

Eber Coelho Paraguassu, Jamille dos Passos Lacerda and WHO

Este artigo é um compartilhamento em forma de cópia literal do original
"Clinical Care for Severe Acute Respiratory Infection": World Health Organization;
2022. Licença [CC BY-NC-SA 3.0 IGO](https://creativecommons.org/licenses/by-nc-sa/3.0/igo/).

Este compartilhamento tem como objetivo impulsionar o conhecimento
sobre esta nova doença chamada COVID 19.

Clinical Care for Severe Acute Respiratory Infection

Toolkit

Update 2022



World Health
Organization

COVID-19 Adaptation



Clinical Care for
Severe Acute
Respiratory Infection

Toolkit

Update 2022

COVID-19 Adaptation



World Health
Organization

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

WHO/2019-nCoV/SARI_toolkit/2022.1

© World Health Organization 2022

Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; <https://creativecommons.org/licenses/by-nc-sa/3.0/igo>).

Under the terms of this licence, you may copy, redistribute and adapt the work for non-commercial purposes, provided the work is appropriately cited, as indicated below. In any use of this work, there should be no suggestion that WHO endorses any specific organization, products or services. The use of the WHO logo is not permitted. If you adapt the work, then you must license your work under the same or equivalent Creative Commons licence. If you create a translation of this work, you should add the following disclaimer along with the suggested citation: "This translation was not created by the World Health Organization (WHO). WHO is not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition".

Any mediation relating to disputes arising under the licence shall be conducted in accordance with the mediation rules of the World Intellectual Property Organization (<http://www.wipo.int/amc/en/mediation/rules/>).

Suggested citation. Clinical care for severe acute respiratory infection: toolkit, update 2022. COVID-19 adaptation. Geneva: World Health Organization; 2022 (WHO/2019-nCoV/SARI_toolkit/2022.1). Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at <http://apps.who.int/iris>.

Sales, rights and licensing. To purchase WHO publications, see <http://apps.who.int/bookorders>. To submit requests for commercial use and queries on rights and licensing, see <https://www.who.int/copyright>.

Third-party materials. If you wish to reuse material from this work that is attributed to a third party, such as tables, figures or images, it is your responsibility to determine whether permission is needed for that reuse and to obtain permission from the copyright holder. The risk of claims resulting from infringement of any third-party-owned component in the work rests solely with the user.

General disclaimers. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by WHO in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by WHO to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall WHO be liable for damages arising from its use.

Contents

FOREWORD	vii
ACKNOWLEDGEMENTS	viii
ABBREVIATIONS	xi
EXECUTIVE SUMMARY	xvii
1. EPIDEMIOLOGY OF SARI	1
Summary	2
1.1 Differential diagnosis of SARI	3
1.2 COVID-19 (SARS-CoV-2) fact sheet	5
1.3 Influenza virus fact sheet.....	7
1.4 Middle East respiratory syndrome coronavirus (MERS-CoV) fact sheet.....	10
1.5 Risk factors for severe disease: influenza vs COVID-19	11
References and resources	12
2. SCREENING, TRIAGE, CLINICAL ASSESSMENT AND MANAGEMENT OF SARI.....	15
Summary	16
2.1 Screening for SARI	18
2.2 Triage for SARI.....	23
2.3 Clinical assessment of acutely ill patients - basic emergency care: ABCDE approach.....	29
2.4 Classification of severity in patients with COVID-19.....	32
2.5 Decision-making algorithm for patients presenting with <u>acute respiratory infection</u> (ARI) (influenza or COVID-19 suspected or known to be circulating).....	34
2.6 Decision-making algorithm for hospitalization of patients with <u>pneumonia</u> (influenza or COVID-19 known to be circulating)	35
2.7 Decision-making support tool for hospitalization and ICU admission for patients with SARI and severe pneumonia.....	36
2.8 Checklist for admission	37
2.9 Checklist for transfer.....	38
2.10 Transfer of critically ill patients: air medevac for COVID-19 patients	39
References and resources.....	42
3. INFECTION PREVENTION AND CONTROL FOR PATIENTS WITH SARI.....	45
Summary	46
3.1 How to implement infection control measures for SARI.....	48
3.2 How to implement infection control measures for ARIs of potential concern.....	49
3.3 Personal protective equipment (PPE).....	50
3.4 How to improve medical mask fit in health care settings.....	52
3.5 Steps to perform a particulate respirator seal check during the putting on of PPE	53
3.6 Hand hygiene.....	54
3.7 The 5 moments for hand hygiene in health care facilities	56

3.8	The “Three Cs”: settings where transmission of the COVID-19 virus spreads more easily	57
3.9	Checklist for aerosol-generating procedures	58
	References and resources	59

4. MONITORING PATIENTS WITH ACUTE RESPIRATORY INFECTION 61

	Summary	62
4.1	AVPU scale: a simple tool for assessing level of consciousness	64
4.2	Pulse oximetry monitoring	65
4.3	Blood gas analysis monitoring	67
4.4	Capnometry (capnography)	68
4.5	National Early Warning Score (NEWS) for adults	69
4.6	Paediatric Early Warning Score (PEWS)	72
4.7	Routine monitoring and care framework for COVID-19 patients	73
4.8	WHO Mild COVID-19 home care bundle for health care workers	75
4.9	Memory aid: key criteria used to assess vital signs in children	77
4.10	Memory aid: key physiological aspects to assess in pregnant women	78
	References and resources	80

5. DIAGNOSTIC TESTING FOR PATIENTS WITH ARI 83

	Summary	84
5.1	Diagnostic testing for SARS-CoV-2 infection	86
5.2	Use of antigen-detection rapid diagnostic testing for SARS-CoV-2	87
5.3	Specimen collection kit for upper respiratory tract specimens	88
5.4	Guideline for specimen storage	92
5.5	Material for specimen transportation	93
5.6	Guideline for specimen transportation	94
5.7	Guide for blood culture collection in patients with SARI	95
	References and resources	96

6. OXYGEN THERAPY 97

	Summary	98
6.1	Indications for oxygen therapy	100
6.2	Memory aid: oxygen delivery devices	101
6.3	Memory aid: oxygen delivery in children	103
6.4	Algorithm to escalate respiratory support in adults and children with pneumonia	104
6.5	Flowchart on how to titrate oxygen in neonates	105
6.6	Flowchart on how to titrate oxygen in children	106
6.7	Flowchart on how to titrate oxygen in adults	107
6.8	Key tips on awake prone positioning	108
6.9	Checklist to troubleshoot warning signs during oxygen therapy delivery	110
6.10	Oxygen supply calculations	112
6.11	Memory aids: oxygen supply sources and distribution	113
6.12	Respiratory care order template for oxygen therapy	117
	References and resources	118

7. THERAPIES FOR SARI (COVID-19, INFLUENZA, BACTERIAL PNEUMONIA): ANTIMICROBIALS AND IMMUNOMODULATORS 121

	Summary	122
7.1	Memory aid: treatment for acute respiratory infections according to severity (when COVID-19 and influenza are circulating)	124

7.2	COVID-19 and therapeutics	128
7.3	Memory aid: invasive fungal infections in patients with COVID-19	145
7.4	Treatment for influenza infection fact sheet	150
	References and resources	152

8. SEPSIS AND SEPTIC SHOCK 155

	Summary	156
8.1	Sepsis and septic shock definitions	158
8.2	Sequential Organ Failure Assessment (SOFA) score	160
8.3	Quick Sequential Organ Failure Assessment (qSOFA).....	161
8.4	Paediatric Logistic Organ Dysfunction (PELOD-2) score	162
8.5	Algorithm on targeted resuscitation in adults with shock	164
8.6	Algorithms on initial resuscitation, and on fluid and vasoactive-inotrope management for children with septic shock.....	165
8.7	Guide to the use of vasopressors in septic shock for adults and children	167
8.8	The five rules for passive leg raise (PLR).....	169
	References and resources	170

9. ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)173

	Summary	174
9.1	Memory aid: diagnosis and classification of ARDS in adults	176
9.2	Memory aid: diagnosis and classification of pARDS in children	177
9.3	Advanced non-invasive oxygen delivery in ARDS: algorithm to escalate supportive respiratory therapy.....	178
9.4	Checklist for rapid sequence intubation procedure in adults and children.....	179
9.5	Considerations for intubation and mechanical ventilation in children.....	181
9.6	List of commonly used medicines and dosage in ICU with ventilated patients (adults, children)	183
9.7	Choice of induction agents in adults	187
9.8	Choice of induction agents in children	188
9.9	Protocol to deliver lung protective ventilation (LPV)	189
9.10	Memory aid: comparison of normal waveforms during volume and pressure-limited ventilation.....	191
9.11	Memory aid: recognizing and interpreting abnormal pressure and flow waveforms during volume control ventilation.....	192
9.12	Guide to distinguishing between the causes of high peak airway pressures: resistance versus compliance	193
9.13	Troubleshooting high peak airway pressures, low tidal volumes, desaturation or haemodynamic instability in ventilated patients.....	194
9.14	Respiratory care pocket card reference	195
9.15	Adult ventilation order set (ARDS).....	204
9.16	Checklist for proning in severe ARDS	205
9.17	Ventilator circuit types, filter and humidifier locations for SARI	207
	References and resources	212

10. MANAGE PAIN, SEDATION AND DELIRIUM.....215

	Summary	216
10.1	Numerical pain assessment scales.....	218
10.2	Behavioural pain assessment scales	219
10.3	Richmond Agitation-Sedation Scale (RASS)	225

10.4	Flowchart and worksheet for the Confusion Assessment Method of the ICU for adults (CAM-ICU).....	226
10.5	Flowchart and worksheet for the Confusion Assessment Method of the ICU for children (pCAM-ICU)	228
10.6	Procedure for assessing attention: attention screening exam (ASE) for adults	231
10.7	Guide to commonly used sedatives in adults	233
10.8	Guide to commonly used opioid analgesics in adults	234
10.9	Guide to using neuromuscular blockers in adults.....	235
10.10	Guide to commonly used antipsychotics (haloperidol) in adults.....	236
10.11	Guide to paediatric analgesics, sedatives and neuromuscular blockers.....	237
	References and resources.....	238
11. LIBERATION FROM INVASIVE MECHANICAL VENTILATION.....		239
	Summary	240
11.1	Algorithm for daily sedation interruption and daily spontaneous breathing trial (SBT)	241
11.2	How to perform a cuff leak test	242
11.3	Respiratory care pocket card reference	244
11.4	Spontaneous breathing trial (SBT) order set	246
	References and resources	247
12. BEST PRACTICES TO PREVENT COMPLICATIONS		249
	Summary	250
12.1	Interventions to prevent complications in hospitalized and critically ill patients with COVID-19.....	251
12.2	Checklist for central venous catheter (CVC) insertion.....	252
12.3	Checklist for preventing ventilator-associated pneumonia (VAP).....	253
12.4	Checklist for preventing urinary tract infections (UTI)	254
12.5	Procedure for providing enteral nutrition (EN) for adults.....	255
12.6	Procedure for providing enteral nutrition (EN): paediatric considerations.....	256
12.7	Algorithm for early mobility in the ICU	258
12.8	Thromboembolic prophylaxis in COVID-19	259
12.9	ABCDE bundle	260
	References and resources.....	263
13. QUALITY IN CRITICAL CARE		265
	Summary	266
13.1	Checklist for ICU daily best practices	268
13.2	Surviving Sepsis Campaign bundles.....	269
13.3	Checklist for high-quality use of invasive mechanical ventilation for ARDS.....	270
13.4	Process for selecting problem to focus on in the ICU and quality improvement process.....	271
13.5	Checklist for initiating, improving, evaluating and sustaining a quality improvement programme	272
	References and resources	273
14. ETHICAL CONSIDERATIONS		275
	Summary	276
14.1	Ethical values and principles	277
14.2	Triage decision process flow	279
14.3	Hospital scarce resource decision-making	280
	References and resources	281

Foreword

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

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

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



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



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

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

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

Acknowledgements

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

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

2022 version

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

WHO would like to thank the following collaborators and reviewers for their contribution to this current 2022 updated version: Angela Aramburo (Royal Brompton Hospital, London, United Kingdom); Diptesh Aryal (University of Toronto Interdepartmental Division of Critical Care and St Michael's Hospital, Canada); Emmanuel Ayebale (Anaesthesia/ICU - Makerere University, Uganda); Tim Baker (Anaesthesia/ICU - Karolinska Institutet, Sweden and United Republic of Tanzania); Rich Branson (Respiratory Care - University of Cincinnati, USA); Lundy Campbell (Anaesthesia - UCSF, USA); Rshan Haniffa (Anaesthesia/ICU - Network for Improving Critical Care Systems and Training, Colombo, Sri Lanka and University College London, United Kingdom); Carolina Haylock-Loor (Anaesthesia/ICU - World Federation of Societies of Anesthesiologists/Honduras); Carolyn Hendrickson (Pulmonary Critical Care Medicine, UCSF, USA); Shevin Jacob (Infectious Disease - Liverpool School of Tropical Medicine, United Kingdom and Uganda); Rich Kallet (Respiratory Care - San Francisco, General Hospital, USA); Niranjan "Tex" Kissoon (University of British Columbia and British Columbia Children's Hospital, Vancouver Canada); Richard Kojan (Alliance for International Medical Action [ALIMA]); Teresa Kortz (Paediatric Critical Care - UCSF, USA); Arthur Kwizera (Anaesthesia/ICU - Makerere University, Uganda); Hans-Jörg Lang; Paula Lister (Queensland Health, Australia); Srinivas Murthy (University of British Columbia, Vancouver Canada); Robert Neighbour (Biomedical Engineer - Diamedica UK Ltd); Beth Riviello (Pulmonary Critical Care Medicine - Beth Israel Deaconess, USA); Cornelius Sendagire (Anaesthesia/ICU - Makerere University, Uganda); Jhuma Sankar (Pediatrics, All India Institute of Medical Sciences, New Delhi, India); Rebecca Silvers (ICU - UCSF, USA); Paul Sonenthal (Pulmonary Critical Care Medicine, Brigham and Women's Hospital, USA); Sky Vanderburg (Pulmonary Critical Care Medicine, UCSF, USA).

Valuable inputs were also provided by many technical staff from different WHO units and their collaborators including: members of the WHO Neurology and COVID-19 Global Forum Acute Clinical Care and Support Working Group: Foad Abd-Allah (Cairo University, African Academy of Neurology, Egypt); Albert Akpalu (University of Ghana, West African College of Physicians); Mashina Chomba

(Columbia University Medical Center, USA); Sherry Chou (University of Pittsburgh School of Medicine, USA); Maria Lucia Brito Ferreira (Department of Neurology, Hospital da Restauração, Brazil); Ericka Fink (Children's Hospital of Pittsburgh, University of Pittsburgh Medical Center, USA); Alla Guekht (Moscow Research and Clinical Center for Neuropsychiatry, Russian Federation); Hoo Fan Kee (Universiti Putra Malaysia); Amir Kheradmand (Johns Hopkins Myelitis and Myopathy Center, USA); Benedict Michael (Institute of Infection and Global Health, University of Liverpool, United Kingdom); Shubham Misra (All India Institute of Medical Sciences, India); Alessandro Padovani (Neurology, Public Health, Disability Unit & Coma Research Centre, Italy); Carlos Pardo-Villamizar (Department of Neurology, Johns Hopkins School of Medicine, USA); Kameshwar Prasad (Department of Neurology, All India Institute of Medical Sciences, India); Erich Schmutzhard (Medical University of Innsbruck, Austria); Jim Sejvar (Centers for Disease Control and Prevention [CDC], USA); Tom Solomon (National Institute for Health Protection Health Protection Research Unit in Emerging and Zoonotic Infections, Department of Neurology, University of Liverpool, United Kingdom); Kiran Thakur (Department of Neurology, Columbia University, USA); Thirugnanam Umapathi (National Neuroscience Institute, Singapore); Andrea Winkler (Department of Neurology, Center for Global Health, Technical University of Munich, Germany); Greta Wood (University of Liverpool, United Kingdom).

Special thanks for the review and updating of several toolkit chapters by specific WHO units (with external collaborators):

- Biomedical equipment team: Ingrid Lara Rendon, Alejandra Velez Ruiz Gaitan, Adriana Velazquez Berumen.
- Co-infections and antimicrobials: Peter Beyer, Tom Chiller (CDC), Nathan Paul Ford, Haileyesus Getahun, Benedikt Huttner, Brendan R Jackson (CDC), Meghan Marie Lyman (CDC), Sarah Paulin, Hatim Sati, Timothy M Uyeki (CDC).
- Epidemiology and influenza, SARS and MERS: Aspen Hammond, Ann Moen, Julia Vfitzner, Maria Van Kerkhove, Katelijn AH Vandemaele, Wenqing Zhang.
- Ethical considerations: Andreas Alois Reis and collaborator Harald Schmidt (Harald Department of Medical Ethics and Health Policy, Perelman School of Medicine, Pennsylvania, USA).
- Infection prevention and control: April Baller, Alice Simniceanu, Victoria Willet.
- Laboratory and sample collection: Céline Barnadas, Christopher William Black, Kazunobu Kojima, Sylvio Menna, Mark Perkins, Corentin Piroux, Gilles Reboux, D Tobias Todsén (University of Copenhagen, Denmark), Karin Von Eije.
- Medevac: Nadine Vahedi, Francesco Barbero, Michelangelo Bortolin, Jorge Durand, Luca Fontana, Flavio Salio, Harald Veen, Robert Wunderlich.
- Pharmaceuticals: Petra Straight (WHO consultant).
- Pharmacovigilance: Noha Iessa, Annick Jannin, Shanthi Narayan Pal.

2020 version

In 2020 (the previous version) the toolkit was adapted for the COVID-19 pandemic by Janet Diaz (Unit Head, Clinical Care, World Health Emergency Programme, WHO, Geneva, Switzerland), Pryanka Relan (Technical Officer, Clinical Services and Systems, WHO, Geneva, Switzerland) and Teresa Kortz (Consultant, WHO, Geneva, Switzerland).

WHO would like to thank the following for their preparation and contribution to the accompanying original PowerPoint presentations under the coordination of Justin Ortiz (University of Washington, Seattle, WA, USA) in December 2009: Neill Adhikari (Sunnybrook Health Sciences Centre and University of Toronto, Toronto, Canada) - Acute hypoxaemic failure in adults with H1N1; Yolanda Bayugo (WHO, Geneva, Switzerland) - Ethics and culture; Cheryl Cohen (National Institute for Communicable Diseases, Johannesburg, South Africa) - Diagnostics and specimen collection, antimicrobial therapy; Charles David Gomersall (Chinese University of Hong Kong, Prince of Wales Hospital, Hong Kong SAR, China) - ICU best practices, weaning; Carlos G Grijalva (Vanderbilt University School of Medicine, Nashville, TN, USA) - Influenza epidemiology; Wendy Hansen (University of Kentucky, Lexington, KY, USA) - Pregnant patient; Shevin Jacob (University of Washington, Seattle, WA, USA) - Severe sepsis and septic

shock management; Paula Lister (Great Ormond Street Hospital, London, United Kingdom) - Paediatric patient; Shabir Madhi (University of the Witwatersrand, Johannesburg, South Africa) - Diagnostics and specimen collection, antimicrobial therapy; Christine Olson (CDC, Atlanta, GA, USA) - Pregnant patient; Daisuke Tamura (Saitama Medical Center Jichi Medical University, Saitama, Japan) - Paediatric patient; Eric Walter (University of Washington, Seattle, WA, USA) - Infection prevention and control; T Eoin West (University of Washington, Seattle, WA, USA) - Clinical management in hospital wards.

Major revisions were completed in 2016. We would like to thank the following globally recognized experts for reviewing those updates: Andre Amaral (Sunnybrook Health Sciences Centre and University of Toronto, Toronto, Canada); Derek Angus (University of Pittsburgh Medical Center, Pittsburg, PA, USA); Ashoke Banarjee (Westmead Hospital, New South Wales, Australia); Rosa Constanza Vallenias Bejar De Villar (Pandemic and Epidemic Diseases, WHO); Martin Dunser (Department of Critical Care, University College of London Hospitals, United Kingdom); Wes Ely Vanderbilt University School of Medicine, Nashville, TN, USA); Nerina Harley (Epworth Health Care, Melbourne, Australia); Rashan Haniffa (Centre for Tropical Medicine, University of Oxford, United Kingdom); Fred Hayden, University of Virginia, Richmond, VA, USA); Rich Kallet (San Francisco General Hospital, CA, USA); Arjun Karki (Patan Academy of Health Sciences, Kathmandu, Nepal); Abdo Khoury (University of Franche-Comté, Medical and Trauma Center, Besançon, France); Niranjana "Tex" Kissoon (British Columbia Children's Hospital and Sunny Hill Health Centre for Children, Vancouver, Canada); Flavia Machado (Federal University of São Paulo, Brazil); Kathryn Maitland (Imperial College, London, United Kingdom); Michael Matthay (University of California, San Francisco, CA, USA); Paul McGinn (St John of God Hospital, Geelong, Victoria, Australia); Andy Petros (Great Ormond Street Hospital, London, United Kingdom); Stephen Playfor (Royal Manchester Children's Hospital, United Kingdom); Kobus Preller (Addenbrooke's Hospital, Cambridge, United Kingdom); Natalia Pshenichnaya (Rostov State Medical University, Russian Federation); Marcus Schultz (Academic Medical Center, Amsterdam, Netherlands); Christopher Seymour (University of Pittsburgh Medical Center, PA, USA); Nehad Shewari (Al Zahra Hospital, Dubai, United Arab Emirates); Sergey Shlapikov (St Petersburg State Medical Academy, Saint Petersburg, Russian Federation); Leo Yee Sin (Tan Tock Seng Hospital, Communicable Disease Centre, Singapore); Owen Tsang, Hospital Authority (Princess Margaret Hospital, Hong Kong SAR, China); Tim Uyeki (CDC, Atlanta, GA, USA); Dat Vu (Hanoi Medical University, National Hospital of Tropical Diseases, Hanoi, Viet Nam); Steven Webb (Royal Perth Hospital, Perth, Australia).

WHO would like to thank the following globally recognized experts for reviewing the materials at various stages of development between 2010 and 2016: Andre Amaral (Sunnybrook Health Sciences Centre and University of Toronto, Toronto, Canada); Edgar Bautista (Instituto Nacional de Enfermedades Respiratorias, Mexico City, Mexico); Satish Bhagwanjee (University of Washington, Seattle, WA, USA); Niranjana Bhat (Johns Hopkins University, Baltimore, MD, USA); Hillary Cohen (Maimonides Medical Center, Brooklyn, NY, USA); Shelly Dev and Gordon Rubinfeld (Sunnybrook Health Sciences Centre, University of Toronto, Toronto, Canada); Wes Ely (Vanderbilt University School of Medicine, Nashville, TN, USA); Sabine Heinrich (Berlin, Germany); Michael Ison (Northwestern University, Chicago, IL, USA); Arjun Karki (Patan Academy of Health Sciences, Kathmandu, Nepal); John Luce (San Francisco General Hospital, CA, USA); Lung Injury Knowledge Network, National Heart, Lung, and Blood Institute (Bethesda, MD, USA); Kirsten Lunghi (San Francisco General Hospital, CA, USA); Kishore Pichamuthu (Vellore, India); Kevin Rooney (Royal Alexandra Hospital, Scotland); Harry Shulman (Sunnybrook Health Sciences Centre and University of Toronto, Toronto, Canada); Monica Thormann (Asociación Panamericana de Infectología, Santo Domingo, Dominican Republic); Timothy Uyeki (CDC, Atlanta, GA, USA); Khai Vu (San Francisco General Hospital, CA, USA); Steven Webb (Royal Perth Hospital, Perth, Australia); Jenson Wong (San Francisco General Hospital, CA, USA).

Valuable inputs were also provided by many technical staff at WHO and special thanks are extended to Sergey Romualdovich Eremin (antimicrobial resistance), Charles Penn (Antiviral Group Committee), Andreas Alois Reis (global health ethics) and their collaborating centres.

