and renal dysfunction Dose-dependent increased HR and blood pressure (due to vagolytic and weak sympathomimetic effects)	Intermediate duration of activity: ~30–45 minutes. Accumulation in hepatic and renal dysfunction	Duration of action: ~45–75 minutes Slight accumulation in hepatic and renal dysfunction	Intermediate duration of activity: ~30–45 minutes. Accumulation in hepatic and renal dysfunction Can be reversed completely by sugammadex when available
Common risks	Appropriate sedation and analgesia should be administered concurrently. HR and blood pressure should be routinely monitored; increases may indicate inadequate sedation or analgesia. ICU-acquired weakness if used for prolonged period			

10.10 Guide to commonly used antipsychotics (haloperidol) in adults

Antipsychotic agents can be used to keep actively delirious patients safer. Haloperidol is a typical antipsychotic that has been available for many years. Atypical antipsychotics can also be used (e.g. quetiapine, olanzapine and risperidone). Dexmedetomidine is a newer agent that has both sedative and anti-delirium effects.

Haloperidol	
Loading dose	Begin with 2–5 mg IV Double dose every 15 minutes until desired effect is achieved **Do not** exceed total of 20 mg/day
Onset	10–20 minutes
Risks	Torsade de pointes arrhythmia, do not use if the QTc interval on ECG is prolonged to > 460 milliseconds Suspect neuroleptic malignant syndrome if patient develops hyperthermia, muscle rigidity and rhabdomyolysis

Dosing recommendations	
Quetiapine	Begin with 25–50 mg po twice or three times daily Increase up to 200 mg po total daily dose (halve dose in elderly)
Olanzipine	Begin with 5–10 mg IV/IM/po Repeat dose in 2 hours to maximum of 30 mg/day
Risperidone	Begin with 1–2 mg po daily Increase to maximum of 6 mg po daily

Side-effects of atypical antipsychotics are prolonged QTc interval and extrapyramidal effects (less common than with typical antipsychotic agents).

10.11 Guide to paediatric analgesics, sedatives and neuromuscular blockers

There are several agents available for analgesia, sedation and neuromuscular blockade. You will need to see which medications your hospital currently has and consider which medications you may want to use in the future. Familiarize yourself with the basic pharmacokinetics and side-effects of any drugs you use. The doses provided below are suggestions and will need titration in individual patients based on the amount of pain and whether the patient is receiving mechanical ventilation. Appropriate sedation and analgesia should be administered concurrently with neuromuscular blockade, which has no sedative or analgesic properties.

Propofol is contraindicated for sedation in children < 16 years old in the ICU because of the risk of propofol infusion syndrome (acidosis and rhabdomyolysis).

	Drug	Enteral dose	Bolus IV dose	IV infusion
Analgesia	Paracetamol	10–15 mg/kg/6hr	10mg/kg q6–8hr	N/A
	Oxycodone	0.05–0.2 mg/kg/4–6hr	N/A	N/A
	Ibuprofen	5–10 mg/kg/6–8hr	N/A	N/A
	Morphine	0.2–0.4 mg/kg/6hr	0.1–0.2 mg/kg	0–40 µg/kg/hr
	Fentanyl	N/A	1–2 µg/kg	0–8 µg/kg/hr
Sedation	Hydromorphone	0.03–0.06 mg/kg/4hr	0.01–0.015 mg/kg	0.003–0.005 mg/kg/hr
	Midazolam	N/A	0.05–0.2 mg/kg	0–4 µg/kg/min
	Diazepam		0.1–0.2 mg/kg	N/A
	Chloral hydrate	30–50 µg/kg/6hr	N/A	N/A
	Triciofos	30–50 µg/kg/6hr	N/A	N/A
	Allmemazine	1 mg/kg/6hr	N/A	N/A
	Ketamine	6–8 mg/kg	0.5–2 mg/kg	0.3–1.22 mg/kg/hr
	Dexmedetomidine	N/A	1 mcg/kg over 10 minutes	0.2–0.7 mcg/kg/hr
	Clonidine	4–5 mcg/kg	1–2 mcg/kg	0.18–3.16 mcg/kg/hr
Neuromuscular blockade	Vecuronium	N/A	0.1 mg/kg as required	0–4 µg/kg/min
	Cisatracurium	N/A	0.1–0.15 mg/kg	0.5–10 µg/kg/min
	Rocuronium	N/A	0.6 mg/kg	0.12 µg/kg/min
	Pancuronium	N/A	0.04–0.1 mg/kg	0.1 mg/kg/h
	Suxamethonium	N/A	1–2 mg/kg	0.3–0.6 mg/kg q5–10min PRN

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11 Liberation from invasive mechanical ventilation

11 Liberation from invasive mechanical ventilation

Summary

Use a daily coordinated spontaneous awakening trial (SAT) with spontaneous breathing trial (SBT) protocol to liberate patients from mechanical ventilation as soon as possible as this improves patient outcomes. In patients who fail SBT, recognize and treat the reason for failure, and try again the next day. In patients who pass SBT, consider extubation after evaluating their ability to protect the airway and clear secretions. After extubation, monitor the patient closely for signs of respiratory failure and the need for prompt re-intubation.

Steps for liberation from invasive mechanical ventilation (IMV)

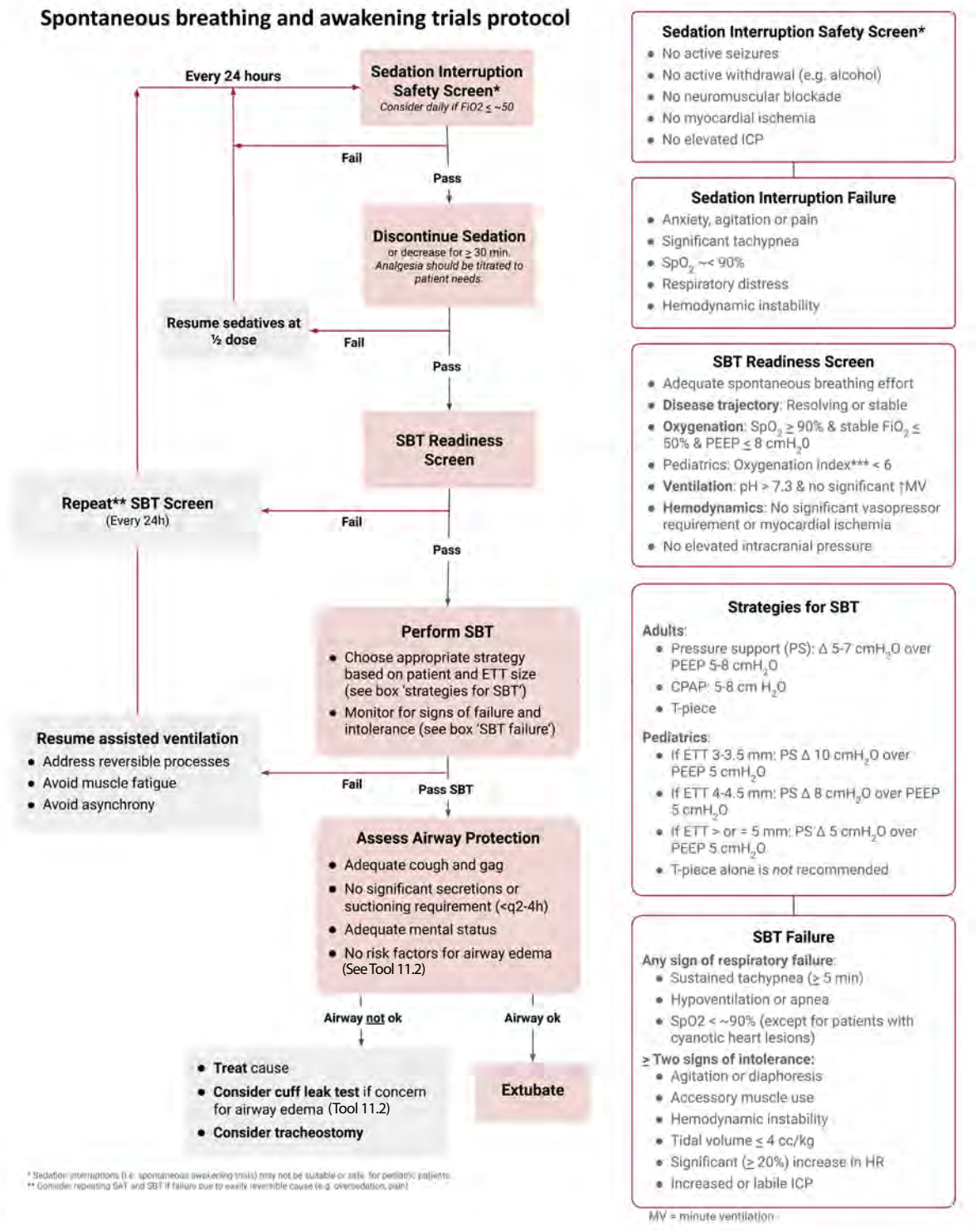
Step 1	Daily assessment for patient readiness to breath spontaneously
Step 2	Conduct the SBT safely
Step 3	Evaluate patient's performance on the SBT
Step 4	Assess safety for extubating
Step 5	Extubate
Step 6	Monitor-record-interpret-respond
Step 7	Deliver quality care: implement as part of ABCDEF protocol

There are limited data to guide the timing of tracheostomy, though routinely this is considered at 10–14 days if the need for prolonged mechanical ventilation persists. During the COVID-19 pandemic, the optimal timing of tracheostomy has been debated. These debates have included arguments to perform tracheostomy as early as possible to assist with early mobilization, reduced sedation requirements, easier pulmonary hygiene and less potential risk for tube malposition. The debates have also included arguments to perform tracheostomy considerably later than routine in order to decrease the chance of health care worker exposure to aerosolized particles during the procedure.

Tools

11.1 Algorithm for daily sedation interruption and daily spontaneous breathing trial (SBT)

This protocol outlines the steps for daily consideration of sedation interruption, spontaneous breathing trial, and extubation – modified by the OpenCriticalCare.org Project from Girard et al. (2008) and MacIntyre (2007).



Source: USAID-STAR-UCSF Open Critical Care Project ().

11.2 How to perform a cuff leak test

Performing a cuff leak test may help to determine that the airway is patent, without swelling.

When an adequate cuff leak is present, it signifies that the patient's airway is unlikely to be profoundly edematous, and the patient is less likely to have post-extubation stridor (PES). Of note, studies of the predictive value of cuff leak tests vary, and generally the cuff leak test is considered to have higher specificity than sensitivity. The presence of a cuff leak does not ensure that the patient's airway will remain open after extubation.

***When an adequate cuff leak is not present,* consider steroids and elevating the head of the bed to reduce swelling; check again in 12–24 hours.**

The lack of a cuff leak makes it more likely that the patient could have post-extubation stridor if steroids are not given prior (Kuriyama et al., 2020; Miller and Cole, 1996).

