Clinical management of COVID-19

Interim guidance
27 May 2020

World Health Organization

This document is the update of an interim guidance originally published under the title “Clinical management of severe acute respiratory infection (SARI) when COVID-19 disease is suspected” on 13 March 2020.

WHO continues to monitor the situation closely for any changes that may affect this interim guidance. Should any factors change, WHO will issue a further update. Otherwise, this interim guidance document will expire 2 years after the date of publication.

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Contents

Foreword

The *Strategic preparedness and response plan* outlines WHO's strategic objectives to end the COVID-19 pandemic and assists national stakeholders with developing a structured approach to their response. The World Health Organization's (WHO) main objectives for COVID-19 are to:

1) slow and stop transmission;

2) provide optimized care for all patients; and

3) minimize the impact of the epidemic on health systems, social services and economic activity.

To achieve these objectives, the WHO *Operational considerations for case management of COVID-19 in health facility and community* describes key actions that should be taken in each transmission scenario: no cases; sporadic cases; clusters of cases; and community transmission, in order to enable timely surge of clinical and public health operations.

This guidance, *Clinical management of COVID-19,* is based on the above strategic priorities, and is intended for clinicians involved in the care of patients with suspected or confirmed COVID-19. It is not meant to replace clinical judgment or specialist consultation but rather to strengthen frontline clinical management. Considerations for special and vulnerable populations, such as paediatric patients, older people and pregnant women, are highlighted throughout the text.

In this document we refer to the **COVID-19 care pathway (Appendix 1).** This describes a coordinated and multidisciplinary care pathway that a patient enters after s/he is **screened to be a suspect COVID-19 case,** and follows the continuum of their care until release from the pathway. The objective is to ensure delivery of safe and quality care while stopping onwards viral transmission. All others enter the health system in the non-COVID-19 pathway. For the most up-to-date technical guidance related to the COVID-19 response, visit WHO Country & Technical Guidance *(1)*.

Methods

The original version of this document was developed in consultation with the International Forum for Acute Care Trialists (InFACT), International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC) and the Surviving Sepsis Campaign. This is the third edition (version 1.3) of this document, which was originally adapted from *Clinical management of severe acute respiratory infection when Middle East respiratory syndrome coronavirus (MERS-CoV) infection is suspected* (WHO, 2019).

For the development of the third version of the COVID-19 clinical guidance, we assembled a formal Guideline Development Group (GDG) comprising individuals with broad expertise spanning multiple specialties and all regions. Confidentiality and declarations of interest were collected and reviewed and no conflict of interest was identified.

Because of the accelerated timeline and very broad scope of the guideline, it was not feasible to undertake a formal GRADE process (PICO questions; systematic reviews; formal documentation of values and preferences and incorporation of considerations of costs, resources, and feasibility). The topics for consideration originated in the WHO interim guidance for MERS, but for COVID-19 were greatly expanded to reflect the full spectrum of illness, from screening to rehabilitation. Published evidence was synthesized under the coordination of the Science Division in rapid systematic reviews, which were pre-circulated to the GDG. The WHO Steering Committee initially drafted the recommendations about interventions based on these reviews and input from expert clinicians participating in twice-weekly clinical network teleconferences. The GDG held four virtual meetings via

teleconference (total of 12 hours) to discuss all previous and new recommendations. Suggested revisions were incorporated into the guidance. Consensus was achieved for all recommendations presented in the final version.

The direction and strength of recommendations are presented using symbols rather than formal GRADE terminology (strong and conditional recommendations with grading of certainty of evidence, or best practice statements).

The GREEN symbol denotes a strong recommendation or a best practice statement in favour of an intervention.

The RED symbol denotes a recommendation or a best practice statement against an intervention.

The YELLOW symbol denotes a conditional recommendation in favour of an intervention, or a recommendation where special care is required in implementation.

This guidance has been significantly expanded to meet the needs of front-line clinicians caring for patients with COVID-19 to ensure quality care. The following sections are entirely new: COVID-19 care pathway, treatment of acute and chronic infections, management of neurological and mental manifestations, noncommunicable diseases, rehabilitation, palliative care, ethical priniciples, and reporting of death. The remaining sections have been substantially expanded. Though not intended to be an exhaustive list, the following bullets highlight some key changes:

- Discontinue transmission-based precautions (including isolation) and release from the COVID-19 care pathway: **For symptomatic patients: 10 days after symptom onset, plus at least 3 days without symptoms (without fever and respiratory symptoms).**
- Treatment of acute co-infections: **For suspected or confirmed mild COVID-19, against the use of antibiotic therapy or prophylaxis. For suspected or confirmed moderate COVID-19, that antibiotics should not be prescribed unless there is clinical suspicion of a bacterial infection.**
- Prevention of complications: **In patients (adults and adolescents) hospitalized with COVID-19, use pharmacological prophylaxis, such as low molecular weight heparin (e.g. enoxaparin), according to local and international standards, to prevent venous thromboembolism, when not contraindicated. For those with contraindications, use mechanical prophylaxis (intermittent pneumatic compression devices).**

And, importantly, key previous recommendations that remain are:

- Antivirals, immunomodulators and other adjunctive therapies: **WHO recommends that the listed drugs not be administered as treatment or prophylaxis for COVID-19, outside the context of clinical trials.**
- Corticosteroids and COVID-19: **WHO recommends against the routine use of systemic corticosteroids for treatment of viral pneumonia.**

Developed by a multidisciplinary panel of health care providers with experience in the clinical management of patients with COVID-19 and other viral infections, including severe acute respiratory virus (SARS) and Middle East respiratory virus (MERS), as well as sepsis and

acute respiratory distress syndrome (ARDS), this guidance should serve as a foundation for optimized clinical care to ensure the best possible chance for survival. The guidance stresses the importance of using investigational therapeutic interventions as part of randomized controlled trials (RCTs) *(2-4)*. For queries, please email: EDCARN@who.int with "COVID-19 clinical question" in the subject line.

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Abbreviations

ALIMA	Alliance for International Medical Action
ALT	alanine aminotransferase
ARDS	acute respiratory distress syndrome
AWaRe	Access, Watch or Reserve (antibiotics)
BiPAP	bilevel positive airway pressure
BP	blood pressure
bpm	beats per minute
COPD	chronic obstructive pulmonary disease
CPAP	continuous positive airway pressure
CRF	case record form
CT	computed tomography
DIC	disseminated intravascular coagulation
ECMO	extracorporeal membrane oxygenation
FiO_2	fraction of inspired oxygen
GDG	Guideline Development Group
GI	gastrointestinal
HFNO	high-flow nasal oxygen
HIV	human immunodeficiency virus
ICU	intensive care unit
IFRC	International Federation of Red Cross and Red Crescent Societies
InFACT	International Forum for Acute Care Trialists
IPC	infection prevention and control
IQR	interquartile range
ISARIC	International Severe Acute Respiratory and emerging Infection Consortium
LRT	lower respiratory tract
LTCF	long-term care facility
MAP	mean arterial pressure
MERS-CoV	Middle East respiratory syndrome coronavirus
MHPSS	mental health and psychosocial support
NCD	noncommunicable disease
NICD	National Institute for Communicable Diseases (South Africa)
NIV	non-invasive ventilation
OI	Oxygenation Index
OSI	Oxygenation Index using SpO_2
PaO_2	partial pressure arterial oxygen
PBW	predicted body weight
PEEP	positive end-expiratory pressure
PICS	post-intensive care syndrome
PPE	personal protective equipment
PUI	person/patient under investigation
RCT	randomized controlled trial
RDT	rapid diagnostic test
RM	recruitment manoeuvre
RT-PCR	reverse transcription polymerase chain reaction
SARS-CoV	severe acute respiratory syndrome coronavirus
SBP	systolic blood pressure
SIRS	systemic inflammatory response syndrome
SOFA	sequential organ failure assessment
SpO2	oxygen saturation
TB	tuberculosis
UNICEF	United Nations Children's Fund
URT	upper respiratory tract
WHO	World Health Organization

1. Background

Coronavirus disease 2019 (COVID-19) is caused by SARS-CoV-2, a newly emergent coronavirus, that was first recognized in Wuhan, China, in December 2019. Genetic sequencing of the virus suggests that it is a betacoronavirus closely linked to the SARS virus. By way of definition, a symptomatic COVID-19 case is a person who has developed signs and symptoms suggestive of COVID-19.

Symptomatic transmission refers to transmission of SARS-CoV-2 from persons with symptoms. Epidemiology and virologic studies suggest that transmission mainly occurs from symptomatic people to others by close contact through respiratory droplets, by direct contact with infected persons, or by contact with contaminated objects and surfaces *(5-8).* Clinical and virologic studies that have collected repeated biological samples from confirmed patients demonstrate that shedding of SARS-CoV-2 is highest in the upper respiratory tract (URT) (nose and throat) early in the course of the disease *(9-11),* within the first 3 days from onset of symptoms *(11-13).* The incubation period for COVID-19, which is the time between exposure to the virus (becoming infected) and symptom onset, is, on average, 5–6 days, but can be up to 14 days. During this period, also known as the "presymptomatic" period, some infected persons can be contagious, from 1–3 days before symptom onset *(13).* It is important to recognize that presymptomatic transmission still requires the virus to be spread via infectious droplets or by direct or indirect contact with bodily fluids from an infected person. An asymptomatic case is a person infected with SARS-CoV-2 who does not develop symptoms.

While most people with COVID-19 develop only mild (40%) or moderate (40%) disease (see Table 2), approximately 15% develop severe disease that requires oxygen support, and 5% have critical disease with complications such as respiratory failure, acute respiratory distress syndrome (ARDS), sepsis and septic shock, thromboembolism, and/or multiorgan failure, including acute kidney injury and cardiac injury *(14)*. Older age, smoking *(15, 16)* and underlying noncommunicable diseases (NCDs), such as diabetes, hypertension, cardiac disease, chronic lung disease and cancer, have been reported as risk factors for severe disease and death, and multivariable analyses have confirmed older age, higher sequential organ failure assessment (SOFA) score and D-dimer > 1 µg/L on admission were associated with higher mortality *(17, 18)* (see Table 2). This study also observed a median duration of viral RNA detection of 20.0 days (IQR 17.0–24.0) in survivors, but COVID-19 viral RNA was detectable until death in non-survivors. The longest observed duration of viral RNA detection in survivors was 37 days *(17, 18).*

COVID-19 is associated with mental and neurological manifestations, including delirium or encephalopathy, agitation, stroke, meningo-encephalitis, impaired sense of smell or taste *(19)* anxiety, depression and sleep problems. In many cases, neurological manifestations have been reported even without respiratory symptoms. Anxiety and depression appear to be common amongst people hospitalized for COVID-19, with one hospitalized cohort from Wuhan, China, revealing over 34% of people experiencing symptoms of anxiety and 28% experiencing symptoms of depression *(20).* An observational case series from France found that 65% of people with COVID-19 in intensive care units (ICUs) showed signs of confusion (or delirium) and 69% experienced agitation *(21).* Delirium, in particular, has been associated with increased mortality risk in the context of COVID-19 *(22).* Moreover, there have been concerns related to acute cerebrovascular disease (including ischaemic and haemorrhagic stroke) in multiple case series from China, France, the Netherlands, and the United States of

America *(20, 21, 23, 24).* Case reports of Guillain-Barré syndrome and meningo-encephalitis among people with COVID-19 have also been reported *(25, 26).*

There are few data on the clinical presentation of COVID-19 in specific populations, such as children and pregnant women. Clinical manifestations of COVID-19 are generally milder in children compared with adults *(27-30).* Relatively few cases of infants confirmed with COVID-19 have been reported; infants also experience mild illness *(29).* However, most recently, an acute presentation with a hyperinflammatory syndrome leading to multiorgan failure and shock has been described *(31),* now described as *multisystem inflammatory syndrome temporally associated with COVID-19 in children and adolescents*. Robust evidence associating underlying conditions with severe illness in children is still lacking. Among 345 children with laboratory-confirmed COVID-19 and complete information about underlying conditions, 23% had an underlying condition, with chronic lung disease (including asthma), cardiovascular disease and immunosuppression most commonly reported *(32).*

There is currently no known difference between the clinical manifestations of COVID-19 in pregnant women and non-pregnant adults of reproductive age.

2. COVID-19 care pathway (see Appendix 1)

We recommend that COVID-19 care pathways be established at local, regional and national levels. COVID-19 care pathways are for persons with suspected or confirmed COVID-19.

A person enters the COVID-19 care pathway after s/he is *screened,* based on a standardized case definition, including assessment of symptoms, and meets criteria for a suspect case.

- **Suspect cases may be referred to as "persons or patients under investigation" (PUIs) in some contexts.**
- **Probable cases are suspect cases for whom testing for SARS-CoV-2 is inconclusive or not available.**
- **Confirmed cases are persons with laboratory confirmation of COVID-19.**

Remarks:

1. All persons with suspected, probable or confirmed COVID-19 should be immediately isolated to contain virus transmission. See Table 3 for IPC considerations in cohorting suspect, probable and confirmed cases separately.

2. Considerations for co-infections and/or chronic diseases must be made within the COVID-19 care pathway.

3. All suspect cases should be tested to determine if they are a ***confirmed*** case. Until proven negative, all suspected cases should remain in the COVID-19 care pathway. If testing is not available, the person becomes a probable case (based on clinical suspicions) and should be cared for in the COVID-19 pathway.

Discontinue transmission-based precautions (including isolation) and release from the COVID-19 care pathway as follows:

- **For symptomatic patients: 10 days after symptom onset, plus at least 3 days without symptoms (without fever and respiratory symptoms).**
- **For asymptomatic patients: 10 days after test positive.**

Remarks:

1. Limited published and pre-published information provides estimates on viral shedding of up to 9 days for mild patients and up to 20 days in hospitalized patients. Additionally, there are reports that patients can remain consistently polymerase chain reaction (PCR) positive for many weeks, or even test PCR positive after days/weeks of a negative test.

2. Please note that the clinical pathway needs to be clearly outlined by countries to follow each patient until outcome, including full recovery. Discharge criteria from clinical care need to take into account the patient's condition, disease experience and other factors.

3. Release from the COVID-19 care pathway is not the same as clinical discharge from a facility or from one ward to another. For example, some patients may still require ongoing rehabilitation, or other aspects of care, beyond release from the COVID-19 care pathway, based on clinical needs in the COVID-19 care pathway. If release from the COVID-19 care pathway coincides with clinical discharge, then several clinical considerations, such as medication reconciliation, plan for follow up with clinical provider in place, review of routine immunization status, among others, should be taken into account.

3. Screening and triage: early recognition of patients with COVID-19

The primary objective of the COVID-19 global response is to slow and stop transmission, find, isolate and test every suspect case, and provide timely appropriate care of patients with COVID-19. The recommended location of care will depend on the epidemiologic scenario and be either at a designated COVID-19 health facility, community facility or, where not possible, at home. Refer to the WHO *Operational considerations for case management of COVID-19 in health facility and community (33).*

We recommend screening all persons at the first point of contact with the health system in order to identify individuals that have suspected or confirmed COVID-19.