Abbreviations

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

CFR	case fatality ratio
CNS	central nervous system
CO	carbon monoxide/cardiac output
CO ₂	carbon dioxide
COPD	chronic obstructive pulmonary disease
COVID-19	coronavirus disease
CPAP	continuous positive airway pressure
CPOT	Critical-Care Pain Observation Tool
CPP	cerebral perfusion pressure
CR	capillary refill
CRP	c-reactive protein
CPR	cardio-pulmonary resuscitation
CrAg	cryptococcal antigen
CRBSI	catheter-related blood stream infection
CSF	cerebrospinal fluid
CT	computerized tomography
CURB-65	confusion, urea, respiratory rate, blood pressure, 65 years (score)
CVC	central venous catheter
CVP	central venous pressure
CXR	chest X-ray
DBP	diastolic blood pressure
DKA	diabetic ketoacidosis
DM	diabetes mellitus
DVT	deep venous thrombosis
ECG	electrocardiogram
ECLS	extracorporeal life support
ECMO	extracorporeal membrane oxygenation
EIA	enzyme immunoassay
EIP	electromagnetic inductance plethysmography
EN	enteral nutrition
ENT	ear, nose and throat
EPAP	expiratory positive airway pressure
ESBL	extended spectrum beta-lactamase
ESI	emergency severity index
ESR	erythrocyte sedimentation rate
ETAT	emergency triage, assessment and treatment
EtCO ₂	end-tidal carbon dioxide
ETT	endotracheal tube
EV-D68	Enterovirus D68
FFP2	filtering face pieces 92%

FiO ₂	fraction of inspired oxygen
FLACC	face, legs, activity, cry, consolability
FM	face mask
GCS	Glasgow Coma Scale
GI	gastrointestinal
GMP	good manufacturing practices
Hb	haemoglobin
HBcAb	hepatitis B core antibody
HBsAg	hepatitis B surface antigen
HCAb	hepatitis C antibody
HCO ₃	blood bicarbonate
HDL	high density lipoprotein
HEPA	high-efficiency particulate air (filter)
HFNC	high-flow nasal cannula
HFNO	high-flow nasal oxygen
HICS	hospital incident command system
HIV	human immunodeficiency virus
HME	heat moisture exchanger
HR	heart rate
ICP	intracranial pressure
ICRC	International Committee of the Red Cross
ICU	intensive care unit
IHR	International Health Regulations
IITT	Interagency Integrated Triage Tool
ILI	influenza-like illness
IL-6	Interleukin-6
IL-6 RB	Interleukin-6 receptor blockers
IM	intramuscular
IMAI	Integrated Management of Adolescent and Adult Illness
IMV	invasive mechanical ventilation
iNO	inhaled nitric oxide
IO	intraosseous
IPC	infection prevention and control
ISO	International Organization for Standardization
IU	international units
IV	intravenous
JVP	jugular venous pressure
LAT	latex agglutination test
LDH	lactate dehydrogenase
LDL	low density lipoprotein

LFA	lateral flow immunochromatographic assay
LOS	length of stay
LPM/L/min	litres per minute
LPV	lung protective ventilation
LR	lactated Ringer's
LRT	lower respiratory tract
MAP	mean arterial pressure
MDR	multidrug-resistant
MERS-CoV	Middle East respiratory syndrome coronavirus
MEWS	modified Early Warning Score
MI	myocardial infarction
MIS-C	multisystem inflammatory syndrome in children
MRI	magnetic resonance image
MRSA	methicillin-resistance Staphylococcus aureus
MSF	Médecins Sans Frontières
MV	minute ventilation
NAAT	nucleic acid amplification testing
NCD	noncommunicable disease
NEWS	National Early Warning Score (adults)
NG	nasogastric
NJ	nasojejunal
NIPPV	nasal intermittent positive pressure ventilation
NIV	non-invasive ventilation
NMB	neuromuscular blockers
NPA	nasopharyngeal airway
NRB	non-rebreather
NS	normal saline
NSAID	non-steroidal anti-inflammatory drugs
N95	filtering less 95%
OG	orogastric
OI	oxygenation index using SpO ₂
OMD	Office of Medical Director
OPA	oropharyngeal airway
OSI	oxygen saturation index
PAD	pain, agitation and delirium
PALS	paediatric advanced life support
PaCO ₂	partial pressure of carbon dioxide
PaO ₂	partial pressure arterial oxygen
pARDS	paediatric acute respiratory distress respiratory
PBW	predicted body weight

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

SBP	systolic blood pressure
SBT	spontaneous breathing trial
SCI	spinal cord injury
ScvO ₂	saturation of central venous blood
SD	standard deviation
S:F	ratio between saturation of oxygen and the fraction of inspired oxygen
SIMV	synchronized intermittent mandatory ventilation
SIRS	systemic inflammatory response syndrome
SmPC	Summary of Product Characteristics (European Union)
SOFA	sequential organ failure assessment
SOP	standard operating procedure
SpO ₂	oxygen saturation
TB	tuberculosis
TBI	traumatic brain injury
TMJ	temporomandibular joint
TNF-inhibitors	tumoral necrosis factor inhibitors
TOF	train-of-four
TT	triage team
TV	tidal volume
ULN	upper limit of normal
URT	upper respiratory tract
US	ultrasound
USP	United States Prescribing Information
UTI	urinary tract infection
VA	veno-arterial
VAP	ventilator-associated pneumonia
VAS	Visual Analogue Scale
VOC	Variant of Concern
VOI	Variant of Interest
VPSA	vacuum pressure swing adsorption
VTE	venous thromboembolism
VTM	viral transport medium
VV	veno-venous
WBC	white cell count
WHO	World Health Organization

Executive summary

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

1. EPIDEMIOLOGY OF SARI

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

UPDATED

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

NEW

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

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

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

UPDATED

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

NEW

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

3. INFECTION PREVENTION AND CONTROL FOR PATIENTS WITH SARI

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

UPDATED

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

NEW

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

4. MONITORING PATIENTS WITH ACUTE RESPIRATORY INFECTION

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

UPDATED

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

NEW

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

5. DIAGNOSTIC TESTING FOR PATIENTS WITH ARI

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

UPDATED

- 5.3 Specimen collection kit for upper respiratory tract specimens

NEW

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

6. OXYGEN THERAPY

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

UPDATED

- 6.9 Checklist to troubleshoot warning signs during oxygen therapy delivery

NEW

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

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

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

NEW

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

8. SEPSIS AND SEPTIC SHOCK

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

UPDATED

- 8.6 Algorithms on initial resuscitation, and on fluid and vasoactive-inotrope management for children with septic shock
- 8.7 Guide to the use of vasopressors in septic shock for adults and children

NEW

- 8.1 Sepsis and septic shock definitions
- 8.2 Sequential Organ Failure Assessment (SOFA) score
- 8.3 Quick Sequential Organ Failure Assessment (qSOFA)
- 8.4 Paediatric Logistic Organ Dysfunction (PELOD-2) score
- 8.5 Algorithm on targeted resuscitation in adults with shock

9. ACUTE RESPIRATORY DISTRESS SYNDROME (ARDS)

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

UPDATED

- 9.1 Memory aid: diagnosis and classification of ARDS in adults
- 9.2 Memory aid: diagnosis and classification of pARDS in children

NEW

- 9.3 Advanced non-invasive oxygen delivery in ARDS: algorithm to escalate supportive respiratory therapy
- 9.4 Checklist for rapid sequence intubation procedure in adults and children
- 9.5 Considerations for intubation and mechanical ventilation in children
- 9.6 List of commonly used medicines and dosage in ICU with ventilated patients (adults, children)
- 9.7 Choice of induction agents in adults
- 9.8 Choice of induction agents in children
- 9.9 Protocol to deliver lung protective ventilation (LPV)
- 9.10 Memory aid: comparison of normal waveforms during volume and pressure-limited ventilation
- 9.11 Memory aid: recognizing and interpreting abnormal pressure and flow waveforms during volume control ventilation
- 9.12 Guide to distinguishing between the causes of high peak airway pressures: resistance versus compliance
- 9.13 Troubleshooting high peak airway pressures, low tidal volumes, desaturation or haemodynamic instability in ventilated patients

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

10. MANAGE PAIN, SEDATION AND DELIRIUM

- Revised formatting of tables, but no new tools.

11. LIBERATION FROM INVASIVE MECHANICAL VENTILATION

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

NEW

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

12. BEST PRACTICES TO PREVENT COMPLICATIONS

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

NEW

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

13. QUALITY IN CRITICAL CARE

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

NEW

- 13.1 Checklist for ICU daily best practices

14. ETHICAL CONSIDERATIONS

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

NEW

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



1

Epidemiology of SARI



1 Epidemiology of SARI

Summary

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

Patients with acute respiratory infection who have history of fever (or measured fever of $\geq 38\text{ }^{\circ}\text{C}$), cough and onset within the last 10 days (symptoms within 10 days) and require hospitalization.

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

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

Tools

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

1.1 Differential diagnosis of SARI

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

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

VIRAL PATHOGENS

Common viral pathogens

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

Less common viral pathogens

- Varicella zoster
- Measles
- Hantavirus

Virus that may constitute a public health emergency of international concern

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

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

- Cytomegalovirus,
 - Herpes simplex viruses
-

BACTERIAL PATHOGENS

Most common bacterial pathogens

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

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

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

Resistant pathogens

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

Resistant pathogens include:

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

OTHER ENDEMIC INFECTIONS

Potential endemic infections

Can co-exist with respiratory infections in endemic areas.

- Malaria, dengue, chikungunya, tuberculosis, HIV

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

COVID-19

Introduction

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

Transmission

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

Clinical features

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

Clinical features continued

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

Prevention

Infection prevention and control and public health interventions

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

Vaccines and medications for prophylaxis

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

Treatment

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

1.3 Influenza virus fact sheet

SEASONAL INFLUENZA VIRUSES

Introduction

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

Human infection

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

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

Transmission

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

Clinical features

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

Prevention

Infection prevention and control and public health interventions

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

Vaccines and medications for prophylaxis

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

Treatment

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

ZOONOTIC INFLUENZA

Introduction

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

Transmission

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

Clinical features

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

Prevention

Infection prevention and control and public health interventions

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

Vaccines and medications for prophylaxis

- Not available.

Treatment

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

NEW INFLUENZA VIRUSES WITH PANDEMIC POTENTIAL

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

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

MERS-CoV

Introduction

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

Transmission

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

Clinical features

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

Prevention


Infection prevention and control and public health interventions

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

Vaccines and medications for prophylaxis

- Not available.

Treatment

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

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

INFLUENZA

Chronic conditions, including:

- cardiac conditions (hypertension and cardiovascular disease)
- chronic lung conditions (asthma or chronic obstructive pulmonary disease [COPD]), endocrine disorders (diabetes)
- neurological disorders (stroke and neurodevelopmental conditions)
- chronic kidney disease
- metabolic disorders
- haematologic disorders
- chronic liver disease
- other immunosuppressed conditions, including cancer and HIV/AIDS and chronic conditions requiring immunosuppressive therapy, such as chronic steroid treatment or chemotherapy

Obesity

Pregnancy and post-partum period (up to 6 weeks)

Older persons (> 65 years old)

Young children (< 59 months)

COVID-19

Chronic conditions, including:

- cardiac conditions (hypertension and cardiovascular disease)
- chronic neurological disorders (e. g. stroke)
- dementia or mental health disorders
- chronic lung disease (e.g. COPD)
- endocrine disorders (diabetes)
- chronic kidney disease
- some immunosuppressed conditions (e.g. cancer, HIV)^a

Obesity

Smoking

In pregnant or recently pregnant: women > 35 years old, obesity, with chronic medical conditions or pregnancy specific disorders (e.g. gestational diabetes and pre-eclampsia/eclampsia)

Unvaccinated against COVID-19

Older persons (> 60 years old)

Note:

^a List of risk factors to be updated as evidence emerges.

References and resources

Abrams JY, Godfred-Cato SE, Oster ME, Chow EJ, Koumans EH, Bryant B et al. Multisystem inflammatory syndrome in children associated with severe acute respiratory syndrome coronavirus 2: a systematic review. *J Pediatr*. 2020;226:45-54.e1.

ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Taylor Thompson B, Ferguson ND, Caldwell E et al. Acute respiratory distress syndrome: the Berlin Definition. *Jama*. 2012;307(23):2526-33.

Church J, Maitland K. Invasive bacterial co-infection in African children with *Plasmodium falciparum* malaria: a systematic review. *BMC Med*. 2014;12:31.

Khemani RG, Smith LS, Zimmerman JJ, Erickson S, Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: definition, incidence, and epidemiology: proceedings from the Pediatric Acute Lung Injury Consensus Conference. *Pediatr Crit Care Med*. 2015;16(5 Suppl. 1):S23-40.

Levin M, Cunningham AJ, Wilson C, Nadel S, Lang HJ, Ninis N et al. Effects of saline or albumin fluid bolus in resuscitation: evidence from re-analysis of the FEAST trial. *Lancet Respir Med*. 2019;7(7):P581-593.

Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. Vital surveillances: the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) - China. *China CDC Weekly*. 2020;2(8):113-22.

Riviello ED, Buregeya E, Twagirumugabe T. Diagnosing acute respiratory distress syndrome in resource limited settings: the Kigali modification of the Berlin definition. *Curr Opin Crit Care*. 2017;23(1):18-23.

Takem EN, Roca A, Cunningham A. The association between malaria and non-typhoid *Salmonella* bacteraemia in children in sub-Saharan Africa: a literature review. *Malar J*. 2014;13:400.

Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P et al. Clinical characteristics of 58 children with a pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2. *JAMA*. 2020;324(3):259-269.

WHO. Country & Technical Guidance - Coronavirus disease (COVID-19). Geneva: World Health Organization; 2021 (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance>, accessed 29 April 2021); information on:

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

- Travel, points of entry and border health
- Virus origin/reducing animal-human transmission

WHO. COVID-19 Clinical management: living guidance. Geneva: World Health Organization; 2021 (<https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1>, accessed 29 April 2021).

WHO. COVID-19 vaccines. World Health Organization: Geneva; 2021 (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines>, accessed 29 April 2021).

WHO. Guidelines for the clinical management of severe illness from influenza virus infections. Geneva: World Health Organization; 2022 (<https://apps.who.int/iris/handle/10665/352453?locale-attribute=fr&>, accessed 26 March 2022).

WHO. How WHO is working to track down the animal reservoir of the SARS-CoV-2 virus. Geneva: World Health Organization; 2020 (<https://www.who.int/news-room/feature-stories/detail/how-who-is-working-to-track-down-the-animal-reservoir-of-the-sars-cov-2-virus>, accessed 29 April 2021).

WHO. Influenza. World Health Organization: Geneva; 2021 (<https://www.who.int/influenza/en/>, accessed 29 April 2021).

WHO. Influenza (Avian and other zoonotic). Geneva: World Health Organization; 2018 ([https://www.who.int/en/news-room/fact-sheets/detail/influenza-\(avian-and-other-zoonotic\)](https://www.who.int/en/news-room/fact-sheets/detail/influenza-(avian-and-other-zoonotic)), accessed 29 April 2021).

WHO. Influenza: burden of disease. Geneva: World Health Organization; 2020 (https://www.who.int/influenza/surveillance_monitoring/bod/en/, accessed 29 April 2021).

WHO. Influenza (seasonal). World Health Organization: Geneva; 2021 ([https://www.who.int/en/news-room/fact-sheets/detail/influenza-\(seasonal\)](https://www.who.int/en/news-room/fact-sheets/detail/influenza-(seasonal)), accessed 29 April 2021).

WHO. Living guideline: drugs to prevent COVID-19. Geneva: World Health Organization; 2021 (<https://www.who.int/publications/i/item/WHO-2019-nCoV-prophylaxes-2021-1>, accessed 29 April 2021).

WHO. Mask use in the context of COVID-19. Geneva: World Health Organization; 2020 ([https://www.who.int/publications/i/item/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-\(2019-ncov\)-outbreak](https://www.who.int/publications/i/item/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-(2019-ncov)-outbreak), accessed 29 April 2021).

WHO. Middle East Respiratory Syndrome Coronavirus (MERS-CoV). Geneva: World Health Organization; 2019 ([https://www.who.int/en/news-room/fact-sheets/detail/middle-east-respiratory-syndrome-coronavirus-\(MERS-CoV\)](https://www.who.int/en/news-room/fact-sheets/detail/middle-east-respiratory-syndrome-coronavirus-(MERS-CoV)), accessed 29 April 2021).

WHO. Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19. Scientific brief. World Health Organization: Geneva; 2020 (<https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19>, accessed 29 April 2021).

WHO. Protocol to investigate non-seasonal influenza and other emerging acute respiratory diseases; Geneva: World Health Organization; 2018 (www.who.int/influenza/resources/publications/outbreak_investigation_protocol/en/, accessed 29 April 2021).

WHO. Readiness for influenza during the COVID-19 pandemic. World Health Organization: Geneva; 2020 (https://apps.who.int/iris/bitstream/handle/10665/336438/WHO-2019-nCoV-Influenza_readiness_COVID-19-2020.1-eng.pdf?ua=1, accessed 29 April 2021).

WHO. Therapeutics and COVID-19: living guidance. Geneva: World Health Organization; 2021 (<https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.1>, accessed 29 April 2021).

WHO. WHO-convened Global Study of the Origins of SARS-CoV-2. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/m/item/who-convened-global-study-of-the-origins-of-sars-cov-2>, accessed 29 April 2021).

WHO. WHO Global technical consultation: global standards and tools for influenza surveillance. Geneva: World Health

Organization; 2011 (https://apps.who.int/iris/bitstream/handle/10665/70724/WHO_HSE_GIP_2011.1_eng.pdf;jsessionid=4830617114FE8C79C84E7E989EEE48E7?sequence=1, accessed 29 April 2021).

WHO. WHO surveillance case definitions for ILI and SARI. Geneva: World Health Organization; 2014 (https://www.who.int/influenza/surveillance_monitoring/ili_sari_surveillance_case_definition/en/, accessed 29 April 2021).

Yang X, Yu Y, Xu J, Shu H, Xia J, Liu H et al. Clinical course and outcomes of critically ill patients with SARS-CoV-2 pneumonia in Wuhan, China: a single-centered, retrospective, observational study. *Lancet Respir Med.* 2020. Epub 2020/02/28. doi: 10.1016/S2213-2600(20)30079-5. PubMed PMID: 32105632.



2

Screening, triage, clinical assessment and management of SARI



2 Screening, triage, clinical assessment and management of SARI

Summary

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

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

1. It is fundamental to set up **systems for reporting and referral of cases from the community** to the appropriate destination for triage, clinical assessment, testing, and/or treatments as per local clinical care pathways and protocols.
2. **After screening at the point of access, triage should be done** with a validated acuity-based triage tool to identify and treat patients needing immediate care. Do not delay emergency care.
3. **After triage, care for all patients should be delivered in designated areas, according to disease severity and acute care needs.** Generally, patients with SARI need acute hospital care because of possible complications such as severe pneumonia, sepsis, organ dysfunction, and/or exacerbation of chronic disease or co-infections. These patients can progress to acute organ failure that may require critical care and admission to ICU for closer monitoring and supportive therapies that cannot be delivered on a general ward. Do not delay ICU admission for these patients.

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

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

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

See WHO guidance for more details:

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

Tools


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

2.1 Screening for SARI

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

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

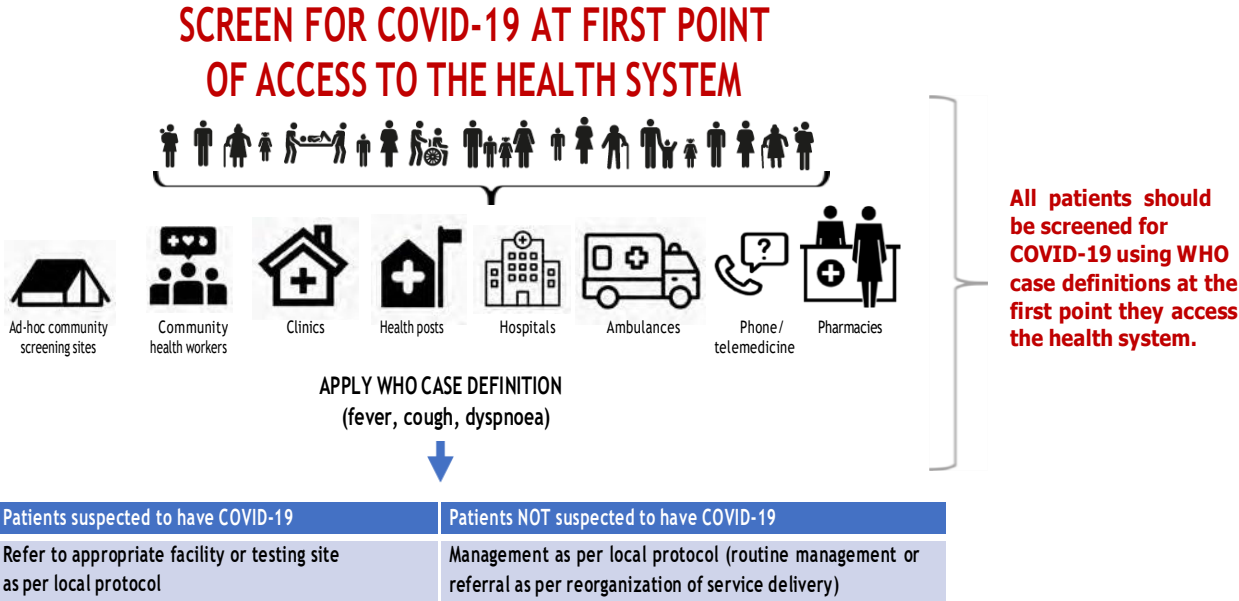
As a precaution, screening should always be done at a distance (> 1 m), with no physical contact.

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

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

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

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



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

2.1.1 Case definition for suspected cases of COVID-19 ()

A. Clinical and epidemiological criteria

Clinical criteria:

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

Epidemiological criteria:

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

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

- acute respiratory infection with history of fever or measured fever of $\geq 38^{\circ}\text{C}$;
- cough;
- onset within the last 10 days; and
- requires hospitalization.

C. A person NOT meeting the clinical AND epidemiological criteria

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

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

Checklist for COVID-19 neurological screening

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

How to use this screening checklist:

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



Adult screening checklist

Loss (ageusia) or decreased sense of taste (dysgeusia)

Loss (anosmia) or decreased sense of smell (hyposmia)

New onset headache

New onset dizziness (including pre-syncope symptoms or syncope)

Confusion (delirium), behavioural changes including agitation, or psychotic symptoms

Decreased consciousness (e.g. somnolence, stupor, unresponsiveness)

New focal or diffuse muscle pain (myalgias) with or without weakness

Worsening of underlying neurological condition

Myoclonus

New onset seizures or increased seizure activity

New onset weakness (paresis, hemiparesis)

Neck stiffness (meningismus)

Trouble with speech

Numbness/tingling (sensory symptoms)

New onset of fatigue

Blurring/loss of vision

Problems passing urine or with bowel movements

Problems with balance in standing or walking



Special considerations in infants and children

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

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

2.1.2 Clinical classification for respiratory infection due to influenza

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

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

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

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

Signs and symptoms of complicated ARI (SARI)

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

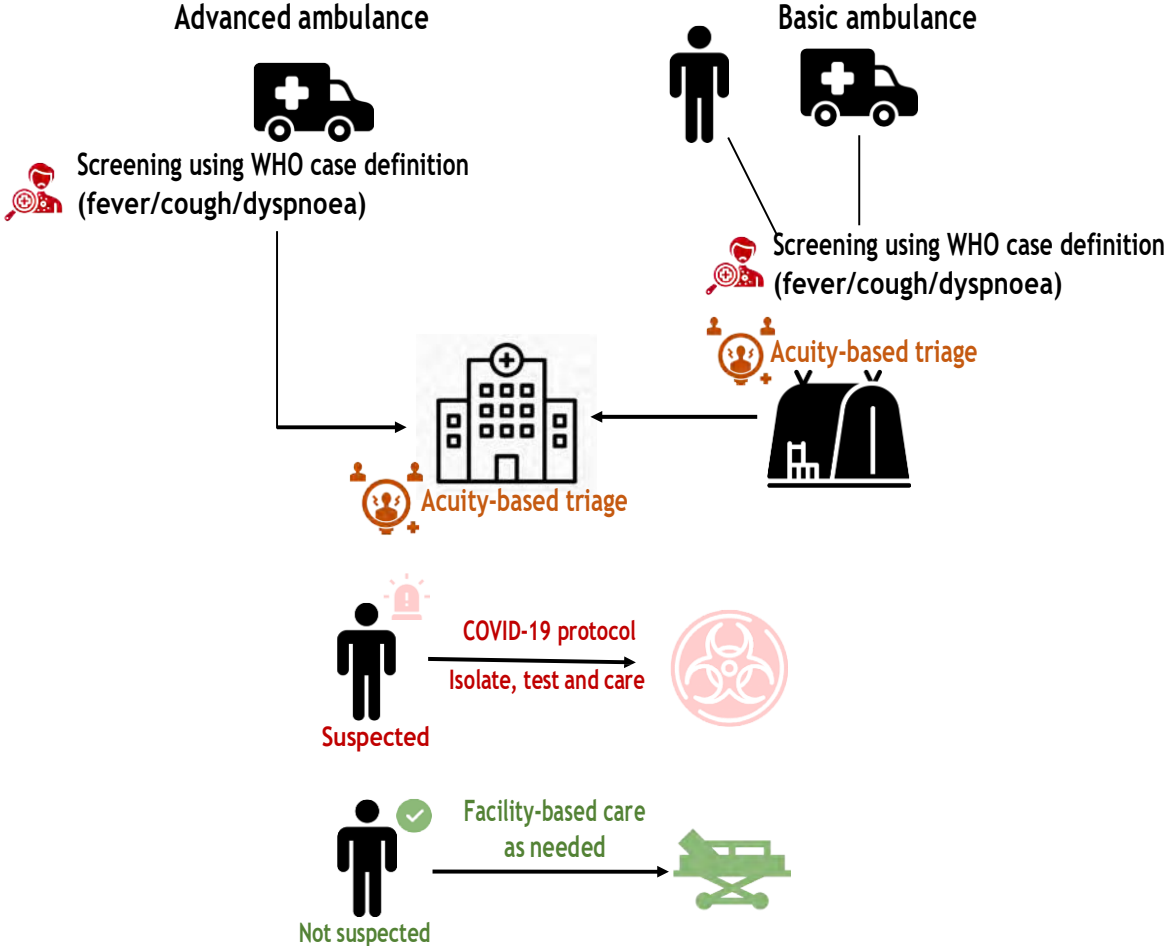
Source: Revision of clinical case definitions: influenza-like illness and severe acute respiratory infection (WHO, 2020).

2.2 Triage for SARI

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

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

TRIAGE AT FACILITY



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

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

EMERGENCY UNIT

DESIGNATING A RESUSCITATION AREA IN THE EMERGENCY UNIT

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

Use of the resuscitation area

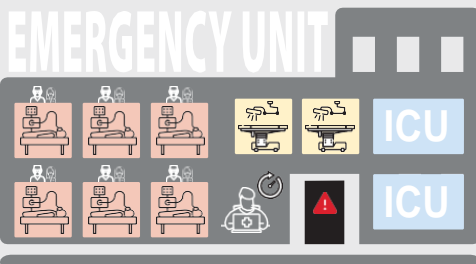


- Upon arrival to the emergency unit, all patients are triaged.
- Patients triaged as “red” are immediately transferred to the resuscitation area.
- Triage personnel alert emergency unit staff as patients are transferred to the resuscitation area (e.g. overhead announcement).
- Pre-hospital providers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



Staff

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



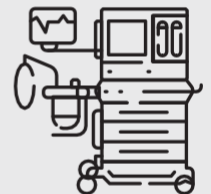
Space

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

Equipment and supplies

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

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



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

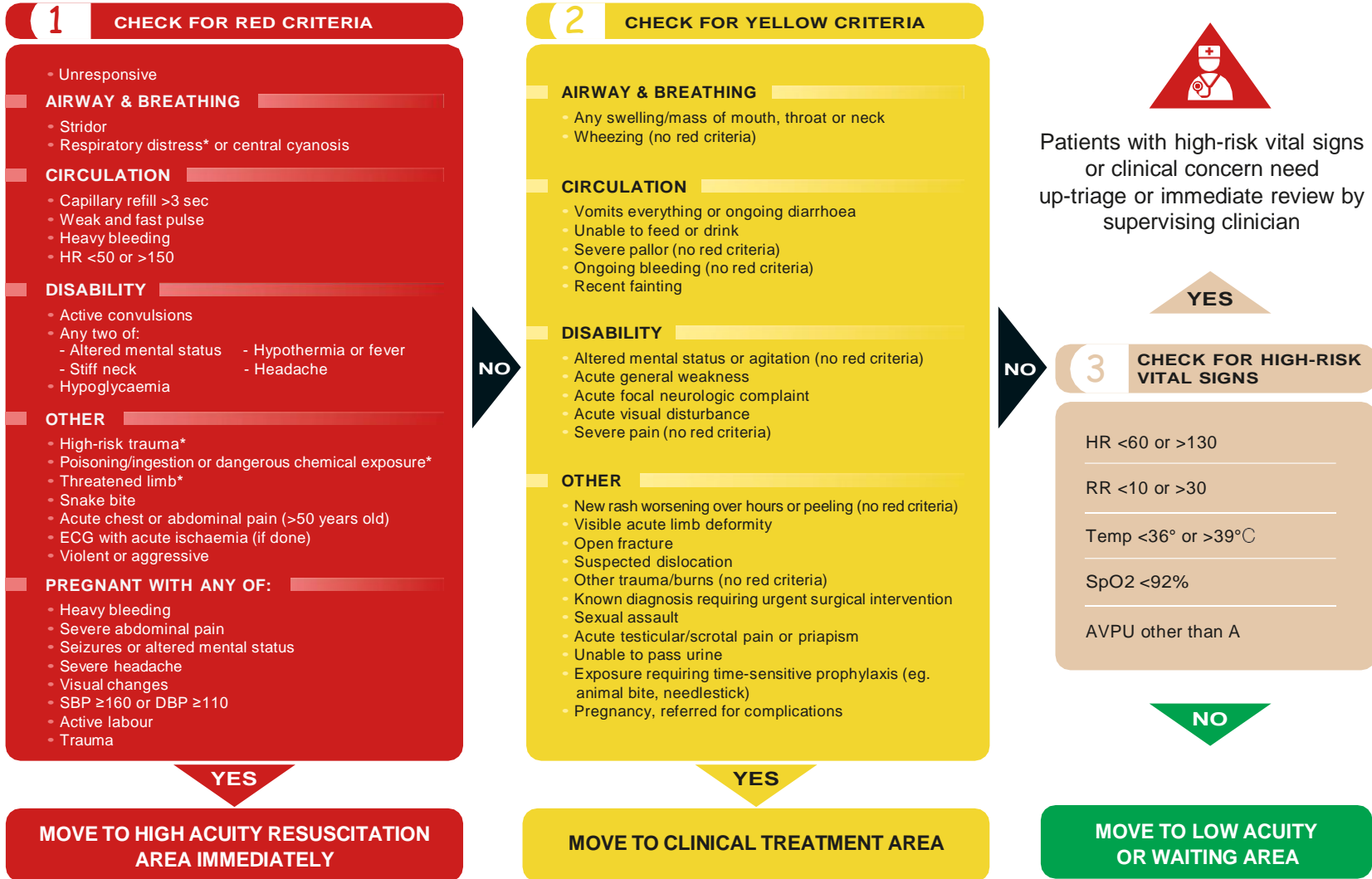
Interagency Integrated Triage Tool (IITT) is a novel triage tool developed in collaboration between WHO, the International Committee of the Red Cross (ICRC) and Médecins Sans Frontières (MSF) to provide an integrated set of protocols for routine triage of adults and children. It can be utilized for facility-based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