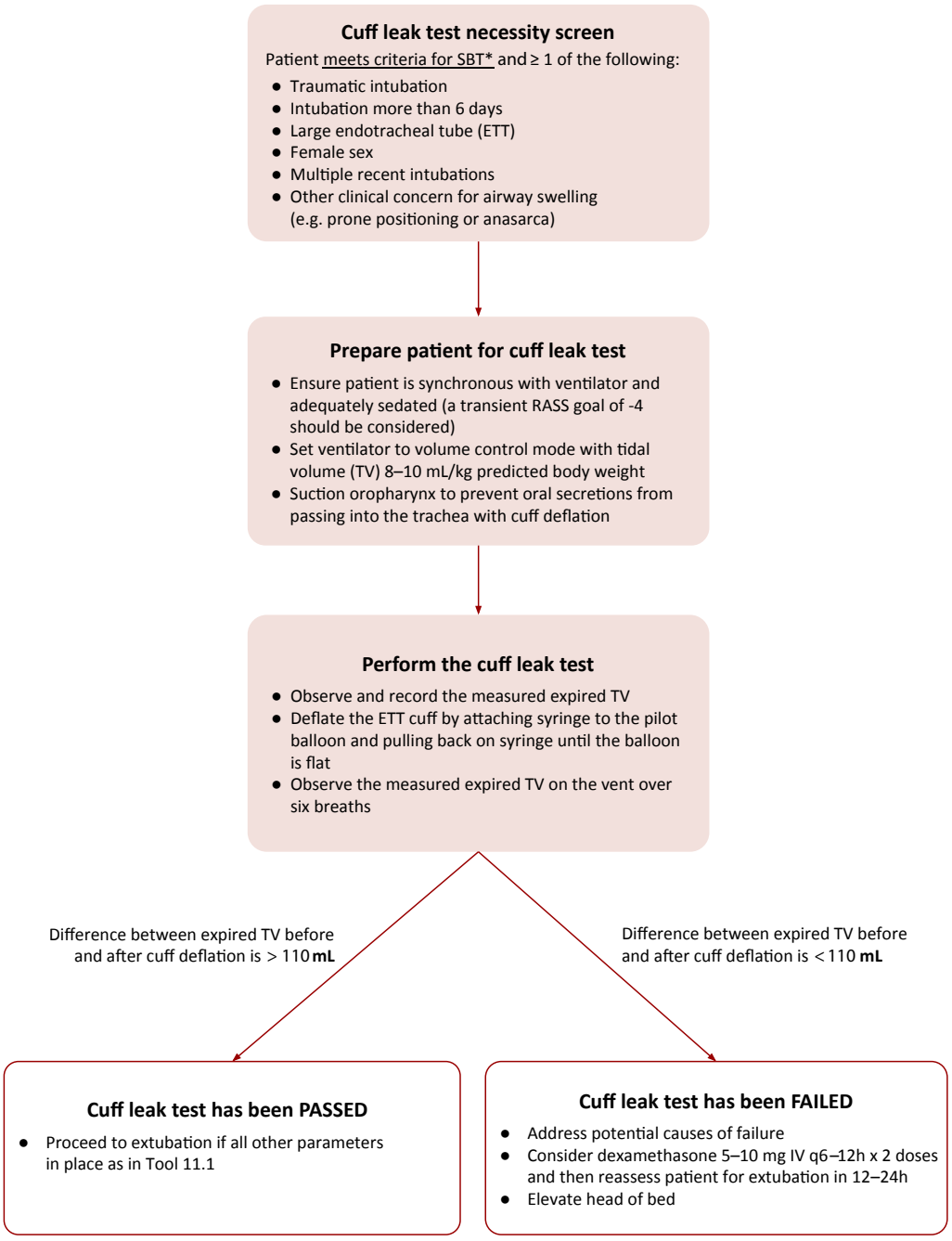
The American Thoracic Society recommends checking a cuff leak in patients with high risk of post-extubation stridor.

Risk factors for post-extubation stridor
neck trauma
prone positioning
anasarca
multiple recent intubations
intubation for > 6 days

Protocol to perform a cuff leak test

1. Ensure proper PPE and IPC for providers as the leak test is an aerosol-generating procedure.
2. Patient should be sedated, or the test done when the patient is asleep (to prevent measurement artifacts).
3. Standard vent settings; volume-controlled ventilation with:
   - TV: 8–10 mL/kg
   - RR: 10–12
   - flow rate: 50–60 L/min.
4. Suction oropharynx (to prevent secretions from passing into the trachea when the ETT cuff is deflated).
5. Measure the expired TV.
6. Deflate the ETT cuff.
7. Re-measure the expired TV over six breaths:
   - cuff leak is the difference in TV with cuff inflated and deflated;
   - > 110 mL difference in expiratory TV before and after cuff down has negative predictive value (NPV) 98% for post-extubation stridor.
8. Reinflation of the cuff.

Cuff leak protocol



*SBT – spontaneous breathing trial criteria (see Tool 11.1).

Source: USAID-STAR-UCSF Open Critical Care Project ( ).

11.3 Respiratory care pocket card reference

The card, which can be printed or saved to your mobile device, ( ) is available in:

- English
- French
- Portuguese
- Spanish.

High Pressures, Desaturations & Dyssynchrony

General Considerations

- ☐ Is the ventilator set to FiO_2 100% while you troubleshoot?
- ☐ Is the patient hemodynamically unstable? If so, consider pressors & urgent evaluation for pneumothorax or severe auto-PEEP.
- ☐ Is the ventilator circuit connected & set correctly?
- ☐ Are breath sounds bilateral? If unilateral, consider mainstem ETT, lobar collapse, atelectasis, and pneumothorax.

High Pressures

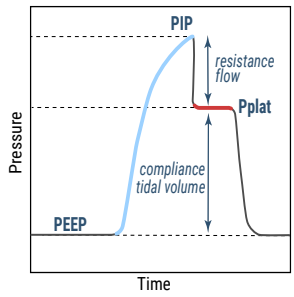
- ☐ Is the patient agitated or asynchronous?
- ☐ Can a suction catheter pass easily through the endotracheal tube? If no, consider kinked tube, biting/bite block, secretions/suction, or replace ETT.
- ☐ What is the Pplat?

Inspiratory Hold

If ↑PIP & ↑Pplat (ΔPplat-PIP<10*)

Dx=Low Compliance

Atelectasis
Pulmonary edema
Pneumothorax
Abdominal distension
Chest wall rigidity
Hyperinflation
Pulmonary fibrosis
ETT in mainstem bronchus



If ↑PIP & normal Pplat (ΔPplat-PIP>10*)

Dx=High Resistance

Secretions
Bronchospasms
Asthma
COPD
Biting
ETT kinked
Small ETT
Circuit filled with water

Troubleshooting low compliance: Decrease V_T & evaluate for breath stacking (auto-PEEP). Consider ↓ PEEP or adjunct therapies for hypoxemia if decrease in PEEP causes desaturations.

Troubleshooting high resistance: Work outside (machine) to inside (alveoli); circuit problem, ETT kink/occlusion/biting, ETT obstructed/mainstem, large airway obstruction (mucous plug), small/medium airway obstruction (bronchospasm); auscultation & passing a suction catheter can quickly eliminate many of these.

Desaturations

- ☐ Is the endotracheal tube in good position? (consider CXR)
- ☐ Is the pulse oximetry waveform good quality?
- ☐ Is there acute hypotension? Evaluate for tension pneumothorax, air trapping and pulmonary embolism
- ☐ Is the source of oxygen faulty or is there an air leak? Check each connection/element sequentially from source of oxygen to the patient.
- ☐ Are there concomitant pressure elevations? If so, see "High Pressures" (next column)
- ☐ Is P:F <150 in setting of worsening ARDS? If so, consider adjunct therapies (above).
- ☐ Are there signs of infection? Consider ventilator-associated pneumonia.

Patient-Ventilator Dyssynchrony

- Detect signs of dyssynchrony: coughing, paradoxical breathing, ventilator alarms (low tidal volumes or high pressures), breath stacking.
- Treat underlying causes: 1) Ineffective triggering (patient or ventilator); 2) Inappropriate triggering (patient inspires while ventilator expires); 3) Auto-triggering (non-respiratory muscle movement triggers ventilator); 4) Flow dyssynchrony (too fast or too slow)

General Approach

- Treat pain or anxiety if present
- If ineffective ventilator triggering change trigger sensitivity, decrease VT or pressure
- Increase V_T to 8 mL/kg and increase flow rate if pressures allow. Consider change to decelerating flow delivery if setting available.
- If still dyssynchronous, paralyze patient (and sedate patient to RASS goal -5)

Discomfort & Delirium

Discomfort (pain, agitation, anxiety) & Delirium

Richmond Agitation Sedation Scale (RASS)

- Ensure appropriate analgesia & sedation to minimize ICU/IMV duration & risk of long-term neuropsychiatric impact.
- **Reassess every ≤4 hours using a standardized scale**
  - Goal RASS -4 to 0 in intubated patients
  - If RASS -4 tor -5 consider lightening sedation unless patient is paralyzed or dyssynchronous with ventilator.
  - Target RASS -5 for paralyzed patients. Never paralyze without sedation
- Perform Daily Sedation Interruptions (DSIs) in non-paralyzed patients to reassess sedation & analgesia needs, which can guide weaning these medications.

Delirium: Prevention & treatment of delirium reduces mortality and ICU/IMV duration

Confusion Assessment Method for the ICU (CAM-ICU)

- Screen every 12h using standardized tool (i.e. CAM-ICU)
- Treat delirium by addressing underlying causes (pain, agitation, anxiety, or physiologic derangements

Ventilator Weaning & Extubation

Spontaneous Breathhing Trial (SBT) Initiation Criteria & Considerations

- **Patient likely to trigger ventilator, stable $FiO_2 \leq 0.50$ adults (≤ 0.40 pediatrics) and PEEP ≤8**
- pH > 7.30. VE < 15 L/min
- ~MAP > 60 mmHg (minimal pressors)
- ICP: non-labile and < 20 mmHg w/ CPP > 60 mmHg
- No MI in previous ~48hr

Weaning Strategies

- Once daily SBT PS Δ5-7 cmH_2O if ETT size > 5 (Δ 8 cmH_2O if ETT 4-4.5; Δ 10 cmH_2O if ETT 3-3.5) in addition to PEEP 5-8 cmH_2O (2nd daily trial ok if failure sedation-related or due to transient issue); Consider additional Δ 3-5 cmH_2O of PS if HME used
- SBT x 30min ~probably as good as SBT x 2hr or longer for most adult patients
- If adult with cardiogenic pulmonary edema risk: Consider 15min T-piece (i.e. no PS or PEEP)
- RSBI (rapid Shallow Breathing Index) = f/V_T ; RSBI is **unreliable**; <80 goal for extubation; sensitive, not specific (if > 105, good predictor of failure)
- Coupling daily sedation interruption, early mobility, & SBT is associated with faster extubation

Extubation Criteria

- Have you fixed the original problem and **no upcoming procedures?**
- Adequate **oxygenation**? (PaO_2 > ~60 on PEEP ≤ 8 cmH_2O, $FiO_2 \leq 0.50$)
- Adequate **ventilation** without excessive **work of breathing?** ($\Delta PaCO_2$ ↑ of < 10 mmHg with remaining pH > 7.30 during SBT)
- **Secretions?** (assess cough strength, suction frequency & secretion volume)
- **Airway protection**? (assess gag, spontaneous cough and GCS)
  - Assess **risk of post-extubation airway obstruction:**
  - Consider cuff leak test if: intubation >6d, trauma, multiple intubations, prolonged prone, flat, volume overload, head/neck trauma, among others

  Cuff Leak Test: 1. pt must be sedated (interaction with vent = incr PIP= incr leak = false reassurance); **2.** Suction oropharynx; **3.** Initiate AC-VC V_T 8 mL/kg, RR 12, Ti: 1.5sec, Flow 50 LPM; **4.** Measure expired V_T; **5.** Deflate cuff and wait 6 breaths; **6.** Measure expired V_T (should ↓ by >110mL to predict low risk of stridor post extubation); **7.** Reinflate cuff

  - Decrease aspiration risk by holding tube feeds for safe interval (~6-8h)
  - Extubation criteria/goals for neuro patients may be different (e.g. visual tracking, swallowing, GCS>10, <40yo)
- **Hemodynamics -** re-intubation of an unstable patient can be lethal

Source: USAID-STAR-UCSF Open Critical Care Project.