Remarks:

1. Screening can be performed in areas such as the emergency unit, outpatient department/primary care clinic, in the community by a community health worker or by telemedicine. In the context of this outbreak, this should be done at a distance (> 1 m). Use a simple set of questions based on the WHO case definition (see Table 2). This is best done by establishing screening protocols at all health access points and during contact tracing activities. Older people and those immunosuppressed may present with atypical symptoms such as fatigue, reduced alertness, reduced mobility, diarrhoea, loss of appetite, delirium and absence of fever *(34-36).* Thus, screening questions may need to be adjusted for certain settings and guided by epidemiologic considerations.

2. Persons with symptoms (see Table 1) that meet the case definition for *suspected* COVID-19 enter into the COVID-19 care pathway and should immediately be given a medical mask and directed to a single room. If a single room is not possible, then group patients with similar clinical diagnosis and based on epidemiological risk factors, with a spatial separation (at least 1 m between patients). Suspected cases should not be cohorted together with confirmed cases (see Table 3).

3. In areas with other endemic infections that cause fever, such as malaria, dengue, tuberculosis (TB) etc., as part of screening, febrile patients should be tested as per routine protocols *(37-41),* irrespective of the presence of respiratory signs and symptoms. Co-infection with COVID-19 may coexist.

4. Large outbreaks have been observed in long-term care facilities (LTCFs) *(35)*. The COVID-19 care pathway should be activated for all residents of LTCFs who are contacts of a confirmed case in that LTCF, including immediate isolation, testing and treatment as needed. The priority focus in these settings should be to ensure the well-being of residents and protect health workers, and implementation of clinical management and IPC that considers the individual's condition and prognosis (such as screening visitors for COVID-19) *(42).*

- **In community settings, community health workers should continue to follow usual protocols for recognition and treatment of other common illnesses and danger signs while activating the COVID-19 care pathway (including for referral as needed) for suspect cases. Refer to WHO/IFRC/UNICEF guidance on *Community-based health care, including outreach and campaigns, in the context of the COVID-19 pandemic (43).***
- **At a health facility, after screening and isolation, triage patients with suspected COVID-19 using a standardized triage tool (such as the Interagency Integrated Triage Tool); and evaluate the patient to determine disease severity (see Table 2).**
    - **Initiate timely care for the acutely ill using a systematic approach, as described in WHO/ICRC *Basic emergency care (44, 45).***
    - **After initial assessment, management and stabilization, refer patient to appropriate COVID-19 care destination: within the health facility (critical care unit or ward), to a different health facility, community facility or home, according to patient medical needs and established COVID-19 care pathways.**

Remarks:

1. Patients with mild and moderate illness may not require emergency interventions or hospitalization; however, isolation is necessary for all suspect or confirmed cases to contain virus transmission. The decision to monitor a suspect case in a health facility, community facility or home should be made on a case-by-case basis. This decision will depend on the clinical presentation, requirement for supportive care, potential risk factors for severe disease, and conditions at home, including the presence of vulnerable persons in the household.

2. Some patients develop severe pneumonia and require oxygen therapy, and a minority progress to critical disease with complications such as respiratory failure or septic shock *(46, 47)* (see Table 2). Early identification of patients with severe disease allows for rapid initiation of optimized supportive care treatments and safe, rapid referral to a designated destination in the COVID-19 care pathway (with access to oxygen and respiratory support).

3. Known risk factors for rapid deterioration, severe disease, and/or increased mortality are: older age (> 60 years) and NCDs such as cardiovascular disease, diabetes mellitus, chronic lung disease, cancer and cerebrovascular disease *(17)*. Patients with one or more of these risk factors should be monitored closely for deterioration. As described above, the decision to monitor in a health facility, community facility or home should be made on a case-by-case basis. This decision will depend on the clinical presentation, requirement for supportive care, risk factors and conditions at home, including the presence of additional vulnerable persons in the household. This may also apply to pregnant and postpartum women with pre-existing or pregnancy-related comorbidities (e.g. pregnancy-induced hypertension, gestational diabetes).

4. Children with suspected or confirmed COVID-19 infection should be kept together with caregivers wherever possible (if caregivers also have suspected or confirmed COVID-19 infection), and cared for in child-friendly spaces, taking into account specific medical, nursing, nutritional, and mental health and psychosocial support needs of children.

Table 1. Symptoms and risk factors associated with COVID-19

Clinical presentation	Presenting signs and symptoms of COVID-19 vary. Most persons experience fever (83–99%), cough (59–82%), fatigue (44–70%), anorexia (40–84%), shortness of breath (31–40%), myalgias (11–35%). Other non-specific symptoms, such as sore throat, nasal congestion, headache, diarrhoea, nausea and vomiting, have also been reported *(17, 48-50)*. Loss of smell (anosmia) or loss of taste (ageusia) preceding the onset of respiratory symptoms has also been reported *(19, 51, 52)*. Older people and immunosuppressed patients in particular may present with atypical symptoms such as fatigue, reduced alertness, reduced mobility, diarrhoea, loss of appetite, delirium, and absence of fever *(34-36)*. Symptoms such as dyspnoea, fever, gastrointestinal (GI) symptoms or fatigue due to physiologic adaptations in pregnant women, adverse pregnancy events, or other diseases such as malaria, may overlap with symptoms of COVID-19 *(53)*. Children might not have reported fever or cough as frequently as adults *(32)*.
Risk factors for severe disease	Age more than 60 years (increasing with age). Underlying noncommunicable diseases (NCDs): diabetes, hypertension, cardiac disease, chronic lung disease, cerebrovascular disease, chronic kidney disease, immunosuppression and cancer have been associated with higher mortality. Smoking.

Table 2. COVID-19 disease severity

Mild disease		Symptomatic patients (Table 1) meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia. See the WHO website for most up-to-date case definitions *(1)*.
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 ≥ 90% on room air *(54)*. **Child** with clinical signs of non-severe pneumonia (cough or difficulty breathing + fast breathing and/or chest indrawing) and no signs of severe pneumonia. Fast breathing (in breaths/min): < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40 *(55)*.

		While the diagnosis can be made on clinical grounds; chest imaging (radiograph, CT scan, ultrasound) may assist in diagnosis and identify or exclude pulmonary complications.
Severe disease	**Severe pneumonia**	**Adolescent or adult** with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO_2 < 90% on room air *(54).* **Child** with clinical signs of pneumonia (cough or difficulty in breathing) + at least one of the following: • Central cyanosis or SpO_2 < 90%; severe respiratory distress (e.g. fast breathing, grunting, very severe chest indrawing); general danger sign: inability to breastfeed or drink, lethargy or unconsciousness, or convulsions *(55,56).* • Fast breathing (in breaths/min): < 2 months: ≥ 60; 2–11 months: ≥ 50; 1–5 years: ≥ 40 *(55).* While 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	**Acute respiratory distress syndrome (ARDS)** ***(57-59)***	**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 factor present. **Oxygenation impairment in adults** *(57, 59)*: • Mild ARDS: 200 mmHg < PaO_2/FiO_2[a] ≤ 300 mmHg (with PEEP or CPAP ≥ 5 cmH_2O).[b] • Moderate ARDS: 100 mmHg < PaO_2/FiO_2 ≤ 200 mmHg (with PEEP ≥ 5 cmH_2O).[b] • Severe ARDS: PaO_2/FiO_2 ≤ 100 mmHg (with PEEP ≥ 5 cmH_2O).[b] **Oxygenation impairment in children:** note OI and OSI.[c] 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.
Critical disease	**Sepsis** *(3,4)*	**Adults:** acute life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection. Signs of organ dysfunction include: altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output *(3),* fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate, or hyperbilirubinemia. **Children:** suspected or proven infection and ≥ 2 age-based systemic inflammatory response syndrome (SIRS) criteria,[e] of which one must be abnormal temperature or white blood cell count.
	Septic shock *(3,4)*	**Adults:** persistent hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥ 65 mmHg and serum lactate level > 2 mmol/L. **Children:** any hypotension (SBP < 5th centile or > 2 SD below normal for age) or two or three of the following: altered mental status; bradycardia or tachycardia (HR < 90 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 *(60, 61).*

Other complications that have been described in COVID-19 patients include acute, life-threatening conditions such as: acute pulmonary embolism, acute coronary syndrome, acute stroke and delirium. Clinical suspicion for these complications should be heightened when caring for COVID-19 patients, and appropriate diagnostic and treatment protocols available.

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[a] If altitude is higher than 1000 m, then the correction factor should be calculated as follows: PaO_2/FiO_2 x barometric pressure/760.

[b] When PaO_2 is not available, $SpO_2/FiO_2 \leq 315$ suggests ARDS (including in non-ventilated patients).

[c] 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). 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.

[d] 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); and 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 *(62).*

[e] 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.

Abbreviations: BP blood pressure; bpm beats per minute; 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; OSI Oxygenation Index using SpO_2; PaO_2 partial pressure arterial 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.

4. Immediate implementation of appropriate IPC measures

Infection prevention and control is a critical and integral part of clinical management of patients. For the most up-to-date, comprehensive WHO guidance see *(63).*

Table 3. How to implement IPC measures for patients with suspected or confirmed COVID-19 *(63)*

Instructions for patients

Ask the suspected patient to wear a medical mask and direct the patient to a separate area, ideally an isolation room/area if available. Keep at least 1 m distance between patients. Instruct all patients to cover nose and mouth during coughing or sneezing with tissue or flexed elbow, dispose of tissues safely immediately after use in a closed bin and perform hand hygiene after contact with respiratory secretions.

Apply standard precautions

Apply standard precautions according to risk assessment for all patients, at all times, when providing any diagnostic and care services. Standard precautions include hand hygiene and the use of personal protective equipment (PPE) when risk of splashes or in contact with patients' blood, body fluids, secretions (including respiratory secretions) and non-intact skin. Standard precautions also include appropriate patient placement; prevention of needle-stick or sharps injury; safe waste management; cleaning and disinfection of equipment; and cleaning of the environment. Best practices for safely managing health care waste, including waste related to surgeries and obstetric care, should be followed.

Apply contact and droplet precautions

For suspected and confirmed COVID-19 patients, contact and droplet or airborne precautions should be applied. Contact precautions prevent direct or indirect transmission from contact with a suspect or confirmed COVID-19 patient and/or contaminated surfaces or equipment (i.e. contact with contaminated oxygen tubing/interfaces).

Contact precautions include gloves and disposable gown. Droplet precautions prevent large droplet transmission of respiratory viruses, and include medical mask and eye protection. Use a medical mask if working within 1 m of the patient. When providing care in close contact with a suspect or confirmed COVID-19 patient use eye protection (face mask or goggles), because sprays of secretions may occur. In particular, use a combination of PPE for contact and droplet precautions (medical mask, eye protection, gloves and gown) when entering room and remove PPE when leaving. Carefully practise hand hygiene using an alcohol-based hand rub if hands are not visibly dirty or soap and water and disposable towels, before PPE use and after PPE removal, and when indicated while providing care, according to the WHO Five Moments for hand hygiene *(64)*. 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 between each patient use. Ensure that health care workers avoid contaminating environmental surfaces that are not directly related to patient care (e.g. door handles and light switches) and refrain from touching their eyes, nose and mouth with potentially contaminated gloved or ungloved hands.

Place all cases in single rooms, or separately group together those with same etiologic diagnosis, such as suspect cases with suspects; probable cases with probable; and confirmed cases with confirmed. In other words, if an etiological diagnosis is not possible, group patients with similar clinical diagnosis and based on epidemiological risk factors. Keep at at least 1 m spatial separation between cases. Suspected or probable cases should not be cohorted together with confirmed cases. Limit patient movement within the institution and ensure that patients wear medical masks when outside their rooms.

Apply airborne precautions when performing aerosol-generating procedures

When performing aerosol-generating procedures (tracheal intubation, non-invasive ventilation, tracheotomy, cardiopulmonary resuscitation, manual ventilation before intubation and bronchoscopy) *(63)* and in settings where aerosol-generating procedures are frequently in place, airborne instead of droplet precautions should be used, in combination with contact precautions. 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 12 air changes per hour or at least 160 L/second/patient in facilities with natural ventilation. Avoid the presence of unnecessary persons/individuals in the room during procedure. Care for the patient in the same type of room after mechanical ventilation begins.

Because of uncertainty around the potential for aerosolization, high-flow nasal oxygen (HFNO), NIV, including bubble CPAP, should be used with airborne precautions until further evaluation of safety can be completed. There is insufficient evidence to classify nebulizer therapy as an aerosol-generating procedure that is associated with transmission of COVID-19. More research is needed.

Note: In situations where TB may co-exist, specific measures may be necessary in addition to the above *(65).*

5. Laboratory diagnosis

For more details, refer to published WHO guidance on specimen collection, processing and laboratory testing and *WHO Laboratory testing strategy recommendations for COVID-19 (66).*

We recommend, for all suspect cases, collection of upper respiratory tract (URT) specimens (nasopharyngeal and oropharyngeal) for testing by reverse transcription polymerase chain reaction (RT-PCR) and, where clinical suspicion remains and URT specimens are negative, to collect specimens from the lower respiratory tract (LRT) when readily available (expectorated sputum, or endotracheal aspirate/bronchoalveolar lavage in ventilated patient). In addition, testing for other respiratory viruses and bacteria should be considered when clinically indicated.

SARS-CoV-2 antibody tests are not recommended for diagnosis of current infection with COVID-19.

Remarks:

1. Use appropriate PPE for specimen collection (droplet and contact precautions for URT specimens; airborne precautions for LRT specimens). When collecting URT samples, use viral swabs (sterile Dacron or rayon, not cotton) and viral transport media. Do not sample the nostrils or tonsils. In a patient with suspected COVID-19, especially with pneumonia or severe illness, a single negative URT sample does not exclude the diagnosis, and additional URT and LRT samples are recommended. LRT (vs URT) samples are more likely to be positive and for a longer period. Clinicians may elect to collect only LRT samples when these are readily available (for example, in mechanically ventilated patients). Sputum induction should be avoided owing to increased risk of aerosol transmission.

2. In hospitalized patients with confirmed COVID-19, repeated URT and LRT samples can be collected, as clinically indicated, but are no longer indicated for release from COVID-19 precautions. The frequency of specimen collection will depend on local epidemic characteristics and resources.

Depending on local epidemiology and clinical symptoms, test for other potential etiologies (e.g. malaria, dengue fever, typhoid fever) as appropriate.