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

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

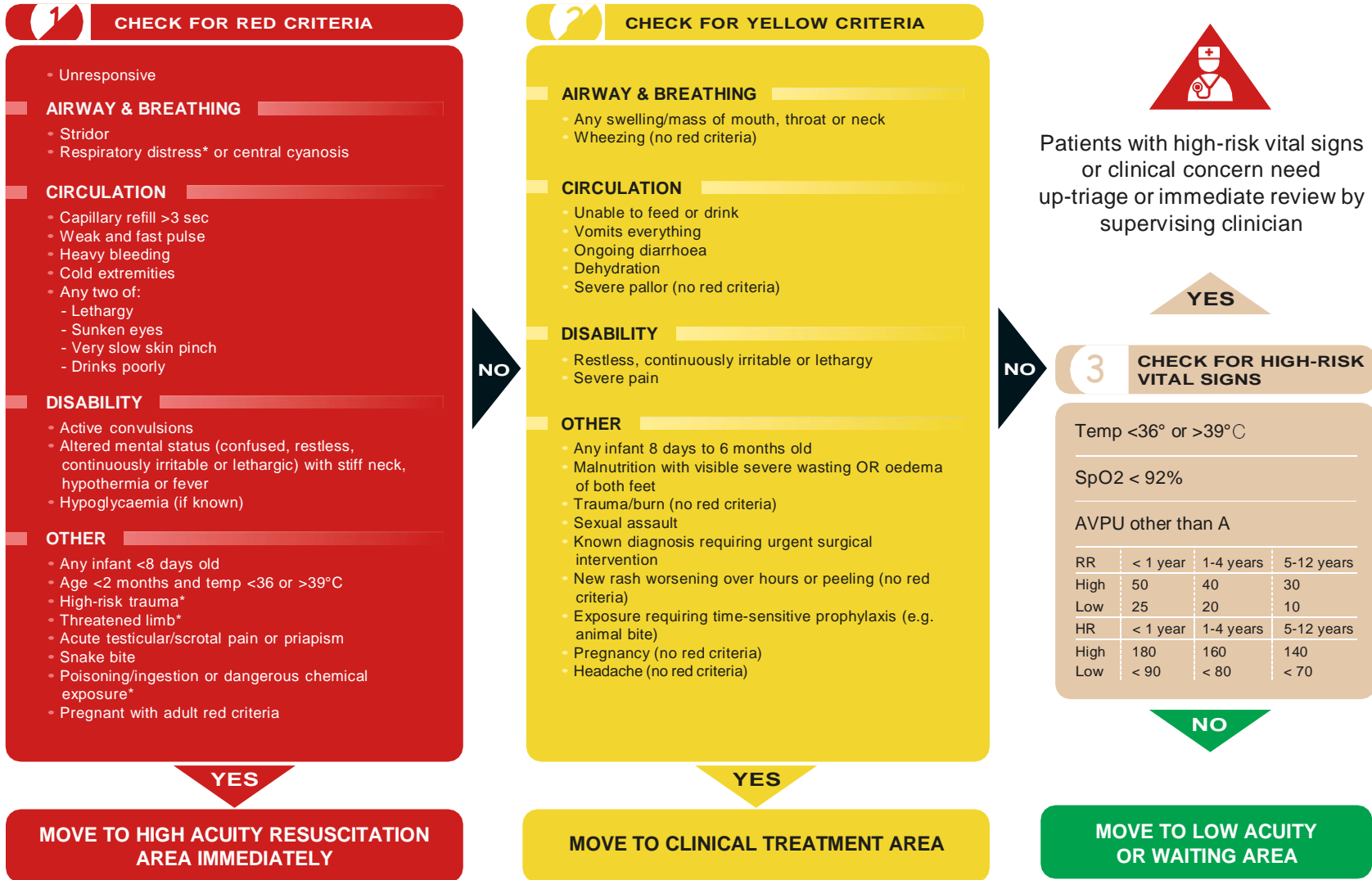
based on red, yellow and green criteria.

Interagency Integrated Triage Tool: ≥ 12 years



*See Reference Card



Interagency Integrated Triage Tool: < 12 years





*See Reference Card

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


High-Risk Trauma Criteria

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

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

 Threatened Limb
A patient presenting with a limb that is: <ul style="list-style-type: none"> • Pulseless OR • Painful and one of the following: pale, weak, numb, or with massive swelling after trauma.

Other High-Risk Criteria

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

 **Ingestion/exposure**

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



© World Health Organization, Médecins sans Frontière (MSF) and the International Committee of the Red Cross (ICRC). Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; <https://creativecommons.org/licenses/by-nc-sa/3.0/igo>).

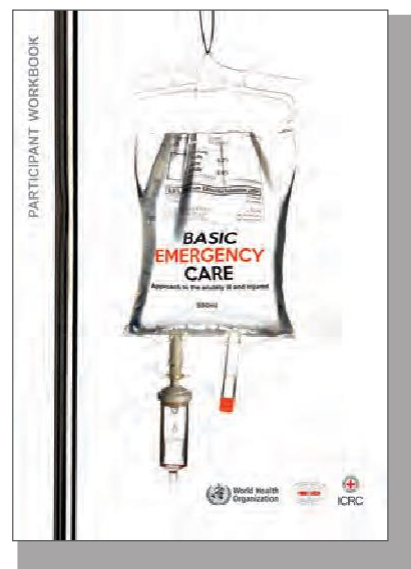
Source: Interagency Integrated Triage Tool (WHO, MSF, ICRC, 2019).

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

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

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





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



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

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

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

	ASSESSMENT FINDINGS	IMMEDIATE MANAGEMENT
Airway 	Unconscious with limited or no air movement	If NO TRAUMA : head-tilt and chin-lift, use OPA or NPA to keep airway open, place in recovery position or position of comfort. If possible TRAUMA : use jaw thrust with c-spine protection and place OPA to keep the airway open (no NPA if facial trauma).
	Foreign body in airway	Remove visible foreign body. Encourage coughing. • If unable to cough: chest/abdominal thrusts/back blows as indicated. • If patient becomes unconscious: CPR.
	Gurgling	Open airway as above, suction (avoid gagging).
	Stridor	Keep patient calm and allow position of comfort. • For signs of anaphylaxis: give IM adrenaline. • For hypoxia: give oxygen.
	Breathing 	Signs of abnormal breathing or hypoxia
Wheeze	Give salbutamol. For signs of anaphylaxis: give IM adrenaline.	
Signs of tension pneumothorax (absent sounds/hyperresonance on one side WITH hypotension, distended neck veins)	Perform needle decompression, give oxygen and IV fluids. Will need chest tube.	
Signs of opiate overdose (AMS and slow breathing with small pupils)	Give naloxone.	
Circulation 	Signs of poor perfusion/shock	If no pulse , follow relevant CPR protocols. Give oxygen and IV fluids.
	Signs of internal or external bleeding	Control external bleeding. Give IV fluids.
	Signs of pericardial tamponade (poor perfusion with distended neck veins and muffled heart sounds)	Give IV fluids, oxygen. Will need rapid pericardial drainage.
Disability 	Altered mental status (AMS)	If NO TRAUMA , place in recovery position.
	Seizure	Give benzodiazepine.
	Seizure in pregnancy (or after recent delivery)	Give magnesium sulphate.
	Hypoglycaemia	Give glucose if < 3.5 mmol/L or unknown.
	Signs of opiate overdose (AMS with slow breathing with small pupils)	Give naloxone.
	Signs of life-threatening brain mass or bleed (AMS with unequal pupils)	Raise head of bed, monitor airway. Will need rapid transfer for neurosurgical services.
Exposure 	Remove wet clothing and dry skin thoroughly	
	Remove jewellery, watches and constrictive clothing	
	Prevent hypothermia and protect modesty	
	Snake bite	Immobilize extremity. Send picture of snake with patient. Call for anti-venom if relevant.

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

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

NORMAL ADULT VITAL SIGNS

Pulse rate: 60-100 beats per minute

Respiratory rate: 10-20 breaths per minute

Systolic blood pressure > 90 mmHg

Oxygen saturation > 92%

Estimating systolic blood pressure

(not reliable in children and the elderly):

Carotid (neck) pulse → SBP ≥ 60 mmHg

Femoral (groin) pulse → SBP ≥ 70 mmHg

Radial (wrist) pulse → SBP ≥ 80 mmHg

SAMPLE History

Signs & symptoms

Allergies

Medications

PMH

Last oral intake

Events

SPECIAL CONSIDERATIONS IN THE ASSESSMENT OF CHILDREN



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



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

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



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

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



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



INFANTS AND CHILDREN HAVE DIFFICULTY MAINTAINING TEMPERATURE

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

DANGER SIGNS IN CHILDREN

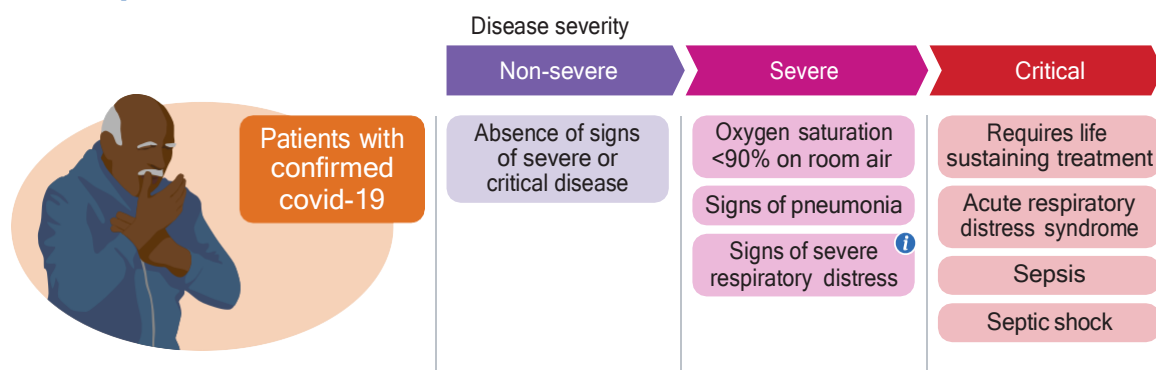
- Signs of airway obstruction (unable to swallow saliva/drooling or stridor).
- Increased breathing effort (fast breathing, nasal flaring, grunting, chest indrawing or retractions).
- Cyanosis (blue colour of the skin, especially at the lips and fingertips).
- Altered mental status (including lethargy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

ESTIMATED WEIGHT in KILOGRAMS for CHILDREN 1-10 YEARS OLD:
 $[\text{age in years} + 4] \times 2$

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

2.4 Classification of severity in patients with COVID-19

Population



Source: A living WHO guideline on drugs for COVID-19 (BMJ, 2020) ([link](#))

Mild disease

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

Moderate disease

Pneumonia Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea, fast breathing) but no signs of severe pneumonia, including $SpO_2 \geq 90\%$ on room air.

Child with cough or difficulty breathing + fast breathing and/or chest indrawing and no signs of severe pneumonia.

Fast breathing: < 2 months: ≥ 60 breaths/min; 2-11 months: ≥ 50 ; 1-5 years: ≥ 40 .

The diagnosis can be made on clinical grounds; chest imaging (radiograph, CT scan, ultrasound) may assist in diagnosis and identify or exclude pulmonary complications.

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

Severe disease

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

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

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

The diagnosis can be made on clinical grounds; chest imaging (radiograph, CT scan, ultrasound) may assist in diagnosis and identify or exclude pulmonary complications.

Critical disease

ARDS

Onset: within 1 week of a known clinical insult (i.e. pneumonia) or new or worsening respiratory symptoms.

Chest imaging: radiograph, CT scan or lung ultrasound: bilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules.

Origin of pulmonary infiltrates: respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echocardiography) to exclude hydrostatic cause of infiltrates/oedema if no risk factors present.

Oxygenation impairment in adults:

Air blood gases (ABG) available

- Mild ARDS: $200 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 300 \text{ mmHg}$ (with PEEP or CPAP $\geq 5 \text{ cmH}_2\text{O}$)
- Moderate ARDS: $100 \text{ mmHg} < \text{PaO}_2/\text{FiO}_2 \leq 200 \text{ mmHg}$ (with PEEP $\geq 5 \text{ cmH}_2\text{O}$)
- Severe ARDS: $\text{PaO}_2/\text{FiO}_2 \leq 100 \text{ mmHg}$ (with PEEP $\geq 5 \text{ cmH}_2\text{O}$).

ABG not available (Kigali modification)

- $\text{SpO}_2/\text{FiO}_2 < 315$ suggests ARDS (including non-ventilated patients)

Oxygen impairment in children: note OI and OSI.^a Use OI when available. If PaO_2 not available, wean FiO_2 to maintain $\text{SpO}_2 \leq 97\%$ to calculate OSI or $\text{SpO}_2/\text{FiO}_2$ ratio:

- Bilevel (NIV or CPAP) $\geq 5 \text{ cmH}_2\text{O}$ via full face mask: $\text{PaO}_2/\text{FiO}_2 \leq 300 \text{ mmHg}$ or $\text{SpO}_2/\text{FiO}_2 \leq 264$
- Mild ARDS (invasively ventilated): $4 \leq \text{OI} < 8$ or $5 \leq \text{OSI} < 7.5$
- Moderate ARDS (invasively ventilated): $8 \leq \text{OI} < 16$ or $7.5 \leq \text{OSI} < 12.3$
- Severe ARDS (invasively ventilated): $\text{OI} \geq 16$ or $\text{OSI} \geq 12.3$.

^a Oxygenation Index (OI) is an invasive measurement of the severity of hypoxaemic respiratory failure and may be used to predict outcomes in paediatric patients. It is calculated as follows: percentage of fraction of inhaled oxygen multiplied by the mean airway pressure (in mmHg), divided by the partial pressure of arterial oxygen (in mmHg), divided by the partial pressure of arterial oxygen (in mmHg). Oxygen Saturation Index (OSI) is a non-invasive measurement and has been shown to be a reliable surrogate marker of OI in children and adults with respiratory failure. OSI replaces PaO_2 with oxygen saturation as measured by pulse oximetry (SpO_2) in the OI equation.

Sepsis

Adults: acute life-threatening organ dysfunction caused by a dysregulated host response to suspect or proven infection. Signs of organ dysfunction include: altered mental status (delirium), difficult or fast breathing, low oxygen saturation, reduced urinary output, fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate or hyperbilirubinaemia.

Children: suspected or proven infection and ≥ 2 age-based systemic inflammatory response syndrome (SIRS) criteria,^b of which one must be abnormal temperature or white blood cell count.

^bSIRS criteria: abnormal temperature ($> 38.5 \text{ }^\circ\text{C}$ or $< 36 \text{ }^\circ\text{C}$); tachycardia for age or bradycardia for age if < 1 year; tachypnoea for age or need for mechanical ventilation; abnormal white blood cell count for age or $> 10\%$ bands.

Septic shock

Adults: persistent hypotension despite volume resuscitation, requiring vasopressor to maintain MAP $\geq 65 \text{ mmHg}$ and serum lactate level $> 2 \text{ mmol/L}$.

Children: any hypotension (SBP < 5 th centile or 2SD below normal for age) or two or three of the following: altered mental status; bradycardia or tachycardia (HR < 90 beats/min [bpm] or < 160 bpm in infants and heart rate < 70 bpm or > 150 bpm in children); prolonged capillary refill (> 2 sec) or weak pulse; fast breathing; mottled or cool skin or petechial or purpuric rash; high lactate; reduced urine output; hyperthermia or hypothermia.

Acute thrombosis

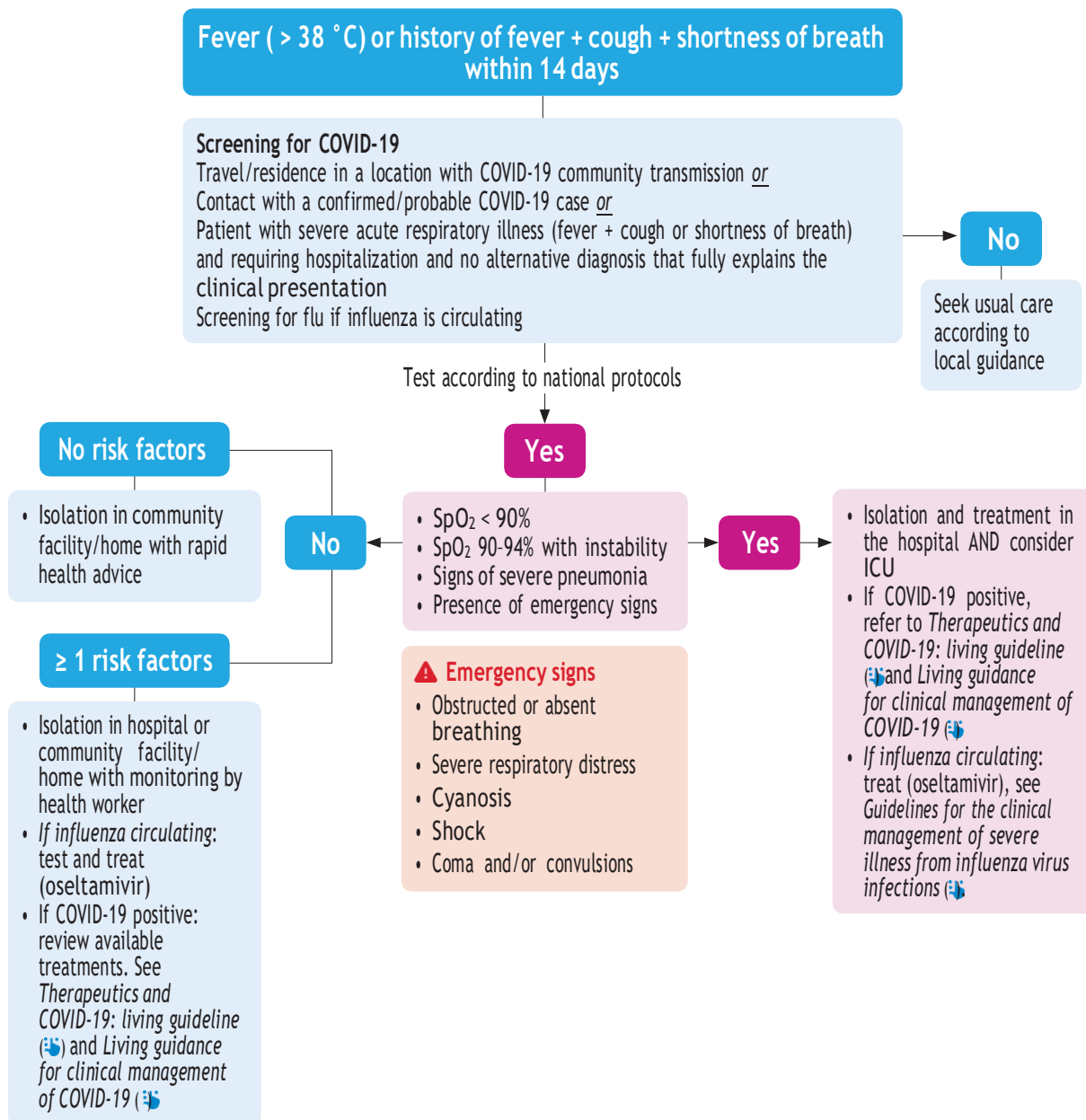
Acute venous thromboembolism (i.e. pulmonary thromboembolism), acute coronary syndrome, acute stroke.

MIS-C

Preliminary case definition: children and adolescents 0-19 years of age with fever ≥ 3 days AND two of the following: rash or bilateral non purulent conjunctivitis or muco-cutaneous inflammation signs (oral, hands or feet); hypotension or shock; features of myocardial dysfunction, pericarditis, valvulitis, or coronary abnormalities (including ECHO findings or elevated troponin/NT-proBNP); evidence of coagulopathy (PT, PTT, elevated D-dimers); acute gastrointestinal problems (diarrhoea, vomiting or abdominal pain); AND elevated markers of inflammation such as ESR, C-reactive protein, or procalcitonin AND no other obvious microbial cause of shock syndrome AND evidence of COVID-19 (RT-PCR, antigen test or serology positive), or likely contact with patients with COVID-19. (See scientific brief, 15 May 2020, WHO: *Multisystemic inflammatory syndrome in children and adolescents temporally related to COVID-19.*)

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

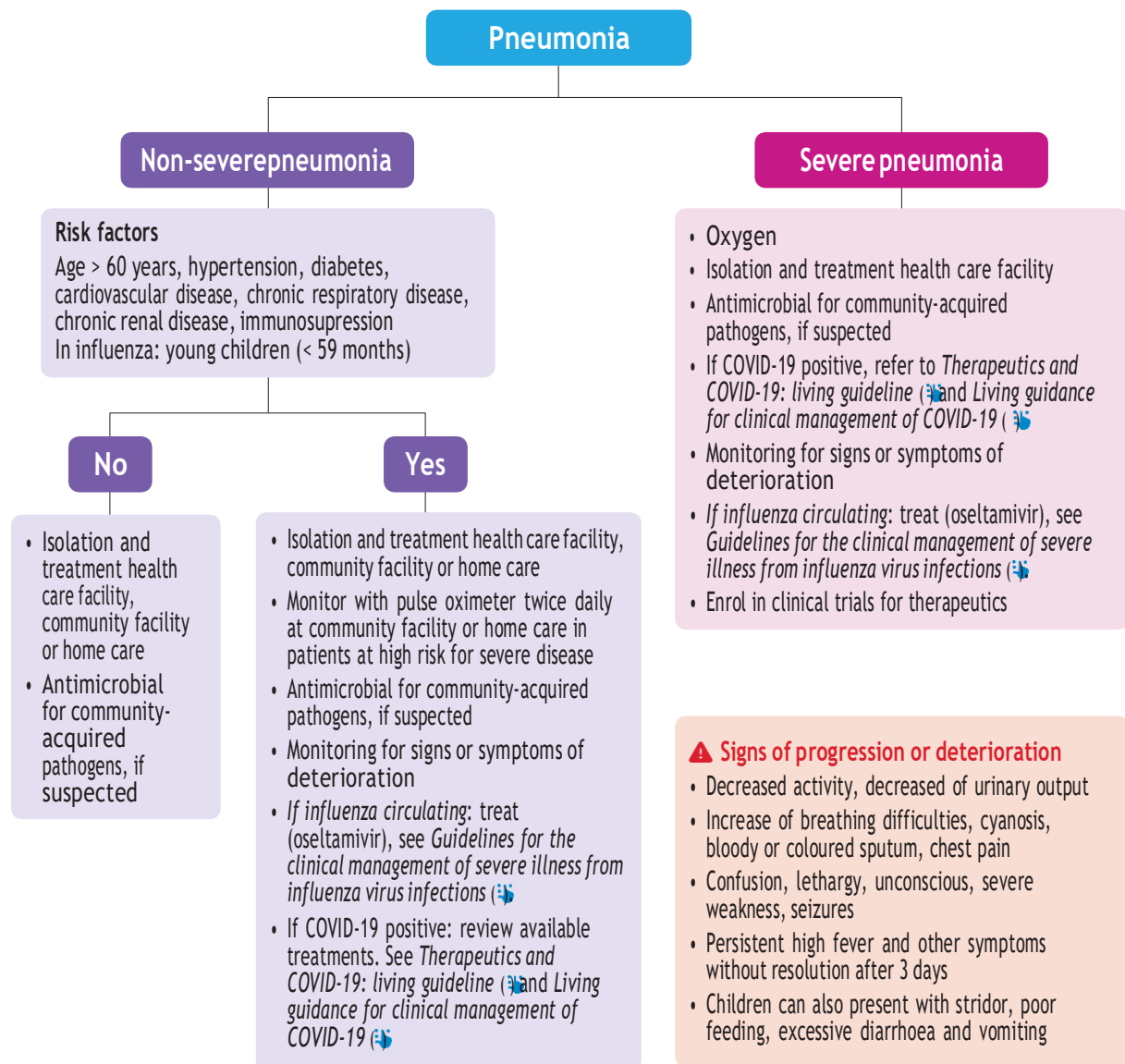
2.5 Decision-making algorithm for patients presenting with acute respiratory infection (ARI) (influenza or COVID-19 suspected or known to be circulating)



Risk factors associated with severe disease

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

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



WHO criteria for severe pneumonia

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

- Cough or difficulty breathing with at least one of the following:
 - central cyanosis or oxygen saturation (SpO₂) < 90%
 - severe respiratory distress (e.g. grunting, very severe chest indrawing)
 - general danger sign (e.g. inability to breastfeed or drink, lethargy or unconscious, convulsions).
- Any or all of the following may also be present:
 - fast breathing (< 2 months ≥ 60 breaths/min; 2-11 months ≥ 50; 1-5 years ≥ 40; 5-15 years ≥ 30).
 - chest indrawing.

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

- RR > 30 breaths/min
- SpO₂ < 90%
- Signs of severe respiratory distress (e.g. inability to speak, use of accessory muscles).

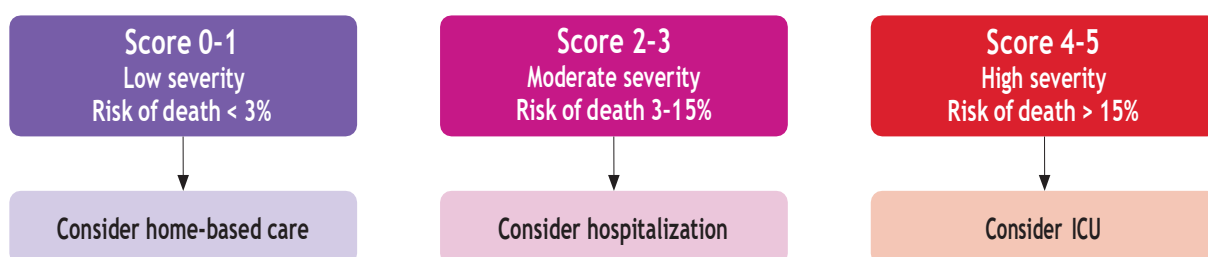
2.7 Decision-making support tool for hospitalization and ICU admission for patients with SARI and severe pneumonia

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

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

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

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



2.8 Checklist for admission

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

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

Checklist for admission

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

2.9 Checklist for transfer

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

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

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

Checklist for transfer

- Patient is stabilized.
- Adequate IPC measures and proper PPE needed, e.g. medical mask for patients with ARI.
- Everything secured: airway, NG tube, IV lines, monitors, endotracheal tubes, ventilator.
- Enough drugs: e.g. vasopressors, sedatives.
- Enough oxygen: adequate oxygen saturation (SpO₂).
- Enough IV fluids: blood pressure adequate.
- Health care workers (e.g. transporters, receiving staff) and receiving unit/ward prepared.