11.4 Spontaneous breathing trial (SBT) order set

Last updated December 2021

Spontaneous Breathing Trial (SBT) Order Set

Surname/Family Name | Name | Attending/Team

Today's Date / / | Patient MRN/Registration # | Age | Sex | Predicted Weight (kg): | Height(cm)

SBT Initiation Criteria:

- FiO2 ≤ 0.50 and PEEP ≤ 8 or OI < 6 in pediatrics patients
- No ↑ in PEEP/FiO2 requirements over past 24hrs
- pH > 7.30 and no significant ↑MV required
- MAP: no significant vasopressor requirement
- ICP: non-labile and in normal range
- No myocardial infarction in previous ~48hr

Tube Feeds During SBT: ☐ Continue Tube Feeds ☐ Hold tube feedings _____hours prior to SBT. If patient fails SBT, resume immediately.

Standard SBT Strategy:

- Daily SBT until patient is extubated, or until at least 3 consecutive failed trials (see below).
- If failure is sedation related can repeat SBT later on same day
- When possible, coordinate with Daily Sedation Interruption/Spontaneous Awakening Trial (adults only)
- Suspend SBT on days when weaning readiness criteria are not met (see protocol for details).
- May withhold SBT for pending special procedures / surgery.

Mode:

- ☐ Default if ETT size > 5mm, Pressure Support (PS) = delta 5-7 cmH2O above PEEP of 5-8 cmH2O; FiO2 ≤ 0.50
- ☐ Default if ETT size 4-4.5mm, Pressure Support (PS) = delta 8 cmH2O above PEEP of 5 cmH2O; FiO2 ≤ 0.50
- ☐ Default if ETT size 3-3.5mm, Pressure Support (PS) = delta 10 cmH2O above PEEP of 5 cmH2O; FiO2 ≤ 0.50
- ☐ T-piece Trial (Consider if resolving cardiogenic pulmonary edema - *Adults only*)
- ☐ CPAP (Consider when VT > 10 mL/kg - *Adults only*)
- ☐ PS = _____ PEEP=_____ FiO2=_____

Duration: ☐ 30 minutes ☐ 2 hours

- Initial intolerance of SBT: PS can be titrated down from PS of 15-20 to SBT settings over 5-30 min.
- Evaluation: RT at bedside for initial 5 min until a 30 min SBT is passed. Full Vent check @ 30 min or 2 hrs.
- Failure Criteria Met: Return to previous ventilator settings (or new written orders for post-SBT). When ARDS Net protocol is in place resume previous ARDS Net settings.

After SBT Passed: ☐ Notify ICU team to evaluate for extubation ☐ Extended SBT as tolerated ☐ Return to prior settings

When Tracheostomy tube is present: Follow orders as written above. When patient passes a 2hr SBT, then:

- ☐ Extend SBT as tolerated if failure criteria met, then return to prior settings
- ☐ Tracheostomy Mask Trials at FiO2 ≤ 0.50 as tolerated. If failure criteria met, then return to SBT PS settings. If these PS settings also are not tolerated then return to prior or newly ordered vent settings.

Difficult to Wean: Initiate only after 3 consecutive SBT failures

PS Range: delta PS 5-20 cmH20 above PEEP 5-8 cm H20; Fi02 ≤ 0.50
Titrate PS as needed to maintain spontaneous RR 25-35 (1-1.5x age adjusted normal) and VT 5-8 mL/kg
Daily Routine: After 2 hrs of stable breathing pattern at a stable PS level, then:

- ☐ PS Decrement challenge: reduce by 3-5 CmH20 every 2-4 hrs
- ☐ Trial Duration: not to exceed _____ hrs/day
- ☐ Notify ICU team when patient passes 2 hr SBT at standard PS settings to evaluate for extubation

Cuff Leak Check: Consider if: intubation > 6 days, neck trauma, multiple intubations, prolonged prone positioning, volume overload

☐ Perform cuff leak PRIOR TO SBT ☐ No cuff leak necessary

1. Pt must be sedated (interaction with vent can incr PIP which can incr leak = false reassurance)
2. Suction oropharynx
3. Initiate AC-VC VT 8 mL/kg, RR 12, Ti: 1.5sec, Flow 50 LPM
4. Measure expired VT
5. Deflate cuff and wait 6 breaths
6. Measure expired VT expired VT (goal is ↓ by >110mL in measure expired VT for adults)
7. Re-inflate cuff

Alternative approach (pediatrics):

1. Sedate patient and suction oropharynx
2. Connect patient to resuscitation bag
3. Place stethoscope over larynx and listen
4. Slowly deflate ETT cuff completely w/cuff manometer
5. Give a breath by slowly squeezing the bag, increasing pressure until audible leak is heard
6. If pressure reaches 30 cmH20 without a leak = failure; if pressure <12 cmH20 with leak = pass; if pressure >20 cm H20 then patient likely to fail
7. Reinflate cuff and resume prior settings

Date (time): _____ **Name:** _____ **Signature:** _____ **Contact #:** _____

TO PRINT MORE Forms scan here

TO LEARN MORE check out this algorithm for SBT, SAT and cuff leak

Source: USAID-STAR-UCSF Open Critical Care Project.

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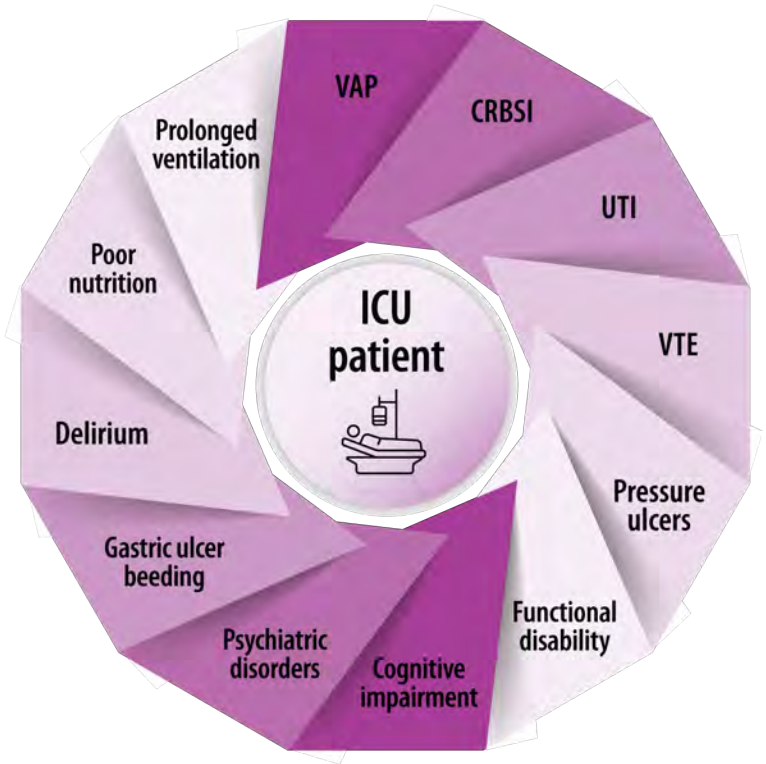
12 Best practices to prevent complications

12 Best practices to prevent complications

Summary

ICU patients are at high risk for complications. This chapter provides tools for implementation of key interventions to reduce the risk of complications in the ICU which include:



Notes: CRBSI – catheter-related bloodstream infection; UTI – urinary tract infection; VAP – ventilator-associated pneumonia; VTE – venous thromboembolism.

Tools

12.1 Interventions to prevent complications in hospitalized and critically ill patients with COVID-19

See WHO *COVID-19 Clinical management: living guidance* (2021).

Anticipated outcome	Interventions
Reduce days of **invasive mechanical ventilation**	• Use weaning protocols that include daily assessment for readiness to breathe spontaneously • Minimize continuous or intermittent sedation, targeting specific titration endpoints (light sedation unless contraindicated) or with daily interruption of continuous sedative infusions • Early mobilization • Implementation as a bundle of care
Reduce incidence of **ventilator-associated pneumonia (VAP)**	• Oral intubation is preferable to nasal intubation in adolescents and adults • Keep patient in semi-recumbent position (head of bed elevation 30–45°) • Use a closed suctioning system; periodically drain and discard condensate in tubing • Use a new ventilator circuit for each patient; once patient is ventilated, change circuit if it is soiled or damaged, but not routinely • Change heat moisture exchanger when it malfunctions, when soiled, or every 5–7 days
Reduce incidence of **catheter-related bloodstream infection (CRBSI)**	• Use a checklist with completion verified by a real-time observer as a reminder of each step needed for sterile insertion and as a daily reminder to remove catheter if no longer needed
Reduce incidence of **pressure ulcers**	• Turn patient every 2 hours
Reduce incidence of **stress ulcers and GI bleeding**	• Give early enteral nutrition (within 24–48 hours of admission) • Administer histamine-2 receptor blockers or proton-pump inhibitors in patients with risk factors for GI bleeding. Risk factors for GI bleeding include: – mechanical ventilation for ≥ 48 hours – coagulopathy – renal replacement therapy – liver disease – multiple comorbidities – higher organ failure score
Reduce the development of **antimicrobial resistance**	Utilize de-escalation protocols as soon as patient is clinically stable and there is no evidence of bacterial infection
Reduce the development of **adverse drug effects**	Expose patient to empiric antimicrobial therapy for the shortest time possible, to prevent nephrotoxicity, cardiac and other side-effects from unnecessary antimicrobial use
Promote appropriate **antimicrobial prescribing and use during the COVID-19 pandemic**	Do not prescribe antibiotics to suspected or confirmed COVID-19 patients with low suspicion of a bacterial infection, to avoid more short-term side-effects of antibiotics in patients and negative long-term consequences of increased antimicrobial resistance

12.2 Checklist for central venous catheter (CVC) insertion

☑ In the literature, a research collaborative found that **using a central line checklist** as a reminder for the inserter **significantly reduced the incidence of central venous catheter-related blood stream infections.** This checklist is adapted from *An intervention to decrease catheter-related blood stream infections in the ICU* (Provonost et al., 2006).

☐ Patient verification, allergies and informed consent.

☐ Hand hygiene before the procedure.

☐ Wear maximal barrier precautions on insertion: full
- ☐ sterile gown
- ☐ face mask
- ☐ face shields
- ☐ sterile gloves
- ☐ hair cover
- ☐ cover the patient in a full sterile sheet from head to toe.

☐ Use chlorhexidine 2% in 70% isopropyl alcohol for skin preparation and apply in a back and forth friction rub motion for 30 seconds.

☐ Let dry completely before puncturing site. It should not be blotted dry.