Remarks:

1. Dual infections with other respiratory infections (viral, bacterial and fungal) have been found in COVID-19 patients *(67)*. As a result, a positive test for a non-COVID-19 pathogen does not rule out COVID-19, or vice versa. At this stage, detailed microbiologic studies are needed in all suspected cases. Both URT and LRT specimens can be tested for other respiratory viruses, such as influenza A and B (including zoonotic influenza A), respiratory syncytial virus, parainfluenza viruses, rhinoviruses, adenoviruses, enteroviruses (e.g. EVD68), human metapneumovirus and endemic human coronaviruses (i.e. HKU1, OC43, NL63, and 229E). LRT specimens can also be tested for bacterial pathogens, including *Legionella pneumophila*.

2. In malaria-endemic areas, patients with fever should be tested for the presence of malaria or other co-infections with validated rapid diagnostic tests (RDTs) or thick and thin blood films and treated as appropriate *(68).* In endemic settings, arbovirus infection (dengue/chikungunya) should also be considered in the differential diagnosis of undifferentiated febrile illness, particularly when thrombocytopenia is present *(37).* Co-infection with COVID-19 virus may also occur and a positive diagnostic test for dengue (e.g. dengue RDTs) does not exclude the testing for COVID-19 *(69)*. If TB is also suspected, collect sputum with specific instructions (e.g. to be done in open area outside the home and away from others) or in an open, well-ventilated space – preferably outside of the health facility *(38).* Staff should not stand near the patient during sample collection.

For COVID-19 patients with severe or critical disease, also collect blood cultures, ideally prior to initiation of antimicrobial therapy *(3)*.

6. Management of mild COVID-19: symptomatic treatment

Patients with mild disease may present to an emergency unit, primary care/outpatient department, or be encountered during community outreach activities, such as home visits or by telemedicine.

We recommend that patients with suspected or confirmed mild COVID-19 be isolated to contain virus transmission according to the established COVID-19 care pathway. This can be done at a designated COVID-19 health facility, community facility or at home (self-isolation).

Remarks:

1. In areas with other endemic infections that cause fever (such as malaria, dengue, etc.), febrile patients should be tested and treated for those endemic infections per routine protocols *(37, 40)*, irrespective of the presence of respiratory signs and symptoms. Co-infection with COVID-19 may occur.
2. The decision to monitor a suspect case with mild COVID-19 in a health facility, community facility or home should be made on a case-by-case basis based on the local COVID-19 care pathway. Additionally, this decision may depend on the clinical presentation, requirement for supportive care, potential risk factors for severe disease, and conditions at home, including the presence of vulnerable persons in the household.
3. If managed at home in self-isolation, refer to WHO guidance on *Home care for patients with COVID-19 presenting with mild symptoms and management of their contacts (70).*

We recommend patients with mild COVID-19 be given symptomatic treatment such as antipyretics for fever and pain, adequate nutrition and appropriate rehydration.

Remark:

At present, there is no evidence to indicate that there are severe adverse events in patients with COVID-19 as a result of the use of non-steroidal anti-inflammatory drugs *(71).*

Counsel patients with mild COVID-19 about signs and symptoms of complications that should prompt urgent care.

Remark:

Patients with risk factors for severe illness should be monitored closely, given the possible risk of deterioration. If they develop any worsening symptoms (such as light headedness, difficulty breathing, chest pain, dehydration, etc.), they should seek urgent care through the established COVID-19 care pathway. Caregivers of children with mild COVID-19 should monitor for signs and symptoms of clinical deterioration requiring urgent re-evaluation. These include difficulty breathing/fast or shallow breathing (for infants: grunting, inability to breastfeed), blue lips or face, chest pain or pressure, new confusion, inability to awaken/not interacting when awake, inability to drink or keep down any liquids. Consider alternative delivery platforms such as home-based, phone, telemedicine or community outreach teams to assist with monitoring *(72)*.

We recommend against antibiotic therapy or prophylaxis for patients with mild COVID-19.

Remark:

Widespread use of antibiotics should be discouraged, as their use may lead to higher bacterial resistance rates, which will impact the burden of disease and deaths in a population during the COVID-19 pandemic and beyond *(73, 74)*.

7. Management of moderate COVID-19: pneumonia treatment

Patients with moderate disease may present to an emergency unit or primary care/outpatient department, or be encountered during community outreach activities, such as home visits or by telemedicine. See Table 2 for definition of pneumonia.

We recommend that patients with suspected or confirmed moderate COVID-19 (pneumonia) be isolated to contain virus transmission. Patients with moderate illness may not require emergency interventions or hospitalization; however, isolation is necessary for all suspect or confirmed cases.

- **The location of isolation will depend on the established COVID-19 care pathway and can be done at a health facility, community facility or at home.**
- **The decision of location should be made on a case-by-case basis and will depend on the clinical presentation, requirement for supportive care, potential risk factors for severe disease, and conditions at home, including the presence of vulnerable persons in the household.**
- **For patients at high risk for deterioration, isolation in hospital is preferred.**

Remark:

In areas with other endemic infections that cause fever (such as malaria, dengue, etc.), febrile patients should be tested and treated for those endemic infections per routine protocols *(37, 40, 41)*, irrespective of the presence of respiratory signs and symptoms. Co-infection with COVID-19 may occur.

We recommend for patients with suspected or confirmed moderate COVID-19, that antibiotics should not be prescribed unless there is clinical suspicion of a bacterial infection.

Remarks:

1. Few patients with COVID-19 experience a secondary bacterial infection. A recent systematic review of patients hospitalized with COVID-19 reported only 8% were reported as experiencing bacterial/fungal co-infection during hospital admission *(75).*

2. Consider in older people, particularly those in LTCFs, and children < 5 years of age, to provide empiric antibiotic treatment for possible pneumonia *(73, 74).* As these patients are not hospitalized, treatment with Access antibiotics (such as co-amoxicillin) is adequate, instead of broad-spectrum antibiotics (Watch and Reserve antibiotics) *(76).*

We recommend close monitoring of patients with moderate COVID-19 for signs or symptoms of disease progression. Provision of mechanisms for close follow up in case of need of escalation of medical care should be available.

Remarks:

1. For patients being treated at home, counselling regarding signs and symptoms of complications (such as difficulty breathing, chest pain, etc.) should be provided to patients and their caregivers. If they develop any of these symptoms, they should seek urgent care through the established COVID-19 care pathway. At this time, there is no evidence to guide the use of pulse oximeters in home settings. Consider alternative delivery platforms such as home-based, phone, telemedicine or community outreach teams to assist with monitoring.

2. For hospitalized patients, regularly monitor vital signs (including pulse oximetry) and, where possible, utilize medical early warning scores (e.g. NEWS2, PEWS) that facilitate early recognition and escalation of treatment of the deteriorating patient *(77).*

8. Management of severe COVID-19: severe pneumonia treatment

All areas where severe patients may be cared for should be equipped with pulse oximeters, functioning oxygen systems and disposable, single-use, oxygen-delivering interfaces (nasal cannula, Venturi mask, and mask with reservoir bag).

Remark:

This includes areas in any part of health facilities, including emergency units, critical care units, primary care/outpatient clinics, as well as pre-hospital settings and ad hoc community facilities that may receive patients with severe COVID-19. See WHO *Oxygen sources and distribution for COVID-19 treatment centres (78).*

We recommend immediate administration of supplemental oxygen therapy to any patient with emergency signs and to any patient without emergency signs and SpO_2 < 90%.

Remarks:

1. Adults with emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma and/or convulsions) should receive emergency airway management and oxygen therapy during resuscitation to target $SpO_2 \geq 94\%$ *(44, 79).* Once the

patient is stable, target > 90% SpO_2 in non-pregnant adults and ≥ 92–95% in pregnant women. Deliver oxygen flow rates using appropriate delivery devices (e.g. use nasal cannula for rates up to 5 L/min; Venturi mask for flow rates 6–10 L/min; and face mask with reservoir bag for flow rates 10–15 L/min). For more details about oxygen titration, refer to the WHO *Clinical care for severe acute respiratory infection toolkit: COVID-19 adaptation (45).*

2. Children with emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma or convulsions) should receive emergency airway management and oxygen therapy during resuscitation to target SpO_2 ≥ 94% *(44, 79, 80)*. Once patient is stable, the target is > 90% SpO_2 *(80)*. Use of nasal prongs or nasal cannula is preferred in young children, as they may be better tolerated.

3. In adults, techniques such as positioning, e.g. high supported sitting, may help to optimize oxygenation, ease breathlessness and reduce energy expenditure *(81).* Prone position for awake, spontaneously breathing patients may also improve oxygenation and the ventilation/perfusion ratio, but evidence is lacking and should be done under clinical trial protocol to assess efficacy and safety.

4. In adult patients with evidence of increased secretion production, secretion retention, and/or weak cough, airway clearance management may assist with secretion clearance. Techniques include gravity-assisted drainage and active cycles of breathing technique. Devices including mechanical insufflation-exsufflation and inspiratory positive pressure breathing should be avoided where possible. Implementation of techniques should be tailored to the individual patient and follow available guidelines *(81).*

Closely monitor patients for signs of clinical deterioration, such as rapidly progressive respiratory failure and shock and respond immediately with supportive care interventions.

Remarks:

1. Patients hospitalized with COVID-19 require regular monitoring of vital signs (including pulse oximetry) and, where possible, utilization of medical early warning scores (e.g. NEWS2, PEWS) that facilitate early recognition and escalation of treatment of the deteriorating patient *(77).*

2. Haematology and biochemistry laboratory testing and electrocardiogram and chest imaging should be performed at admission and as clinically indicated to monitor for complications, such as acute respiratory distress syndrome and acute liver injury, acute kidney injury, acute cardiac injury, disseminated intravascular coagulation (DIC) and/or shock. Application of timely, effective and safe supportive therapies is the cornerstone of therapy for patients who develop severe manifestations of COVID-19.

3. Monitor patients with COVID-19 for signs or symptoms suggestive of venous or arterial thromboembolism, such as stroke, deep venous thrombosis, pulmonary embolism or acute coronary syndrome, and proceed according to hospital protocols for diagnosis (such as laboratory tests and/or imaging) and further management.

4. After resuscitation and stabilization of the pregnant woman, fetal well-being should be monitored. The frequency of fetal heart rate observations should be individualized based on gestational age, maternal clinical status (e.g. hypoxia) and fetal conditions.

Use cautious fluid management in patients with COVID-19 without tissue hypoperfusion and fluid responsiveness.

Remark:

Patients with COVID-19 should be treated cautiously with intravenous fluids; aggressive fluid resuscitation may worsen oxygenation, especially in settings where there is limited availability of mechanical ventilation *(82)*. This applies to both children and adults.

9. Management of critical COVID-19: acute respiratory distress syndrome (ARDS)

The mortality in hospitalized and critically ill patients has varied substantially in different case series throughout the pandemic. The following recommendations are aligned with current international standards for management of all cause ARDS *(3, 92)*.

The following recommendations pertain to adult and paediatric patients with mild ARDS who are treated with non-invasive or high-flow nasal oxygen (HFNO) systems.

In selected patients with COVID-19 and mild ARDS, a trial of HFNO, non-invasive ventilation – continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP) may be used. Refer to Table 2 for definitions of mild, moderate and severe ARDS.

Remarks:

1. Patients with hypoxaemic respiratory failure and haemodynamic instability, multiorgan failure or abnormal mental status should not receive HFNO or NIV in place of other options such as invasive ventilation.

2. Patients receiving a trial of HFNO or NIV should be in a monitored setting and cared for by personnel experienced with HFNO and/or NIV and capable of performing endotracheal intubation in case the patient acutely deteriorates or does not improve after a short trial (about 1 hour). Intubation should not be delayed if the patient acutely deteriorates or does not improve after a short trial.

3. Adult HFNO systems can deliver 60 L/min of gas flow and FiO_2 up to 1.0. Paediatric circuits generally only handle up to 25 L/min, and many children will require an adult circuit to deliver adequate flow. When considering delivering HFNO or NIV outside the usual care settings, evaluating oxygen capacity is important to ensure the higher flow rates required for these devices can be maintained. See WHO *Oxygen sources and distribution for COVID-19 treatment centres (78)*.

4. Because of uncertainty around the potential for aerosolization, HFNO, NIV, including bubble CPAP, should be used with airborne precautions until further evaluation of safety can be completed. If these interventions are performed outside of private rooms in ICUs with appropriate ventilation systems installed, then cohorting of patients requiring these interventions in designated wards will facilitate the implementation of airborne precautions, ensuring all staff entering wear appropriate PPE and adequate environmental ventilation is ensured.

5. Compared with standard oxygen therapy, HFNO may reduce the need for intubation *(83).* Patients with hypercapnia (exacerbation of obstructive lung disease, cardiogenic pulmonary oedema), haemodynamic instability, multiorgan failure or abnormal mental status should generally not receive HFNO, although emerging data suggest that HFNO may be safe in patients with mild-moderate and non-worsening hypercapnia *(83-85)*. Evidence-based guidelines on HFNO do not exist, and reports on HFNO in patients infected with other coronaviruses are limited *(85).*

6. NIV guidelines make no recommendation on use in hypoxaemic respiratory failure (apart from cardiogenic pulmonary oedema, postoperative respiratory failure and early NIV for immunocompromized patients) or pandemic viral illness (referring to studies of SARS and pandemic influenza) *(83).* Risks include delayed intubation, large tidal volumes, and injurious transpulmonary pressures. Limited data suggest a high failure rate in patients with other viral infections such as MERS-CoV who receive NIV *(86).*

7. In situations where mechanical ventilation might not be available, bubble nasal CPAP may be a more readily available alternative for newborns and children with severe hypoxaemia *(87)*.

The following recommendations pertain to adult and paediatric patients with ARDS who need intubation and invasive mechanical ventilation.

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

Remark:

Patients may continue to have increased work of breathing or hypoxaemia even when oxygen is delivered via a face mask with reservoir bag (flow rates of 10–15 L/min, which is typically the minimum flow required to maintain bag inflation; FiO_2 0.60–0.95). Hypoxaemic respiratory failure in ARDS commonly results from intrapulmonary ventilation-perfusion mismatch or shunt and usually requires mechanical ventilation *(3).*

We recommend that endotracheal intubation be performed by a trained and experienced provider using airborne precautions.

Remark:

Patients with ARDS, especially young children or those who are obese or pregnant, may desaturate quickly during intubation. Pre-oxygenation with 100% FiO_2 for 5 minutes, and use of a face mask with reservoir bag is preferred. When possible, avoid bag-valve mask ventilation to reduce exposure to aerosols. Rapid-sequence intubation is appropriate after an airway assessment that identifies no signs of difficult intubation *(88-90).*

The following recommendations pertain to mechanically ventilated adult and paediatric patients with ARDS *(3, 92).*

We recommend implementation of mechanical ventilation using lower tidal volumes (4–8 mL/kg predicted body weight [PBW]) and lower inspiratory pressures (plateau pressure < 30 cmH_2O).