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

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

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

Pre-flight patient assessment

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

Pre-flight physiological considerations	<p>Altitude exposure imposes hypoxia and gas expansion in body cavities.</p> <ul style="list-style-type: none">• Consider supplemental oxygen, ventilation and low-altitude flight paths.• Prepare for any deterioration and for conditions induced by the aerospace environment.• Plan for early endotracheal intubation:<ul style="list-style-type: none">– Pre-emptive intubation is recommended for patients with the potential of respiratory decompensation during aeromedical transport.• Anaemia: fit to fly if Hb \geq 95g/L. If, due to chronic disease and compensation, Hb \geq 80 g/L is acceptable. If lower or if concurrent lung or cardiac disease, consider transfusion.
Pre-flight checklist	<ul style="list-style-type: none">• Allocate key roles.• Flight crew must include a specialized intensive care flight physician and nurse, that are knowledgeable about flight physiology, experienced in inter-facility air-transfer and the management of critical care patients/ intubated patients.• Precise SOPs (e.g. correct use and handling of PPE/environmental cleaning and decontamination); every crew member and service staff (e.g. aircraft cleaning) strictly adhere to SOPs.• Medevac personnel to ensure that patient receives instruction on in-flight IPC measures.• Written informed consent and signed liability waiver forms from patient and/or relatives along with outline of intention to transfer must occur before the transfer.• Clear communication and agreement between coordination mechanism, transferring and receiving facility:<ul style="list-style-type: none">– Formal agreement from the receiving facility.– Ensure full and up-to-date medical records on patient's clinical condition, treatment received, intention to transfer, mode and timeline of transfer and communicate them to flight crew and receiving facility.• Equipment check: monitoring devices (ECG, blood pressure, pulse oximetry, capnography, defibrillators, pacing devices, aeronautical oxygen systems, oxygen, suction, face mask, filter, breathing circuit, respiratory support device, equipment to manage sedation, intubation, ventilation, cardiovascular support, infusion devices, medications including resuscitation drugs, point-of-care testing (POCT) for e.g. arterial blood gases analysis, etc. All equipment must be certified for aeronautical use.• Check resuscitation medications.• Be prepared to deepen anaesthesia and administer additional catecholamines during transport.

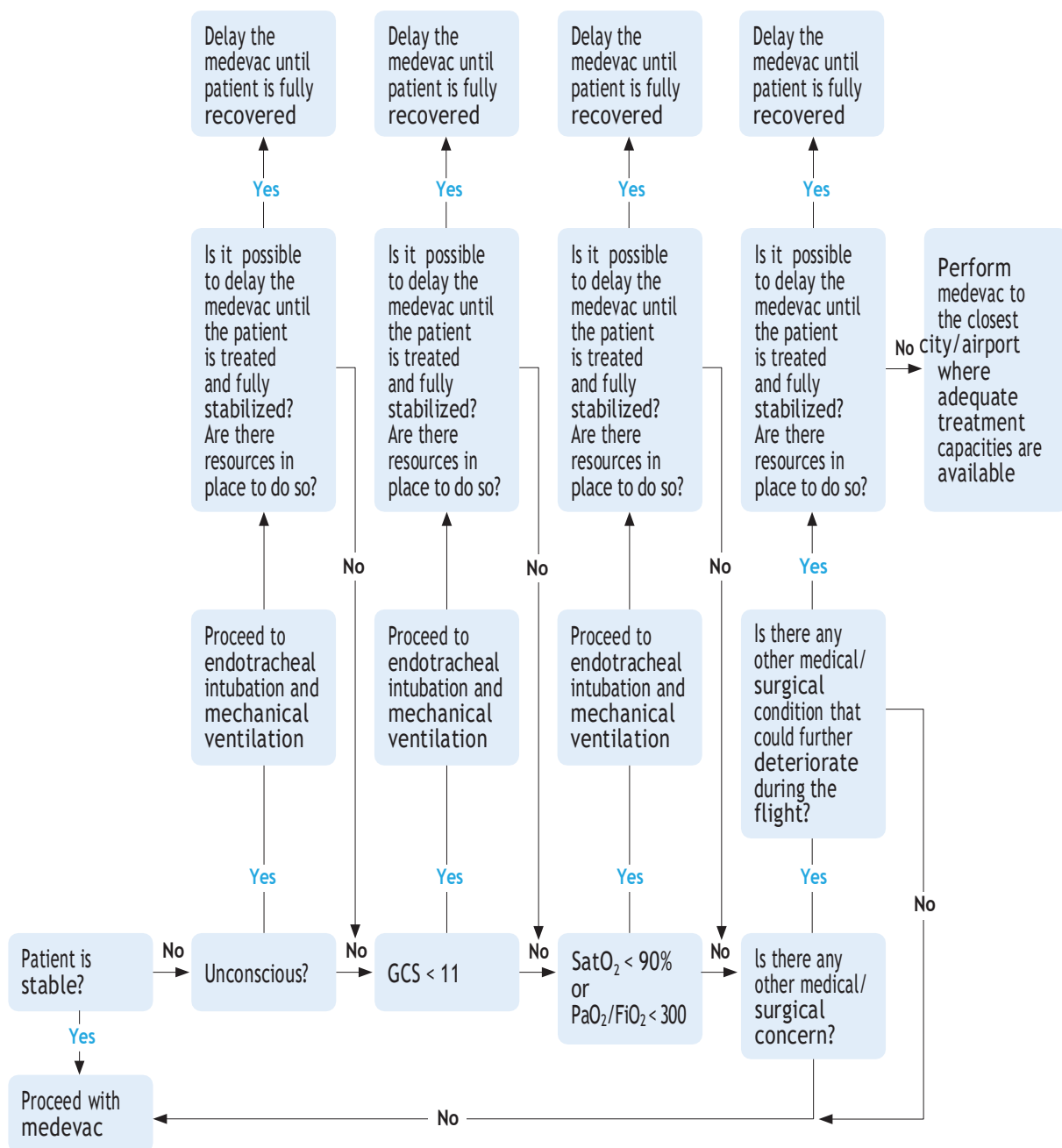
In-flight checklist

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

Post-flight checklist

- SOPs on decontamination.
- SOPs on safe equipment handling.
- SOPs on safe waste disposal.
- SOPs on personnel monitoring.

Medevac algorithm



Notes: GCS - Glasgow Coma Scale; PaO₂/FiO₂ - ratio of partial pressure arterial oxygen and fraction of inspired oxygen; SatO₂ - oxygen saturation.

Minimize risk of in-flight transmission

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

Rotary wing	<ul style="list-style-type: none">• The cockpit should be isolated through use of the aircraft blind.
Fixed wing	<ul style="list-style-type: none">• Use of barriers such as screens or curtains may provide some level of protection for personnel positioned in the cockpit, and their effectiveness is reliant on airflow and the movement of airborne particles within the aircraft.• Air-conditioning (if applicable) should be selected in non-recirculating mode.<ul style="list-style-type: none">– Pressurized aircraft: if available, aircraft recirculation should be deselected.– If cabin air recirculation is selected, then HEPA filtration is preferred. Aircraft ventilation should remain on at all times during transport of respiratory patients, including during ground delays.

References and resources

- Adhikari NK, Fowler RA, Bhagwanjee S, Rubenfeld GD. Critical care and the global burden of critical illness in adults. *Lancet*. 2010;376(9749):1339-1346.
- Albrecht R, Knapp J, Theiler L, Eder M, Pietsch U. Transport of COVID-19 and other highly contagious patients by helicopter and fixed-wing air ambulance: a narrative review and experience of the Swiss air rescue Rega. *Scand J Trauma Resusc Emerg Med*. 2020;28(1):40. doi: 10.1186/s13049-020-00734-9. PMID: 32410706; PMCID: PMC7222521.
- ARHQ. Emergency severity index: a triage tool for emergency department care. Version 4. Implementation handbook 2012. Washington (DC): Agency for Research and Healthcare Quality; 2012 (<https://www.ahrq.gov/patient-safety/settings/emergency-dept/esi.html>, accessed 30 June 2021).
- Assiri A, McGeer A, Perl TM, Price CS, Al Rabeeah AA, Cummings DAT et al. Hospital outbreak of Middle East respiratory syndrome coronavirus. *N Engl J Med*. 2013;369:407-16.
- Australian Government. Coronavirus (COVID-19) early medical aero-medical evacuation of covid-19 cases and contacts from remote communities. 2020 (https://www.health.gov.au/sites/default/files/documents/2020/08/coronavirus-covid-19-early-aero-medical-evacuation-of-covid-19-cases-and-contacts-from-remote-communities_1.pdf).
- Australian Government. Information for aeromedical retrieval of patients with COVID-19. 2020 (<https://www.health.gov.au/sites/default/files/documents/2020/03/coronavirus-covid-19-information-for-aeromedical-retrieval-of-patients.pdf>).
- BTS. British Thoracic Society guidelines for the management of community acquired pneumonia in adults. London: British Thoracic Society; 2009 (<https://www.brit-thoracic.org.uk/quality-improvement/guidelines/pneumonia-adults/>, accessed 30 June 2021).
- Cardoso LT, Grion CM, Matsuo T, Anami EH, Kauss IA, Seko L et al. Impact of delayed admission to intensive care units on mortality of critically ill patients: a cohort study. *Crit Care*. 2011;15(1):R28.
- Crouse HL, Torres F, Vaides H, Walsh MT, Ishigami EM, Cruz AT et al. Impact of an emergency triage assessment and treatment (ETAT)-based triage process in the paediatric emergency department of a Guatemalan public hospital. *Paediatr Int Child Health*. 2016;36(3):219-24.
- De Wit AJ, Coates B, Cheesman MJ, Hanlon GR, House TG, Fisk B. Airflow characteristics in aeromedical aircraft: considerations during COVID-19. *Air Med J*. 2021;40(1):P54-P59 ([https://www.airmedicaljournal.com/article/S1067-991X\(20\)30256-X/fulltext](https://www.airmedicaljournal.com/article/S1067-991X(20)30256-X/fulltext)).
- Duchateau FX, Verner L, Cha O, Corder B. Decision criteria of immediate aeromedical evacuation. *J Travel Med*. 2009;16(6):391-4. doi: 10.1111/j.1708-8305.2009.00340.x. PMID: 19930378.
- Gibbs SG, Herstein JJ, Le AB, Beam EL, Cieslak TJ, Lawler JV et al. Review of literature for air medical evacuation high-level containment transport. *Air Med J*. 2019;38(5):359-365. doi: 10.1016/j.amj.2019.06.006. Epub 2019 Jul 18. PMID: 31578975; PMCID: PMC7128392.
- Guan WJ, Ni ZY, Hu Y, Liang WH, Ou CQ, He JX et al. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med*. 2020. doi: 10.1056/NEJMoa2002032.
- Harris S, Singer M, Rowan K, Sanderson C. Delay to admission to critical care and mortality among deteriorating ward patients in UK hospitals: a multicentre, prospective, observational cohort study. *Lancet*. 2015;385(suppl 1):S40.
- Hegewald MJ, Crapo RO. Respiratory physiology in pregnancy. *Clin Chest Med*. 2011;32(1):1-13 (<https://www.ncbi.nlm.nih.gov/pubmed/21277444>, accessed 25 June 2019).
- Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet*. 2020;395:497-506.
- Kashani KB, Farmer JC. The support of severe respiratory failure beyond the hospital and during transportation. *Curr Opin Crit Care*. 2006;12(1):43-9. doi: 10.1097/01.ccx.0000198057.35212.3e. PMID: 16394783.
- Lim WS, Smith DL, Wise MP, Welham SA. British Thoracic Society community acquired pneumonia guideline and the NICE pneumonia guideline: how they fit together. *BMJ Open Respiratory Research*. 2015;2(1):e000091.
- Lyznicki JM, Williams MA, Deitchman SD, Howe JP 3rd; Council on Scientific Affairs, American Medical Association. Medical oxygen and air travel. *Aviat Space Environ Med*. 2000;71(8):827-31. PMID: 10954360.
- NATO. Aeromedical evacuation standardization agreement. STANAG No. 3204 (Edition 6). Brussels: North Atlantic Treaty Organization, Military Organization for Standardization, unclassified 15 July 1999.
- Poston JT, Patel BK, Davis AM. Management of critically ill adults With COVID-19. *JAMA*. 2020; 323(18):1839-1841. PMID: 32215647.
- Radonovich LJ Jr, Cheng J, Shenal BV, Hodgson M, Bender BS. Respirator tolerance in health care workers. *JAMA*. 2009;301(1):36-8. doi: 10.1001/jama.2008.894. PMID: 19126810.
- Sammito S, Post J, Ritter DM, Hossfeld B, Erley OM. European aeromedical evacuation transports with COVID-19 patients. *Der Notarzt* 2020;36(05):263-270. doi: 10.1055/a-1208-4806.
- Schwabe D, Kellner B, Henkel D, Pilligrath HJ, Krummer S, Zach S et al. Long-distance aeromedical transport of patients with COVID-19 in fixed-wing air ambulance using a portable isolation unit: opportunities, limitations and mitigation strategies. *Open Access Emerg Med*. 2020;12:411-419 (<https://doi.org/10.2147/OAEM.S277678>).
- Teichman PG, Donchin Y, Kot RJ. International aeromedical evacuation. *N Engl J Med*. 2007;356(3):262-70. doi: 10.1056/NEJMra063651. PMID: 17229953.
- WHO. Clinical aspects of pandemic 2009 influenza A (H1N1) virus infection. Writing Committee of the WHO Consultation on Clinical Aspects of Pandemic (H1N1) 2009 Influenza. *N Engl J Med*. 2010;362:1708-1719.

WHO. Country & Technical Guidance - Coronavirus disease (COVID-19) [website]. Geneva: World Health Organization; 2020 (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance>).

WHO. Emergency triage assessment and treatment (ETAT) [website]. Geneva: World Health Organization; 2020 (<https://apps.who.int/iris/handle/10665/43386>, accessed 30 June 2021).

WHO. Global epidemiological surveillance standards for influenza. Geneva: World Health Organization; 2013.

WHO. IMAI district clinician manual: hospital care for adults and adolescents. Guidelines for the management of common illnesses with limited resources. Volume 1. Geneva: World Health Organization; 2012 (<https://apps.who.int/iris/handle/10665/77751>, accessed 30 June 2021).

WHO. Pocket book of hospital care for children. Guidelines for the management of common illnesses with limited resources (second edition). Geneva: World Health Organization; 2013 (<https://apps.who.int/iris/handle/10665/81170>, accessed 30 June 2021).

WHO. Update on human cases of highly pathogenic avian influenza A (H5N1) virus infection. WER. 2012;13(87):117-123 (<https://www.who.int/publications/i/item/who-wer-8713-117-123>, accessed 30 June 2021).

WHO. Updated guideline: paediatric emergency triage, assessment and treatment: care of critically-ill children. Geneva: World Health Organization; 2016 (<http://www.ncbi.nlm.nih.gov/books/NBK350528/>, accessed 30 June 2021).

WHO. WHO recommendations for prevention and treatment of pre-eclampsia and eclampsia. Geneva: World Health Organization; 2011 (https://www.who.int/reproductivehealth/publications/maternal_perinatal_health/9789241548335/en/, accessed 30 June 2021).

WHO/ICRC. Basic emergency care (BEC): approach to the acutely ill and injured. Geneva: World Health Organization and International Committee of the Red Cross; 2018 (<https://www.who.int/publications/i/item/basic-emergency-care-approach-to-the-acutely-ill-and-injured>, accessed 30 June 2021).

Wu Z, McGoogan J. Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China. Summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. doi:10.1001/jama.2020.2648.

Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020. doi: 10.1016/S0140-6736(20)30566-3.

Zumla A, Hui D, Perlman S. Middle East respiratory syndrome. Lancet. 2015;386(9997):995-1007.



3

Infection prevention and control for patients with SARI



3 Infection prevention and control for patients with SARI

Summary

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

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

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

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

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

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

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

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

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

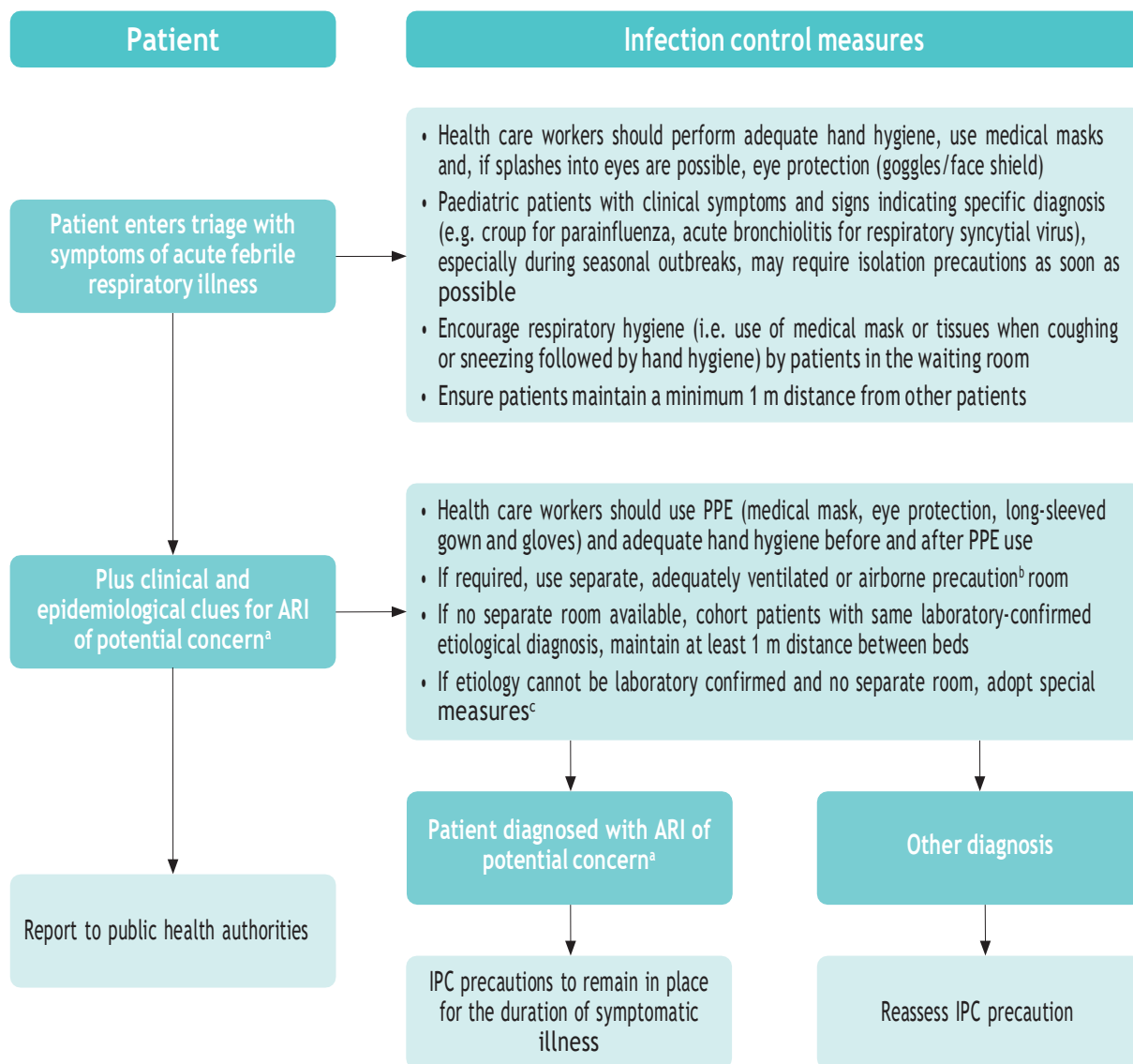
Tools

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

3.1 How to implement infection control measures for SARI

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

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



^a ARIs of potential concern include SARS, COVID-19, new influenza virus causing human infection (e.g. human cases of avian influenza) and novel pathogens causing ARIs that can cause outbreaks with high morbidity and mortality. Clinical and epidemiological clues include severe disease in a previously healthy host, exposure to household member or close contact with severe ARI, cluster of cases, travel, exposure to ill animals or laboratory.

^b Airborne precaution rooms include both mechanically and naturally ventilated rooms with ≥ 12 air changes per hour and controlled direction of airflow.

^c The term “special measures” means allowing patients with epidemiological and clinical information suggestive of a similar diagnosis to share a room, but with a spatial separation of at least 1 m.

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

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

Instructions for patients	<p>Give suspect patient a medical mask and direct the patient to a separate area; an isolation room if available. If not possible to separate the patient, try to keep at least 1 m distance between suspected patients and other patients in the waiting room.</p> <p>All patients in the waiting room should have a mask and should practise respiratory hygiene (cover their nose and mouth during coughing or sneezing with a tissue or flexed elbow) and perform hand hygiene after contact with respiratory secretions (such as coughing, sneezing or blowing nose).</p>
Apply droplet precautions	<p>Droplet precautions prevent transmission of respiratory viruses through respiratory droplets that are expelled when an infected person speaks, coughs, or sneezes.</p> <p>Place patients in single rooms, or group those with the same etiological diagnosis together, maintaining at least 1 m distance between beds. If an etiological diagnosis is not possible, group patients with similar clinical diagnosis and based on epidemiological risk factors, with a spatial separation. Limit patient movement within the institution and ensure that patients wear medical masks when being taken outside their rooms.</p> <p>When providing care in close contact with a patient with respiratory symptoms (e.g. coughing or sneezing), use a medical mask and eye protection (face mask or goggles), because sprays of secretions may occur.</p> <p><i>Note:</i> The risk of COVID-19 spreading is especially high in places where the three Cs overlap: Crowded places, Close-contact settings (especially where people have conversations very near each other) and Confined and enclosed spaces with poor ventilation (see Tool 3.7).</p>
Apply contact precautions	<p>Contact precautions prevent direct or indirect transmission from contact with contaminated surfaces or equipment (i.e. contact with contaminated oxygen tubing/interfaces). PPE for contact precautions are a long-sleeved gown and gloves.</p> <p>Hand hygiene followed by putting on PPE for contact and droplet precautions (medical mask and eye protection) should be applied when entering the room. Remove PPE when leaving the room, and practise hand hygiene following PPE removal.</p> <p>If possible, use either disposable or dedicated equipment (e.g. stethoscopes, blood pressure cuffs, pulse oximeters and thermometers). If equipment needs to be shared among patients, clean and disinfect items between each patient use.</p> <p>Ensure that health workers refrain from touching their eyes, nose and mouth with potentially contaminated gloved or ungloved hands.</p> <p>Avoid contaminating environmental surfaces that are not directly related to patient care (e.g. door handles and light switches). Avoid medically unnecessary movement and transport of patients. Practise hand hygiene frequently.</p>
Apply airborne precautions when performing an aerosol-generating procedure	<p>Ensure that health workers performing, or in the room during, an aerosol-generating procedure (e.g. open suctioning of respiratory tract, tracheal intubation, non-invasive ventilation, tracheotomy, bronchoscopy, cardiopulmonary resuscitation) use the appropriate PPE, including gloves, long-sleeved gowns, eye protection, and fit-tested particulate respirators (N95 or equivalent, or higher level of protection). A scheduled fit test should not be confused with a user's seal check before each use.</p> <p>Whenever possible, use adequately ventilated single rooms when performing aerosol-generating procedures, meaning negative pressure rooms with a minimum of 6-12 air changes per hour (e.g. equivalent to 40-80 L/s/patient for a 4 × 2 × 3 m³ room) or at least 160 L/s/patient in facilities with natural ventilation.</p> <p>Avoid the presence of unnecessary individuals in the room.</p> <p>Care for the patient in the same type of room after mechanical ventilation begins.</p>

3.3 Personal protective equipment (PPE)

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

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

HOW TO GUIDE - PUTTING ON PPE FOR CONTACT/DROPLET PRECAUTIONS

1 Perform hand hygiene

Alcohol based handrub
Rub hands for 20–30 seconds.

or

Water and soap
Wash hands for 40–60 seconds.



2 Put on the gown



3 Put on the mask

Medical mask.



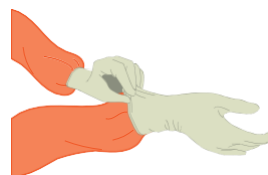
4 Put on eye protection

Put on face shield or goggles.



5 Put on gloves

Ensure glove is placed over the cuff of the gown.



Full PPE



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

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

Order is important

1 Remove gloves



2 Remove the gown

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



3 Perform hand hygiene

Alcohol based handrub

Rub hands for 20–30 seconds.

or

Water and soap

Wash hands for 40–60 seconds.



4 Remove eye protection

Remove face shield or goggles.



5 Remove the mask

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



6 Perform hand hygiene

Alcohol based handrub

Rub hands for 20–30 seconds.

or


Water and soap

Wash hands for 40–60 seconds.




World Health
Organization


3.4 How to improve medical mask fit in health care settings

 World Health Organization


How to improve medical mask fit in health care settings









When linking ear loops behind the head




When using knot-and-tuck method





Clean hands thoroughly before putting on and before and after taking off your mask

 <p>Attach a clean connector to link ear loops together**</p>	 <p>Fold the mask horizontally</p>
 <p>Place the medical mask colour-side facing outward, attach ear loops behind ears</p>	 <p>Make a knot on both ear loops as close to the edge of the mask as possible</p>
 <p>Attach ear loops using connector behind head tightly</p>	 <p>Push the extra material under the mask inward to ensure no gaps on both sides</p>



Adjust the wire at the bridge of the nose and ensure there are no gaps between the mask and your face at the sides of your nose, cheeks, and under your chin.

**Find a clean practical connector to link your ear loops, it can be

adjustable rope silicone

**If a surface is used to fold and manipulate the mask, clean the surface first using a cloth wipe with soap and water, followed by disinfection using a cloth wipe soaked in 70-90% alcohol OR 0.1% sodium hypochlorite (or comparable hospital grade disinfectant) and allow for least 1 minute contact time before surface is used.

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



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



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



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



- 4 Place fingertips of both hands at the top of the metal nosepiece. Mould the nosepiece (**using two fingers of each hand**) to the shape of your nose. (Pinching the nosepiece using one hand may result in less effective respirator performance.) Cover the front of the respirator with both hands, being careful not to disturb the position of the respirator.

A. Positive seal check

Exhale sharply.

A positive pressure inside the respirator = no leakage.

If leakage, adjust position and/or tension straps.

Reset the seal.

Repeat the steps until respirator is sealed properly.

B. Negative seal check

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

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

3.6 Hand hygiene

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

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

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

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

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

How to Handwash?

WASH HANDS WHEN VISIBLY SOILED! OTHERWISE, USE HANDRUB

🕒 Duration of the entire procedure: 40–60 seconds



Wet hands with water;



Apply enough soap to cover all hand surfaces;



Rub hands palm to palm;



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



Palm to palm with fingers interlaced;



Backs of fingers to opposing palms with fingers interlocked;



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



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



Rinse hands with water;



Dry hands thoroughly with a single use towel;



Use towel to turn off faucet;



Your hands are now safe.

How to Handrub?

RUB HANDS FOR HAND HYGIENE! WASH HANDS WHEN VISIBLY SOILED

⌚ Duration of the entire procedure: 20–30 seconds



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



Rub hands palm to palm;



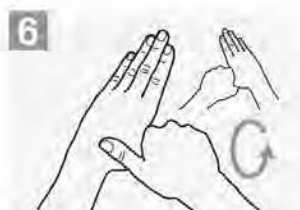
Right palm over left dorsum with interlaced fingers and vice versa;



Palm to palm with fingers interlaced;



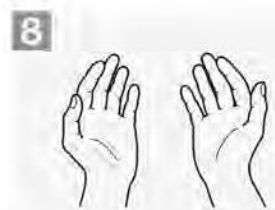
Backs of fingers to opposing palms with fingers interlocked;



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



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



Once dry, your hands are safe.