☐ Choose the optimal site: subclavian or internal jugular vein preferred in adults; internal jugular or femoral vein preferred in children depending on age.

☐ Once in place, evaluate the continuing need for the central line on a daily basis.

☐ Remove line immediately when no longer needed or when non-functional.

12.3 Checklist for preventing ventilator-associated pneumonia (VAP)

☑ In order to prevent VAP, a complication of endotracheal intubation and invasive mechanical ventilation, consider the following procedures, when possible:

- ☐ Oral intubation instead of nasal intubation.
- ☐ Keep the patient in a semi-recumbent position (head of bed elevated up to ≥ 30–45°).
- ☐ Use a closed suctioning system.
- ☐ Periodically drain and remove condensation in tubing.
- ☐ Use a new ventilator circuit for each patient. Change if soiled or damaged.
- ☐ Do not routinely change ETT or ventilator circuit, only if they malfunction.
- ☐ Change heat and moisture exchanger when malfunctions, soiled, or every 5–7 days.
- ☐ Perform regular antiseptic oral care with chlorhexidine gel or mouthwash.
- ☐ Discontinue invasive ventilation in a safe and prompt manner: Daily
  - ☐ sedation interruption of continuous sedative infusions. Daily evaluation for SBT readiness (see Chapter 11).
  - ☐ Extubation to non-invasive ventilation when appropriate (i.e. primarily for patients ventilated because of a COPD exacerbation, and only in centres with sufficient expertise in non-invasive ventilation).
  - ☐ ABCDE bundle.

Note: Note: Heat and moisture exchangers (HME) are not routinely used in infants and small children as they significantly increase dead space. Use heated humidifiers instead.

When HMEs are used, ensure the size of the selected filter is appropriate for the size of the patient to minimize dead space and calculate/account for increased dead space in the circuit when choosing ventilator settings (and target minute ventilation).

12.4 Checklist for preventing urinary tract infections (UTI)

☑ Prevention of UTI requires an appropriate technique for catheter insertion as well as appropriate management of indwelling catheters. Consider the following procedures when possible:

Catheter insertion

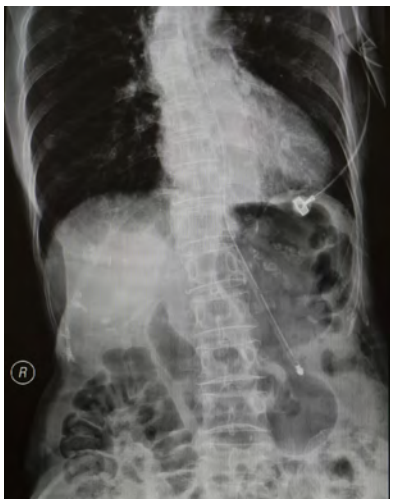
- ☐ Insert catheter only when necessary.
- ☐ Hand hygiene before procedure.
- ☐ Use aseptic technique and sterile equipment.
- ☐ Use as small a catheter as possible, consistent with proper drainage.

Catheter management

- ☐ Maintain unobstructed urine flow.
- ☐ Empty collection bag regularly:
  - ☐ Separate collecting container for each patient.
  - ☐ Do not allow draining spigot to touch collecting container.
- ☐ Keep collecting bag below level of bladder at all times.
- ☐ Cleaning urethral meatus with antiseptic is unnecessary. Routine cleaning is adequate.
- ☐ Secure catheter to prevent movement and urethral traction.
- ☐ Sterile, continuously closed drainage system.
  - ☐ Do not disconnect catheter and drainage tube unless catheter must be irrigated.
  - ☐ Replace collecting system aseptically and after disinfecting catheter-tubing junction if the following occur:
    - break in aseptic technique
    - disconnection
    - leakage.
- ☐ Daily check and remove as soon as there is no indication.

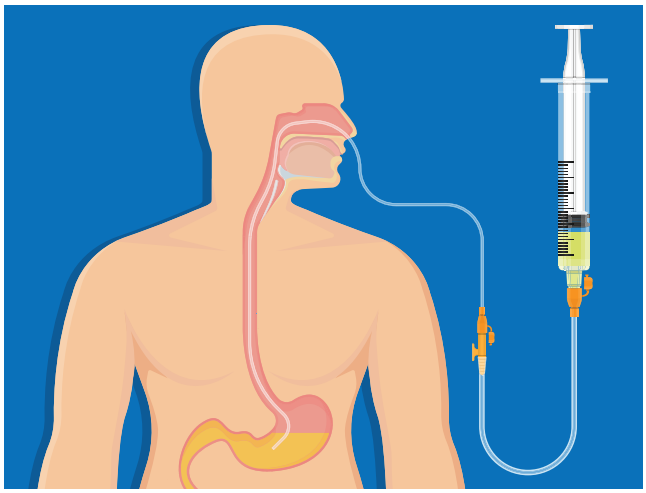
12.5 Procedure for providing enteral nutrition (EN) for adults

The goal is to start enteral nutrition, even in small volumes, as soon as the patient is stable.



This tool can be used to start enteral nutrition.

1. Place a feeding tube.
2. Confirm placement with radiograph (gastric [NG] or small bowel [NJ] feeding are acceptable).
3. Once the feeding tube has been confirmed, start with an infusion of up to **30 mL/hr of clear fluid or feed**.
4. Aspirate the NG tube every 4 hours.
5. Gradually increase the volume of feed with the aim of building up to full feeding within 48 hours.



Feeding intolerance

Intolerance of feeding may result from poor gastric emptying and lead to high residual gastric volumes.

The absolute value that is too high and should prompt cessation of tube feeds is not clear.

Stop feeding when:

- volumes high (between 250–500 mL)
- clinical signs of intolerance (abdominal pain, abdominal distension and diarrhoea).

None of the features are specific for feed intolerance.

Possible treatments include advancing the feeding tube into the small bowel (can be done at the bedside) or adding prokinetic medications (e.g. metoclopromide intravenously).

Note: With an NJ tube, only continuous feeds can be delivered (no bolus) and residuals cannot be checked.

Set caloric target and aim to reach this within a few days

Estimate the patient's daily caloric needs, or basal energy expenditure (BEE). Adjust for fever and stress:

- BEE (kcal/day) = 25 × body weight (kg)
- fever: BEE × 1.1 (for each degree above the normal body temperature)
- mild to moderate stress: BEE × 1.2–1.4
- moderate to severe stress: BEE × 1.4–1.6.

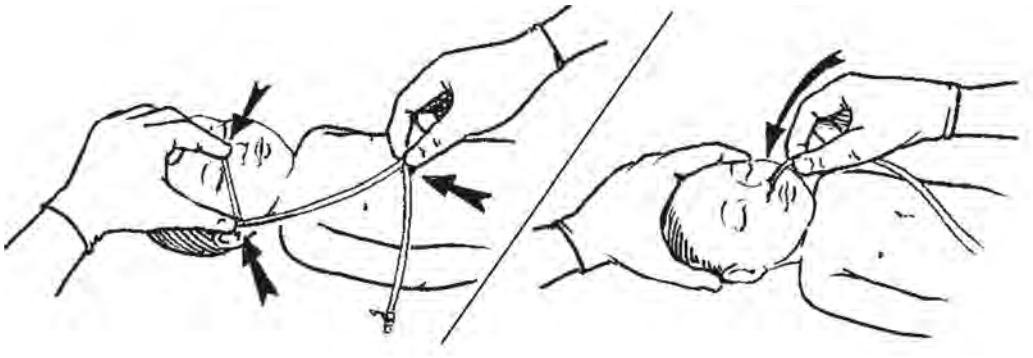
Estimate your patient's daily protein requirements:

- normal 1.2– 2.0 g/kg
- hypercatabolism: 2–3 g/kg
- ratio of non-protein calories to nitrogen (70:1–100:1).

Note: Hypocaloric feeding (40–60% of non-protein caloric needs) may be as beneficial as full caloric feeds (> 70%).

12.6 Procedure for providing enteral nutrition (EN): paediatric considerations

Enteral feeding via NG tube is the preferred method of providing maintenance fluid.



Source: Pocket book of hospital care for children (WHO, 2013).

Initial fitting

1. Measure the distance from the nose to the ear and then to the epigastrium.
2. Insert NG tube to the measured distance.
3. Check correct placement of tube:
   - check the pH of aspirate using pH indicator strips
   - position can be seen on chest X-ray
   - if in doubt remove and replace.
4. Secure the NG tube by taping to the cheek avoiding upwards pressure on the nares.
5. Once correct placement has been confirmed, flush the tube with water. It is now safe to use the tube for administration of feed and medication.
6. Flush the NG tube with sterile water after administration of NG drugs otherwise it will block.

Ongoing checks

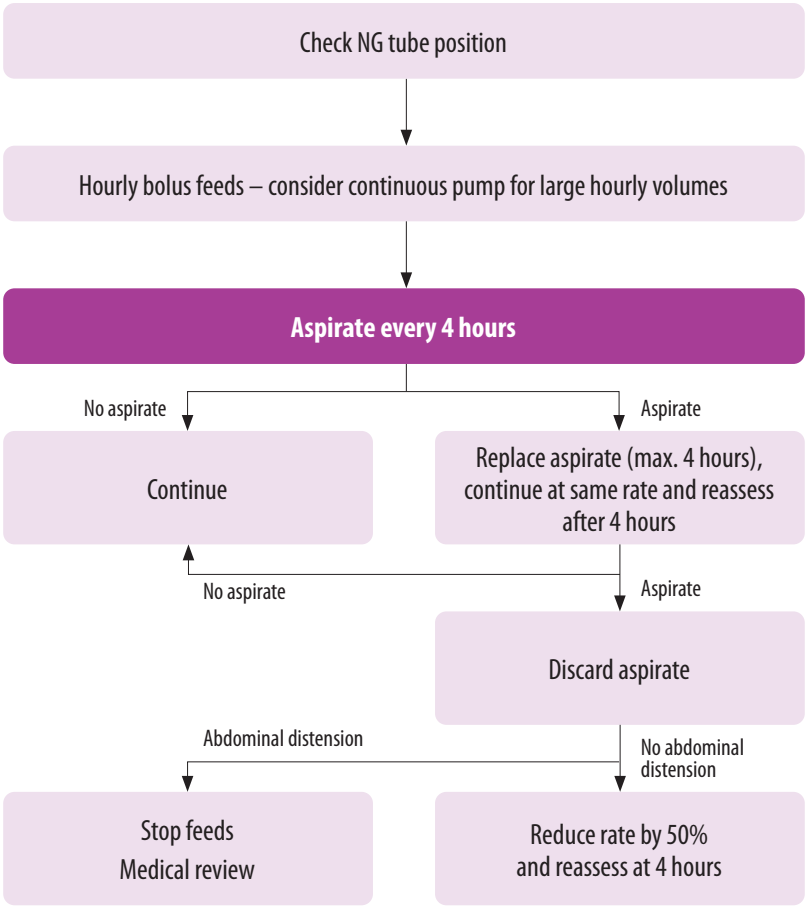
Check the position of the NG tube:

- before each use
- every 6 hours if continuous feeds
- after episodes of vomiting or retching, increased respiratory distress or excessive coughing
- if the tube looks dislodged (i.e. with more tubing visible).

NG tube sizes

This is only a rough guide; the bore of tube must fit easily in the child's nostril.