Remarks for adults:

The implementation of mechanical ventilation using lower tidal volumes and lower inspiratory pressures is a strong recommendation from a clinical guideline for patients with ARDS *(3),* and is also suggested for patients with sepsis-induced respiratory failure who do not meet ARDS criteria *(3).* The initial target tidal volume is 6 mL/kg PBW; tidal volume up to 8 mL/kg PBW is allowed if undesirable side-effects occur (e.g. dyssynchrony, pH < 7.15). Permissive hypercapnia is permitted. Ventilator protocols are available *(91).* The use of deep sedation may be required to control respiratory drive and achieve tidal volume targets.

Remarks for children:

In children, a lower level of plateau pressure (< 28 cmH_2O) is targeted, and a lower target of pH is permitted (7.15–7.30). Tidal volumes should be adapted to disease severity: 3–6 mL/kg PBW in the case of poor respiratory system compliance, and 5–8 mL/kg PBW with better preserved compliance *(92).*

In adult patients with severe ARDS (PaO_2/FiO_2 < 150) prone ventilation for 12–16 hours per day is recommended.

Remarks:

1. Application of prone ventilation is recommended for adult patients, preferably for 16 hours per day, and may be considered for paediatric patients with severe ARDS but requires sufficient human resources and expertise to be performed safely; protocols (including videos) are available *(93, 94).*

2. There is little evidence on prone positioning in pregnant women with ARDS; this could be considered in early pregnancy. Pregnant women in the third trimester may benefit from being placed in the lateral decubitus position.

Use a conservative fluid management strategy for ARDS patients without tissue hypoperfusion and fluid responsiveness.

Remarks for adults and children:

This has also been recommended in another international guideline *(3)*. The main effect is to shorten the duration of ventilation. A sample protocol for implementation of this recommendation is available *(95).*

In patients with moderate or severe ARDS, a trial of higher positive end-expiratory pressure (PEEP) instead of lower PEEP is suggested and requires consideration of benefits versus risks. In COVID-19, we suggest the individualization of PEEP where during titration the patient is monitored for effects (beneficial or harmful) and driving pressure.

Remarks:

1. PEEP titration requires consideration of benefits (reducing atelectrauma and improving alveolar recruitment) versus risks (end-inspiratory overdistension leading to lung injury and higher pulmonary vascular resistance). Tables are available to guide PEEP titration based on the FiO_2

required to maintain SpO_2 *(91).* In younger children, maximal PEEP pressures are 15 cmH_2O. Although high driving pressure (plateau pressure − PEEP) may more accurately predict increased mortality in ARDS compared with high tidal volume or plateau pressure *(96)*, data from RCTs of ventilation strategies that target driving pressure are not currently available.

2. A related intervention of recruitment manoeuvres (RMs) is delivered as episodic periods of high CPAP (30–40 cmH_2O), progressive incremental increases in PEEP with constant driving pressure, or high driving pressure; considerations of benefits vs risks are similar. Higher PEEP and RMs were both conditionally recommended in a clinical practice guideline. For PEEP, the guideline considered an individual patient data meta-analysis *(97)* of three RCTs. However, a subsequent RCT of high PEEP and prolonged high-pressure RMs showed harm, suggesting that the protocol in this RCT should be avoided *(98).* Monitoring of patients to identify those who respond to the initial application of higher PEEP or a different RM protocol and stopping these interventions in non-responders are suggested *(99)*.

In patients with moderate-severe ARDS (PaO_2/FiO_2 < 150), neuromuscular blockade by continuous infusion should not be routinely used.

Remark:

A trial found that this strategy improved survival in adult patients with moderate-severe ARDS (PaO_2/FiO_2 < 150) without causing significant weakness *(100),* 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 *(101).* Intermittent or 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.

Avoid disconnecting the patient from the ventilator, which results in loss of PEEP, atelectasis and increased risk of infection of health care workers.

Remarks:

1. Use in-line catheters for airway suctioning and clamp endotracheal tube when disconnection is required (for example, transfer to a transport ventilator).

2. Manual hyperinflation should be avoided and ventilator hyperinflation used instead, if indicated *(81).*

In patients with excessive secretions, or difficulty clearing secretions, consider application of airway clearance techniques. These should be performed only if deemed medically appropriate *(81)*.

The following recommendations pertain to adult and paediatric patients with ARDS in whom lung protective ventilation strategy fails to achieve adequate oxygenation and ventilation.

In settings with access to expertise in extracorporeal membrane oxygenation (ECMO), consider referral of patients who have refractory hypoxaemia (e.g. including a ratio of partial pressure of arterial oxygen [PaO_2] to the fraction of inspired oxygen [FiO_2] of < 50 mmHg for 3 hours, a PaO_2:FiO_2 of < 80 mmHg for > 6 hours) despite lung protective ventilation.

Remarks for adults:

An RCT of ECMO for adult patients with ARDS was stopped early and found no statistically significant difference in the primary outcome of 60-day mortality between ECMO and standard medical management (including prone positioning and neuromuscular blockade) *(102).* However, ECMO was associated with a reduced risk of the composite outcome that consisted of mortality and crossover to ECMO treatment *(104),* and a post-hoc Bayesian analysis of this RCT showed that ECMO is very likely to reduce mortality across a range of prior assumptions *(212).* In patients with MERS, ECMO vs conventional treatment was associated with reduced mortality in a cohort study *(2).* ECMO is a resource-intensive therapy and should be offered only in expert centres with a sufficient case volume to maintain expertise and staff volume and capacity to apply the IPC measures required (*103, 104*). In children, ECMO can also be considered in those with severe ARDS, although high-quality evidence for benefit is lacking *(92).*

10. Management of critical COVID-19: septic shock

Recognize septic shock in adults when infection is suspected or confirmed AND vasopressors are needed to maintain mean arterial pressure (MAP) ≥ 65 mmHg AND lactate is ≥ 2 mmol/L, in the absence of hypovolaemia (see Table 2).

Recognize septic shock in children with any hypotension (systolic blood pressure [SBP] < 5th centile or > 2 SD below normal for age) or two or more of the following: altered mental status; bradycardia or tachycardia (HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children); prolonged capillary refill (> 2 sec) or feeble pulses; tachypnoea; mottled or cold skin or petechial or purpuric rash; increased lactate; oliguria; hyperthermia or hypothermia (see Table 2).

Remarks:

1. In the absence of a lactate measurement, use blood pressure (i.e. MAP) and clinical signs of perfusion to define shock.

2. Standard care includes early recognition and the following treatments to be done immediately, within 1 hour of recognition: antimicrobial therapy, and initiation of fluid bolus and vasopressors for hypotension *(3).* The use of central venous and arterial catheters should be based on resource availability and individual patient needs. Detailed guidelines from the Surviving Sepsis Campaign and WHO are available for the management of septic shock in adults *(3)* and children *(55, 105)*. Alternate fluid regimens are suggested when caring for adults and children in resource-limited settings *(106, 107).*

The following recommendations pertain to resuscitation strategies for adult and paediatric patients with septic shock.

In resuscitation for septic shock in adults, give 250–500 mL crystalloid fluid as rapid bolus in first 15–30 minutes.

In resuscitation for septic shock in children, give 10–20 mL/kg crystalloid fluid as a bolus in the first 30–60 minutes.

Fluid resuscitation may lead to volume overload, including respiratory failure, particularly with ARDS. If there is no response to fluid loading or signs of volume overload appear (e.g. jugular venous distension, crackles on lung auscultation, pulmonary oedema on imaging, or hepatomegaly), then reduce or discontinue fluid administration. This step is particularly important in patients with hypoxaemic respiratory failure.

Remarks:

1. Crystalloids include normal saline and Ringer's lactate.

2. Determine the need for additional fluid boluses (250–500 mL in adults; 10–20 mL/kg in children) based on clinical response and improvement of perfusion targets and reassess for signs of fluid overload after each bolus. Perfusion targets include MAP (> 65 mmHg or age-appropriate targets in children), urine output (> 0.5 mL/kg/hr in adults; 1 mL/kg/hr in children), and improvement of skin mottling and extremity perfusion, capillary refill, heart rate, level of consciousness, and lactate.

3. Consider dynamic indices of volume responsiveness to guide volume administration beyond initial resuscitation based on local resources and experience *(3).* These indices include passive leg raises, fluid challenges with serial stroke volume measurements, or variations in systolic pressure, pulse pressure, inferior vena cava size, or stroke volume in response to changes in intrathoracic pressure during mechanical ventilation.

4. In pregnant women, compression of the inferior vena cava can cause a decrease in venous return and cardiac preload and may result in hypotension. For this reason, pregnant women with sepsis and or septic shock may need to be placed in the lateral decubitus position to off-load the inferior vena cava *(108).*

5. Clinical trials conducted in resource-limited settings comparing aggressive versus conservative fluid regimens suggest higher mortality in patients treated with aggressive fluid regimens *(106, 107).* Refer to the WHO/ICRC *Basic emergency care (Shock module)* for an initial approach and management of shock in resource limited settings *(44).*

Do not use hypotonic crystalloids, starches or gelatins for resuscitation.

Remark:

Starches are associated with an increased risk of death and acute kidney injury compared with crystalloids. The effects of gelatins are less clear, but they are more expensive than crystalloids *(3, 109)*. Hypotonic (vs isotonic) solutions are less effective at increasing intravascular volume. Surviving Sepsis guidelines also suggest albumin for resuscitation when patients require substantial amounts of crystalloids, but this conditional recommendation is based on low-quality evidence *(3).*

In adults, administer vasopressors when shock persists during or after fluid resuscitation. The initial blood pressure target is MAP ≥ 65 mmHg in adults and improvement of markers of perfusion.

In children, administer vasopressors if signs of fluid overload are apparent or the following persist after two fluid bolus:

- **signs of shock such as altered mental state;**
- **bradycardia or tachycardia (HR < 90 bpm or > 160 bpm in infants and HR < 70 bpm or > 150 bpm in children);**
- **prolonged capillary refill (> 2 seconds) or feeble pulses;**
- **tachypnoea; mottled or cool skin or petechial or purpuric rash; increased lactate; oliguria persists after two repeat boluses;**
- **or age-appropriate blood pressure targets are not achieved *(105)*.**

Remarks:

1. Vasopressors (i.e. norepinephrine, epinephrine, vasopressin and dopamine) are most safely given through a central venous catheter at a strictly controlled rate, but it is also possible to safely administer them via peripheral vein *(110)* and intraosseous needle. Monitor blood pressure frequently and titrate the vasopressor to the minimum dose necessary to maintain perfusion and prevent side-effects. A recent study suggests that in adults 65 years or older a MAP 60–65 mmHg target is equivalent to ≥ 65 mmHg *(111)*.

2. Norepinephrine is considered the first-line treatment in adult patients; epinephrine or vasopressin can be added to achieve the MAP target. Because of the risk of tachyarrhythmia, reserve dopamine for selected patients with low risk of tachyarrhythmia or those with bradycardia.

3. In children, epinephrine is considered the first-line treatment, while norepinephrine can be added if shock persists despite optimal dose of epinephrine *(4)*.

If central venous catheters are not available, vasopressors can be given through a peripheral IV, but use a large vein and closely monitor for signs of extravasation and local tissue necrosis. If extravasation occurs, stop infusion. Vasopressors can also be administered through intraosseous needles.

If signs of poor perfusion and cardiac dysfunction persist despite achieving MAP target with fluids and vasopressors, consider an inotrope such as dobutamine.

Remark:

No RCTs have compared dobutamine with placebo for clinical outcomes.

11. Prevention of complications in hospitalized and critically ill patients with COVID-19

Thromboembolism

Coagulopathy is common in patients with severe COVID-19, and both venous and arterial thromboembolism have been reported *(23, 24, 112-114).*

- **In patients (adults and adolescents) hospitalized with COVID-19, use pharmacological prophylaxis, such as low molecular weight heparin (such as enoxaparin), according to local and international standards, to prevent venous thromboembolism, when not contraindicated *(115).* For those with contraindications, use mechanical prophylaxis (intermittent pneumatic compression devices).**
- **Monitor patients with COVID-19, for signs or symptoms suggestive of thromboembolism, such as stroke, deep venous thrombosis, pulmonary embolism or acute coronary syndrome. If these are clinically suspected, proceed immediately with appropriate diagnostic and management pathways.**

Adverse effects of medications

- **Careful consideration should be given to the numerous, clinically significant side-effects of medications that may be used in the context of COVID-19, as well as drug-drug interactions between medications, both of which may affect COVID-19 symptomatology (including effects on respiratory, cardiac, immune and mental and neurological function). Both pharmacokinetic and pharmacodynamic effects should be considered.**

Remarks:

1. The risk of relevant side-effects and drug-drug interactions relating to COVID-19 symptomatology include sedation, cardiotoxicity via QTc-prolongation and respiratory suppression, and these may be dose-dependent (i.e. increase with escalating doses). For this reason, care should be taken that minimum effective doses of medications with dose-dependent negative effects are used and for the shortest durations possible.

2. Use medications that carry the least risk possible for drug-drug interactions with other medications the person may be receiving. Psychotropic medications with sedative proprieties, such as benzodiazepines, can worsen respiratory function. Some, psychotropic medications have QTc-prolonging activity (such as some antipsychotics and some antidepressants). Use medications that carry the least risk possible for side-effects that may worsen COVID-19 symptomatology, including sedation, respiratory or cardiac function, risk of fever or other immunological abnormalities, or coagulation abnormalities.

Other complications

These interventions are based on Surviving Sepsis *(3)* or other guidelines *(116-119),* and are generally limited to feasible recommendations based on high-quality evidence. Recent publications have encouraged best practices to continue during the COVID-19 outbreak *(120).* See the WHO *Clinical care for severe acute respiratory infection toolkit: COVID-19 adaptation* for practical tools to assist implementation *(45).*

Table 3. Prevention of complications

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 of the above as a bundle of care (may also reduce delirium); such as the **A**wakening and **B**reathing **C**oordination, **D**elirium assessment/management, and **E**arly mobility (ABCDE)
Reduce incidence of ventilator-associated pneumonia	• Oral intubation is preferable to nasal intubation in adolescents and adults • Keep patient in semi-recumbent position (head of bed elevation 30–45º) • 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	• 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, and higher organ failure score
Reduce the development of antimicrobial resistance Reduce the development of adverse drug effects Promote appropriate antimicrobial prescribing and use during the COVID-19 pandemic *(121)*	• Utilize de-escalation protocols as soon as patient is clinically stable and there is no evidence of bacterial infection • Expose patient to empiric antimicrobial therapy for the shortest time possible, to prevent nephrotoxicity, cardiac and other side-effects from unnecessary antimicrobial use • 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. Antivirals, immunomodulators and other adjunctive therapies for COVID-19

We recommend that the following drugs not be administered as treatment or prophylaxis for COVID-19, outside of the context of clinical trials:

- **Chloroquine and hydroxychloroquine (+/- azithromycin), including but not limited to:**
- **Antivirals, including but not limited to:**
  - **Lopinavir/ritonavir**
  - **Remdesivir**
  - **Umifenovir**
  - **Favipiravir**
- **Immunomodulators, including but not limited to:**
  - **Tocilizumab**
  - **Interferon-β-1a**
- **Plasma therapy.**

Remarks:

1. Existing published literature on the agents listed above is mostly observational in nature, with few clinical trials; and does not provide high-quality evidence in favour of any of these agents. In addition, important side-effects have been described *(122-131).*
   - **Chloroquine and hydroxychloroquine +/- azithromycin:** each can cause QT prolongation and taken together can increase the risk of cardiotoxicity.
   - **Lopinavir/ritonavir:** the most common adverse effects are gastrointestinal.
   - **Remdesivir:** elevation of hepatic enzymes, GI complications, rash, renal impairment and hypotension.
   - **Umifenovir:** diarrhoea, nausea.
   - **Favipiravir:** QT interval prolongation.
   - **Interferon-β-1a:** pyrexia, rhabdomyolysis.
   - **Tocilizumab:** URT infections, nasopharyngitis, headache, hypertension, increased alanine aminotransferase (ALT), injection site reactions.