3.7 The 5 moments for hand hygiene in health care facilities

Your 5 Moments for Hand Hygiene




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

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

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


Avoid the Three Cs

Be aware of different levels of risk in different settings.




There are certain places where COVID-19 spreads more easily:

1




Crowded places
with many people nearby

2

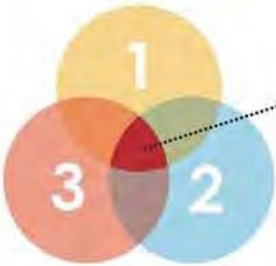


Close-contact settings
Especially where people have close-range conversations

3




Confined and enclosed spaces
with poor ventilation




The risk is higher in places where these factors overlap.

Even as restrictions are lifted, consider where you are going and #StaySafe by avoiding the Three Cs.


WHAT SHOULD YOU DO?




Avoid crowded places and limit time in enclosed spaces




Maintain at least 1 m distance from others



When possible, open windows and doors for ventilation



Keep hands clean and cover coughs and sneezes



Wear a mask, especially when you can't physically distance

If you are unwell, stay home unless you need to seek urgent medical care.

3. Infection prevention and control for patients with SARI 57

3.9 Checklist for aerosol-generating procedures

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

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

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

Checklist for aerosol-generating procedures

- Perform hand hygiene before and after patient contact and before and after PPE use.
- All health workers present should wear the following PPE:
 - A facial particulate respirator (e.g. European Union FFP2 or United States of America National Institute for Occupational Safety and Health-certified N95). Perform a seal check.
 - Eye protection (e.g. goggles or a face shield).
 - A clean, non-sterile, long-sleeved gown.
 - Gloves (some of these procedures require sterile gloves).
- Make sure adequately ventilated room:
 - For mechanically ventilated rooms: Ensure ≥ 6 -12 air changes per hour plus control of airflow direction, ideally 12 air changes per hour for new constructions, with a recommended negative pressure differential of ≥ 2.5 Pa (0.01 inch water gauge) to ensure that air flows from the corridor into the patient room.
 - For natural ventilation: The recommended average natural ventilation rate is 160 L/s/patient.
- Social distancing - avoid unnecessary individuals in the room.

References and resources

CDC. Interim guidance on infection control measures for 2009 H1N1 Influenza in healthcare settings, including protection of healthcare personnel. Atlanta (GA): Centers for Disease Control and Prevention; 2010 (https://www.cdc.gov/h1n1flu/guidelines_infection_control.htm, accessed 3 June 2021).

Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. *PLoS One*. 2012;7(4):e35797.

WHO. Advice on the use of masks in the community setting in Influenza A(H1N1) outbreaks: interim guidance. Geneva: World Health Organization; 2009.

WHO. Coronavirus disease (COVID-19): How is it transmitted? Geneva: World Health Organization; 2020 (Coronavirus disease (COVID-19): How is it transmitted? (who.int), accessed 3 June 2021).

WHO. Coronavirus disease (COVID-19) technical guidance: infection prevention and control / WASH [website]. Geneva: World Health Organization; 2020 (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance-publications?publicationtypes=d198f134-5eed-400d-922e-1ac06462e676>, accessed 3 June 2021).

WHO. How to handwash? [poster]. Geneva: World Health Organization; 2009 (https://www.who.int/gpsc/5may/How_To_HandWash_Poster.pdf, accessed 3 June 2021).

WHO. Infection prevention and control during health care when coronavirus disease (COVID-19) is suspected or confirmed: interim guidance. 29 June 2020. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/i/item/WHO-2019-nCoV-IPC-2020.4>, accessed 3 June 2021).

WHO. Infection prevention and control of epidemic- and pandemic-prone acute respiratory infections in health care. WHO guidelines. Geneva: World Health Organization; 2014 (<https://www.who.int/publications/i/item/infection-prevention-and-control-of-epidemic-and-pandemic-prone-acute-respiratory-infections-in-health-care>, accessed 3 June 2021).

WHO. Rational use of personal protective equipment for coronavirus disease (COVID-19). Geneva: World Health Organization; 2020 (Personal protective equipment for COVID-19 (who.int), accessed 3 June 2021).

WHO. Severe acute respiratory infections treatment centre. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/i/item/10665-331603>, accessed 3 June 2021).

WHO IPC posters:

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



4

Monitoring patients with acute respiratory infection



4 Monitoring patients with acute respiratory infection

Summary

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

Pulse oximetry is used to monitor oxygen saturation (SpO₂). It is an essential tool that should be available at all first access health points, where patients with ARI are assessed to inform triage, clinical assessment and appropriate referral and/or treatment plans. Pulse oximeter is also an essential tool to monitor patients for signs of clinical deterioration or improvement that may require change in clinical management interventions.

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

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

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

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

Tools

- 4.1 AVPU scale: a simple tool for assessing level of consciousness
- 4.2 Pulse oximetry monitoring
- 4.3 Blood gas analysis monitoring
- 4.4 Capnometry (capnography)
- 4.5 National Early Warning Score (NEWS) for adults
- 4.6 Paediatric Early Warning Score (PEWS)
- 4.7 Routine monitoring and care framework for COVID-19 patients
- 4.8 WHO Mild COVID-19 home care bundle for health care workers
- 4.9 Memory aid: key criteria used to assess vital signs in children
- 4.10 Memory aid: key physiological aspects to assess in pregnant women

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

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

A

ALERT: Patient is aware of the examiner, responds to the environment on their own, follows commands, opens eyes spontaneously, and tracks objects.

V

VERBAL: Patient does not open eyes spontaneously, but does in response to a verbal stimulus and reacts meaningfully to the verbal stimulus.

P

PAIN: Patient does not open eyes spontaneously, but does in response to pain and may move, moan, or cry in response to pain.

U

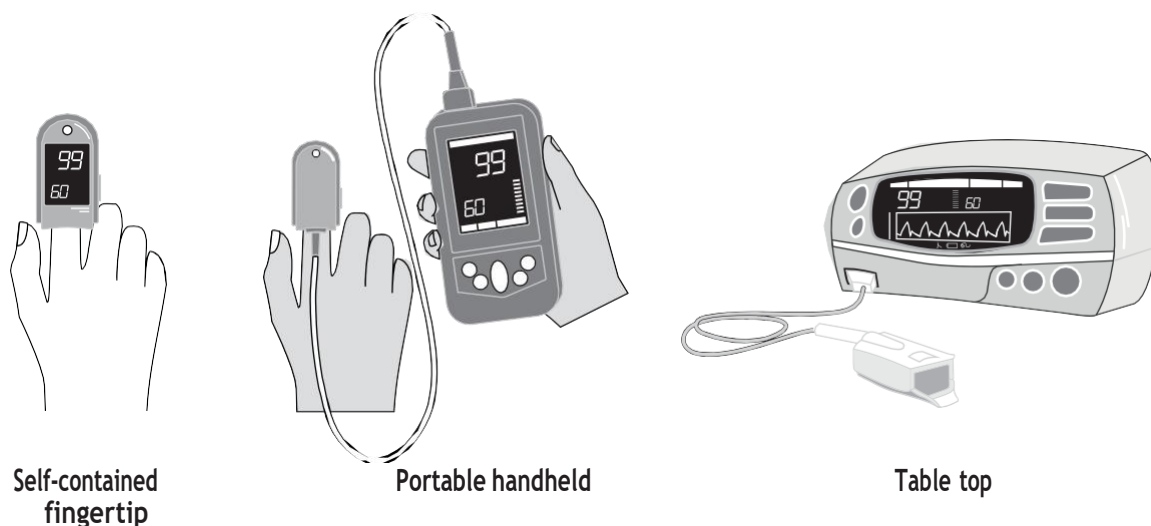
UNRESPONSIVE: Patient does not respond to verbal or painful stimuli.

4.2 Pulse oximetry monitoring

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

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

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



✓ BENEFITS

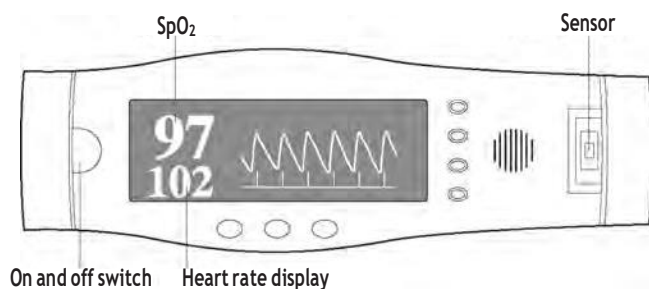
- Accurate
- Fast
- Easy to use
- Non-invasive
- Portable

⚠ LIMITATIONS

- Requires a pulsatile signal - challenging with motion or poor perfusion.
- Does not measure ventilation (PaCO₂).
- False readings can be due to many factors including abnormal haemoglobin (Hb), carbon monoxide (CO) poisoning.
- Remember to remove nail polish if present!

Note: Oxygen partial pressures in the atmosphere are lower at higher altitudes. Therefore, patients at facilities in higher altitudes may require higher flow rates for longer duration for adequate therapy compared with patients at sea level. If the altitude is higher than 1000 m, then a correction factor should be calculated to define ARDS: PaO₂/FiO₂ × barometric pressure/760.

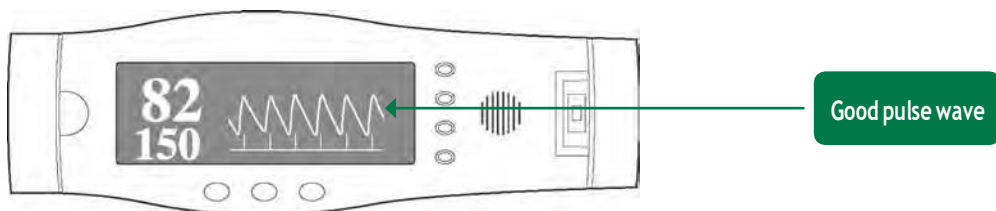
Pulse oximeter displaying normal SpO₂ reading



This image shows a pulse oximeter with a normal oxygen saturation (SpO₂) reading (pulse rate = 102 bpm; SpO₂ = 97%) and a plethysmographic (pulse) wave (i.e. the waveform corresponds with arterial pulsation and rate) indicating a good arterial trace and a valid reading.

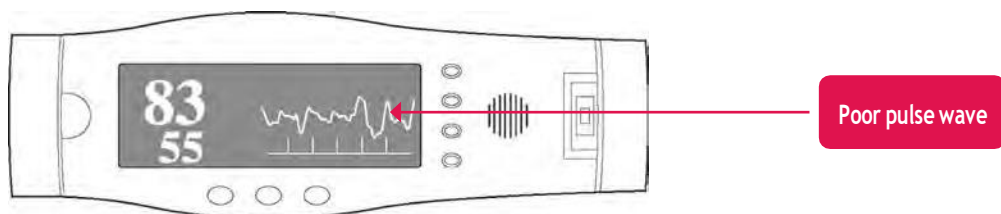
Note: Not all pulse oximeters may display a plethysmograph or signal quality, and without this feature, interpretation of the data must be done cautiously.

Pulse oximeter displaying abnormal SpO₂ reading



In this image (pulse rate = 150 bpm; SpO₂ = 82%), the pulse oximeter has a good plethysmographic wave, indicating a valid arterial trace. Therefore, the SpO₂ reading, which is abnormally low (82%), is likely accurate and indicates that the patient is hypoxaemic. Oxygen should be given. Note the increased heart rate, which is common in seriously ill patients.

Pulse oximeter showing a poor plethysmography (pulse) wave



In this image, the SpO₂ reading is 83% (pulse rate 55 bpm) with a poor pulse wave. The poor pulse wave raises concern that the reading of 83% may not be correct. Multiple factors may cause a poor waveform, including patient movement, poor probe placement, or poor perfusion (shock).

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

4.3 Blood gas analysis monitoring

Blood gas analysis can be used to measure the pH, partial pressure of oxygen (PaO₂), and partial pressure of carbon dioxide (PaCO₂) in arterial, venous or capillary blood.

The pH is a direct indicator of overall acid-base status in arterial, capillary and venous blood. The probable cause of pH disturbances can be inferred only from the PaCO₂ and blood bicarbonate (HCO₃) concentration (or the base excess or deficit). In the absence of blood gas analysis, there is no accurate surrogate for assessing acid-base status.

Acidosis is a process that lowers the extracellular fluid pH (pH < 7.35). This can be caused by a fall in the serum bicarbonate concentration (metabolic acidosis with low pH and HCO₃) or an elevation of PaCO₂ (respiratory acidosis with low pH and high PaCO₂). Acidosis (metabolic or respiratory) is commonly seen when there is major disturbance of the circulation or oxygen delivery, as in severe hypoxaemia due to SARI, ARDS, sepsis and septic shock.

Arterial blood gas analysis can be used for monitoring changes in response to therapy, including ventilator changes. Venous blood and capillary blood may be easier to monitor than arterial blood but should not be used for oxygen level determination. The CO₂ level in arterial, capillary or venous blood helps in assessing and monitoring alveolar ventilation, but peripheral venous values can be inaccurate. While SpO₂ can often be used as a surrogate for PaO₂, end-tidal CO₂ (EtCO₂) measurement has limitations when deployed as a surrogate for PaCO₂ (see Tool 4.4). Direct measurement of PaCO₂ is an important diagnostic tool in patients with SARI and ARDS to help guide protocolized lung protective ventilation.



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

Blood gas analysis provides information on oxygenation, ventilation and circulation, but can also inform about electrolyte concentrations (particularly sodium and potassium) which can be measured in the same blood sample by some analysers, such as point of care. Electrolyte abnormalities are common in critically ill patients with SARI and it may be useful for them to be measured for diagnosis and monitoring, besides pH, HCO₃, PaCO₂ and PaO₂.

✓ BENEFITS

- Measures pH, HCO₃, PaCO₂, PaO₂.
- Informs about ventilation and acidosis.
- May be used to measure lactate, haemoglobin, potassium (e.g. point of care analysers).

⚠ LIMITATIONS

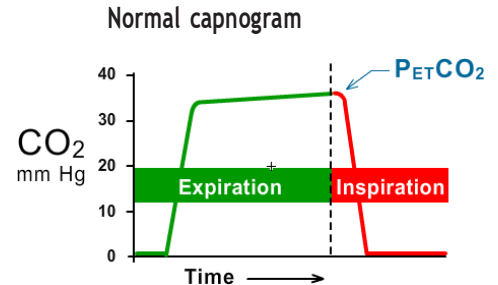
- Invasive arterial puncture.
- Special (heparinized) syringe.
- Rapid transfer (on ice if > 20 minutes) to laboratory.
- Blood gas analyser machine (e.g. I-STAT).
- CO level not detected on all machines.

4.4 Capnometry (capnography)

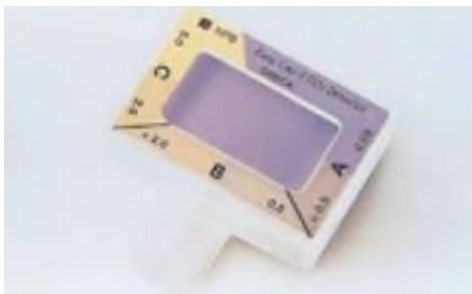
Capnometry is the non-invasive measurement of EtCO₂ partial pressure. This is achieved by shining infrared light through exhaled gas and detecting absorption, from which EtCO₂ partial pressure can be derived.

Capnography is the non-invasive measurement of EtCO₂ in exhaled breath expressed as the CO₂ concentration over time. The relationship of CO₂ concentration to time is graphically represented by the CO₂ waveform (capnogram).

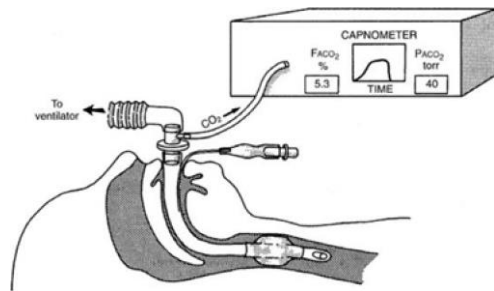
Capnography can be done in line with the breathing circuit, at the hub of the endotracheal tube (i.e. mainstream) or by continuously sampling gas from the exhaled breath of a patient or from a breathing circuit (e.g. nasal, nasal-oral cannula) to a detector (i.e. sidestream). Mainstream systems are configured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



Colorimetric end-tidal CO₂ (EtCO₂) detectors



Sidestream capnometry system



Source: Thoracic Key (2021).

CO₂ monitors are either quantitative or qualitative. Quantitative devices measure the precise EtCO₂ as a number (capnometry) or a number and a waveform (capnography). Qualitative devices (e.g. colorimetric detectors) report the range in which the EtCO₂ falls as opposed to a precise value. For example, the colour in the colorimetric end-tidal CO₂ (EtCO₂) detector may change when the endotracheal tube is not correctly placed. EtCO₂ measurements can be used to monitor and manage ventilation and circulation.

✓ BENEFITS

- Measures EtCO₂ tension in expired air from sampling gas in respiratory circuit.
- In normal lungs, EtCO₂ is about 3-5 mmHg less than PaCO₂.
- Confirms endotracheal intubation.
- Assess perfusion (during CPR).

⚠ LIMITATIONS

- Inaccurate if there is no discernible plateau: e.g. airflow obstruction.
- Underestimates PaCO₂ when there is decreased lung perfusion:
 - pulmonary emboli
 - hypotension
 - high PEEP
 - severe ARDS
 - emphysema.

¹ If there is significant dead space in the circuit (e.g. large filters or heat moisture exchangers) or the patient's lungs (e.g. ARDS), capnography may significantly underestimate PaCO₂ and will have limited utility for guiding titration of ventilation.



4.5 National Early Warning Score (NEWS) for adults

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

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

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

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

Chart 1: NEWS scoring system

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

Source: Royal College of Physicians (2017).

Chart 2: NEWS thresholds and triggers

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

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

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

Source: Royal College of Physicians (2017).

Chart 3: Clinical response to NEWS trigger thresholds

NEWS score	Monitoring frequency	Clinical response
0	Minimum 12 hourly	<ul style="list-style-type: none"> Continue routine NEWS monitoring
Total 1-4	Minimum 4-6 hourly	<ul style="list-style-type: none"> Inform registered nurse, who must assess the patient Registered nurse decides whether increased frequency of monitoring and/or escalation of care is required
3 in single parameter	Minimum 1 hourly	<ul style="list-style-type: none"> Registered nurse to immediately inform the medical team caring for the patient Registered nurse to request urgent assessment by a clinician or team with core competencies in the care of acutely ill patients Provide clinical care in an environment with monitoring facilities
Total 5 or more Urgent response threshold	Minimum 1 hourly	<ul style="list-style-type: none"> Registered nurse to inform medical team caring for the patient, who will review and decide whether escalation of care is necessary
Total 7 or more Emergency response threshold	Continuous monitoring of vital signs	<ul style="list-style-type: none"> Registered nurse to immediately inform the medical team caring for the patient - this should be at least at specialist registrar level Emergency assessment by a team with critical care competencies, including practitioner(s) with advanced airway management skills Consider transfer of care to a level 2 or 3 clinical care, i.e. higher dependency unit or ICU Clinical care in an environment with monitoring facilities

Source: Royal College of Physicians (2017).

Chart 4: NEWS 2 observation chart

NEWS key		FULL NAME												
0 1 2 3		DATE OF BIRTH						DATE OF ADMISSION						
	DATE													DATE
	TIME													TIME
A+B Respirations Breaths/min	≥25													≥25
	21–24													21–24
	18–20													18–20
	15–17													15–17
	12–14													12–14
	9–11													9–11
≤8													≤8	
A+B SpO ₂ Scale 1 Oxygen saturation (%)	≥96													≥96
	94–95													94–95
	92–93													92–93
	≤91													≤91
SpO₂ Scale 2† Oxygen saturation (%) Use Scale 2 if target range is 88–92%, eg in hypercapnic respiratory failure †ONLY use Scale 2 under the direction of a qualified clinician	≥97 _{on O₂}													≥97 _{on O₂}
	95–96 _{on O₂}													95–96 _{on O₂}
	93–94 _{on O₂}													93–94 _{on O₂}
	≥93 _{on air}													≥93 _{on air}
	88–92													88–92
	86–87													86–87
84–85													84–85	
≤83%													≤83%	
Air or oxygen?	A=Air													A=Air
	O ₂ L/min													O ₂ L/min
	Device													Device
C Blood pressure mmHg Score uses systolic BP only	≥220													≥220
	201–219													201–219
	181–200													181–200
	161–180													161–180
	141–160													141–160
	121–140													121–140
	111–120													111–120
	101–110													101–110
	91–100													91–100
	81–90													81–90
	71–80													71–80
	61–70													61–70
	51–60													51–60
≤50													≤50	
C Pulse Beats/min	≥131													≥131
	121–130													121–130
	111–120													111–120
	101–110													101–110
	91–100													91–100
	81–90													81–90
	71–80													71–80
	61–70													61–70
	51–60													51–60
	41–50													41–50
	31–40													31–40
	≤30													≤30
	D Consciousness Score for NEWS onset of confusion (no score if chronic)	Alert												
Confusion														Confusion
V														V
P														P
U														U
E Temperature °C	≥39.1°													≥39.1°
	38.1–39.0°													38.1–39.0°
	37.1–38.0°													37.1–38.0°
	36.1–37.0°													36.1–37.0°
	35.1–36.0°													35.1–36.0°
	≤35.0°													≤35.0°
NEWS TOTAL														TOTAL
Monitoring frequency														Monitoring
Escalation of care Y/N														Escalation
Initials														Initials

Source: Royal College of Physicians (2017).



4.6 Paediatric Early Warning Score (PEWS)

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

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

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

Notes: CR time - capillary refill time; HR - heart rate; RR - respiratory rate; SBP - systolic blood pressure; SpO₂ - peripheral oxygen saturation.

Source: Parshuram et al. (2011).

4.7 Routine monitoring and care framework for COVID-19 patients

To be adapted by context and local care pathway.

Routine monitoring and care framework

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

Routine monitoring and care framework continued

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

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

Notes:

- ^a **Patients with ≥ 1 risk factor and mild disease** who are not hospitalized should use pulse oximetry monitoring at home as part of a package of care (telemedicine, home hospitalization programmes) including patient and provider education and appropriate follow up and report to health worker on a daily basis. The rest of the vital signs, such as temperature, RR, HR, BP, are recommended to be reported to the health care provider who follows up the patient at home if the equipment is available at home.
- ^b **Patients without risk factors and moderate disease** can be initially managed at home with self-monitoring and reporting to a health worker if any complication or emergency signs occur.
- ^c **Patients with ≥ 1 risk factor and moderate disease** should, preferably, be referred to a health care facility for monitoring and treatment. If this is not possible, patients can be initially managed at home, preferably monitored by a health worker (telemedicine, home hospitalization programmes) at least once daily; and patients should record vital signs as detailed in the table above and report to the health worker on a daily basis.
- ^d **The need for monitoring of vital signs (SpO₂, HR, RR, BP) and physical examination** should be assessed by health care provider who follows up the patient at home with telemedicine or home hospitalization programmes (ensure the equipment is available).

Risk factors for severe disease

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

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

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

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



World Health Organization



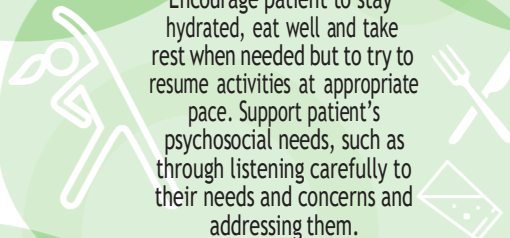
WHO Mild COVID-19 HOME CARE BUNDLE FOR HEALTH CARE WORKERS*



Instruct patient to stay in isolation, preferably in separate room with adequate ventilation. Ensure good flow of fresh air and open windows where possible. Minimize close contact with others (households and/or visitors). If within 1 m of others, patient should wear a mask, and caregivers should wear PPE. Wash your hands regularly.



If there is fever, treat with antipyretic, such as paracetamol. There is no need for antibiotics unless bacterial infection is suspected. In areas with other endemic infections (e.g. malaria, TB, dengue), follow routine treatment protocols for fever. Advise patient taking medications for chronic conditions (e.g. diabetes or hypertension) to continue with them.



Encourage patient to stay hydrated, eat well and take rest when needed but to try to resume activities at appropriate pace. Support patient's psychosocial needs, such as through listening carefully to their needs and concerns and addressing them.



Advise patient to monitor for worsening of symptoms, such as chest pain, fast or difficulty breathing (at rest or while speaking), fast heart rate, palpitations, confusion, altered mental status, or any other emergency signs. If present, instruct patient to call for emergency help according to national protocols.



EMERGENCY SIGNS:
Obstructed or absent breathing, severe respiratory distress, cyanosis, shock, coma and/or convulsions.



If patient is at risk for severe disease[†], monitor oxygen saturation with pulse oximeter, at least twice a day. If SpO₂ is <90%, instruct patient to call for emergency help. If SpO₂ is between 90-94%, call for urgent help, as this range may be an early sign for deterioration in someone with previously normal lungs. Oral corticosteroids may be prescribed at this time.

See *Therapeutics and COVID-19: living guideline* (📄) and *Living guidance for clinical management of COVID-19* (📄).

[†]Risk factors for severe disease includes: older age (> 60 years), hypertension, diabetes, cardiac disease, chronic lung disease, cerebrovascular disease, dementia, mental disorders, chronic kidney disease, immunosuppression (including HIV), obesity, cancer and unvaccinated against COVID-19. In pregnant or recently pregnant: women > 35 years old, obesity, with chronic medical conditions or pregnancy specific disorders (e.g. gestational diabetes and pre-eclampsia/eclampsia).



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

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

Severe disease

Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnoea) plus one of the following: respiratory rate > 30 breaths/min; severe respiratory distress; or SpO₂ < 90% on room air at rest.

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

- SpO₂ < 90%
- Very severe chest wall indrawing, grunting, central cyanosis or presence of any other general danger sign (inability to breastfeed or drink, lethargy or unconsciousness or convulsions).

Critical COVID-19

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



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

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

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

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

ADDITIONAL REFERENCES

WHO patient leaflet for the self-management of symptoms

<https://www.euro.who.int/en/health-topics/health-emergencies/coronavirus-covid-19/publications-and-technical-guidance/2020/support-for-rehabilitation-self-management-after-covid-19-related-illness-2020-produced-by-who/europe>

WHO Healthy at Home

<https://www.who.int/campaigns/connecting-the-world-to-combat-coronavirus/healthyathome>

© World Health Organization 2021

<https://www.who.int/publications/i/item/clinical-management-of-covid-19>

<https://www.who.int/teams/health-care-readiness-clinical-unit/covid-19>



World Health
Organization



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

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

Key tips for assessing a sick child

Blood pressure measurement in children

- Cuff should cover to $\frac{3}{4}$ of the upper arm, calf or thigh.
- Cuffs that are too small or too large give falsely high readings.
- Child should be at rest and not distressed (this will falsely elevate the reading).

To perform capillary refill (CR) assessment

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

Weight estimates in children

It is always best to weigh children rather than estimate their weight.

In an emergency, weight can be estimated in visibly well-nourished children.

- Term infants: 2.5-4.5 kg.
- 6 months of age: 5-7 kg.
- After 1 year of age: (age in years + 4) × 2 kg.

Criteria to define severe malnutrition

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

Signs of respiratory distress

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

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

Item sub-score

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

Source: Adapted from Hegewald and Crapo (2011).