Description of patient	Tubes sizes
< 2 kg, preterm	4 Fr
2–4 kg	6 Fr
Term to 1 year	8 Fr
Younger children	10 Fr
Older children and adolescents	12 Fr
Small adult	14 Fr
Large adult	16 Fr


Check NG tube position
Hourly bolus feeds – consider continuous pump for large hourly volumes
Aspirate every 4 hours
No aspirate
Aspirate
Continue
Replace aspirate (max. 4 hours), continue at same rate and reassess after 4 hours
No aspirate
Aspirate
Discard aspirate
Abdominal distension
No abdominal distension
Stop feeds
Medical review
Reduce rate by 50% and reassess at 4 hours

12.7 Algorithm for early mobility in the ICU

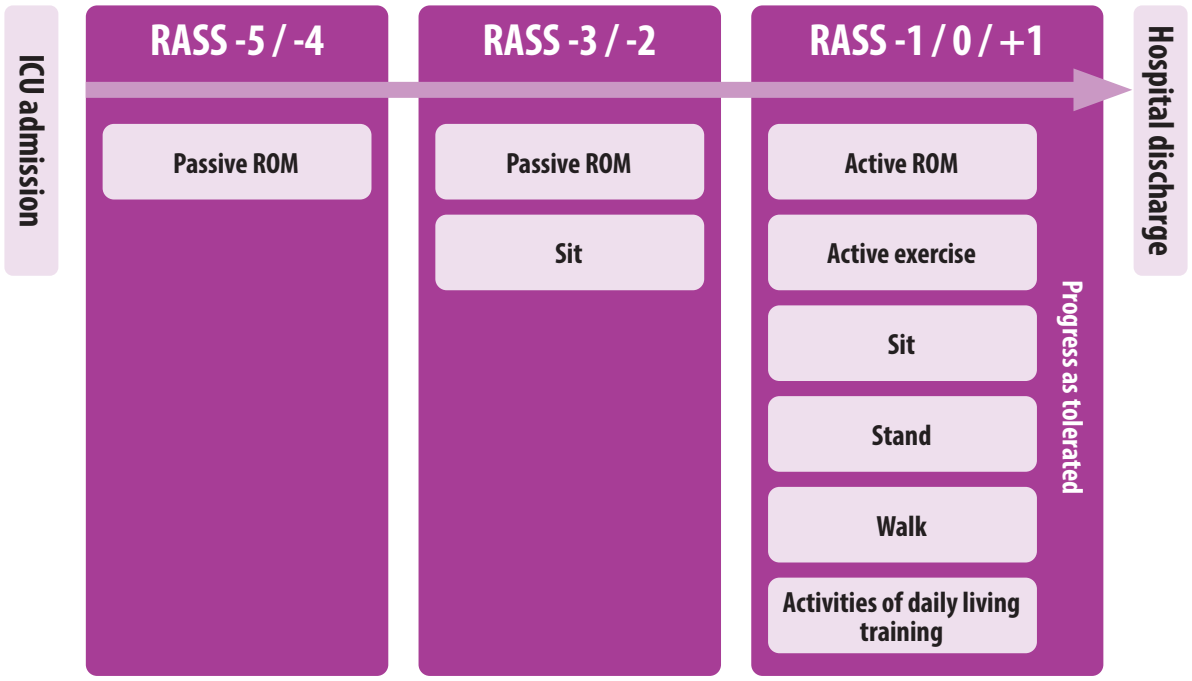
An adapted early mobility algorithm is presented below. It is adapted from Balas et al. (2014).

The patient's level of consciousness will be determined prior to the daily physical rehabilitation session using the Richmond Agitation-Sedation Scale.

- **A patient who is only arousable to physical stimulation (RASS -4/-5**) will undergo passive range of motion (ROM) exercises.
- **Once a patient can open their eyes to voice (RASS -2/-3),** passive ROM exercises will be performed, and the patient will be placed in the chair position in bed.
- Finally, **once a patient is alert and calm (RASS -1/+1),** they will progress from active ROM up through ambulation as they are able.

Sessions will continue until hospital discharge or a patient meets certain functional milestones. Early mobility in select intubated patients is feasible when adequate staff are available and safety assessment has been completed.

Physical rehabilitation protocol



12.8 Thromboembolic prophylaxis in COVID-19

Coagulopathy is common in patients with severe COVID-19, and both venous and arterial thromboembolism have been reported.

Monitor patients with COVID-19 for signs or symptoms suggestive of thromboembolism, such as stroke, deep vein thrombosis, pulmonary embolism or acute coronary syndrome. If these are clinically suspected, proceed immediately with appropriate diagnosis and management pathways.

In hospitalized patients with COVID-19 without an established indication for higher dose anticoagulation, WHO recommends to administer standard thromboprophylaxis dosing of anticoagulation (rather than therapeutic or intermediate dosing).

Type of heparin	Dose	Comments
Enoxaparin	40 mg/day SC	Clinical observation if < 45 kg (women) or < 57 kg (men): risk of bleeding
		BMI > 40 mg/m^2 or weight >120 kg: 40 mg/12h SC
Unfractionated heparin (UFH)	5000 units/12h or 8h SC	BMI > 40 mg/m^2 or weight >120 kg: 7500 units/12h or 5000 units/8h
Tinzaparin	4500 units/day SC	BMI > 40 mg/m^2 or weight >120 kg: 9000 units/day
Dalteparin	5000 units/day SC	BMI > 40 mg/m^2 or weight >120 kg: 5000 units/12h
Fondaparinux	2.5 mg/day SC	

Notes:
SC – subcutaneous injection.
In renal failure, reduce dose of low molecular weight heparin (LMWH) (except dalteparin).
Patients on thromboprophylaxis dosing of anticoagulation do not require monitoring, except for platelet count monitoring after 5–7 days if UFH is used.
Dosing should be adjusted according to body weight/BMI and renal function according to local protocols.

Use mechanical prophylaxis if moderate VTE risk, in patient at risk of bleeding:
- intermittent pneumatic compression devices;
- graduated compression stockings.

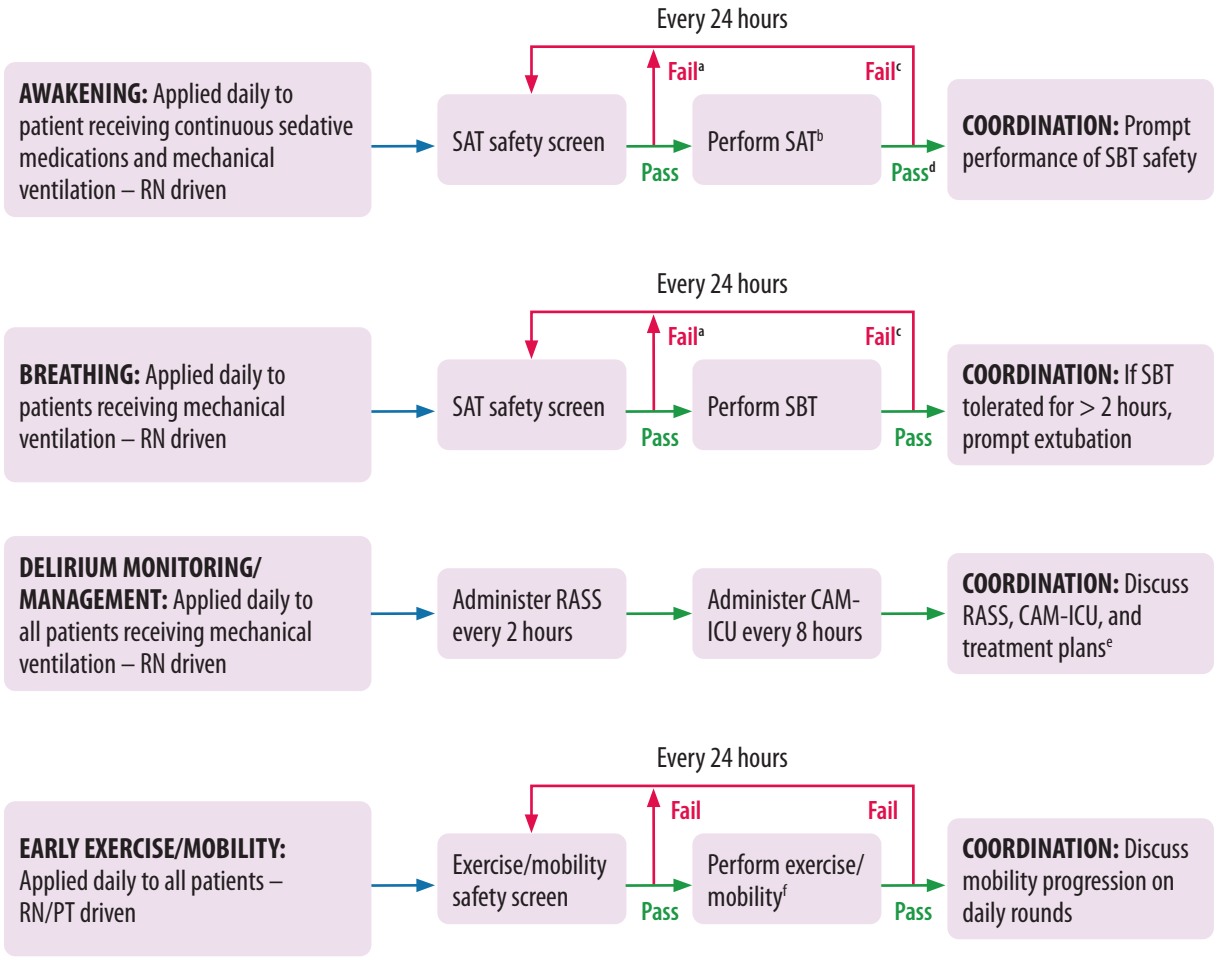
Switch to pharmacologic agent once risk of bleeding has decreased.

12.9 ABCDE bundle

This algorithm is adapted from Balas et al. (2014). Implementing this bundle reduced the time patients spent on invasive mechanical ventilation by 3 days. Additionally, patients experienced less delirium and were more likely to be mobilized.

Adapt this bundle to fit your ICU and implement using a quality improvement mechanism.

ABCDE bundle algorithm



Notes:

[a] Continuous sedative medications maintained at previous rate if spontaneous awakening trail (SAT) safety screen failure. Mechanical ventilation continued, and continuous sedative medications restarted at half the previous dose only if needed due to SBT safety screen failure.

[b] Continuous sedative infusions stopped, and sedative boluses held. Bolus doses of opioid medications allowed for pain. Continuous opioid infusions maintained only if needed for active pain.

[c] Continuous sedative medications restarted at half the previous dose, and then titrated to sedation target if SAT failed. Interdisciplinary team determines possible causes of SAT/SBT failure during rounds. Mechanical ventilation restarted at previous settings, and continuous sedative medications restarted at half the previous dose only if needed if SBT failed.

[d] SAT pass if the patient can open their eyes to verbal stimulation without failure criteria (regardless of trial length) or does not display any of the failure criteria after 4 hours of shutting off sedation.

[e] Each day on interdisciplinary rounds, the RN will inform the team of the patient's target RASS score, actual RASS score, CAM-ICU status, and sedative and analgesic medications the patients is receiving. If delirium is detected, team will discuss possible causes, eliminate risk factors, and employ non-pharmacologic management strategies.