2. This recommendation has not changed and is consistent with previous WHO guidance documents and other international grade-based guidelines *(132).*

3. Outside of clinical trials, the following criteria should be met for access to investigational therapeutics: 1) no proven effective treatment exists; 2) it is not possible to initiate clinical studies immediately; 3) data providing preliminary support of the intervention's efficacy and safety are available, at least from laboratory or animal studies, and use of the intervention outside clinical trials has been suggested by an appropriately qualified scientific advisory committee on the basis of a favourable risk–benefit analysis; 4) the relevant country authorities, as well as an appropriately qualified ethics committee, have approved such use; 5) adequate resources are available to ensure that risks can be minimized; 6) the patient's informed consent is obtained; and 7) the emergency use of the intervention is monitored and the results are documented and shared in a timely manner with the wider medical and scientific community *(133).*

13. Corticosteroid therapy and COVID-19

We recommend against the routine use of systemic corticosteroids for treatment of viral pneumonia.

Remarks:

1. A systematic review and meta-analysis of the impact of corticosteroid therapy on outcomes of persons with SARS-CoV-2, SARS-CoV and MERS-CoV revealed corticosteroids did not significantly reduce the risk of death, did not reduce hospitalization duration, ICU admission rate and/or use of mechanical ventilation, and had several adverse effects *(134).* A systematic review of observational studies of corticosteroids administered to patients with SARS reported no survival benefit and possible harms (avascular necrosis, psychosis, diabetes and delayed viral clearance) *(135).* A systematic review of observational studies in influenza found a higher risk of mortality and secondary infections with corticosteroids; the evidence was judged as very low to low quality owing to confounding by indication *(136)*. A subsequent study that addressed this limitation by adjusting for time-varying confounders found no effect on mortality *(137).* Finally, a study of patients receiving corticosteroids for MERS used a similar statistical approach and found no effect of corticosteroids on mortality but delayed LRT clearance of MERS-CoV *(138)*.

2. Given the lack of effectiveness and possible harm, routine corticosteroids should be avoided unless they are indicated for another reason. Other reasons may include exacerbation of asthma or chronic obstructive pulmonary disease (COPD), septic shock or ARDS, and risk/benefit analysis needs to be conducted for individual patients.

3. A recent guideline issued by an international panel and based on the findings of two recent large RCTs makes a conditional recommendation for corticosteroids for all patients with sepsis (including septic shock) *(139).* Surviving Sepsis guidelines, written before these RCTs were reported, recommend corticosteroids only for patients in whom adequate fluids and vasopressor therapy do not restore haemodynamic stability *(3).* In addition, a recent trial reported that corticosteroids may reduce mortality in moderate-severe ARDS *(140).* Clinicians considering corticosteroids for a patient with COVID-19 and sepsis must balance the potential small reduction in mortality with the potential downside of prolonged shedding of coronavirus in the respiratory tract, as has been observed in patients with MERS *(84, 138, 141).* If corticosteroids are prescribed, monitor and treat hyperglycaemia, hypernatraemia and hypokalaemia. Monitor for recurrence of inflammation and signs of adrenal insufficiency after stopping corticosteroids, which may have to be tapered. Because of the risk of *Strongyloides stercoralis* hyperinfection with steroid therapy, diagnosis or empiric treatment should be considered in endemic areas if steroids are used *(142).*

4. WHO recommends antenatal corticosteroid therapy for women at risk of preterm birth from 24 to 34 weeks of gestation when there is no clinical evidence of maternal infection, and adequate childbirth and newborn care is available. However, in cases where the woman presents with mild COVID-19, the clinical benefits of antenatal corticosteroid might outweigh the risks of potential harm to the mother. In this situation, the balance of benefits and harms for the woman and the preterm newborn should be discussed with the woman to ensure an informed decision, as this assessment may vary depending on the woman's clinical condition, her wishes and that of her family, and available health care resources.

5. WHO has prioritized the evaluation of corticosteroids in clinical trials to assess safety and efficacy and there are many ongoing clinical trials *(143).*

14. Treatment of other acute and chronic infections in patients with COVID-19

The prevalence of acute co-infections or secondary infections coinciding with COVID-19 has been not adequately described but appears to be low *(75)*, and will be based on local factors and endemic or other emerging infections *(48, 73, 74, 121).* Antibiotic overuse increases the risk of emergence and transmission of multidrug-resistant bacteria. Infections with multidrug-resistant bacteria are more difficult to treat, and associated with increased morbidity and mortality.

Acute co-infections

We recommend for patients with:

- **suspected or confirmed mild COVID-19, against the use of antibiotic therapy or prophylaxis;**
- **suspected or confirmed moderate COVID-19, that antibiotics should not be prescribed unless there is clinical suspicion of a bacterial infection;**
- **suspected or confirmed severe COVID-19, the use of empiric antimicrobials to treat all likely pathogens, based on clinical judgment, patient host factors and local epidemiology, and this should be done as soon as possible (within 1 hour of initial assessment if possible), ideally with blood cultures obtained first. Antimicrobial therapy should be assessed daily for de-escalation.**

Remarks:

1. For patients with severe disease, early and appropriate empiric antimicrobial therapy *(3)* can be administered in the emergency unit and/or pre-hospital setting. Empiric antibiotic treatment should be based on the clinical diagnosis (community-acquired pneumonia, health care-associated pneumonia [if infection was acquired in health care setting] or sepsis), local epidemiology and susceptibility data, and national treatment guidelines. Choose antibiotics with the least ecologic impact based on data and guidance from your own institution, region or country (e.g. of the Access group of the AWaRe classification) *(76).* The AWaRe classification categorizes antibiotics into three different groups (**A**ccess, **Wa**tch and **Re**serve) based on their indication for common infectious syndromes, their spectrum of activity, and their potential for increasing antibiotic resistance. The AWaRe classification is a tool for antibiotic stewardship at local, national and global levels with the aim of optimizing antibiotic use and reducing antibiotic resistance.

2. Treatment of other co-infections may be based on a laboratory-confirmed diagnosis or epidemiological criteria. For example, in malaria endemic areas, when a malaria RDT is also positive, antimalarials should be initiated as soon as possible as per local protocol *(40).* Or, when there is ongoing local circulation of seasonal influenza, empiric therapy with a neuraminidase inhibitor should be considered for patients with severe disease or at risk for severe influenza. If TB co-infection is suspected or confirmed, then follow local TB treatment protocols *(41).*

3. Empiric antibiotic therapy should be de-escalated on the basis of microbiology results and clinical judgment. Regularly review the possibility of switching of intravenous to oral route of administration and provide targeted treatment based on microbiologic results.

4. Duration of empiric antibiotic treatment should be as short as possible; generally 5–7 days.

5. An increase in antibiotic use during the pandemic may cause adverse reactions such as *Clostridioides difficile* infections, with clinical disease ranging from diarrhoea and fever to colitis *(144)*. Antibiotic stewardship programmes should be put into place or continue among COVID-19 patients.

Chronic infections

It is currently unknown whether immunosuppression caused by chronic co-infections such as human immunodeficiency virus (HIV) puts persons at greater risk for severe COVID-19 disease. However, people living with HIV with advanced disease have an increased risk of opportunistic infections (notably TB) and related complications in general. Facility-based HIV testing services should continue and those newly diagnosed should start antiretroviral therapy as soon as possible. For people living with HIV already on treatment, continuity of antiretroviral therapy and prophylaxis for co-infections is essential, with multi-month prescribing.

15. Management of neurological and mental manifestations associated with COVID-19

People with COVID-19 are at high risk for delirium, and sometimes delirium may be a presenting feature without respiratory symptoms (see Chapter 3). Anxiety and depressive symptoms may constitute common reactions for people in the context of COVID-19 diagnosis, especially for those who may be hospitalized, due to concerns for one's own health or the health of others, the need for physical isolation (which can lead to social isolation), potential risk of death, concerns over the risk of infecting others, and concerns over leaving family members alone who may need care. Stressors particular to COVID-19 include: fear of falling ill and dying, fear of being socially excluded/placed in quarantine, loss of livelihood and loss of loved ones, and feelings of helplessness, boredom and loneliness due to being isolated. These stressors may trigger new symptoms or exacerbate underlying mental or neurological conditions. Patients with pre-existing mental health conditions and substance abuse disorders may also be adversely impacted. People with COVID-19 are at higher risk for sleep problems owing to acute stress responses, as well as additional reasons for those who are hospitalized such as environmental factors, invasive medical procedures (e.g. mechanical ventilation) and the frequent combination of multiple medications possibly disrupting sleep patterns *(145, 146).*

Delirium

We recommend, in patients with COVID-19, that measures to prevent delirium, an acute neuropsychiatric emergency, be implemented; and patients be evaluated using standardized protocols, for the development of delirium. If detected, then immediate evaluation by a clinician is recommended to address any underlying cause of delirium and treat appropriately.

Remarks:

1. Manage any underlying cause of delirium by monitoring oxygenation and fluid status, correcting metabolic or endocrine abnormalities, addressing co-infections, minimizing the use of medications that may cause or worsen delirium, treating withdrawal from substances, understanding and minimizing the effects of any harmful drug-drug interactions and maintaining normal sleep cycles as much as possible *(147)*.

2. In patients receiving invasive ventilation, minimize continuous or intermittent sedation, targeting specific titration endpoints (light sedation unless contraindicated) or with daily interruption of continuous sedative infusions, to reduce delirium *(147).*

3. In patients experiencing agitation (defined as marked restlessness or excessive motor activity, often accompanied by anxiety), use calming communication strategies and attempt to reorient the person. Acute pain due to physical illness or air hunger should be considered as triggers for agitation and need to be addressed immediately. If the person continues to be agitated despite the strategies described above and is experiencing severe distress, it may be necessary to use psychotropic medications *(148)*.

4. When using antipsychotic medications for agitation, consider side-effects that may worsen symptomatology, including sedation, respiratory or cardiac function, risk of fever or other immunological abnormalities, or coagulation abnormalities and any potential drug-drug interactions between these and other medications. Use minimum effective doses of antipsychotic medications at the lowest frequency and for the shortest duration possible, with doses adjusted according to age, medical co-morbidities and degree of distress *(149).* For severe agitation, low doses of haloperidol (administered orally or by intramuscular injection) can be considered, while carefully monitoring for adverse effects such as QT prolongation *(150).*

5. If haloperidol is contraindicated due to the patient's clinical condition (e.g. prolonged QT interval, recent myocardial infarction, Parkinson's Disease, Lewy-Body dementia, etc.), other antipsychotic medications with safer cardiovascular profiles may be used after careful consideration of other risks (such as respiratory suppression or sedation) and drug-drug interactions.

6. If the patient remains severely agitated despite the strategies described above, benzodiazepines can be added, with preference given to those with shorter half-lives and lower risk of drug-drug interactions (such as lorazepam); lowest doses should be used and for the shortest duration possible. The intravenous route should be avoided *(150)*.

Mental health and psychosocial support

We recommend providing basic mental health and psychosocial support (MHPSS) for all persons with suspected or confirmed COVID-19 by asking them about their needs and concerns, and addressing them *(151).*

Remarks:

1. Given the stress that COVID-19 may create at individual and family levels, the high prevalence of common mental health conditions among women in the antenatal and postpartum period, and the acceptability of programmes aimed at them, interventions for

MHPSS targeted to mothers need to be more widely implemented. Prevention services should be available in addition to services that treat mental health conditions.

2. Basic psychosocial support skills are essential for management of all patients and they represent an integral part of the care to be provided for different groups, including children, older adults, pregnant women and others affected by COVID-19.

3. This recommendation is consistent with the Inter-Agency Standing Committee briefing note about mental health and psychosocial aspects of COVID-19 *(151)* and WHO recommendations on providing access to support based on psychological first aid principles to people in acute distress exposed recently to a traumatic event *(152).*

4. Ask people about their needs and concerns around diagnosis, prognosis, and other social, family or work-related issues. Listen carefully, try to understand what is most important to the person at this moment, and help them work out what their priorities are and link them with relevant resources and services.

5. Give accurate information on the person's condition and treatment plans in easily understood and non-technical language, as lack of information can be a major source of stress. Help people address urgent needs and concerns, and help with decision-making, as necessary. Help connect people with loved ones and social support, including through phone or internet as appropriate.

6. MHPSS and follow up should continue after the person is discharged from hospital to ensure their symptoms are not worsening and they are continuing to do well. This can be provided through telehealth, where available and appropriate.

7. Parents and caregivers who may need to be separated from their children, and children who may need to be separated from their primary caregivers, should have access to appropriately trained health or non-health workers for MHPSS. MHPSS should be appropriately adapted for the needs of children, taking into consideration their social and emotional development, learning and behaviour *(151).*

We recommend prompt identification and assessment for anxiety and depressive symptoms in the context of COVID-19 and to initiate psychosocial support strategies and first-line interventions, for the management of new anxiety and depressive symptoms.

Remarks:

1. For people who are experiencing symptoms of anxiety, psychosocial support strategies such as psychological first aid, stress management, and brief psychological interventions based on the principles of cognitive behavioural therapy should be considered *(152, 153).*

2. For relieving anxiety causing severe distress that is not responsive to psychosocial support strategies, benzodiazepines can be considered, specifically in the hospital setting. Benzodiazepines should only be used with extreme caution with preference for those with shorter half-lives and lower risk of drug-drug interactions (such as lorazepam). Lowest doses should be used and for the shortest duration possible; high doses and longer term use should be avoided *(154).* Benzodiazepines carry the risks of confusion and respiratory suppression, may worsen traumatic stress reactions, can produce tolerance and dependence, and are known to be prescribed indiscriminately in many emergencies.