Immune system

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

Cardiovascular

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

Respiratory

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

Maternal-fetal dyad

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

Key tips for complications in pregnant women

Tips regarding preterm labour

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

Tips for managing respiratory distress

- Keep SpO₂ ≥ 92-95%.
- Do not delay intubation for worsening respiratory distress. Be prepared for difficult airway!

Tips for managing hypotension

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

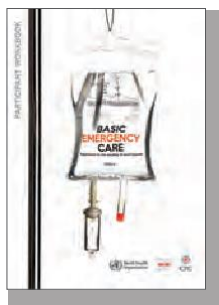
Tips regarding antimicrobial therapy

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

References and resources

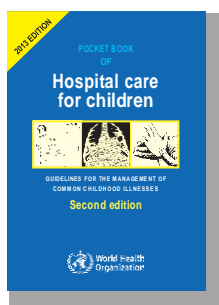
- Abbott TE, Vaid N, Ip D, Cron N, Wells M, Torrance HD et al. A single-centre observational cohort study of admission National Early Warning Score (NEWS). *Resuscitation*. 2015;92:89-93.
- Brown SR, Martinez-Garcia D, Agulnik A. Scoping review of Pediatric Early Warning Systems (PEWS) in resource-limited and humanitarian settings. *Front Pediatr*. 2019;6:410. doi 10.3389/fped.2018.00410.
- Burch VC, Tarr G, Morroni C. Modified early warning score predicts the need for hospital admission and in-hospital mortality. *Emerg Med J*. 2008;25(10):674-678.
- Cook TM, Woodall N, Frerk C, Fourth National Audit Project. Major complications of airway management in the UK: results of the Fourth National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society: Part 1: Anaesthesia. *Br J Anaesth*. 2011;106(5):617-31.
- Cook TM, Woodall N, Harper J, Benger J, Fourth National Audit Project. Major complications of airway management in the UK: results of the Fourth National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society: Part 2: Intensive care and emergency departments. *Br J Anaesth*. 2011;106(5):632-42.
- Frankel HL, Kirkpatrick AW, Elbarbary M, Blaivas M, Desai H, Evans D et al. Guidelines for the appropriate use of bedside general and cardiac ultrasonography in the evaluation of critically ill patients. Part I: general ultrasonography. *Crit Care Med*. 2015;43(11):2479-502.
- Ingham J, Macnaughton PD. Measurement of pO₂, pCO₂, pulse oximetry and capnography. *Anaesthesia & Intensive Care Medicine*. 2005;6(12):413-415.
- Jaber S, Jung B, Corne P, Sebbane M, Muller L, Chanques G et al. An intervention to decrease complications related to endotracheal intubation in the ICU: a prospective, multi-center study. *Int Care Med*. 2010;36(2):248-55.
- Magder S. Understanding central venous pressure: not a preload index? *Curr Opin Crit Care*. 2015;21(5):369-75.
- Marik PE, Baram M, Vahid B. Does central venous pressure predict fluid responsiveness? A systematic review of the literature and the tale of seven mares. *Chest*. 2008;134(1):172-8.
- Marino PL. *The ICU book* (third edition). Philadelphia (PA): Lippincott Williams and Wilkins; 2007.
- National Heart, Lung, and Blood Institute ARDS Clinical Trials Network, Wiedemann HP, Wheeler AP, Bernard GR, Thompson BT, Hayden D et al. Comparison of two fluid-management strategies in acute respiratory distress syndrome. *N Engl J Med*. 2006;354(24):2564-75.
- Parshuram CS, Duncan HP, Joffe AR, Farrell CA, Lacroix JR, Middaugh KL et al. Multicentre validation of the bedside paediatric early warning score: a severity of illness score to detect evolving critical illness in hospitalised children. *Crit Care*. 2011;15(4):R184.
- RCP. National Early Warning Score (NEWS) 2 [website]. London: Royal College of Physicians (<https://www.rcplondon.ac.uk/projects/outputs/national-early-warning-score-news>, accessed 5 July 2021).
- Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med*. 2001;345(19):1368-77.
- Silcock DJ, Corfield AR, Gowens PA, Rooney KD. Validation of the National Early Warning Score in the prehospital setting. *Resuscitation*. 2015;89:31-5.
- Subbe CP, Kruger M, Rutherford P, Gemmel L. Validation of a modified Early Warning Score in medical admissions. *QJM*. 2001;94(10):521-6.
- Wollner E, Nourian MM, Booth W, Conover S, Law T, Lilaonitkul M et al. Impact of capnography on patient safety in high and low-income settings: a scoping review. *Br J Anaesth*. 2020;125(1):e88-e103.

Key resources for supporting the management of SARI



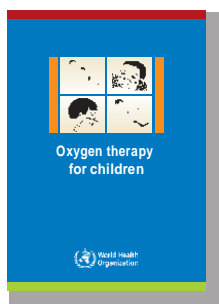
Basic emergency care (BEC): approach to the acutely ill and injured (2018) ([📄](#))

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



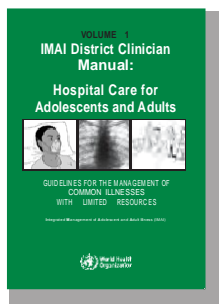
Pocket book of hospital care for children: guidelines for the management of common illnesses with limited resources (second edition) (2013) ([📄](#))

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



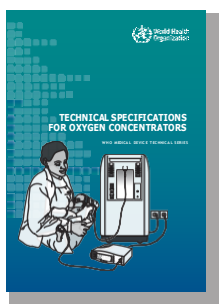
Oxygen therapy for children (2016) ([📄](#))

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



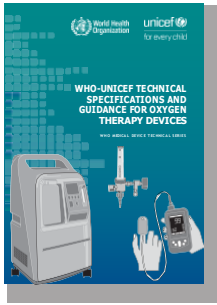
IMAI district clinician manual: hospital care for adolescents and adults. Guidelines for the Management of common illnesses with limited resources (2011) ([📄](#))

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



Technical specifications for oxygen concentrators (2015) ([📄](#))

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



WHO-UNICEF technical specifications and guidance for oxygen therapy devices (2019) ([📄](#))

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



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

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

5

Diagnostic testing for patients with ARI



5 Diagnostic testing for patients with ARI

Summary

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

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

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

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

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

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

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

See WHO *Diagnostic testing for SARS-CoV-2 infection* (). [↗](#)


See WHO *TB guidelines: recent updates* (). [↗](#)

See WHO *Malaria testing* (). [↗](#)

Tools

- 5.1 Diagnostic testing for SARS-CoV-2 infection
- 5.2 Use of antigen-detection rapid diagnostic testing for SARS-CoV-2
- 5.3 Specimen collection kit for upper respiratory tract specimens
 - 5.3.1 Nasopharyngeal swab technique
 - 5.3.2 Posterior pharyngeal swab or throat swab technique
 - 5.3.3 Tracheal aspirate technique
- 5.4 Guideline for specimen storage
- 5.5 Material for specimen transportation
- 5.6 Guideline for specimen transportation
- 5.7 Guide for blood culture collection in patients with SARI


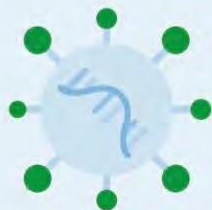

5.1 Diagnostic testing for SARS-CoV-2 infection

 World Health Organization

Diagnostic testing for SARS-CoV-2 infection

Countries need to test for **SARS-CoV-2** according to the national strategy, using available and approved diagnostic tests. WHO recommends testing of all **SARS-CoV-2** suspected cases.

Types of tests:

 <h4>Nucleic acid amplification testing</h4> <p><i>Detects genetic material of the virus</i></p> <p>Uses upper respiratory specimens* to diagnose acute SARS-CoV-2 infection. Nucleic acid amplification testing (NAAT), for example RT-PCR, is the reference method for detection of acute SARS-CoV-2 infection. Results: usually available within 24 hours. Testing takes 30 minutes to 4 hours (depending on the test), but transport to the testing laboratory can add hours to days.</p>	 <h4>Antigen</h4> <p><i>Detection rapid diagnostic testing – detects viral protein(s)</i></p> <p>Uses upper respiratory specimens* to diagnose acute SARS-CoV-2 infection. Performance is best within first 5-7 days of symptoms. Results: within 15-30 minutes, not requiring laboratory infrastructure.</p>	 <h4>Antibody testing</h4> <p><i>Detects antibodies against the virus</i></p> <p>Uses serum/plasma or whole blood specimens to detect antibodies generated by prior SARS-CoV-2 infection or vaccination. SARS-CoV-2 antibodies are usually detectable 1-2 weeks after infection or vaccination. Results: within 24 hours; point of care tests within 10-30 mins.</p>
--	--	--

*Some NAA tests and some Ag-RDTs are designed to work on upper respiratory track samples or saliva
For more information: https://www.youtube.com/watch?v=PhdSdJu_QXI

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

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

World Health Organization

Use of antigen-detection rapid diagnostic testing

WHO recommends that all suspected cases be tested for SARS-CoV-2

Antigen-detection diagnostic testing
Uses upper respiratory specimen or saliva to test for SARS-CoV-2 infection by detecting viral proteins (e.g. nucleoprotein).
Can be used outside of clinical and laboratory settings, including in communities ()*

Antigen-detection rapid diagnostic tests (Ag-RDT), with adequate performance (>80% sensitivity and >97% specificity compared to a NAAT reference assay) are easy to use, can rapidly detect SARS-CoV-2 infection and do not require laboratory infrastructure.

HOW, WHEN, WHERE:
Ag-RDTs are used to detect **acute SARS-CoV-2 infection** and are best used for:

- 1 CASE FINDING**
As a **primary case-detection tool** for testing all suspected cases.
Can be used to detect SARS-CoV-2 in many settings including in health facilities, testing centers, care homes, prisons, schools, communities where there is ongoing transmission.
- 2 CONTACT TRACING**
To identify infection among **asymptomatic contacts of cases** (1)
- 3 OUTBREAK INVESTIGATIONS**
To **confirm suspected outbreaks of COVID-19** among symptomatic individuals, especially in closed or semi-closed settings including schools, care-homes, cruise ships, prisons, work-places and dormitories, etc
- 4 MONITOR TRENDS**
To **monitor trends in disease incidence in communities**, and particularly among frequently exposed workers, including health and care workers, irrespective of symptoms.

*AgRDT testing should be performed by trained individuals. WHO training materials can be found here: <https://extranet.who.int/hslp/content/sars-cov-2-antigen-rapid-diagnostic-test-training-package>

¹ Ag-RDTs can be used to test asymptomatic contacts of confirmed cases, even if the Ag-RDT is not specifically authorized for this use.

For more information see WHO guidance September 2020 <https://www.who.int/publications/i/item/antigen-detection-in-the-diagnosis-of-sars-cov-2-infection-using-rapid-immunoassays>

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

5.3 Specimen collection kit for upper respiratory tract specimens

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

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

Required items

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

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



© WHO/Tim Healing

Technique

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

Swabs

The type of swab used is very important.

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

5.3.1 Nasopharyngeal swab technique

Required materials

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

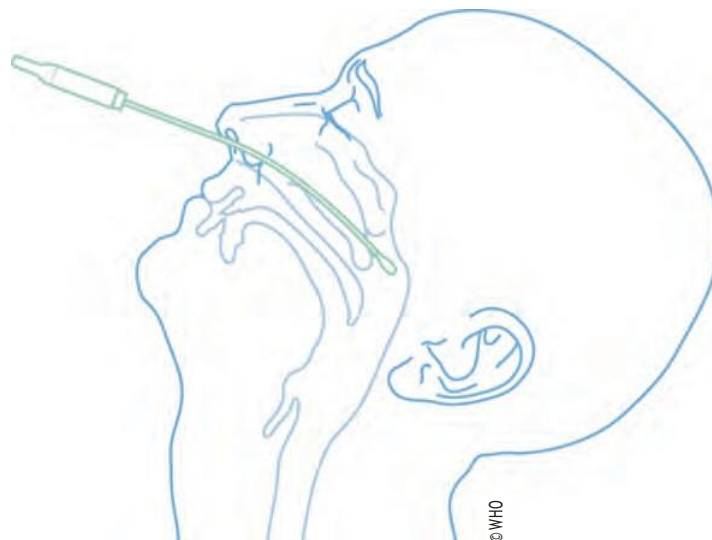
Technique

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



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

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



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

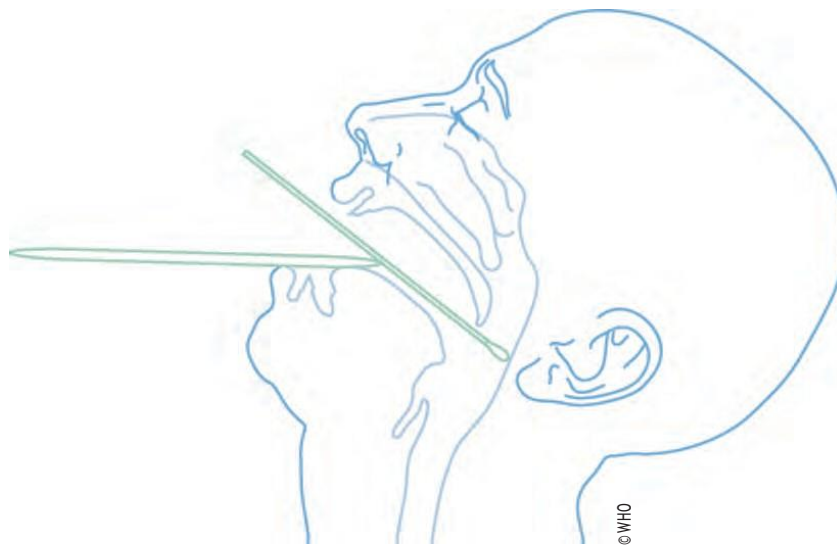
5.3.2 Posterior pharyngeal swab or throat swab technique

Required materials

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

Technique

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



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

5.3.3 Tracheal aspirate technique

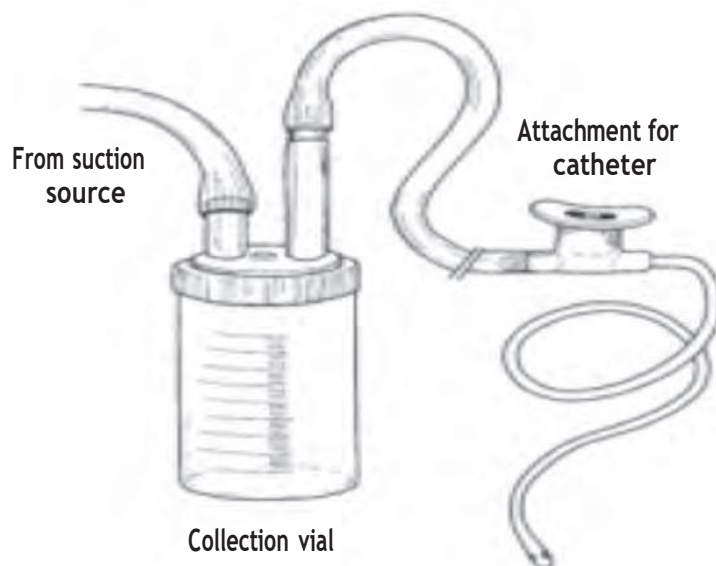
Intended for patients intubated and receiving invasive mechanical ventilation (IMV).

Required materials

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

Technique

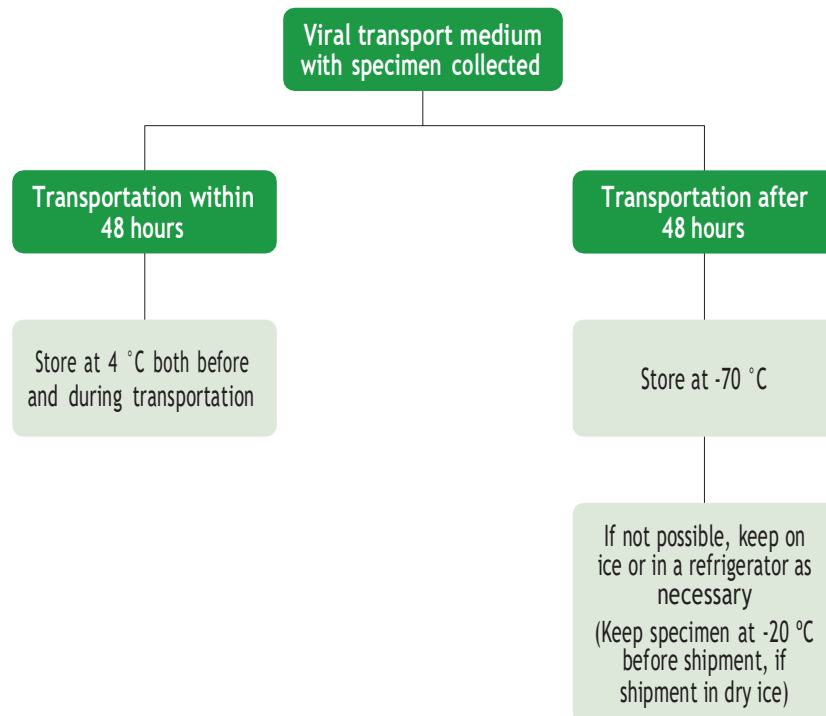
1. Apply standard, contact, droplet and airborne precautions.
2. Prepare patient: pre-oxygenate with 100% fraction of inspired oxygen (FiO₂). Give adequate sedation.
3. Attach mucous trap to catheter and suction outlet. Turn on suction to make sure functioning. Then turn it off.
4. When you are ready, disconnect ventilator tubing from endotracheal tube.
5. Without applying suction, insert sterile suction catheter apparatus into endotracheal tube, about 2-3 cm beyond tip.
6. Apply suction and collect sample into the mucous trap. Hold trap upright to prevent secretions from going into the pump. Slowly withdraw catheter. Replace ventilator tubing.
7. If inadequate sample, instil 3-5 mL of sterile saline, give two insufflations/deep breaths and apply suction.
8. After collection, immediately transport specimen to laboratory for viral testing and bacteriology.
9. Store in refrigerator (2-8 °C) for maximum 24 hours.
10. If delay, store in freezer < -20 °C.



5.4 Guideline for specimen storage

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

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



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

Viral transport medium information

Possible suppliers

Local laboratory and commercial supplier.

Description

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

Stock management

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

Conservation

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

5.5 Material for specimen transportation

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

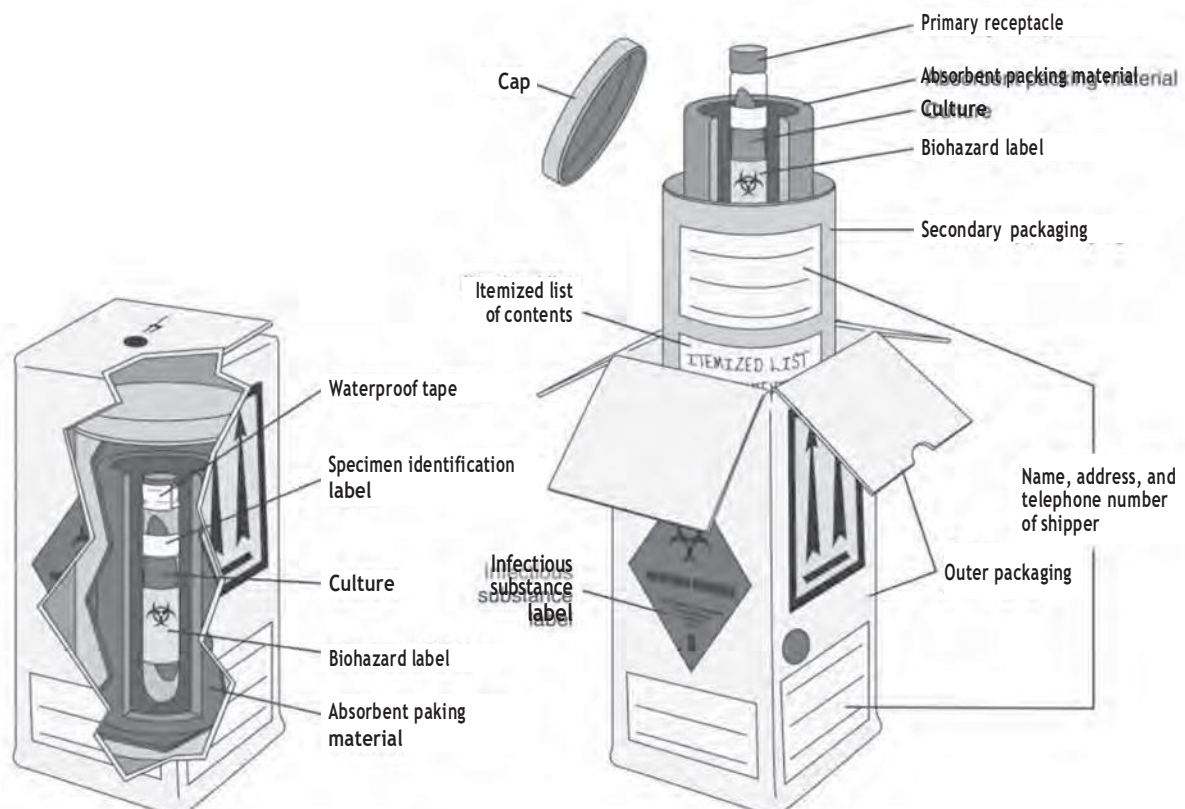
Required materials

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



Packing and labelling of infectious substances not refrigerated

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



For more details review:

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

5.6 Guideline for specimen transportation



1 Envelop the cryo-tube with blotting paper.



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



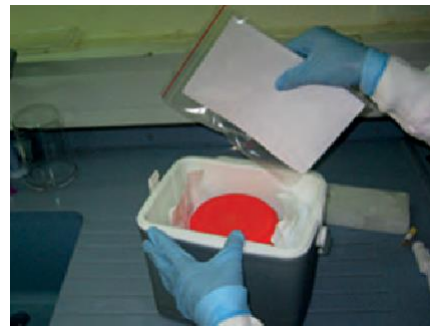
▫ Place the primary waterproof container in bubble wrap or a shock-absorbing material.



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



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



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

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



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

5.7 Guide for blood culture collection in patients with SARI

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

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

Required materials

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

Technique

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

Contaminated blood culture

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

This may lead to misdiagnosis and prolonged antimicrobial use.

References and resources

- ANZIC Influenza Investigators, Webb SA, Pettilä V, Seppelt I, Belloma R, Bailey M et al. Critical care services and 2009 H1N1 influenza in Australia and New Zealand. *N Engl J Med*. 2009;361(20):1925-1934.
- Chanez P, Holz O, Ind PW, Djukanovic R, Maestrelli P, Sterk PJ. Sputum induction. Report of Working Group 1. *Eur Res J*. 2002;20(suppl 37):3s-8s.
- Domínguez-Cherit G, Lapinsky SE, Macias AE, Pinto R, Espinosa-Perez L, de la Torre A et al. Critically ill patients with 2009 influenza A(H1N1) in Mexico. *JAMA*. 2009;302(17):1880-1887.
- Gill J, Sheng ZM, Ely SF, Guinee DG, Beasley MB, Suh J et al. Pulmonary pathologic findings of fatal 2009 pandemic influenza A(H1N1) viral infections. *Arch Pathol Lab Med*. 2010;134(2):235-243.
- Heymann DL (editor). *Control of communicable diseases manual* (20th edition). Washington (DC): APHA Press; 2014.
- Kumar A, Zarychanski R, Pinto R, Cook DJ, Marshall J, Lacroix J et al. Critically ill patients with 2009 influenza A(H1N1) in Canada. *JAMA*. 2009;302(17):1872-1879.
- Lister P. Swine-origin influenza virus H1N1, seasonal influenza virus, and critical illness in children. *Lancet*. 2009;374:605-07.
- Novel Swine-Origin Influenza A (H1N1) Virus Investigation Team. Emergence of a novel swine-origin influenza A(H1N1) virus in humans. *N Engl J Med*. 2009;360:2605-2615.
- WHO. Clinical management of human infection with pandemic (H1N1) 2009: revised guidance. Geneva: World Health Organization; 2009.
- WHO. Clinical management of severe acute respiratory infection when Middle East respiratory syndrome coronavirus (MERS-CoV) infection is suspected: interim guidance. Geneva: World Health Organization; 2019 (https://www.who.int/csr/disease/coronavirus_infections/case-management-ipc/en/, accessed 4 June 2021).
- WHO. Diagnostic testing for SARS-CoV-2: interim guidance. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/i/item/diagnostic-testing-for-sars-cov-2>, accessed 15 June 2021).
- WHO. Fact sheets for avian influenza, seasonal influenza and Middle East respiratory syndrome coronavirus (MERS-CoV) are updated regularly and available on the following WHO websites: [https://www.who.int/news-room/fact-sheets/detail/influenza-\(avian-and-other-zoonotic\)](https://www.who.int/news-room/fact-sheets/detail/influenza-(avian-and-other-zoonotic)); <http://www.who.int/mediacentre/factsheets/fs211/en/>; <http://www.who.int/mediacentre/factsheets/mers-cov/en/>, accessed 5 July 2021).
- WHO. Guidance on regulations for the transport of infectious substances 2019-2020. Geneva: World Health Organization; 2019 (<https://www.who.int/ihr/publications/WHO-WHE-CPI-2019.20/en/>, accessed 4 June 2021).
- WHO. Influenza (Avian and other zoonotic). Geneva: World Health Organization; 2018 ([https://www.who.int/en/news-room/fact-sheets/detail/influenza-\(avian-and-other-zoonotic\)](https://www.who.int/en/news-room/fact-sheets/detail/influenza-(avian-and-other-zoonotic)), accessed 29 April 2021).
- WHO. Information for laboratory diagnosis of pandemic (H1N1) 2009 virus in humans - revised. Geneva: World Health Organization; 2009 (https://www.who.int/csr/resources/publications/swineflu/diagnostic_recommendations/en/, accessed 4 June 2021).
- WHO. Instructions for storage and transport of suspected or confirmed human and animal specimens and virus isolates of pandemic (H1N1). Geneva: World Health Organization; 2009 (https://www.who.int/influenza/gisrs_laboratory/logistic_activities/transport_storage_specimens_isolates/en/, accessed 4 June 2021).
- WHO. Laboratory biosafety guidance related to coronavirus disease (COVID-19): interim guidance. Geneva: World Health Organization; 2020 ([https://www.who.int/publications/i/item/laboratory-biosafety-guidance-related-to-coronavirus-disease-\(covid-19\)](https://www.who.int/publications/i/item/laboratory-biosafety-guidance-related-to-coronavirus-disease-(covid-19)), accessed 4 June 2021).
- WHO. Laboratory testing strategy recommendations for COVID-19: interim guidance. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/i/item/laboratory-testing-strategy-recommendations-for-covid-19-interim-guidance>, accessed 15 June 2021).
- WHO. Recommendations on the use of rapid testing for influenza diagnosis. Geneva: World Health Organization; 2005.
- WHO. Regional Office for Europe guidance for sentinel influenza surveillance in humans. Copenhagen: WHO Regional Office for Europe; 2011 (<https://apps.who.int/iris/handle/10665/107265>, accessed 4 June 2021).
- WHO. Safe transport of pandemic influenza A (H1N1) 2009 virus cultures, isolates and patient specimens as Biological Substance, Category B. Geneva: World Health Organization; March 2010.
- WHO. SARS-CoV-2 antigen rapid diagnostic test training package. Geneva: World Health Organization: WHO Health Security Learning Platform; 2021 (<https://extranet.who.int/hslp/content/sars-cov-2-antigen-rapid-diagnostic-test-training-package>, accessed 4 June 2021).
- WHO. Transmission dynamics and impact of pandemic influenza A (H1N1) 2009 virus. *WER*. 2009;84(46):477-484.