[f] Each eligible patient is encouraged to be mobile at least once a day, with the specific level of activity geared to their readiness. Patients progress through a three-step process, embarking on the highest level of physical activity they can tolerate. Progress includes sitting on edge of bed, standing at bedside and sitting in chair, and walking a short distance. Use of the protocol ends when the patient is discharged from the ICU.

CAM-ICU = confusion assessment method for the intensive care unit; PT – physical therapist; RASS – Richmond Agitation-Sedation Scale; RN – registered nurse; RT – respiratory therapist; SAT – spontaneous awakening trial; SBT – spontaneous breathing trial.

ABCDE bundle safety screen questions and success/fail criteria

ABCDE bundle component	Safety screen criteria: conditions for exclusion	Pass/fail criteria: conditions denoting failure
Spontaneous awakening trial	1. Active seizures 2. Alcohol withdrawal 3. Neuromuscular blockade 4. Control of increased ICP 5. ICP > 20 mmHg 6. Receiving ECMO 7. Documentation of MI in past 24 hours 8. Current RASS > 2	1. RASS score > 2 for ≥ 5 minutes 2. Pulse oximetry < 88% for ≥ 5 minutes 3. Respirations > 35 BPM for ≥ 5 minutes 4. Acute cardiac arrhythmia 5. ICP > 20 mmHg 6. Two or more of the following: (heart rate increase ≥ 20 BPM, heart rate < 55 BPM, use of accessory muscles, abdominal paradox, diaphoresis or dyspnoea)
Spontaneous breathing trial	1. Chronic ventilator dependence 2. Pulse oximeter reading < 88% 3. FiO_2 > 50% 4. Set PEEP > 7 5. ICP > 20 mmHg 6. Receiving mechanical ventilation in attempt to control ICP 7. Documentation of MI in past 24 hours 8. Increasing doses of vasopressor medications 9. Lack of inspiratory effort	1. RR > 35 BPM for ≥ 5 minutes 2. RR < 8 3. Pulse oximetry < 88% > 5 minutes 4. ICP > 20 mmHg 5. Mental status changes 6. Acute cardiac arrhythmia 7. Two or more of the following: • use of accessory muscles • abdominal paradox diaphoresis • dyspnoea
Early exercise/ mobility	1. RASS -3 2. FiO_2 > 0.6 3. Set PEEP > 10 cmH_20 4. Increasing doses of vasopressor infusions in the last 2 hours 5. Evidence of active MI 6. Administration of a new antiarrhythmic agent 7. Receiving therapies that restricted mobility (e.g. ECMO, open-abdomen, etc.) 8. Injuries in which mobility is contraindicated (e.g. unstable fractures, etc.)	1. Symptomatic drop in mean arterial pressure 2. Heart rate < 50 or > 130 BPM ≥ 5 minutes 3. RR < 5 or > 40 BPM ≥ 5 minutes 4. Systolic blood pressure > 180 mmHg ≥ 5 minutes 5. Pulse oximetry < 88% ≥ 5 minutes 6. Marked ventilator dyssynchrony 7. Patient distress 8. New arrhythmia or evidence of active MI 9. Concern for airway device integrity or endotracheal removal 10. Fall to knees

Notes: ABCDE – Awakening and Breathing Coordination, Delirium Monitoring/Management and Early Mobility Bundle; BPM – beats per minute; ECMO – extracorporeal membrane oxygenation; FiO_2 – fraction of inspired oxygen; ICP – intracranial pressure; MI – myocardial ischaemia; PEEP – positive end-expiratory pressure; RASS – Richmond Agitation-Sedation Scale; RR – respiratory rate.

Bedside checklist for ABCDE protocol

Date:_____/_____/_____

A B C Awakening and Breathing Coordination

	Check if yes or indicate reasons
SAT screen passed? If not, why?	
SAT done? If not, why?	
SBT screened passed? If not, why?	
SBT done? If not, why?	
SAT and SBT coordinated/paired?	

D Delirium nonpharmacologic interventions

Intervention	Check if done
Pain assessment/management	
Orientation	
Sensory (eyes/ears)	
Sleep (nonpharm)	
Check any intervention that was performed during your shift (including night shift)	

E Early Exercise and mobility

Intervention	Check if done
Active ROM	
Sitting up on side of bed	
Standing	
Walking	
Check any level of activity the patient performed during your shift (including night shift)	

Notes: ROM – range of motion; SAT – spontaneous awakening trial; SBT – spontaneous breathing trial.

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13 Quality in critical care

13 Quality in critical care

Summary

Quality elements	Description
Safety	Avoiding harm to people for whom the care is intended.
Timeliness	Reducing waiting times and sometimes harmful delays for both those who receive and those who give care.
Effectiveness	Providing evidence-based health care services to those who need them.
Efficiency	Maximizing the benefit of available resources and avoiding waste.
Equity	Providing care that does not vary because of age, sex, gender, race, ethnicity, geography, religion, socio-economic status, linguistic or political affiliation.
Patient-centredness	Providing care that responds to individual preferences, needs and values in health services that are organized around the needs of people.

Systematic and continuous quality improvement work is essential because health care delivery is complex and imperfect, even with the best efforts. Quality measures are related to ICU resources/structure, processes of care and patient outcomes. The focus should be on processes of care, instead of hard-to-measure outcomes.

Use the iterative, real-time, **plan-do-act-check** cycle to test changes/improvement.

Create an inclusive team and culture of change for a successful and sustainable quality improvement programme.

See further information on quality interventions see the WHO *Handbook for national quality policy and strategy* ( ).

Tools

13.1 Checklist for ICU daily best practices
13.2 Surviving Sepsis Campaign bundles
13.3 Checklist for high-quality use of invasive mechanical ventilation for ARDS
13.4 Process for selecting problem to focus on in the ICU and quality improvement process
13.5 Checklist for initiating, improving, evaluating and sustaining a quality improvement programme

13.1 Checklist for ICU daily best practices

ICU Daily Rounding Checklist			
Can **sedation** be reduced?	❑ Yes	❑ NA	❑ No
Can **analgesia** be reduced?	❑ Yes	❑ NA	❑ No
Is **delirium** being assessed, addressed and prevented?	❑ Yes	❑ NA	❑ No
Spontaneous awakening trial and/or **Spontaneous breathing trial** candidate?	❑ Yes	❑ NA	❑ No
Total **fluid balance goal** reviewed? And targeting: _____ [12h] [24h]	❑ Yes	❑ NA	❑ No
Is the patient at goals for **lung protective ventilation**?	❑ Yes	❑ NA	❑ No
Head of bed elevation (30 degrees)	❑ Yes	❑ NA	❑ No
Skin breakdown assessment (prevention) completed	❑ Yes	❑ NA	❑ No
Is enteral **nutrition** at goal?	❑ Yes	❑ NA	❑ No
Is blood **glucose** at goal?	❑ Yes	❑ NA	❑ No
Deep venous thrombosis prophylaxis?	❑ Yes	❑ NA	❑ No
Gastric ulcer prophylaxis? If coagulopathy (INR>1.5, PTT>2x normal, Plt < 50k), mechanical ventilation > 48h, history of GI bleed/ulcer within past year, TBI, SCI or burn, or if ≥2 minor risk factors (sepsis, ICU stay >1 week, occult GI bleed > 6 days, glucocorticoid therapy, NSAID use, antiplatelet use)	❑ Yes	❑ NA	❑ No
Can **Antibiotics** be narrowed or discontinued?	❑ Yes	❑ NA	❑ No
Early **mobility** candidate and physical therapy consulted?	❑ Yes	❑ NA	❑ No
Is **foley** catheter needed?	❑ Yes	❑ NA	❑ No
Is **central venous/arterial catheter** needed?	❑ Yes	❑ NA	❑ No
Has the **family** been updated?	❑ Yes	❑ NA	❑ No
Are the patient's **goals** of care and code status current?	❑ Yes	❑ NA	❑ No

TBI - traumatic brain injury; SCI - spinal cord injury; GI - gastrointestinal; PT - physical therapy; Plt - platelet; NSAID - non steroidal anti-inflammatory drugs.

DISCLAIMER: This tool is intended to serve as a framework for local modification in accordance with local resources, standards and guidelines. This is intended to be educational in nature and is not a substitute for clinical decision making based on the medical condition presented. It is the responsibility of the user to ensure all information contained herein is current and accurate by using published references. Table based in part on ABCDEF Guidelines - *Critical Care Medicine*, 2018

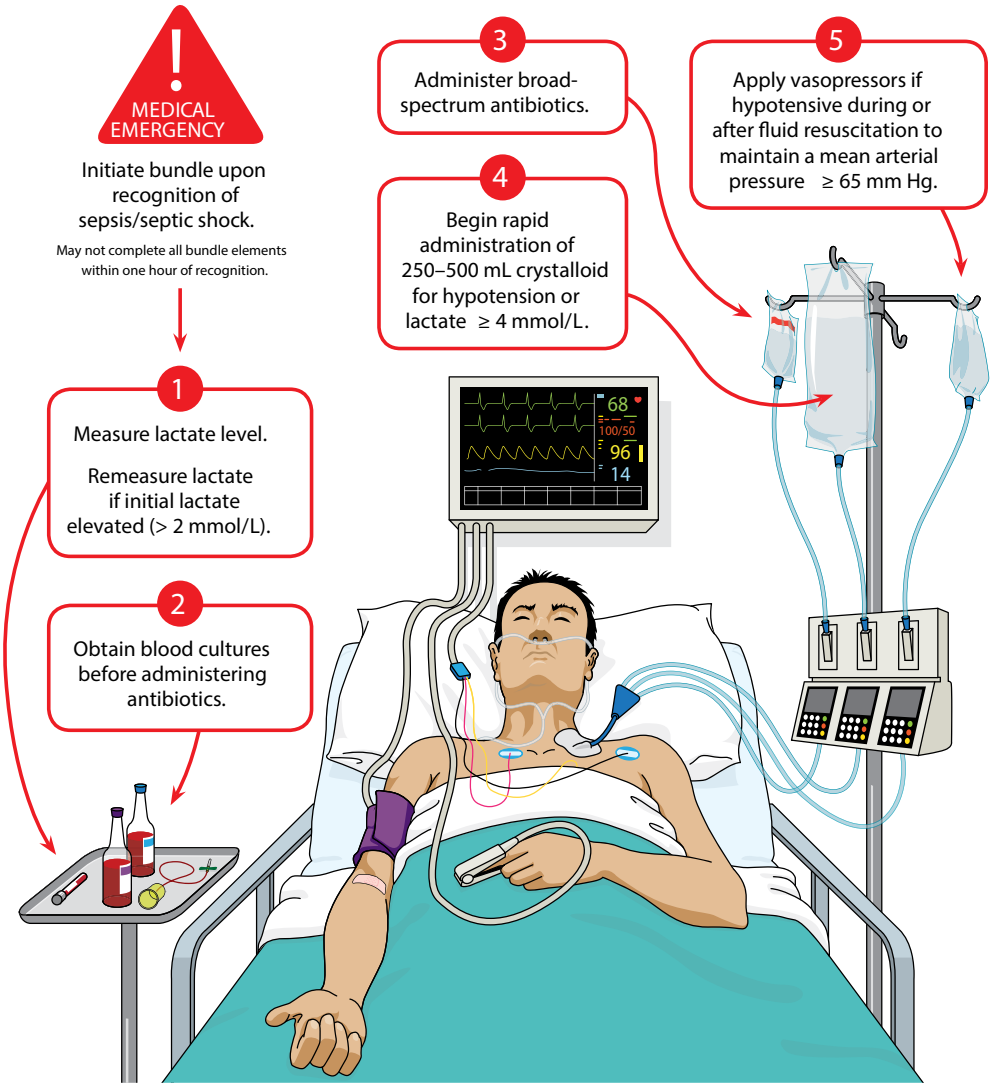
Source: Open Critical Care Project ().

