Clinical management of COVID-19

LIVING GUIDELINE
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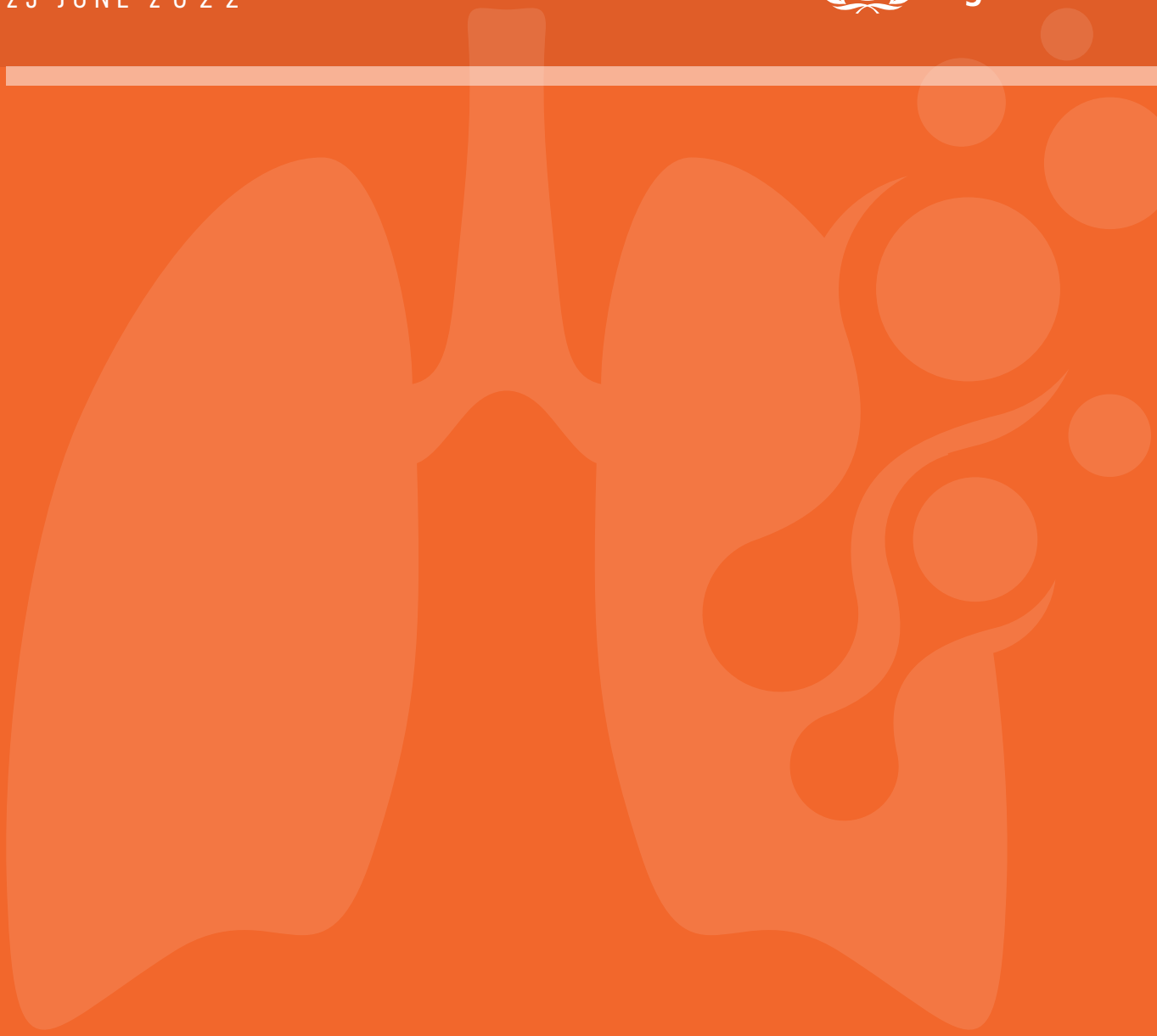
World Health Organization



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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.

Sections

Foreword

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

1) suppress transmission;

2) provide optimized care for all patients, and save lives;

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 [1]* describes key actions that should be taken in different scenarios: no cases; sporadic cases; clusters of cases; and community transmission, in order to enable delivery of clinical and public health services in a timely fashion. This guideline 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 and the public health response. Considerations for special and vulnerable populations, such as paediatric patients, older people and pregnant women, are highlighted throughout the text.

This guideline is a product of the contributions of several WHO team members and independent experts from all over the world. The WHO is deeply grateful to each of the contributors for their time and expertise.

In this document we refer to the **COVID-19 care pathway (Annex 1).** This describes a coordinated and multidisciplinary care pathway that a patient enters after they are **screened for COVID-19 and becomes a suspect/confirmed 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 *[2]*.

Summary

Info Box

Clinical guideline: What are the interventions to manage patients with COVID-19?

Target audience: The target audience is anyone broadly involved directly or indirectly in the care of patients with COVID-19, i.e. clinicians, allied health care workers, and hospital administrators.

Current practice: The evidence base for clinical management of COVID-19 is increasing rapidly. Numerous randomized and observational trials are underway to inform practice. This version of *Clinical management of COVID-19: living guideline* includes three new recommendations.