6

Oxygen therapy

6 Oxygen therapy

Summary

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

Oxygen delivery (DO_2) = cardiac output (CO) × oxygen content in arterial blood (CaO_2)

- $CaO_2 = 1.34 \times (Hb) \times SpO_2 + (0.003 \times PaO_2)$
- $CO = SV \times HR$

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

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

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

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

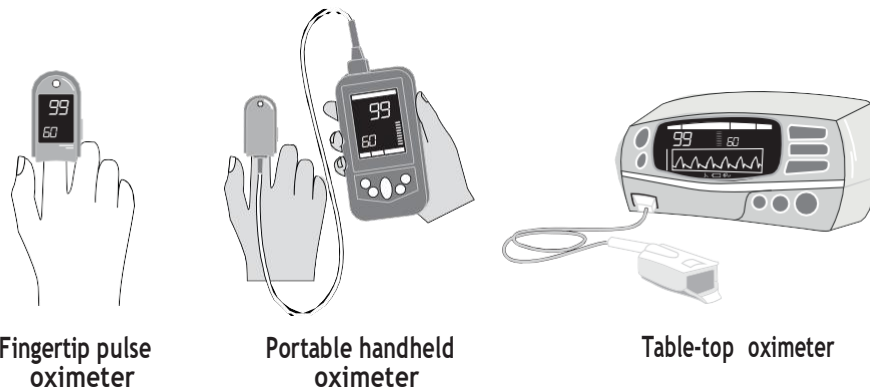
3. Oxygen saturation (% SpO_2) and oxygen partial pressure (PaO_2) are the measured oxygen levels in blood, the former measured by pulse oximeter and the latter by blood gas analyser.



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

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

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



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

Oxygen delivery devices should be selected based on the oxygen needs of the patient and include nasal cannulas, conventional face masks, Venturi face masks and face masks with reservoir bag. If patients require higher levels of oxygen flow (> 10-15 L/min) to reach SpO₂ targets, and/or have other signs of acute respiratory failure, other respiratory support options, that can deliver higher flows and/or positive pressure support should be considered. These include:

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

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

Rational oxygen use delivers the least amount of oxygen necessary to achieve SpO₂ goals. Although avoiding hypoxaemia is the primary goal of oxygen therapy, it is important to remember that giving a patient more oxygen than they need to meet the SpO₂ goal can be harmful and more rapidly deplete oxygen supplies. Therefore, titration up and down of oxygen therapy and trials of oxygen weaning should be performed on a regular basis (see how to titrate oxygen with different devices: Tools 6.5-6.7). Oxygen sources should routinely be checked for quality, including oxygen concentration and flow or pressure output.

Tools

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

6.1 Indications for oxygen therapy

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

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

- **SpO₂ < 90%** (if patient is haemodynamically stable)
- **SpO₂ < 94%** (if patient with any **emergency signs, with or without respiratory distress**)
- **SpO₂ < 92–95%** (if pregnant)

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

Supplemental oxygen therapy should be provided immediately to achieve the following SpO₂ targets:

SpO₂ targets

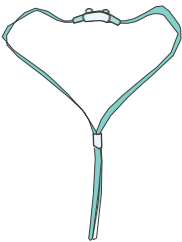
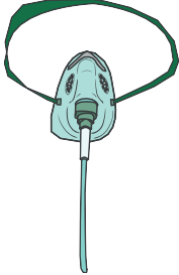
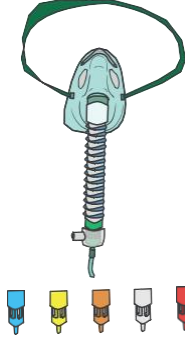
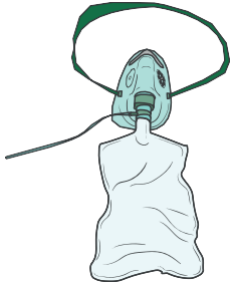
SpO₂ ≥ 90% in adults and children


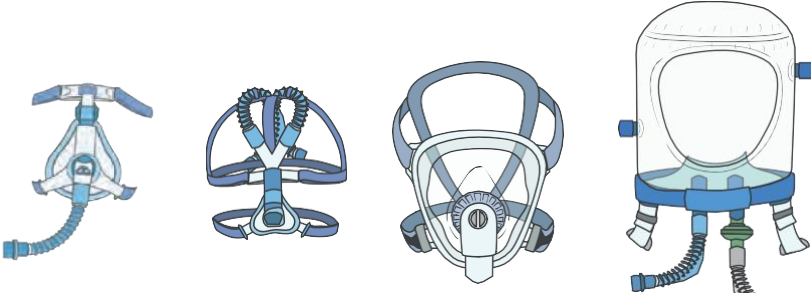
SpO₂ ≥ 92-95% in pregnant patients

SpO₂ ≥ 94% if child or adult with signs of multi-organ failure, including shock, alteration of mental status, severe anaemia, and/or during resuscitation. Once stabilized, resume target SpO₂ ≥ 90%.



6.2 Memory aid: oxygen delivery devices

Non-invasive O ₂ delivery devices			
<p>Nasal cannula</p> 	<p>Face mask</p> 	<p>Venturi face mask</p> 	<p>Face mask reservoir bag</p> 
O ₂ flow 1–5 L/min ^a	O ₂ flow 5–10 L/min	O ₂ flow 2–15 L/min	O ₂ flow 10–15 L/min
FiO ₂ 0.23–0.35 ^b	FiO ₂ 0.30–0.50 ^b	FiO ₂ 0.24–0.6 ^b	FiO ₂ 0.5–0.95 ^b


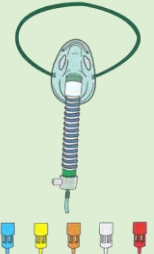

Advanced non-invasive O ₂ delivery devices				
<p>High-flow nasal oxygen</p> 	<p>BiPAP/CPAP</p> 			
	<p>Oronasal</p>	<p>Nasal</p>	<p>Full face</p>	<p>Helmet</p>
O ₂ flow 10–60 L/min ^a	O ₂ flow ~10–80 L/min ^c			
FiO ₂ 0.23–1.0 ^b	FiO ₂ 0.21–1.0 ^b			

^a O₂ flow ranges differ for neonates, children and adults; see Tool 6.2 for ranges by age.

^b Delivered O₂ concentration depends on multiple factors including the concentration of the oxygen source and the patient's respiratory pattern (e.g. peak inspiratory flow and minute ventilation).

^c O₂ consumption for BiPAP/CPAP is widely variable depending on device used and the leak of the system.

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

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

Disclaimer: This table is intended to provide information from the technical point of view about oxygen delivery devices, including flow rate ranges, achievable FiO₂, and possible oxygen sources that can be used with each device. Clinical decisions should determine the methods of administration of oxygen therapy and device selection.

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



6.3 Memory aid: oxygen delivery in children

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

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



Practical considerations

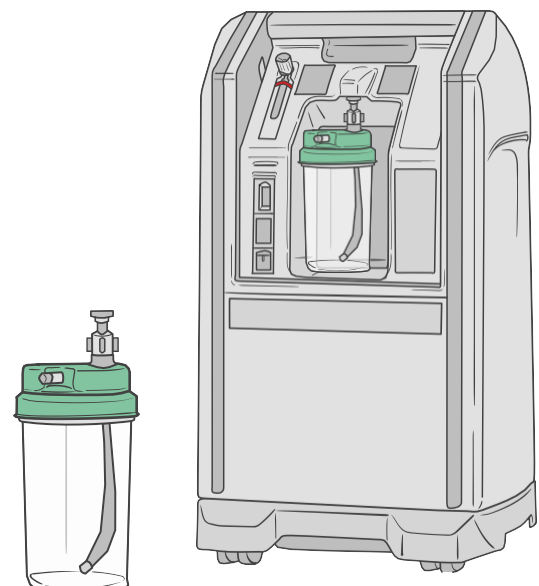
- **Fitting:** The distal prong should fit well into the nostril (premature infants: 1 mm; infants weighing up to 10 kg: 2 mm). The prongs should be secured with a piece of tape on the cheeks near the nose as shown. Care should be taken to keep the nostrils clear of mucus to avoid blockage.

- **Humidification:**

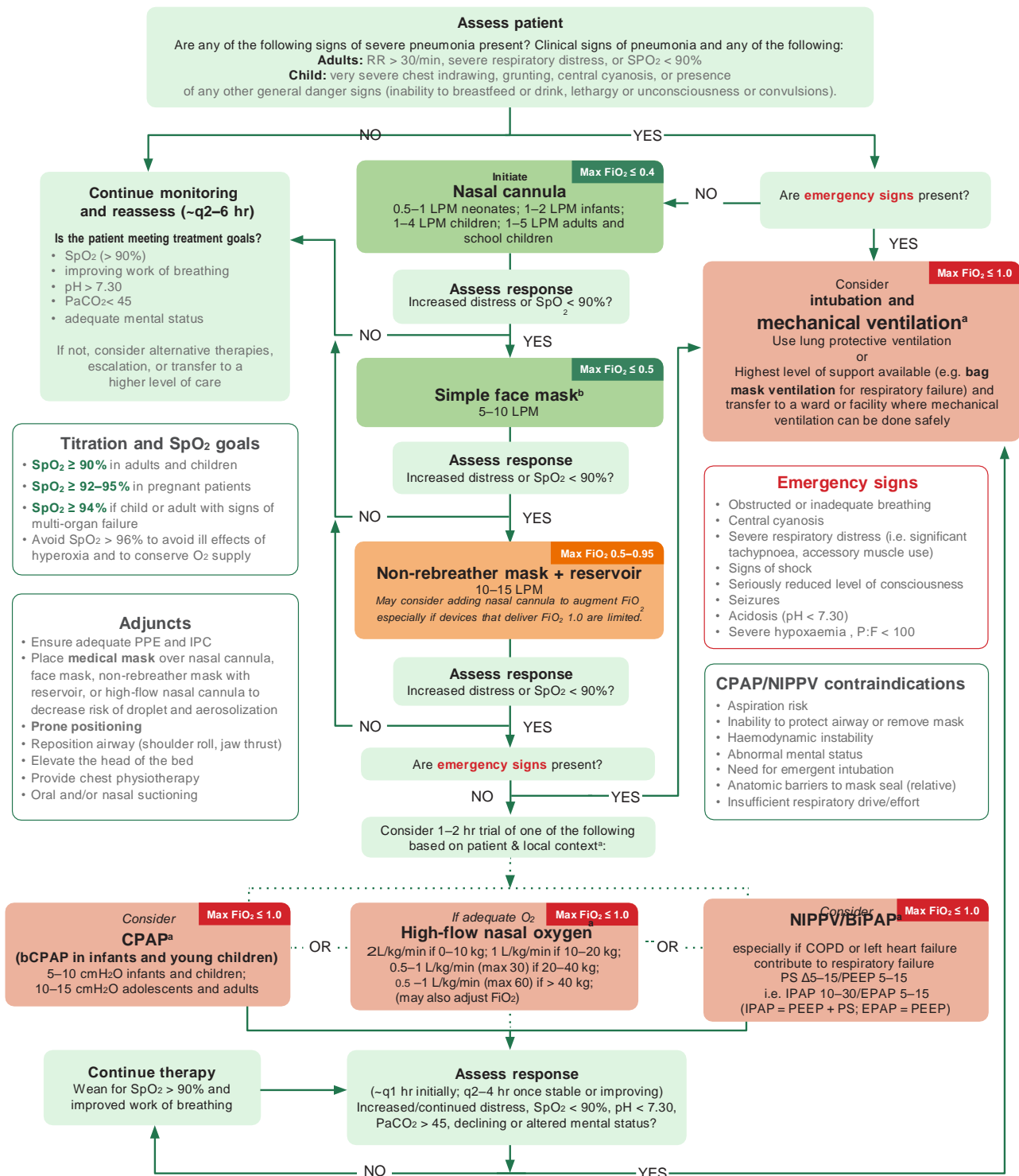
When oxygen is delivered at standard flow rate (0.5-1 L/min for a neonate, 1-2 L/min for an infant, 1-4 L/min for an older child) through nasal prongs, humidification is not necessary.

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

- Humidification is essential when cold oxygen is delivered from a cylinder, compared with concentrators (mainly in tropical countries), as normally concentrators provide oxygen at room temperature.
- Bubble humidifiers reduce the dryness of the oxygen supplied by bubbling the gas through water at room temperature. They must be filled with clean water at least once a day (distilled water or tap water that has been boiled and cooled). The water level in the humidifier should be checked twice daily and topped up as necessary. The humidifier equipment must be washed and disinfected regularly to prevent bacterial colonization.



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

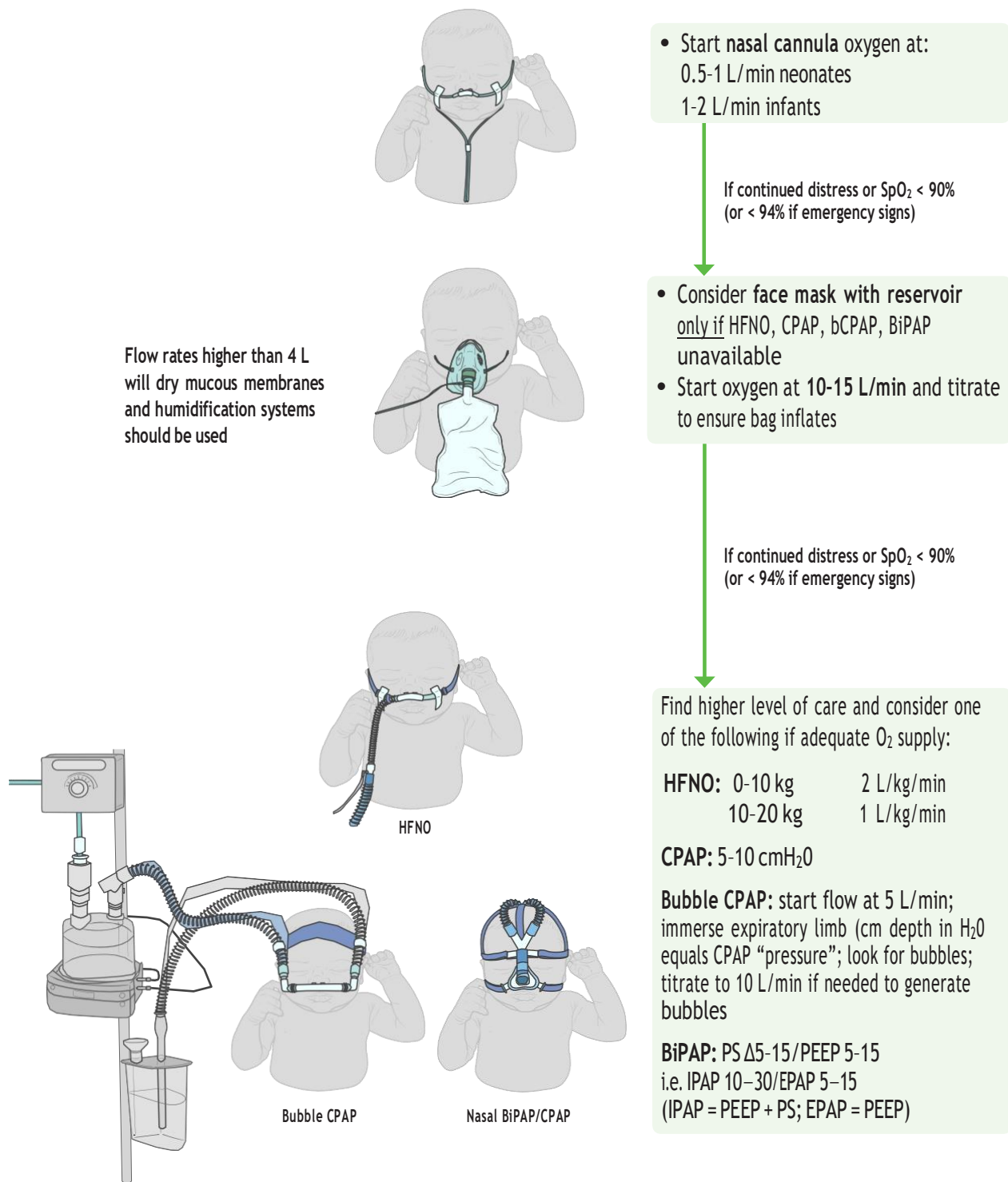


^a Selection of optimal delivery device should be based on local clinician's judgment and risk-benefit assessment tailored to the individual patient, global and local outcomes data, as well as local resources including O₂ supply, skill of personnel, availability of consumables, monitoring and therapeutic adjuncts, among other factors.
^b Venturi/entrainment face masks deliver FiO₂ 24–60%, depending on flow rate and device setup

LPM (litres per minute), EPAP (expiratory positive airway pressure), PS (pressure support), COPD (chronic obstructive pulmonary disease), SpO₂ (oxygen saturation), PaCO₂ (arterial partial pressure of carbon dioxide), P:F (ratio between arterial partial pressure of oxygen and the fraction of inspired oxygen – FiO₂), CPAP (continuous positive airway pressure), bCPAP (bubble CPAP), NIPPV (non-invasive positive pressure ventilation), BiPAP (bi-level positive airway pressure); Δ – change.

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

6.5 Flowchart on how to titrate oxygen in neonates

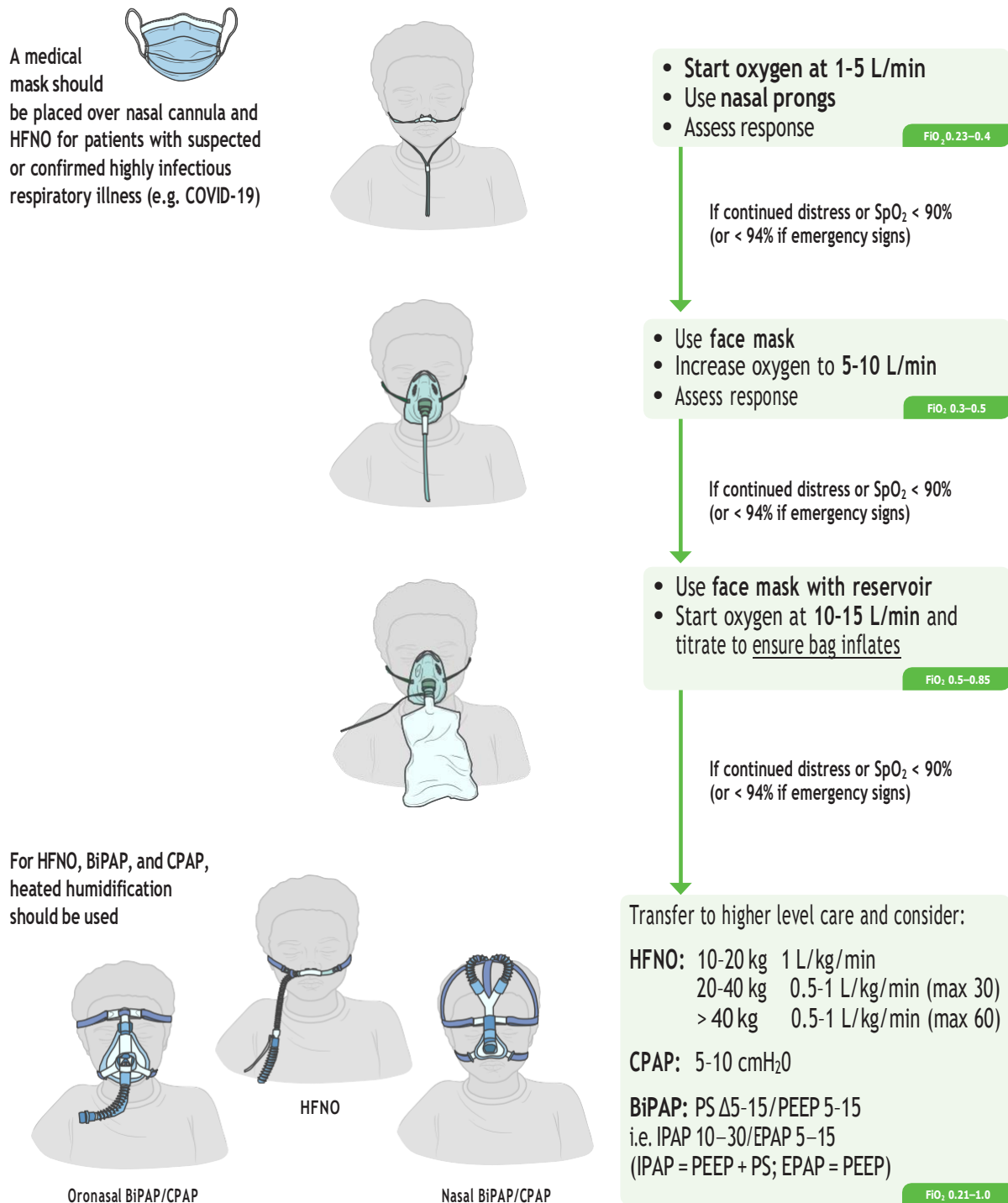


If continued respiratory distress or $SpO_2 < 90\%$ on 15 L/min, consider intubation and invasive mechanical ventilation (clinical management decisions should be made based on individual patient characteristics, local resources and expertise).

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

Source: USAID-STAR-UCSF OpenCriticalCare.org Project (illustrations Holly Sullivan) (1)

6.6 Flowchart on how to titrate oxygen in children

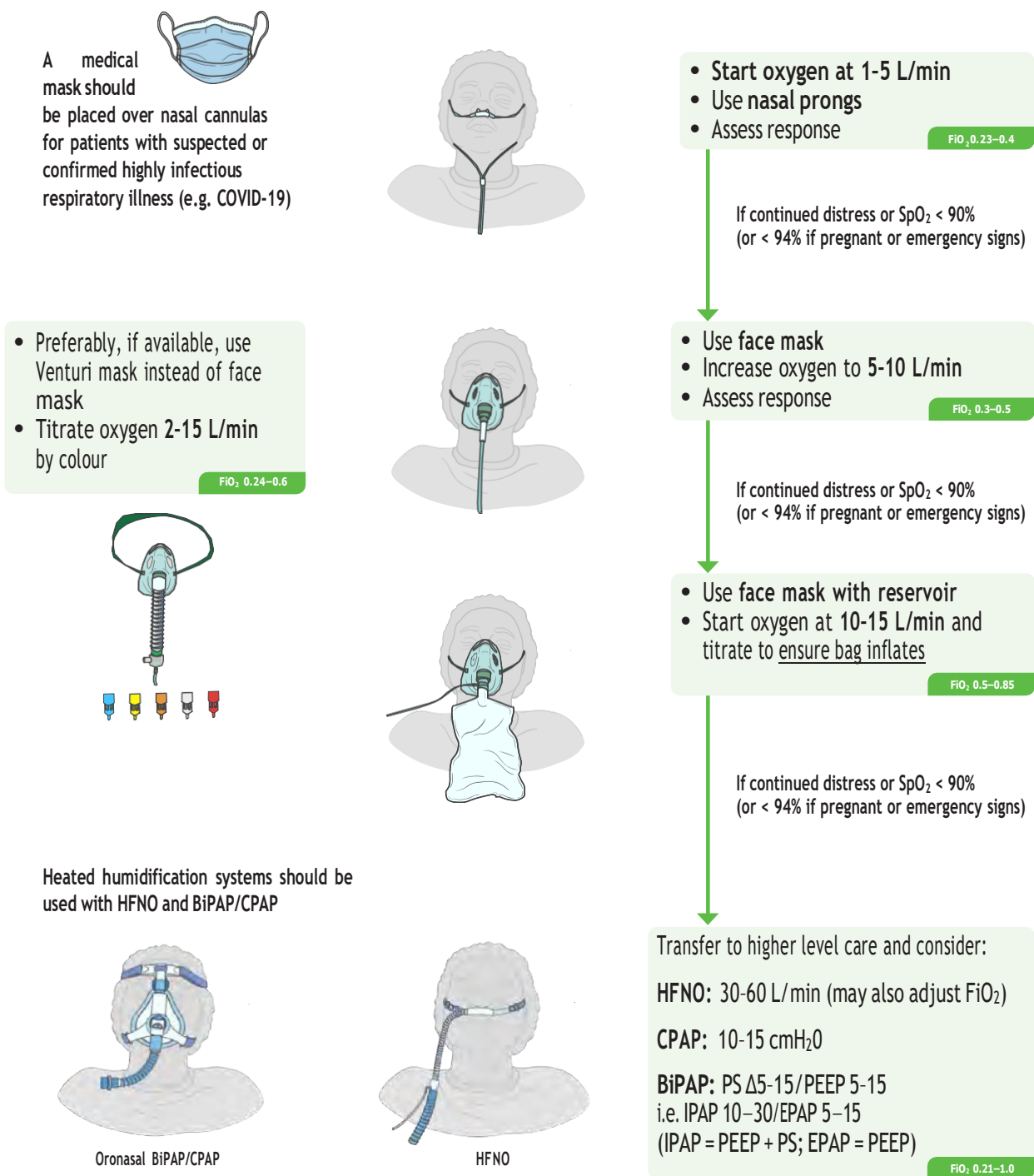


If continued respiratory distress or SpO₂ < 90% on 15 L/min, consider intubation and invasive mechanical ventilation (clinical management decisions should be made based on individual patient characteristics, local resources and expertise).

Wean O₂ flow and avoid SpO₂ 100% to avoid ill effects of hyperoxia and excess O₂ consumption.

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

6.7 Flowchart on how to titrate oxygen in adults



If continued respiratory distress or SpO₂ < 90% on 15 L/min, consider intubation and invasive mechanical ventilation (clinical management decisions should be made based on individual patient characteristics, local resources and expertise).

Wean O₂ flow and avoid SpO₂ 100% to avoid ill effects of hyperoxia and excess O₂ consumption.

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

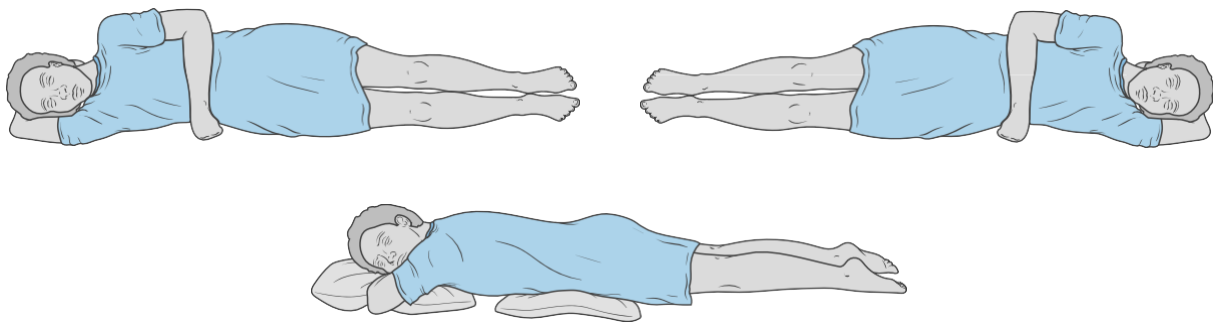
6.8 Key tips on awake prone positioning

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

The WHO COVID-19 Clinical Guideline Development Group conditionally recommends:

Awake prone positioning of patients severely ill and hospitalized with COVID-19 requiring supplemental oxygen (including high-flow nasal cannula) or non-invasive ventilation.

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



Source: USAID-STAR-UCSF OpenCriticalCare.org Project (illustrations Holly Sullivan) ([🇺🇸](#)).