To DOWNLOAD or PRINT more

13.2 Surviving Sepsis Campaign bundles

Hour-1 bundle: initiate bundle upon recognition of sepsis/septic shock

May not complete all elements within first hour.



Remember

1. Act quickly upon sepsis and septic shock recognition;
2. Minimize time to treatment – sepsis and septic shock are medical emergencies;
3. Monitor closely for response to interventions;
4. Communicate sepsis status in hand-offs.

Consider using an adapted version of this tool to monitor performance for sepsis care. This bundle was recently revised based on the most recent version of these tools. See the Surviving Sepsis Campaign – adult patients website for full details.

The Paediatric Surviving Sepsis Campaign Bundle can be found in Chapter 8 (Tool 8.6) or on the Surviving Sepsis – paediatric patients website.

13.3 Checklist for high-quality use of invasive mechanical ventilation for ARDS

☑ Consider using this tool if you are using IMV to deliver quality care to your patients with ARDS.

Technical competence

- ☐ Type of mechanical ventilator available.
- ☐ Able to deliver internal PEEP 5–20 cmH_2O.
- ☐ Able to measure plateau airway pressure.
- ☐ Able to deliver FiO_2 100%.
- ☐ Able to titrate FiO_2.
- ☐ Able to titrate tidal volumes from 4–10 mL/kg.
- ☐ Intubation equipment readily available. See full WHO specifications for mechanical ventilators (☝).
- ☐ Infection prevention materials readily available (airborne precautions). Skilled person to intubate available.
- ☐ Skilled personnel to use and troubleshoot IMV. Arterial blood gas analyser available and working. Pulse oximeter available and working.
- ☐ Supply chain for ventilator consumables (circuits, filters).
- ☐ Skilled personnel and equipment for biomedical/ventilator troubleshooting and preventive maintenance.

Safety

- ☐ Protocols and equipment for difficult airway (e.g. backup personnel, equipment and plan – e.g. cricothyrotomy).
- ☐ Plan for IMV complications (e.g. chest tube for pneumothorax, sedation for agitation).
- ☐ Protocols for prevention while on IMV (e.g. daily SBT evaluation, daily sedation interruption, VAP prevention).
- ☐ Protocols for lung protective ventilation. See OpenCritical Care Respiratory care order set (protocol) templates (☝).

Process measures

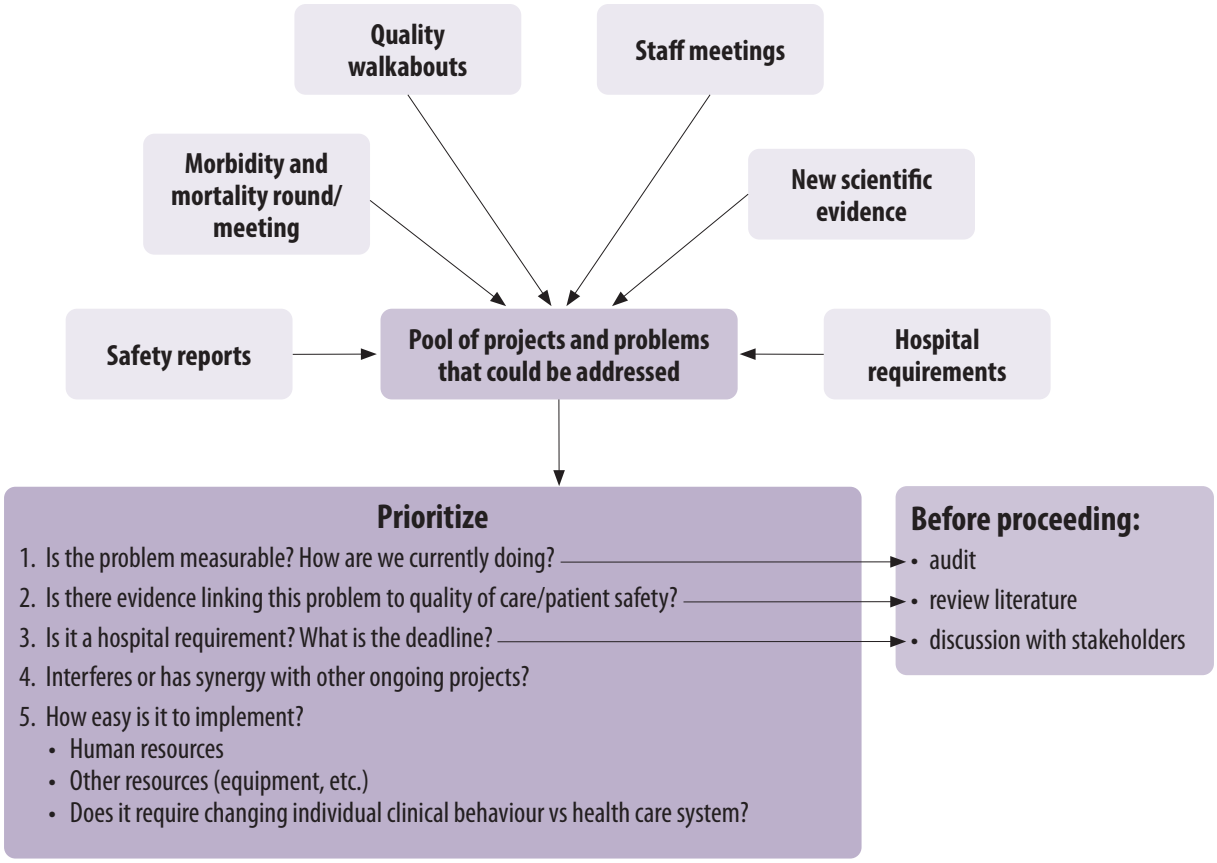
- ☐ Process measures (e.g. lung protective targets met).

Outcome measures

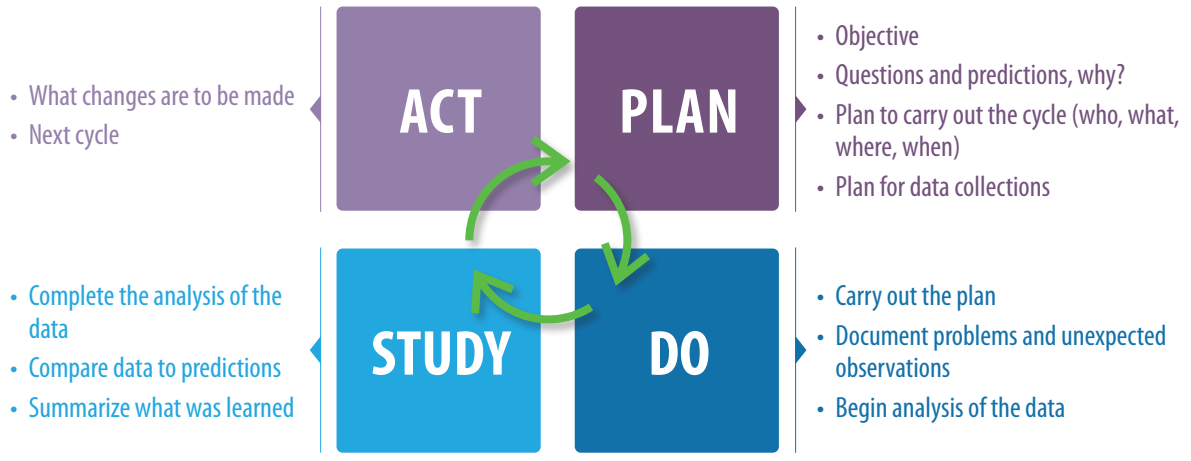
- ☐ Complications (e.g. VAP, pneumothorax).

13.4 Process for selecting problem to focus on in the ICU and quality improvement process

This flowchart provides a framework for selecting a problem to focus on for quality improvement among the many that might be considered.



Essential steps in the **plan-do-study-act** cycle:



Source: Adapted from Dr Andre Amaral, Sunnybrook Health Sciences Centre and University of Toronto, Canada.

13.5 Checklist for initiating, improving, evaluating and sustaining a quality improvement programme

☑ This checklist provides steps for initiating, improving, evaluating and sustaining a quality improvement programme in the ICU (adapted from Curtis et al., 2006).

Initiating or improving a quality improvement programme

- ☐ Do background work: identify motivation, support team and develop strong leadership. Prioritize potential projects and choose the projects to begin.
- ☐ Prepare for the project by operationalizing the measures, building support for the project and developing a business plan.
- ☐ Do an environmental scan to understand the current situation (structure, process or outcome), the potential barriers, opportunities and resources for the project.
- ☐ Create a data collection system to provide accurate baseline data and document improvement.
- ☐ Create a data reporting system that will allow clinicians and other stakeholders to see and understand the problem and the improvement.
- ☐ Introduce strategies to change clinician behaviour and create the change that will produce improvement.

Evaluating and sustaining a quality improvement programme

- ☐ Determine whether the target is changing with ongoing observation, periodic data collection and interpretation.
- ☐ Modify behaviour change strategies to improve, regain or sustain improvements.
- ☐ Focus on sustaining interdisciplinary leadership and collaboration for the quality improvement programme.
- ☐ Develop and sustain support from the hospital leadership.

Common ICU quality indicators

- ☐ Deep venous thrombosis prophylaxis – number of patients receiving prophylaxis per eligible day.
- ☐ Stress ulcer prophylaxis – percentage of patients receiving prophylaxis per eligible day.
- ☐ Ventilator-associated pneumonia prevention strategies – percentage of patients receiving VAP bundle per eligible day.
- ☐ Central venous catheter blood stream infection prevention strategies – percentage of patients receiving checklist per eligible central venous catheter insertion.

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14 Ethical considerations

14 Ethical considerations

Summary

During a pandemic, the need for critical care services can exceed available resources.
Triage decisions may need to be made on how to allocate scarce resources and prioritize patients.

Before patients are prioritized, allocation planners need to prioritize among often mutually exlusive substantive values and principles.

Key values and principles include: maximizing the number of lives or life-years saved; first come, first served; allocating in ways that reduces, rather than maintains or increases inequities; however, there is neither international nor, typically, national consensus on which values and principles to include and/or how to rank them.

Public engagement in pandemic preparedness is essential to develop a prioritization strategy that is fair, transparent and builds trust.

Tools

14.1 Ethical values and principles

Ethical analysis involves identifying relevant principles, applying them to a particular situation, and making judgements about how to weigh competing principles when it is not possible to satisfy them all.

The fundamental ethical challenge in triage is how to justify who to initially allocate a ventilator to when there are insufficient resources for all patients who require one, and under what circumstances patients might be removed from ventilators.

Ethical triage requires:

- first, identifying relevant substantive and procedural principles;
- second, processes to apply these principles in a transparent way to particular situations; and
- third, monitoring that triage accomplishes its goals and that there are no unintended consequences.

While there is international agreement on the need for transparent processes, consensus on substantive principles is elusive at the international level and typically also at national level.