New recommendations: In this update, the Guideline Development Group (GDG) makes three new recommendations:

- Conditional recommendation to use high-flow nasal oxygen (HFNO) rather than standard oxygen therapy for patients with severe and critical COVID-19 with acute hypoxaemic respiratory failure (AHRF) not requiring emergency intubation;
- Conditional recommendation to use continuous positive airway pressure (CPAP) rather than standard oxygen therapy for patients with severe and critical COVID-19 with AHRF not requiring emergent intubation;
- Conditional recommendation to use non-invasive ventilation rather than standard oxygen therapy for patients with severe and critical COVID-19 with AHRF not requiring emergent intubation.

Rationale for the new recommendations:

The recommendations were triggered by the availability of new evidence (five randomized controlled trials [RCTs] specific to COVID-19). Two systematic reviews/meta-analysis (one based on a direct PICO - COVID-19 patients and the other based on an indirect PICO of patients with acute respiratory distress syndrome (ARDS) and hypoxemic respiratory failure) provided the data for the development of these recommendations. The rationale for the broad recommendation around the use of these devices over standard oxygen therapy is explained in detail in the respective sections; key factors guiding these recommendations were the impact (benefit) of these devices on four prioritized critical outcomes: mortality, need for invasive mechanical ventilation, hospitalization, and ICU length of stay. The recommendations are conditional based on the quality and certainty of the evidence.

For sub-questions such as the choice of interface (helmet vs face mask etc.) or between-device comparisons, the GDG chose not to make a recommendation either due to the absence of direct data or the uncertainty.

How this guideline was created? A GDG of content experts, clinicians, patients, ethicists, and methodologists produced recommendations following standards for trustworthy guideline development using the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach. No conflict of interest was identified for any panel member or other contributors to the guideline development process. This living guideline represents an innovation from the World Health Organization (WHO), driven by the urgent need for global collaboration to provide trustworthy and evolving COVID-19 guidance informing policy and practice worldwide.

The latest evidence: The GDG's recommendations for non-invasive advanced respiratory support options for patients with severe and critical COVID-19 with AHRF not requiring emergent intubation were informed by the results of two systematic reviews, one evaluating the use of these interventions in patients with COVID-19 (direct PICO) and the other evaluating the use of these interventions in patients with non-COVID-19 ARDS (indirect PICO).

Understanding the recommendations:

When moving from evidence to recommendations, the GDG considered a combination of evidence assessing relative benefits and harms, values and preferences, equity and feasibility issues. For severe and critical COVID-19 patients with AHRF not requiring intubation, the GDG recognized that: HFNO may reduce mortality and need for invasive mechanical ventilation (IMV; direct PICO, low certainty); and probably decreases hospital length of stay (direct PICO, moderate certainty evidence) when compared with standard oxygen therapy (SOT); that CPAP may reduce mortality and length of stay (direct PICO, low certainty) and probably decreases the need for IMV (moderate certainty) when compared with SOT; and that non-invasive ventilation (NIV) probably reduces mortality and IMV (indirect PICO, moderate certainty) and may decrease hospital length of stay (indirect PICO, low certainty). The GDG emphasized that appropriate resources such as trained staff and infrastructure, as as oxygen supply, need to be in place for implementation.

Abbreviations

ADL	activities of daily living
AGP	aerosol-generating procedure
AHRF	acute hypoxaemic respiratory failure
ARDS	acute respiratory distress syndrome
AWaRe	Access, Watch or Reserve (antibiotics)
BiPAP	bilevel positive airway pressure
BMI	body mass index
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
DVT	deep vein thrombosis
ECMO	extracorporeal membrane oxygenation
EOS	end of study
FiO2	fraction of inspired oxygen
GDG	Guideline Development Group
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HFNO	high-flow nasal oxygen
HIV	human immunodeficiency virus
ICU	intensive care unit
IFRC	International Federation of Red Cross and Red Crescent Societies
IMV	invasive mechanical ventilation
IPC	infection prevention and control
IQR	interquartile range
IVIG	intravenous immune globulin
LOS	length of stay
LRT	lower respiratory tract
LTCF	long-term care facility
MAGIC	Magic Evidence Ecosystem Foundation
MAP	mean arterial pressure
MERS-CoV	Middle East respiratory syndrome coronavirus
MHPSS	mental health and psychosocial support

MIS-C	multisystem inflammatory syndrome in children
NAAT	nucleic acid amplification test
NCD	noncommunicable disease
NICU	neonatal intensive care unit
NIV	non-invasive ventilation
OI	Oxygenation Index
OSI	Oxygenation Index using SpO2
PaO2	partial pressure arterial oxygen
PBW	predicted body weight
PEEP	positive end-expiratory pressure
PICO	population, intervention, comparator, outcome
PICS	post-intensive care syndrome
PPE	personal protective equipment
PTSD	post-traumatic stress disorder
PUI	person/patient under investigation
QNS	quality assurance of norms and standards
RCT	randomized controlled trial
RDT	rapid diagnostic test
RM	recruitment manoeuvre
RT-PCR	reverse transcription polymerase chain reaction
SARS-CoV-2	severe acute respiratory syndrome coronavirus
SBP	systolic blood pressure
SIRS	systemic inflammatory response syndrome
SOFA	sequential organ failure assessment
SOT	standard oxygen therapy
SpO2	oxygen saturation