3. For people who are experiencing symptoms of depression, brief psychological interventions based on the principles of cognitive behavioural therapy, problem-solving treatment and relaxation training can be considered *(149).*

4. If a person's anxiety or depressive symptoms persist beyond recovery from COVID-19 and/or discharge from the hospital, then an underlying anxiety or depressive disorder may be suspected, and a mental health professional should be consulted and these conditions should be managed appropriately. Refer to the *mhGAP Intervention Guide for mental, neurological and substance use disorders in non-specialized health settings (155).*

5. It is important to ask about thoughts or acts of self-harm, particularly during COVID-19, due to risk factors for self-harm and suicide such as sense of isolation, loss of a loved one, job, or financial loss and hopelessness. Remove possible means of self-harm, activate psychosocial support, follow up with the person, and consult a mental health professional as necessary. Refer to the *mhGAP Intervention Guide for mental, neurological and substance use disorders in non-specialized health settings (155).*

We recommend psychosocial support strategies as the first-line interventions for management of sleep problems in the context of acute stress.

Remarks:

1. Sleep hygiene advice (including avoiding the use of psychostimulants such as caffeine, nicotine or alcohol), and stress management (including relaxation techniques and mindfulness practices) are effective in reducing sleep problems and may be offered. Psychological interventions based on the principles of cognitive behavioural therapy may also be considered.

2. For people who are hospitalized for COVID-19, additional causes of insomnia may include environmental factors (e.g. excessive light and noise at night), anxiety, delirium, agitation, pain or air hunger. Identifying and promptly addressing underlying causes should be prioritized before using any pharmacological sleep aids.

16. Noncommunicable diseases and COVID-19

Pre-existing NCDs, including cardiovascular disease, diabetes, chronic respiratory disease, hypertension and cancer, have been identified as independent risk factors for death *(18).*

We recommend when caring for patients with suspected and confirmed COVID-19 that have underlying NCDs to continue or modify previous medical therapy according to the patient's clinical condition.

Antihypertensive drugs should not routinely be stopped in patients with COVID-19, but therapy may need to be adjusted based on general considerations for patients with acute illness, with particular reference to maintaining normal blood pressure and renal function.

Remark:

SARS-CoV-2 uses the ACE 2 receptor for entry into cells. It has been suggested that antihypertensive drugs that exert their effect by inhibiting ACE or blocking the ACE 2 receptor may either aggravate or ameliorate the clinical course of patients with COVID-19 *(156).* To date, there are no studies that can substantiate this, and it is generally advised to continue these medications unless there are other reasons to stop these (e.g. hyperkalaemia, hypotension or acute deterioration in renal function) *(157).*

17. Rehabilitation for patients with COVID-19

As COVID-19 is a novel disease, the rehabilitation needs for patients recovering from COVID-19 are anticipated based on evidence from the general critical care population. Based on this evidence, it is expected that acute interventions for the management of patients with severe and critical COVID-19, including mechanical ventilation, sedation and/or prolonged bed rest, may result in a range of impairments including (but not limited to) physical deconditioning, respiratory, swallow, cognitive and mental health impairments *(145, 158-168).* These symptoms are collectively referred to as post-intensive care syndrome (PICS) *(169).* Older people and patients of all ages with chronic diseases, may be most susceptible to its impacts *(170-173).* Patients recovering from severe COVID-19 who did not require admission to an ICU may also experience some degree of these symptoms *(174).*

For the following patient groups, routinely assess for mobility, functional, swallow, cognitive impairments and mental health concerns, and, based on that assessment, determine discharge readiness, and rehabilitation and follow-up requirements:

- **patients that are in or have been discharged from intensive care;**
- **older patients that have experienced severe cases; and**
- **patients that exhibit signs of any of these impairments.**

Remark:

Use standardized assessment instruments, where available and appropriate *(175)* to detect the presence and severity of impairments related to physical function, respiratory function, cognition, nutrition, communication, swallow, activities of daily living and psychosocial needs (or any other impairments). Consider these in the context of the person's individual situation, including pre-admission status, social support, home environment and access to rehabilitation follow up. Particular consideration should be given to older people, those with disability and those with co-morbidities, who may have more complex requirements *(176, 177).* Involve the person, family and caregivers in the assessment and decision-making regarding rehabilitation and discharge planning.

Where rehabilitation needs are identified, refer for inpatient, outpatient or community-based follow up as indicated and based on rehabilitation needs.

Remarks:

1. Ensure that appropriate IPC is available at designated rehabilitation areas that are caring for patients with COVID-19 that remain infectious.

2. When a patient no longer requires an acute hospital bed for medical needs and requires inpatient rehabilitation, then refer to a rehabilitation ward or facility with capacity to deliver the level of care required.

3. When a patient does not require inpatient rehabilitation but would benefit from rehabilitation follow up post-discharge, refer to outpatient or community-based services according to local service availability. Consider which options have the least barriers to attendance/service utilization and, where available and appropriate, refer to services delivered through telehealth, particularly where IPC measures prevent in-person consultations. Ensure patients are provided with education and information resources for self-management, especially when barriers to accessing rehabilitation follow up are anticipated.

Provide tailored rehabilitation programmes from post-acute to long term, according to patient needs.

Remarks:

1. Ensure access to multidisciplinary rehabilitation where patients can access professionals whose skill sets align with their needs. This may include physiotherapists, occupational therapists, speech and language therapists, mental health and psychosocial providers and, in complex cases, physical and rehabilitation medicine doctors. However, rehabilitation workforce composition may vary by context and in different parts of the world.

2. Rehabilitation programmes should be orientated around patient needs and goals and may entail exercises; education and advice on self-management strategies (including for cognition, swallow and activities of daily living); respiratory techniques (such as breathing exercises and techniques); provision of assistive products; caregiver support and education; peer-to-peer groups; stress management; and home modification.

3. Complement rehabilitation with educational resources, such as information leaflets regarding anticipated symptoms, exercises, and self-management and guidance for caregivers.

4. Where long-term rehabilitation needs associated with severe respiratory illness and PICS are apparent, such as persisting fatigue, reduced exercise tolerance and difficulty with activities of daily living, for example, patients may benefit from pulmonary rehabilitation programmes (or similar) in the community *(176).* If the etiology of symptoms is unclear, a specialist rehabilitation assessment can be considered. This may require involvement of relevant specialists, primary health care providers (general practitioners), rehabilitation professionals, mental health and psychosocial providers, and social care services for coordinated care.

18. Caring for women with COVID-19 during and after pregnancy

There are limited data on the clinical presentation, and maternal and perinatal outcomes of COVID-19 disease during or after pregnancy. Current findings should be cautiously interpreted given the small sample sizes and limitations in study design. As of 24 April 2020, data show a prevalence and patterns of clinical presentation in pregnancy that are broadly similar to the general population. But these findings are restricted to women who were managed in hospitals for any reason, with limited data on women postpartum. Studies varied in the rigor of ascertaining mother-to-child transmission. So far, there is no confirmed mother-to-child transmission.

Similarly, evidence of increased adverse maternal or neonatal outcomes is uncertain, and limited to infection in the third trimester, with some cases of prelabour rupture of membranes, fetal distress and preterm birth reported. Existing evidence has not identified major risks of complications in babies born to mothers with COVID-19.

This section builds on existing recommendations from WHO on pregnancy and infectious diseases and provides additional remarks for the management of pregnant and recently pregnant women.

We recommend all pregnant women with history of contact with a person with confirmed COVID-19 be carefully monitored, considering asymptomatic transmission of COVID-19 may be possible.

Pregnant or recently pregnant women with suspected or confirmed mild COVID-19 may not require acute care in hospital, unless there is concern for rapid deterioration or an inability to promptly return to hospital; but isolation to contain virus transmission is recommended, and can be done at a health facility, community facility or at home, according to established COVID-19 care pathways.

Remarks:

1. Counsel pregnant and recently pregnant women about maternal and newborn signs, including COVID-19 danger signs and maternal perception of decreased fetal movements, and advise them to seek urgent care if they develop any worsening of illness or other danger signs, such as danger signs of pregnancy (including: bleeding or leaking fluid from the vagina, blurry vision, severe headaches, weakness or dizziness, severe abdominal pain, swelling of face, fingers, feet, inability to tolerate foods or liquids, convulsions, difficulty breathing, decrease in fetal movements). Update birth preparedness and complication readiness plans so they know when and where to seek care.

2. In pregnant and postnatal women that are being cared for at home in self-isolation, self-care interventions should be encouraged. Routine antenatal or postnatal health visits in health facilities should be postponed, and delivery of antenatal and postnatal counselling and care, and follow up or other reasons should instead be conducted via alternative platforms such as home-based, phone or telemedicine *(178, 179)*. For women requiring abortion services, consider alternate modes of abortion services, including self-management of medical abortion up to 12 weeks' gestation, where women have access to accurate information and to a health care provider at any stage of the process. Postponing abortion care may lead to increased morbidity and mortality where individuals resort to unsafe abortion practices as abortion service delivery is time-bound by gestational limits prescribed by the law *(180).* If postponed, health visits should be rescheduled until after the period of self-isolation following national guidelines and advice, and in consultation with the health care provider. See the *WHO Consolidated guideline on self-care interventions for health (181).*

3. Counsel women about healthy diet, mobility and exercise, intake of micronutrients for herself and her infant, tobacco use and second-hand smoke exposure, use of alcohol and other substances, as per WHO guidelines on antenatal and postnatal care. Clinical enquiry about the possibility of gender-based violence should be strongly considered, where there is the capacity to provide a supportive response (including referral where appropriate) and where the WHO minimum requirements are met. See resource *(182).*

Pregnant and recently pregnant women with suspected, probable or confirmed COVID-19, should have access to woman-centred, respectful skilled care, including midwifery, obstetric, fetal medicine and neonatal care, as well as mental health and psychosocial support, with readiness to care for maternal and neonatal complications.

Remarks:

1. Woman-centred, respectful, skilled care refers to care organized for and provided to all women in a manner that maintains their dignity, privacy and confidentiality, ensures freedom from harm and mistreatment, and enables informed choice. During labour and childbirth this includes a companion of choice, pain relief, mobility during labour and birth position of choice.

2. Screen birth companions using the standardized case definition. If the companion has suspected or confirmed COVID-19, arrange for an alternative, healthy birth companion in consultation with the woman. Emphasize to any and all companions the importance of IPC measures during labour, childbirth and the mother's and newborn's postnatal stay in the health facility, including appropriate training on and use of PPE and movement restriction in the health care facility.

Mode of birth should be individualized, based on obstetric indications and the woman's preferences. WHO recommends that induction of labour and caesarean section should only be undertaken when medically justified and based on maternal and fetal condition. COVID-19 positive status alone is not an indication for caesarean section. See *WHO recommendations for induction of labour (183).*

Remarks:

1. Emergency birth and pregnancy termination decisions are challenging and based on many factors such as gestational age, severity of maternal condition, and fetal viability and well-being.

2. Interventions to accelerate labour and childbirth (e.g. augmentation, episiotomy, operative vaginal birth) should only be undertaken if medically justified and based on maternal and fetal clinical condition. See *WHO recommendations: intrapartum care for a positive childbirth experience (184).*

3. Delayed umbilical cord clamping (not earlier than 1 minute after birth) is recommended for improved maternal and infant health and nutrition outcomes. The risk of transmission of COVID-19 through blood is likely to be minimal. There is no evidence that delaying cord clamping increases the possibility of viral transmission from the mother to the newborn. The proven benefits of a 1–3 minute delay, at least, in clamping the cord outweigh the theoretical, and unproven, harms.

4. Individualized decisions should be taken about postponing planned (elective) induction or caesarean section in pregnant women with suspected or confirmed mild COVID-19 *(182).*

Pregnant and recently pregnant women who have recovered from COVID-19 and been released from the COVID-19 care pathway, should be enabled and encouraged to receive routine antenatal, postpartum, or postabortion care, as appropriate. Additional care should be provided if there are any complications.

Remarks:

1. All pregnant women with or recovering from COVID-19 should be provided with counselling and information related to the potential risk of adverse pregnancy outcomes.

2. Women's choices and rights to sexual and reproductive health care should be respected regardless of COVID-19 status, including access to contraception and safe abortion to the full extent of the law *(180).*

19. Feeding and caring for infants and young children of mothers with COVID-19

Relatively few cases have been reported of infants confirmed with COVID-19; those that have been reported experienced mild illness. Of 115 mother-child pairs from 17 articles where the mother is confirmed to be infected with COVID-19, 13 children had COVID-19 (4 breastfed, 5 formula-fed, 2 mix-fed, 2 unreported feeding practice). Twenty mothers had breastmilk samples tested for the presence of SARS-CoV-2 RNA particles by RT-PCR; 7 of them had children with COVID-19 (2 breastfed,1 formula fed, 2 mix-fed, 2 unreported). Of the 20 with breastmilk tested, 18 had negative results and 2 had positive results. One of the two mothers whose breastmilk sample was positive for SARS-CoV-2, had a mix-fed child who was not infected with COVID-19; the other one had a child with COVID-19 (feeding practice was not reported) *(185-195)*.

Breastfeeding protects against morbidity and death in the post-neonatal period and throughout infancy and childhood. The protective effect is particularly strong against infectious diseases that are prevented through both direct transfer of antibodies and other anti-infective factors and long-lasting transfer of immunological competence and memory. See WHO *Essential newborn care and breastfeeding (196)*. Therefore, standard infant feeding guidelines should be followed with appropriate precautions for IPC.

Recommendations on the care and feeding of infants whose mothers have suspected or confirmed COVID-19 promote the health and well-being of the mother and infant. Such recommendations must consider not only the risks of infection of the infant with the COVID-19 virus, but also the risks of serious morbidity and mortality associated with not breastfeeding or the inappropriate use of breastmilk substitutes as well as the protective effects of skin-to-skin contact and kangaroo mother care. In light of the current evidence, WHO has concluded that mothers with suspected or confirmed COVID-19 should not be separated from their infants. Mother-infant contact and holding enhances thermoregulation and other physiological outcomes, significantly reduces mortality and morbidity, and improves child and parental attachment. Overall, the recommendation to keep mothers and their children together is based on several important benefits that outweigh the potential (and likely mild) harms of COVID-19 transmission to the child.

We recommend that mothers with suspected or confirmed COVID-19 should be encouraged to initiate and continue breastfeeding. From the available evidence, mothers should be counselled that the benefits of breast-feeding substantially outweigh the potential risks of transmission.