Historically, the dominant trend underlying triage frameworks has been to focus on maximizing benefits; and allocation frameworks comprised clinical measures such as prognosis that help ensure that triage saves the most lives, or the most life-years. However, drawing on such frameworks in the COVID-19 pandemic made clear that maximizing benefits has a tendency to exacerbate exisiting inequities due to the social and political determinants of health. For example, considering prior comorbidities, remaining life expectancy, or even seemingly objective measures such as the Sequential Organ Failure Assessment (SOFA) score, tend to favour economically and otherwise priviledged population groups, while simultaneously disadadvantaging less priviledged groups. A major challenge is, therefore, how to weigh competing principles when it is not possible to satisfy them all.

Key ethical principles and descriptions (in alphabetical, not lexical, order)

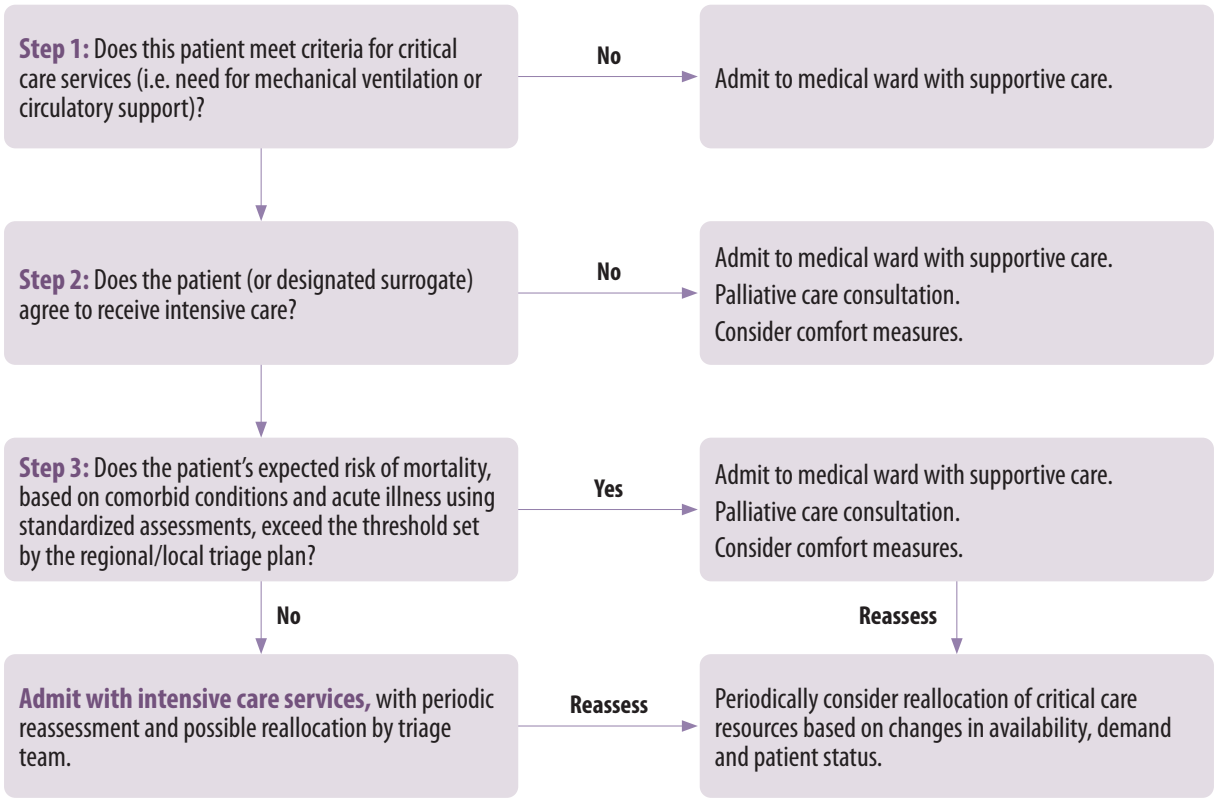
Ethical principle	Description
Autonomy	Enabling, and letting individuals make their own choices based on their values and preferences.
Equity	• Treating the same those who have the same needs, and treating differently those with different needs, which usually requires reducing, rather than maintaining, or worse, exacerbating, avoidable unfair differences in opportunities or health outcomes. • Equity important if policies appear to systematically disadvantage groups already experiencing disproportionate discrimination, injustice or other forms of disadvantage.
First come, first served	Allocates resoures by respecting the temporal sequence of requests. Typically this assumes that all those requesting resources are reasonably equal in their ability to access services.
Informed consent	Process in which a competent individual authorizes a course of action based on sufficient relevant information, without coercion or undue inducement.
Instrumental value	Giving priority to those who have made, or are likely to make, relevant contributions, for example, essential key health care staff.
Justice	Encompasses *equity* – fairness in the distribution of resources, opportunities and outcomes – and procedural justice – a fair process for making important decisions.
Liberty	Includes a broad range of social, religious and political freedoms (e.g. freedom of movement, peaceful assembly, speech), many of which are protected as fundamental human rights.
Life cycle	Captures the notion that it is desirable that everyone should be able to live a life of normal length, and that, while all deaths are tragic, deaths of individuals who are younger are more tragic than those of people near the end of normal life expectancy.
Maximizing benefits	Actions or policies are right insofar as they maximize benefits. Most commonly this is understood to require policies that save the most lives or life-years.
Procedural justice	Includes: • Due process – acknowledgement of people and give opportunity to be heard. • Transparency – clear, accurate information about the basis for decisions and the decision-making process. • Inclusiveness/community engagement – ensuring all relevant stakeholders participate. • Accountability – allocating and enforcing responsibility for decisions. • Oversight – ensuring appropriate mechanisms for monitoring and review.
Respect for persons	Treating individuals in recognition of our common humanity, dignity and inherent rights. Key aspects include: autonomy; informed consent; privacy; confidentiality; social, religious and cultural beliefs; important relationships (e.g. family); and transparency and truth telling in public health and research.
Random selection	Assumes that everyone is equal irrespective of factors such as age, comorbidities, prognosis or other factors and should have an equal chance that can be implemented through a lottery, coin-toss or similar methods. Sometimes proposed as a secondary principle, for example, for patients with similar prognosis.
Solidarity	Social relations in which a group, community, nation or global community stands together. Justifies collective action in the face of common threats and supports efforts to overcome inequalities that undermine the welfare of minorities and groups that suffer discrimination.

Source: Adapted from *Guidance for managing ethical issues in infectious disease outbreaks* (WHO, 2016); *WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination*, 14 September 2020 (WHO, 2020).

14.2 Triage decision process flow

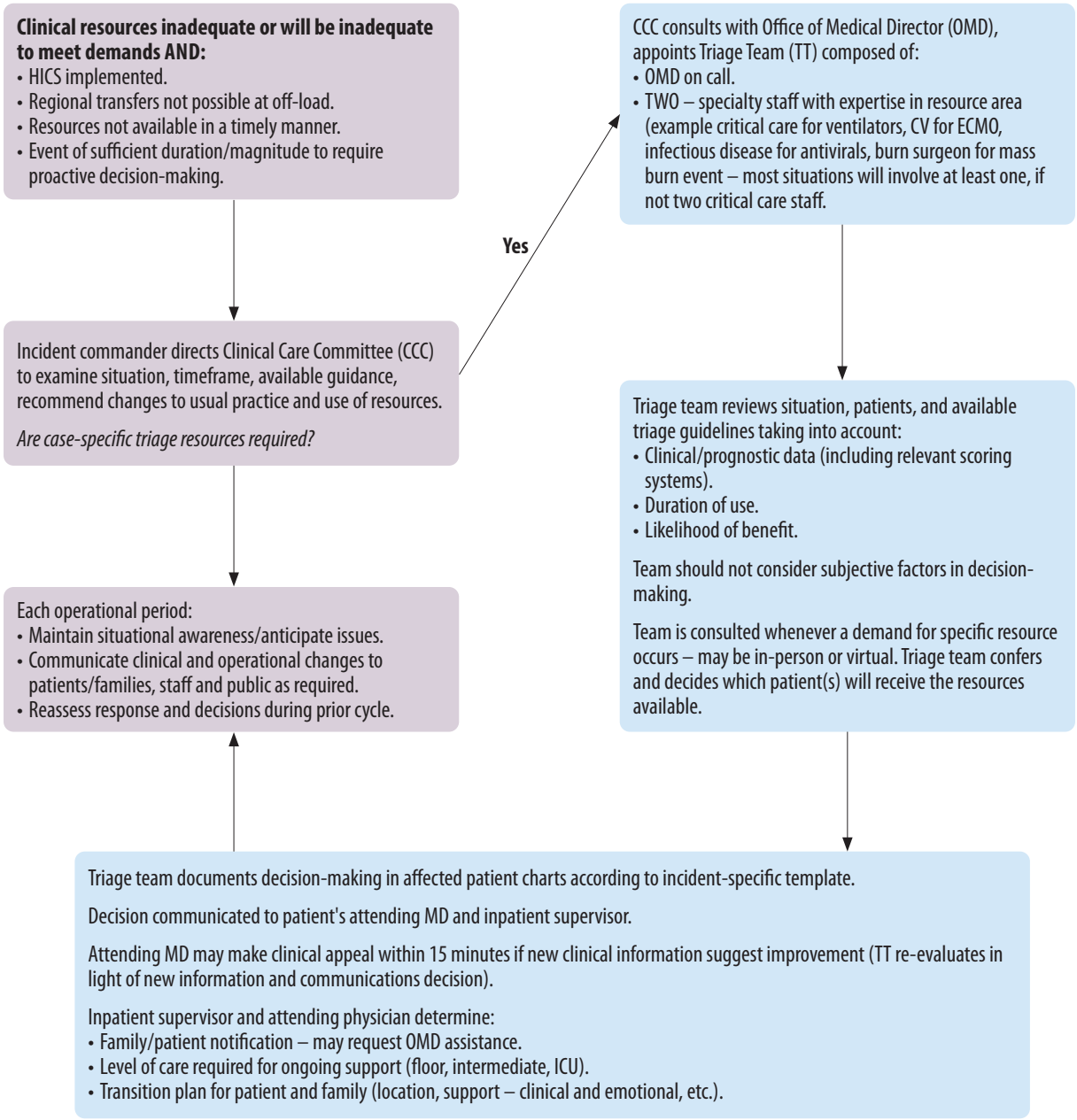
This is adapted from the 2020 *Triage of scarce critical care resources in COVID-19 an implementation guide for regional allocation* (Expert Panel Report of the Task Force for Mass Critical Care and the American College of Chest Physicians) (Maves et al., 2020). It is presented as a framework only, and has not been validated in any population.

Triage decision algorithm



Source: Maves et al. (2020).

14.3 Hospital scarce resource decision-making



Notes: Algorithm and plan does not apply to immediate, reactive triage decisions in the early phase of a disaster (e.g. ED, trauma surgery) or to non-emergency circumstances (specialty providers will engage colleagues in decision-makng). This algorithm is a summary of select actions in the HCMC Crisis Care Annex which should be referred to for further details.
CCC = clinical care committee; CV = cardiovascular specialist; ECMO = extracorporeal membrane oxygenation; HICS = hospital incident command system; MD = medical doctor; OMD = office of medical director; TT = triage team.

Source: Maves et al. (2020).

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