Remarks:

WHO recognizes that the recommendation for an infected mother to be in close contact with her baby may appear to contradict other IPC measures that include isolation of persons infected with COVID-19 virus *(41)*. However, the balance of risks is significantly different for infants than for adults. In infants, the risk of COVID-19 infection is low, the infection is typically mild or asymptomatic, and the consequences of not breastfeeding or separation of mother and child can be significant. At this point it appears that COVID-19 in infants and children represents a much lower risk to survival and health than the other infections and conditions that breastfeeding is protective against. This protection is especially important when health and other community services are themselves under pressure. In contrast, the risks associated with COVID-19 in adults are much higher and more severe. Improved communication is needed to address the uncertainties and confusion among programme managers, health workers and communities on this issue.

Table 4. Summary of recommendations when mother with COVID-19 is caring for infant

	Interventions
Mother infant contact at birth	Mothers should not be separated from their infants unless the mother is too sick to care for her baby. If the mother is unable to care for the infant another competent family caregiver should be identified. Mother and infant should be enabled to remain together while rooming-in throughout the day and night and practise skin-to-skin contact, including kangaroo mother care, especially immediately after birth and during establishment of breastfeeding, whether they or their infants have suspected or confirmed COVID-19 virus infection. Neonates born to mothers with suspected or confirmed COVID-19 should be breastfed within 1 hour of birth. Mothers should apply appropriate IPC. Early and uninterrupted skin-to-skin contact between mothers and infants should be facilitated and encouraged as soon as possible after birth, while applying necessary measures for IPC. This applies also to infants who are born preterm or low birth weight. If the newborn or infant is ill and requires specialist care (such as neonatal unit), arrangements should be made to allow the mother free access to the unit, with appropriate IPC measures. Earlier initiation of breastfeeding results in greater benefits. This may be relevant to mothers who give birth by caesarean section, after an anaesthetic, or those who have medical instability that precludes initiation of breastfeeding within the first hour after birth.
During early childhood	Infants should be breastfed exclusively during the first 6 months after birth, as breastmilk provides all the nutrients and fluids they need. From 6 months of age, breastmilk should be complemented with a variety of adequate, safe and nutrient-dense foods. Breastfeeding should continue up to 2 years of age or beyond. Breastfeeding counselling, basic psychosocial support and practical feeding support should be provided to all pregnant women and mothers with infants and young children if they or their infants and young children have suspected or confirmed COVID-19 infection.
If feeding is interrupted	In situations when severe illness in a mother prevents her from caring for her infant or prevents her from continuing direct breastfeeding, mothers should be encouraged and supported to express milk, and the breastmilk provided safely to the infant, while applying appropriate IPC measures. In the event that the mother is too unwell to breastfeed or express breastmilk, explore the viability of feeding with donor human milk. If this is not possible, consider wet nursing (defined as another woman breastfeeds the child) or appropriate breastmilk substitutes, informed by feasibility, safety, sustainability, cultural context, acceptability to mother and service availability.

	Mothers who are not able to initiate breastfeeding during the first hour after delivery should still be supported to breastfeed as soon as they are able. Assistance should be provided after recovery for relactation to re-establish a milk supply and continue breastfeeding.
Practices the mother should perform during all infant and childcare	Perform frequent hand hygiene with soap and water or alcohol-based hand rub, especially before contact with her child. Perform respiratory hygiene: sneeze or cough into a tissue and immediately dispose of the tissue. Hands should immediately be washed with soap and water or alcohol-based hand rub. Clean and disinfect surfaces with which the mother has been in contact. Wear a medical mask until symptom resolution and criteria for release from isolation have been met. Additionally, breastfeeding mothers should be helped to clean her chest with soap and water if she has been coughing on it before breastfeeding. She does not need to wash her breasts prior to every breastfeed. While mothers are recommended to wear medical masks, if the mother does not have a medical mask, she should still be encouraged to continue breastfeeding as the benefits of breastfeeding outweigh the potential risks of transmission of the virus when breastfeeding while applying other IPC measures.
Best practices for breast-feeding	Health facilities providing maternity and newborn services should enable a mother to breastfeed for as often and for as long as she wishes. Minimizing disruption to breastfeeding will require health care practices that enable a mother to breastfeed. All mothers should receive practical support to enable them to initiate and establish breastfeeding and manage common breastfeeding difficulties. This support should be provided by appropriately trained health care professionals and community-based lay and peer breastfeeding counsellors. There should be no promotion of breastmilk substitutes, feeding bottles and teats, pacifiers or dummies in any part of facilities providing maternity and newborn services, or by any of the staff. Health facilities and their staff should not give feeding bottles and teats or other products that are within the scope of the International Code of Marketing of Breast-milk Substitutes and its subsequent related WHA resolutions, to infants. If the mother is too unwell to breastfeed or express breastmilk, explore the best alternatives to breastfeeding a newborn or young infant, in priority order, as follows: 1) donor human milk should be fed if available from a human milk bank; 2) if supplies are limited, prioritize donor human milk for preterm and low birthweight newborns; 3) wet nursing may be an option depending on acceptability to mothers and families, availability of wet nurses and services to support mothers and wet nurses. COVID-19 testing of a woman who is a potential wet nurse is not required. Prioritize wet nurses for the youngest infants. In settings where HIV is prevalent, prospective wet nurses should undergo HIV counselling and rapid testing where available. In the absence of testing, if feasible, undertake HIV risk assessment. If HIV risk assessment or counselling is not possible, facilitate and support wet nursing; 4) breastmilk substitutes may be used as a last resort.

20. Caring for older people with COVID-19

Older age has been reported as a risk factor for increased mortality in those affected by COVID-19. Other risk factors that have been reported are: smoking, diabetes, hypertension, cerebrovascular disease, cancer and chronic lung disease. Since older people are often affected by these conditions as well, they are potentially at the highest risk for fatality. Those with frailty are one of the most vulnerable populations. Refer to the WHO guidance *Integrated care for older people (ICOPE) (197)* for person-centred and coordinated model of care.

We recommend that older people be screened for COVID-19 at the first point of access to the health system, be recognized promptly if they are suspected to have COVID-19 and treated appropriately according to established COVID-19 care pathways. This should occur in all settings where older people may seek care; included but not limited to facility-based emergency units, primary care, prehospital care settings and LTCFs.

Remark:

Older patients may present with atypical symptoms (including delirium) of COVID-19 (see Table 1); health workers should take this into account during the screening process.

Identify if there is an advance care plan for patients with COVID-19 (such as desires for intensive care support) and respect their priorities and preferences. Tailor the care plan to be in line with patients' expressed wishes and provide the best care irrespective of treatment choice.

We recommend a review of medication prescriptions to reduce polypharmacy and prevent medicine interactions and adverse events for those being treated with COVID-19.

Remarks:

1. Older people are at greater risk of polypharmacy, as a result of newly prescribed medications, inadequate medication reconciliation, and a lack of coordination of care, all of which increases the risk of negative health consequences. If medications are prescribed for mental and neurological manifestations of COVID-19 in older adults, this should be done with extreme caution given the increased susceptibility to drug side-effects and drug interactions with other prescribed medications.

2. Over 20% of adults over 60 years have pre-existing mental or neurological conditions for which they may already be taking medications before infection *(198)*. If a person has a previously diagnosed mental or neurological condition and is already on medications, consider how these medications (or withdrawal from them) may affect their COVID-19 symptoms. Stopping or adjusting the dosage of medications in people with COVID-19 are decisions that require careful risk-benefit analyses and when possible, consultation with a specialist is advised.

Ensure multidisciplinary collaboration among community workers, physicians, nurses, pharmacists, physiotherapists, occupational therapists, social workers, mental health and psychosocial providers and other health care professionals in the decision-making process to address multimorbidity and functional decline *(197).*

Remarks:

1. Physiological changes with age lead to declines in intrinsic capacity such as malnutrition, cognitive decline, depressive symptoms, and those conditions interact at several levels. These interactions require an integrated approach to the screening, assessment and management of older people *(197).*

2. Hearing and vision impairments become more prevalent among older adults and may pose a communication barrier, especially when masks prevent lip reading and decrease vocal clarity. Cognitive decline may also need to be considered when communicating with older patients. Such impairments should be identified early so that health workers involved in their care can adjust their communication accordingly *(199).*

3. Older people who experience COVID-19, including those admitted to ICU and/or treated with protracted oxygen therapy and bed rest, are more likely to experience pronounced functional decline and require coordinated rehabilitation care after acute hospitalization (see Chapter 17: Rehabilitation for patients with COVID-19).

4. Ensure that chronic infections are diagnosed and treated appropriately in older people. Other infections such as TB may mimic or co-exist with COVID-19 and therefore pass unrecognized, causing increased mortality *(38, 39, 41).*

21. Palliative care and COVID-19

Palliative care is a multifaceted, integrated approach to improving the quality of life of adults and paediatric patients and their families facing the problems associated with life-threatening illness such as COVID-19. Palliative care focuses on prevention and relief of suffering by means of early identification, assessment and treatment of physical, psychosocial and spiritual stressors. Palliative care includes but is not limited to end-of-life care *(200)*. Palliative interventions should be integrated with curative treatment *(200).* Basic palliative care, including relief of dyspnoea or other symptoms and social support, should be practised by all doctors, nurses, social workers and others caring for persons affected by COVID-19 *(200, 201).* Refer to the WHO guide *Integrating palliative care and symptom relief into responses to humanitarian emergencies and crises (200).*

We recommend to identify, in all patients with COVID-19, if they have an advance care plan for COVID-19 (such as desires for intensive care support) and respect their priorities and preferences to tailor the care plan and provide the best care irrespective of treatment choice.

Palliative care interventions should be made accessible at each institution that provides care for persons with COVID-19.

Remarks:

1. All interventions described in Appendix 3 should be accessible at each institution that provides care for persons with COVID-19. Efforts should be made to assure accessibility of interventions at home *(200)*.

2. Palliative care includes but is not limited to end-of-life care. Palliative interventions should be integrated with curative treatment. Basic palliative care, including relief of dyspnoea or other symptoms and social support, should be practised by all doctors, nurses, social workers and others caring for persons affected by COVID-19.

3. In hospitals, palliative care does not require a separate ward or department. Palliative care can be provided in any setting.

4. Consider opioids and other pharmacologic and non-pharmacologic interventions for relief of dyspnoea that is refractory to treatment of the underlying cause and/or as part of end-of-life care *(202)*. The narrow therapeutic margin of opioids in the management of dyspnoea requires that opioids are prescribed in accordance with evidence-based treatment protocols and that patients are closely monitored to prevent negative unintended effects due to inappropriate use of opioids. Providers should reference their institutional standards regarding the potential use of opioids for dyspnoea in patients with COVID-19.

22. Ethical principles for optimum care during the COVID-19 pandemic

Ethics are central to the clinical care of COVID-19 patients in the same way that ethics pertains to all patients. Clinical care involves using clinical expertise to do what is best for patients within a relationship of care. This section provides a brief introduction to some of the ethical considerations that are important to remember in the context of COVID-19 *(203, 204)*.

Ethical considerations that affect all persons affected by COVID-19

Equal moral respect: Every person is equally valuable. Treatment and care decisions should be based on medical need and not on irrelevant or discriminatory features such as **ethnicity, religion, sex, age, disability or political affiliation**. Patients with similar health problems or symptoms must receive equal treatment and care. Showing moral respect means involving patients and their caregivers in decision-making to the greatest extent possible, explaining options and limitations in treatment.

Duty of care: Every patient is owed the best possible care and treatment available in the circumstances. Even when resources need to be rationed during a crisis, health care professionals and frontline workers have a duty of care to promote their patients' welfare within available resources. Health care professionals and frontline workers are also owed a duty of care. In this regard, appropriate PPE for health care professionals and frontline workers should be provided to promote their safety and well-being. This is a benefit to them but also to the whole of society by ensuring that they are available to support the clinical response for as long as possible.

Non-abandonment: It follows from consideration of equal moral respect and duty of care, that no person in need of medical care should ever be neglected or abandoned. Care will

extend to families and friends of patients and options to maintain communication with them should be explored. Palliative care must be accessible for all patients with respiratory failure for whom ventilatory support will be withheld or withdrawn.

Protection of the community: Appropriate IPC should be in place, respected and enforced. Such actions protect patients, health care professionals and the community. During a pandemic the focus should be on both clinical care for patients and the promotion of public health.

Confidentiality: All communications between patient and clinician must remain confidential except in the case of compelling public health concerns (e.g. contact tracing and surveillance etc.) or other accepted justifications for breach of confidentiality. Private individual information must be kept secure unless it is a justified breach.

We recommend that hospitals and health systems at local, regional, national and global level plan prepare and be ready to surge clinical care capacity (staff, structure, supplies and systems) in order to be able to provide appropriate care of all COVID-19 patients and maintain essential health services *(33, 205).*

Allocation of scarce resources: We recommend that each institution should establish a plan for what to do in situations of resource scarcity to cover the allocation or access to critical medical interventions (such as oxygen, intensive care beds and/or ventilators). Such a plan should establish a clear overall aim.

Decision-making regarding allocation: Part of planning for scarcity is ensuring that a fair system of decision-making for allocation is in place.

Remarks:

1. Personnel familiar with the medical triage criteria and allocation protocols, who are distinct from the clinical treating team are one option. Allocation decisions should be done according to the established plan and regularly reviewed. If necessary, there should be a reallocation of a resource that was previously allocated where it is not proving beneficial.

2. For example, the aim might be to ensure the best possible use of limited resources based upon chosen medical criteria. Triage criteria should seek to balance medical utility and equity, and ease of implementation. The same criteria should be applied for all patients with similar levels of need, regardless of COVID-19 status.

We recommend that it be clear when decision-making will move from routine allocation to pandemic allocation, so that institutions do not move too soon to restrict access in anticipation of possible future scarcity that might not arise.

Remarks:

1. It should be clear what the “tipping point” is to change to pandemic allocation (e.g. a declaration by a ministry of health, or hospitals reaching ICU bed and ventilator capacity). This should take into account maximizing surge clinical capacity.

2. Whatever method is chosen should be subject to a fair process, such as using the following procedural principles:

- **Inclusiveness:** Input should be obtained from the most affected population(s).
- **Transparency:** The mechanism should be easily accessible and understandable at an elementary school level and in all major languages in the institution's catchment area.
- **Accountability:** A mechanism should be available to review the application of an approved triage protocol, or requests to review a particular decision, in light of novel or updated clinical information or other concerns.
- **Consistency:** Allocation principles should be applied consistently.

We recommend that caregivers should be:

- **Given access to adequate training in caregiving, including IPC.**
- **Given access to appropriate and adequate PPE.**
- **Exempted from travel restrictions that would preclude caring for the patient.**
- **Be given access to psychological, social and spiritual care, and also to respite and bereavement support as needed.**

Remark:

Caregivers are at risk for the same types of psychological, social and spiritual distress as patients. They are also at risk for becoming infected. Basic mental health and psychosocial support should be provided for all caregivers by asking them about their needs and concerns, and addressing them *(206)*.

23. Reporting of death during the COVID-19 pandemic

We recommend the use of emergency ICD codes as outlined in the *International guidance for certification and coding of COVID-19 as cause of death (208).* As there are six types of coronaviruses, we recommended not to use "coronavirus" in place of COVID-19.

Remarks:

1. The primary goal is to identify all deaths due to COVID-19. A death due to COVID-19 is defined for surveillance purposes as a death resulting from a clinically compatible illness, in a probable or confirmed COVID-19 case, unless there is a clear alternative cause of death that cannot be related to COVID-19 disease (e.g. trauma). There should be no period of complete recovery from COVID-19 between illness and death. A death due to COVID-19 may not be attributed to another disease (e.g. cancer) and should be counted independently of pre-existing conditions that are suspected of triggering a severe course of COVID-19.

2. Specification of the causal sequence leading to death in Part 1 of the certificate is important. For example, in cases when COVID-19 causes pneumonia, sepsis and acute respiratory distress; then pneumonia, sepsis and acute respiratory distress should be included, along with COVID-19, in Part 1. Certifiers should include as much detail as possible based on their knowledge of the case, from medical records, or about laboratory testing *(207)*.

3. The use of official terminology, COVID-19, should be used for all certification of this cause of death. COVID-19 should be recorded on the medical certificate as cause of death for all decedents where the disease caused, or is assumed to have caused, or contributed to death. This helps to reduce uncertainty for the classification or coding and to correctly monitor these deaths.

24. Clinical research during the COVID-19 pandemic

There are many ongoing clinical trials testing various potential antivirals; these are registered on https://clinicaltrials.gov/, the Chinese Clinical Trial Registry (http://www.chictr.org.cn/abouten.aspx) and on the WHO website: Living mapping and living systematic review of COVID-19 studies *(208)*. For more information about the WHO research roadmap see https://www.who.int/teams/blueprint/covid-19

We recommend to collect standardized clinical data on all hospitalized patients to improve understanding of the natural history of the disease and contribute data to the WHO Global COVID-19 Clinical Data Platform.

Remarks:

1. Member States are invited to contribute anonymized clinical data to the WHO Global COVID-19 Clinical Data Platform; contact: COVID_ClinPlatform@who.int to get log-in credentials. This will serve to inform the public health and clinical response.

2. Three case record forms (CRFs) are now available: These can be accessed on the WHO website *(209)*.
    - Rapid CRF
    - Pregnancy CRF
    - Multisystem inflammatory syndrome temporally associated with COVID-19 CRF.

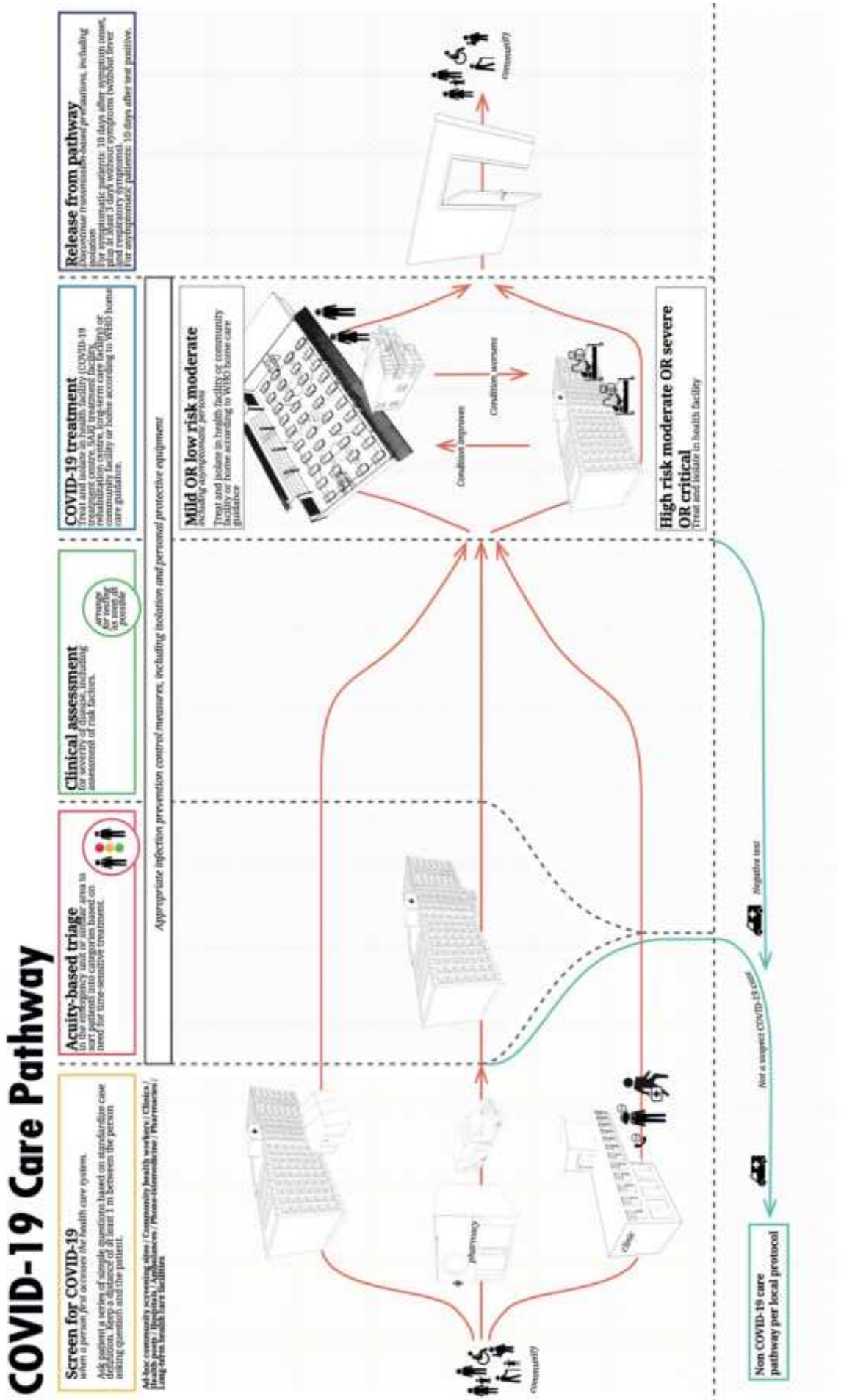
3. Clinical characterization research protocols are also available *(210)*.

The WHO Solidarity trial is a randomized clinical trial that is a currently enrolling. For more information see the WHO website *(211)*.

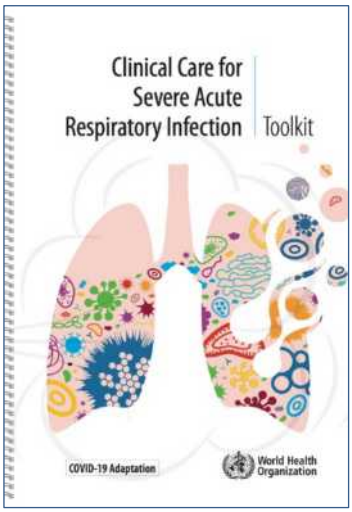
Remark:

Older age is reported to be a predictor of mortality in patients with COVID-19. The systematic exclusion of older adults from research activities or from accessing investigational therapeutic agents is not justified *(204)*.

Appendix 1: COVID-19 care pathway

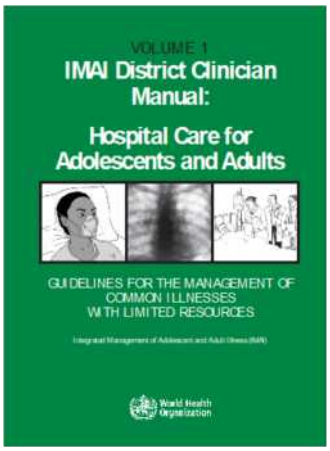


Appendix 2: Resources for supporting clinical management of COVID-19



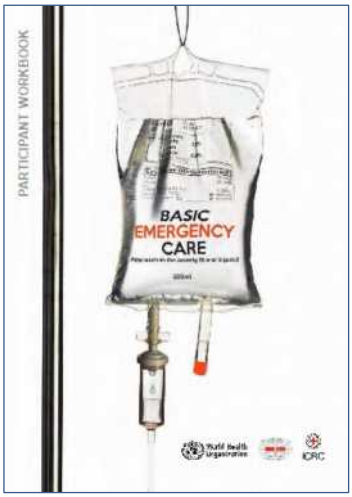
Clinical care for severe acute respiratory infection toolkit: COVID-19 adaptation (2020)

This toolkit is intended for clinicians working in acute care hospitals in low- and middle-income countries, managing adult and paediatric patients with acute respiratory infection, including severe pneumonia, acute respiratory distress syndrome, sepsis and septic shock. The main objective is to provide some of the necessary tools that can be used to care for the critically ill patient from hospital entry to hospital discharge.
https://www.who.int/publications-detail/clinical-care-of-severe-acute-respiratory-infections-tool-kit



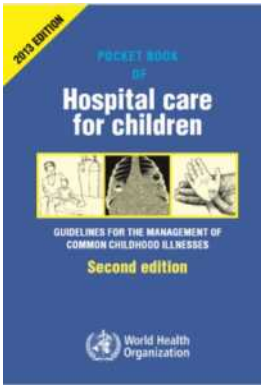
IMAI District clinician manual: hospital care for adolescents and adults. Guidelines for the management of common illnesses with limited resources (2011)

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 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.
https://www.who.int/hiv/pub/imai/imai2011/en/



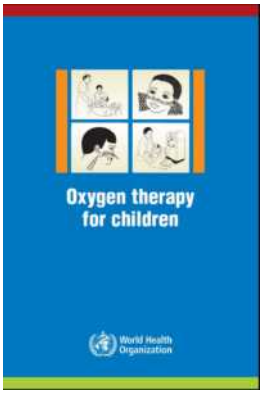
WHO-ICRC Basic emergency care: approach to the acutely ill and injured (2018)

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. 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.
https://www.who.int/publications-detail/basic-emergency-care-approach-to-the-acutely-ill-and-injured



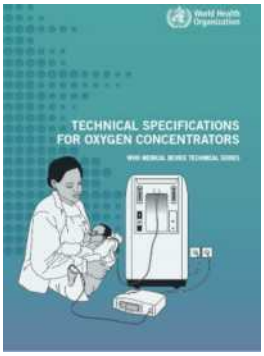
Pocket book of hospital care for children: guidelines for the management of common childhood illnesses (second edition) (2013)

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.
https://www.who.int/maternal_child_adolescent/documents/child_hospital_care/en/



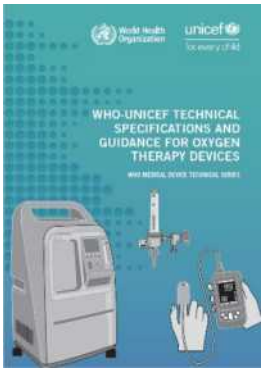
Oxygen therapy for children (2016)

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.
http://www.who.int/maternal_child_adolescent/documents/child-oxygen-therapy/en/



Technical specifications for oxygen concentrators (2015)

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.
https://www.who.int/medical_devices/publications/tech_specs_oxygen-concentrators/en/



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 groups. It aims to support ministries of health to ensure that oxygen supply is available, as well as to raise awareness of the importance of appropriate selection, procurement, maintenance, and use of medical devices, both capital equipment and single-use devices.
https://www.who.int/medical_devices/publications/tech_specs_oxygen_therapy_devices/en/

Appendix 3: Palliative care therapies

The following table has been adapted from *Integrating palliative care and symptom relief into responses to humanitarian emergencies and crises: a WHO guide*, available here in full: https://apps.who.int/iris/handle/10665/274565

Table A3.1 Essential package of palliative care: interventions, medicines, equipment, human resources and social supports

	Inputs			
Interventions	**Medicines[a]**	**Equipment**	**Human resources[b]**	**Social supports**
Prevention and relief of pain or other physical suffering,[c] acute or chronic, related to COVID-19	– Amitriptyline, oral – Bisacodyl (senna), oral – Dexamethasone, oral and injectable – Diazepam, oral and injectable – Diphenhydramine (chlorpheniramine, cyclizine, or dimenhydrinate), oral and injectable – Fluconazole, oral – Fluoxetine, oral – Furosemide, oral and injectable – Haloperidol, oral and injectable – Hyoscine butylbromide, oral and injectable – Ibuprofen (naproxen, diclofenac, or meloxicam), oral – Lactulose (sorbitol or polyethylene glycol), oral – Loperamide, oral – Metaclopramide, oral and injectable – Metronidazole, oral, to be crushed for topical use – Morphine, oral immediate release and injectable – Naloxone, injectable – Omeprazole, oral – Ondansetron, oral and injectable[d] – Oxygen – Paracetamol, oral – Petroleum jelly	– Pressure-reducing mattresses – Nasogastric drainage and feeding tubes – Urinary catheters – Opioid lock boxes – Flashlights with rechargeable batteries (if no access to electricity) – Adult diapers or cotton and plastic	– Doctors (with basic palliative care training) – Nurses (with basic palliative care training) – Community health workers (if available)	

Prevention and relief of psychological suffering,[e] acute or chronic, related to COVID-19	– Amitriptyline, oral – Dexamethasone, oral and injectable – Diazepam, oral and injectable – Diphenhydramine (chlorpheniramine, cyclizine or dimenhydrinate), oral and injectable – Fluoxetine, oral – Haloperidol, oral and injectable – Lactulose (sorbitol or polyethylene glycol), oral	– Adult diapers or cotton and plastic	– Doctors (with basic palliative care training) – Nurses (with basic palliative care training) – Social workers or psychologists – Community health workers (if available)	
Prevention and relief of social suffering, acute or chronic, related to COVID-19			– Social workers – Community health workers (if available)	– Income and in-kind support[f]
Prevention and relief of spiritual suffering, related to COVID-19			– Local spiritual counsellors	

[a] Based on WHO Model List of Essential Medicines (2015). Acceptable alternative medicines are in parentheses: ( )

[b] Doctors may be local or foreign and may be surgeons, anaesthesiologists, intensivists, infectious disease specialists, paediatricians, general practitioners, palliative care specialists, or others. Nurses may include nurse-anaesthetists.

[c] Other physical suffering includes breathlessness, weakness, nausea, vomiting, diarrhoea, constipation, pruritus, bleeding, wounds and fever.

[d] Only at hospitals that provide cancer chemotherapy or radiotherapy.

[e] Psychological suffering includes anxiety, depressed mood, confusion or delirium, dementia and complicated grief.

[f] Only for patients living in extreme poverty and for one caregiver per patient. Includes cash transfers to cover housing, children's school tuition, transportation to health care facilities or funeral costs; food packages; and other in-kind support (blankets, sleeping mats, shoes, soap, toothbrushes, toothpaste).

Source: Integrating palliative care and symptom relief into responses to humanitarian emergencies and crises: a WHO guide (2018).

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