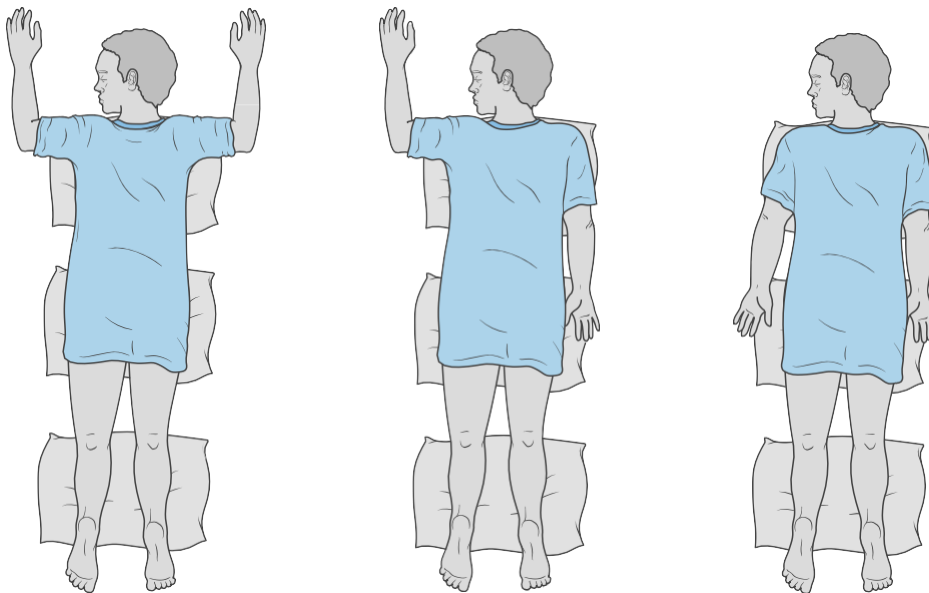
Indications and contraindications for awake prone positioning

Characteristics of patients appropriate for prone position

- Awake and alert.
- Capable of communicating and moving independently.
- Patient must be able get help if they have discomfort or pain.
- Patient must be able to supinate independently, if needed.
- Haemodynamically stable.
- Able to protect their airway.
- Able to be closely monitored by workers with experience with prone positioning.

Contraindications to prone positioning

- Need for immediate intubation.
- Haemodynamically unstable (tachycardia, hypotension).
- Spinal instability.
- Altered mental status or reduced ability to protect the airway.
- Unable to readily call for help if needed.
- Caution if nausea or vomiting.
- Not enough human resources in the unit to monitor.



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

Proning positioning tips

Characteristics of patients appropriate for prone position

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

Rotation and timed position changes

- Regimens vary, and target being in awake prone position 8-12 hours/day, broken into shorter periods over the day.
For example, some institutional protocols describe rotational protocols, with patients changing position on a regular schedule (e.g. every 1 hour changing position, with positions rotating from prone, to lying on right side, to sitting straight upright, to lying on left side, to prone again, etc.).

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

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

6.9 Checklist to troubleshoot warning signs during oxygen therapy delivery

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

Checklist to troubleshoot warning signs during oxygen therapy delivery

Equipment

Is the measurement correct?

Repeat measurement:

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

Is there technical difficulty in delivering treatments?

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

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

Checklist to troubleshoot warning signs during oxygen therapy delivery

Patient and treatments

Is there an alternate or additional diagnosis?

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

Is the patient getting appropriate therapy for the correct diagnosis?

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

Is our treatment causing harm?

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

If the patient's mental status deteriorates despite SpO₂ > 90%, consider the following:

- Manage airway, assist ventilation if needed - do not wait for arterial blood gas results if the patient requires assisted ventilation on clinical grounds.
- Check arterial blood gas, if available, to evaluate ventilation. CO₂ retention causing acute respiratory acidosis will not be detected with SpO₂ alone.
- Consider alternate causes of altered mental status and treat appropriately (e.g. acute central nervous system [CNS] event, electrolyte abnormalities, low glucose).

6.10 Oxygen supply calculations

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

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

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

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

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




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

Useful links:

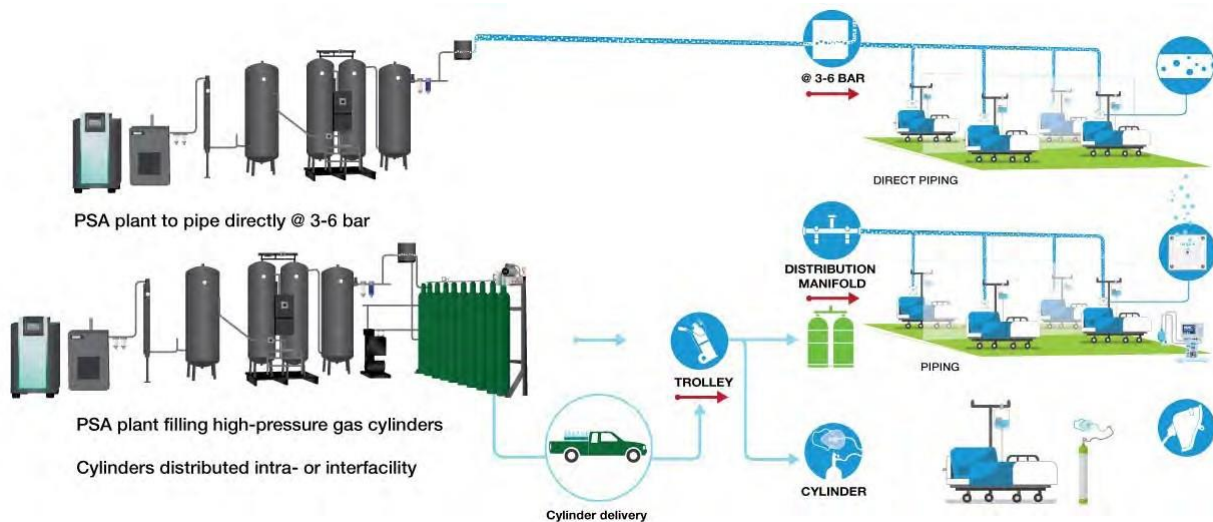
- [USAID Open Critical Care.org Project oxygen supply and demand calculator](#) (🔗)
- [UNICEF: Oxygen system planning tool](#) (🔗)
- [PATH: Oxygen delivery toolkit](#) (🔗)

6.11 Memory aids: oxygen supply sources and distribution

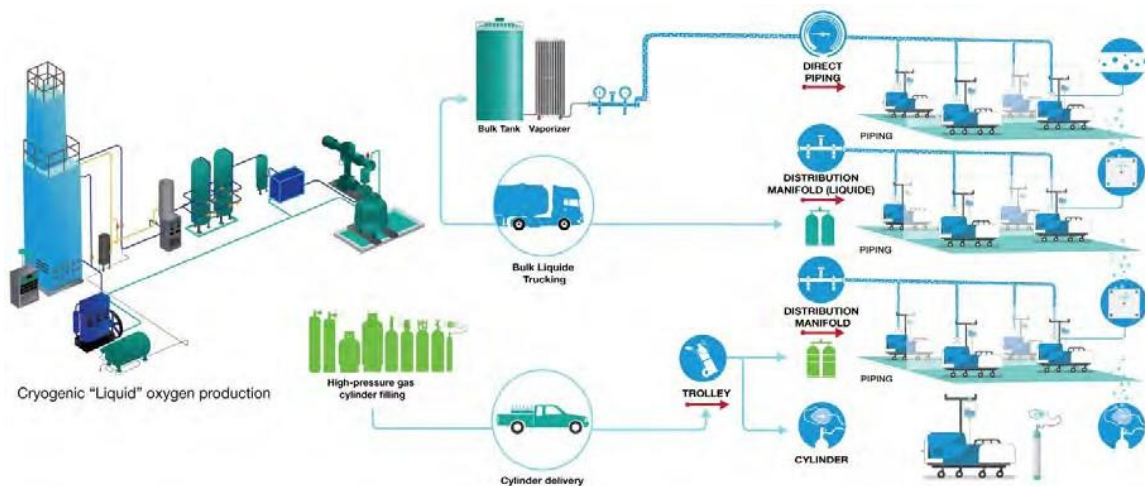
Overview of oxygen supply sources

	PSA bedside concentrators	PSA or VSA O ₂ generator plants	Cryogenic liquid
Description	 <p>Different flow rates, typical: 5, 8 or 10 L/min- medical use</p>	 <p>Different sizes and configurations: single and duplex 2-200+ Nm³/hr</p>	 <p>Produced mainly for heavy industry; serves medical sector where GMP allows</p>
Requirements	<ul style="list-style-type: none"> Situated onsite, bedside. Continuous and reliable electrical source. Device-specific spares needed. Timely technical maintenance (preventive every 6 months). Need for IPC measures as is situated bedside. 	<ul style="list-style-type: none"> Various own/operate models. Often situated onsite. Continuous and reliable electrical source during plant and booster operations. Detailed technical and financial planning for long-term operations and maintenance (~20 years). 	<ul style="list-style-type: none"> Third party responsible for production and supply chain. Plants must be offsite. Bulk liquid tanks with passive vaporization for onsite storage (specialized materials). Capital expenditure (CAPEX) and operating expenses (OPEX) are very high; borne by third party.
Additional considerations	<ul style="list-style-type: none"> Difficult to optimize for at-scale needs. Not suitable for high-flow or higher-pressure needs (e.g. patient ventilators). Depending on the capacity and oxygen therapy, flow could be split among patients. 	<ul style="list-style-type: none"> Need > 4 technicians for 24/7 operation. Continuous supply at all atmospheric pressures. Supply can be piped bedside and/or plant can fill cylinders to be used bedside or transported elsewhere. 	<ul style="list-style-type: none"> Goods and service contract. Product can be used via high-pressure gas cylinders or piped bedside from bulk tank.

Primary system: PSA plan



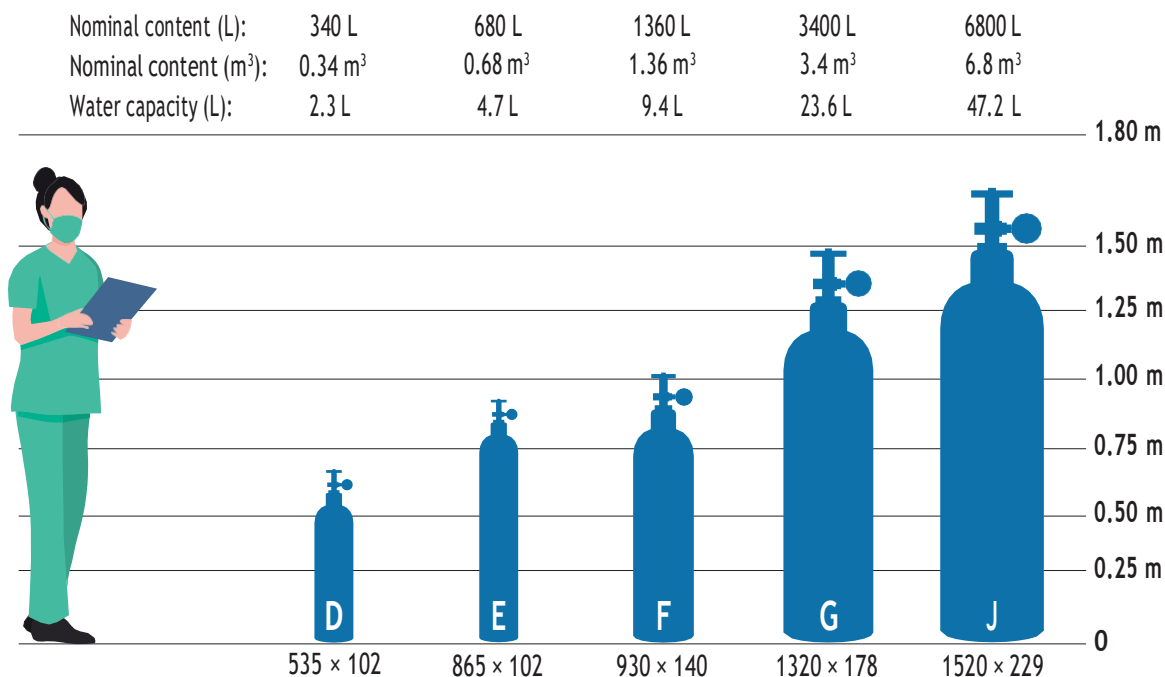
Primary system: cryogenic liquid oxygen



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

Cylinders

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



Note: dimensions: height × diameter mm

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

Cylinder size

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

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

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

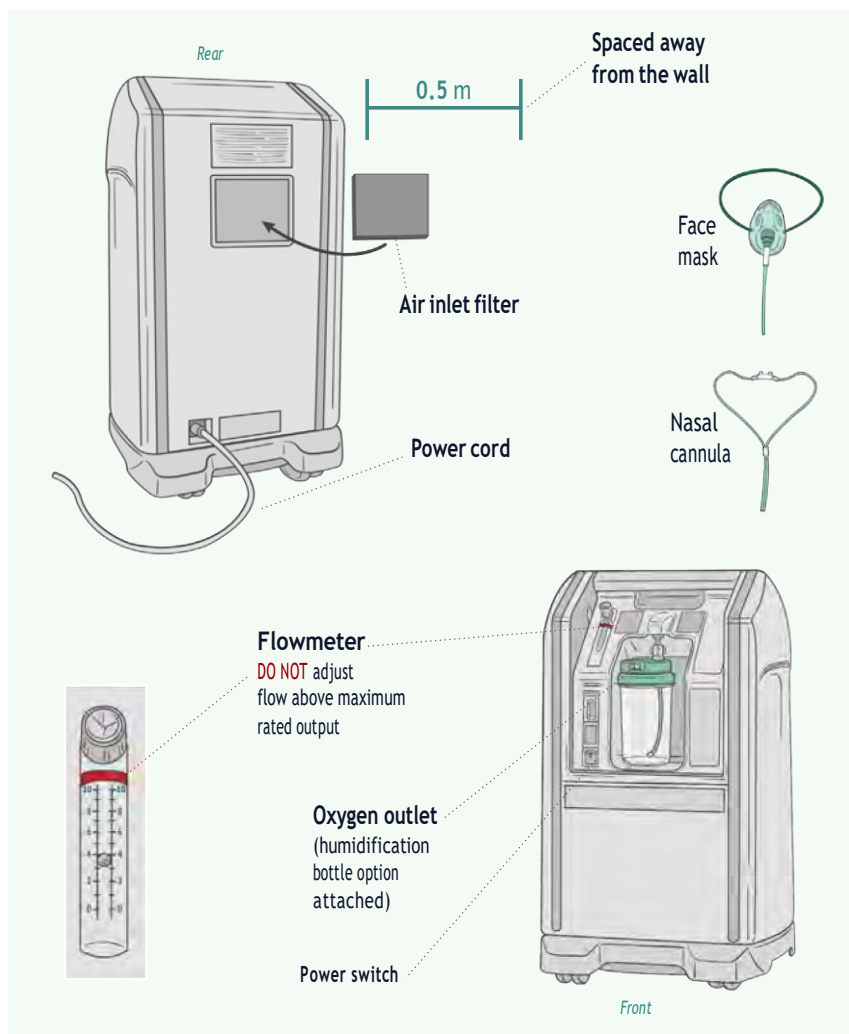
Duration of cylinders

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

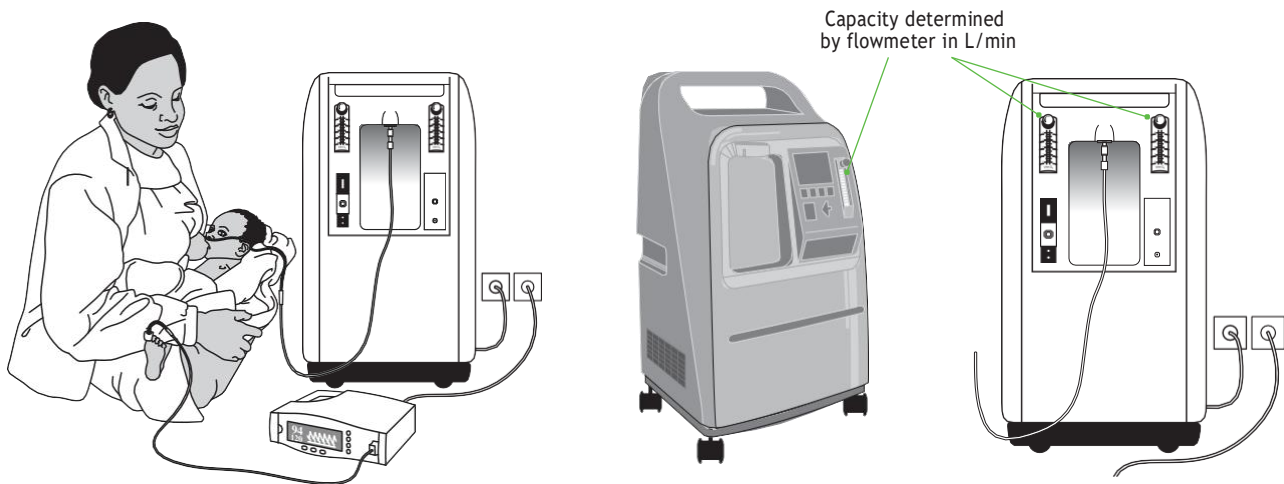
Top row: duration of cylinder

Bottom row: number of cylinders required/24 hr

Concentrators



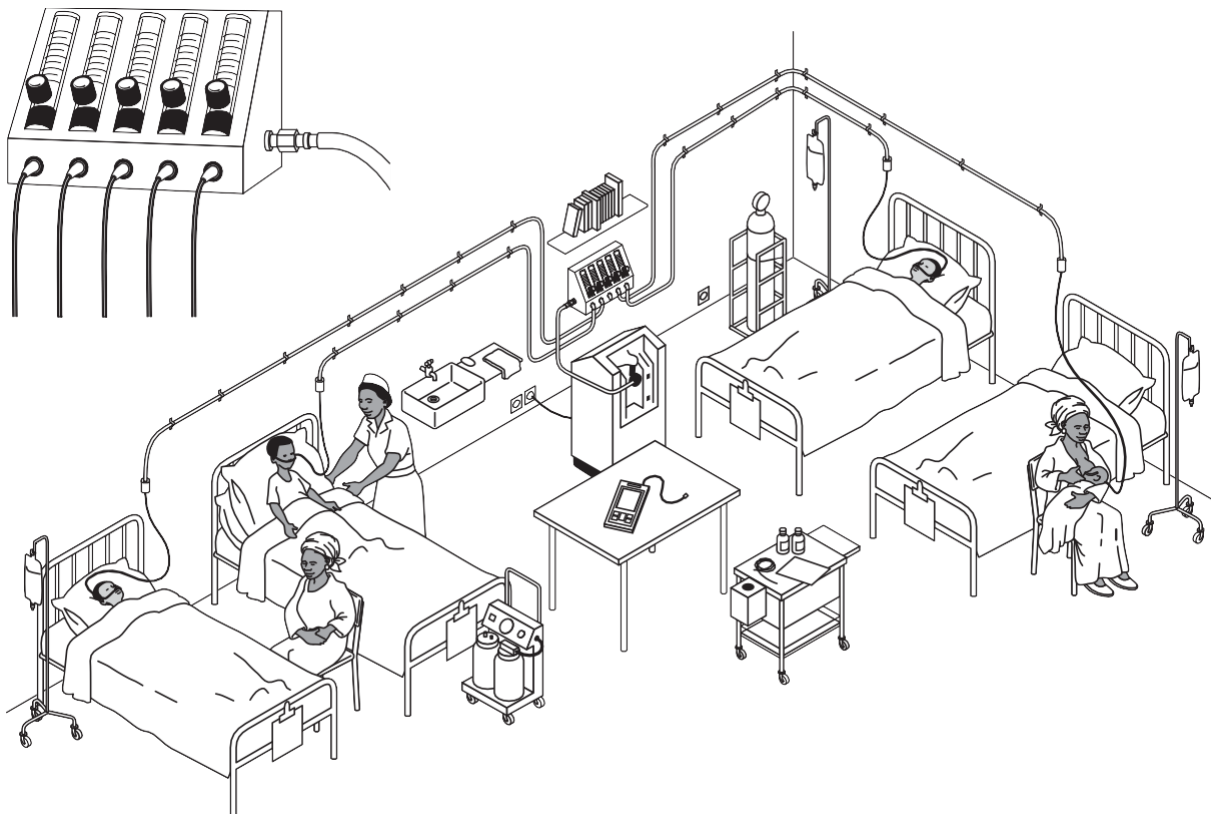
Source: USAID-STAR-UCSF OpenCriticalCare.org Project. (i)



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

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

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



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

6.12 Respiratory care order template for oxygen therapy

Last updated 27 May 2021

Hospital name/Logo		Oxygen therapy order set v1.2																
Surname/Family name		Name		Attending/Team														
Date / /	ID number	Age	Sex	Weight (kg)	Height (cm)													
CHOOSE A DELIVERY DEVICE																		
<input type="checkbox"/>	Nasal cannula	<input type="checkbox"/> Titrate flow rate _____ litres per minute (0.5–1 LPM neonates; 1–2 LPM infants; 1–4 LPM children; 1–5 LPM adults) to maintain oxygen saturation (SpO ₂) by pulse oximeter to goal > _____ (consider 90–94% for most patients)* or <input type="checkbox"/> Set flow rate at: _____ litres per minute (typical range 0.5–5 LPM) <input type="checkbox"/> Attach room temperature bubble humidifier and change sterile/distilled H ₂ O: [per protocol every] or [q _____ hours] (consider if > 4 LPM, especially in paediatrics, though evidence of benefit is lacking)																
<input type="checkbox"/>	Simple face mask	<input type="checkbox"/> Titrate flow rate from 5–10 litres per minute to maintain oxygen saturation (SpO ₂) by pulse oximeter to goal > _____ (consider 90–94% for most patients)* or <input type="checkbox"/> Set flow rate at: _____ litres per minute (typical range 5–10 LPM) <input type="checkbox"/> Attach room temperature bubble humidifier and change sterile/distilled H ₂ O: [per protocol every] or [q _____ hours] (consider especially in paediatrics, though evidence of benefit is lacking)																
<input type="checkbox"/>	Face mask with reservoir bag	<input type="checkbox"/> Titrate flow rate from 10–15 litres per minute to maintain oxygen saturation (SpO ₂) by pulse oximeter to goal > _____ (consider SpO ₂ goal 90–94% for most patients) or <input type="checkbox"/> Set flow rate at: _____ litres per minute (typical range 10–15 LPM) Attach room temperature bubble humidifier and change sterile/distilled H ₂ O: [per protocol every] or [q _____ hours]																
<input type="checkbox"/>	Venturi mask	<input type="checkbox"/> Select Venturi device adapter (or setting) (FiO ₂ 24–60%) to maintain oxygen saturation (SpO ₂) by pulse oximeter to goal > _____ (consider 90–94% for most patients) or <input type="checkbox"/> Set flow rate at _____ litres per minute for FiO ₂ adapter: _____ (O ₂ input flow rate determined by specific adapter used. Always refer to manufacturer's insert) 24% 2–4 LPM; 28% 4–5 LPM; 35% 8–10 LPM; 40% 10–12 LPM; 60% 12–15 LPM (colour may vary by manufacturer) Note: Do not use humidifiers with Venturi masks as moisture may affect accuracy of FiO ₂																
<input type="checkbox"/>	High-flow nasal cannula (HFNO)	<input type="checkbox"/> Set flow rate: _____ litres per minute and titrate FiO ₂ (typical range 0.40–1.0) to maintain oxygen saturation (SpO ₂) goal > _____ (consider SpO ₂ goal 90–94% for most patients) If patient trajectory is improving and tolerating < _____ LPM flow (typical < 20 LPM for adults or < 4 LPM for children) and < _____ FiO ₂ (typical 0.40), then consider trial on standard nasal cannula or <input type="checkbox"/> Titrate flow rate with 1.0 FiO ₂ oxygen to maintain oxygen saturation (SpO ₂) by pulse oximeter to goal > _____ (consider SpO ₂ goal 90–94% for most patients) <div style="text-align: center; margin-top: 10px;"> <table border="0"> <tr> <td>Typical flow rates by patient weight:</td> <td>0–10 kg</td> <td>= 2 L/kg/min</td> </tr> <tr> <td>as tolerated by patient; can titrate for work of breathing up to max. above</td> <td>10–20 kg</td> <td>= 1 L/kg/min</td> </tr> <tr> <td></td> <td>20–40 kg</td> <td>= 0.5–1 L/kg/min (max. 30 LPM)</td> </tr> <tr> <td></td> <td>> 40 kg</td> <td>= 0.5–1 L/kg/min if > 40 kg (max. 60 LPM)</td> </tr> </table> </div> (Mandatory) Attach active heat and humidification system and change with sterile/distilled water. [Change every _____ hours]					Typical flow rates by patient weight:	0–10 kg	= 2 L/kg/min	as tolerated by patient; can titrate for work of breathing up to max. above	10–20 kg	= 1 L/kg/min		20–40 kg	= 0.5–1 L/kg/min (max. 30 LPM)		> 40 kg	= 0.5–1 L/kg/min if > 40 kg (max. 60 LPM)
Typical flow rates by patient weight:	0–10 kg	= 2 L/kg/min																
as tolerated by patient; can titrate for work of breathing up to max. above	10–20 kg	= 1 L/kg/min																
	20–40 kg	= 0.5–1 L/kg/min (max. 30 LPM)																
	> 40 kg	= 0.5–1 L/kg/min if > 40 kg (max. 60 LPM)																
Pulse oximetry		In addition to routine monitors, check oxygen saturation (SpO ₂):	<input type="checkbox"/> Continuously	<input type="checkbox"/>	Every _____ [hours] [minutes]													

* SpO₂ goal ≥ 90% in adults and children; SpO₂ goal ≥ 92–95% in pregnant patients; SpO₂ goal ≥ 94% if child or adult with signs of multi-organ failure, including shock, alteration of mental status, severe anaemia and/or ongoing resuscitation. (Once stabilized, resume target SpO₂ ≥ 90%.)

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



TO PRINT MORE forms scan here



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

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

References and resources

- ACPRC. The active cycle of breathing techniques. United Kingdom: Association of Chartered Physiotherapists in Respiratory Care (https://www.acprc.org.uk/Data/Publication_Downloads/GL-05ACBT.pdf, accessed 31 May 2021).
- APSF. FAQ on anesthesia machine use, protection and decontamination during COVID-19 pandemic. Rochester (MN): Anesthesia Patient Safety Foundation; 2021 (<https://www.apsf.org/faq-on-anesthesia-machine-use-protection-and-decontamination-during-the-covid-19-pandemic/#filter>, accessed 31 May 2021).
- Bronchiectasis Toolbox. Modified gravity assisted drainage and positioning for children. 2020 (<https://bronchiectasis.com.au/paediatrics/airway-clearance/modified-postural-drainage>, accessed 31 May 2021).
- Coppo A, Bellani G, Winterton D, DiPierro M, Sorio A, Faverio P et al. Feasibility and physiological effects of prone positioning in non-intubated patients with acute respiratory failure due to COVID-19 (PRON-COVID): a prospective cohort study. *Lancet Respiratory Medicine*. 2020;8(8):P765-774 ([https://doi.org/10.1016/S2213-2600\(20\)30268-X](https://doi.org/10.1016/S2213-2600(20)30268-X), accessed 31 May 2021).
- Ding L, Wang L, Ma W, He H. Efficacy and safety of early prone positioning combined with HFNC or NIV in moderate to severe ARDS: a multi-center prospective cohort study. *Crit Care*. 2020;24(1):28 (<https://doi.org/10.1186/s13054-020-2738-5>, accessed 31 May 2021).
- Duke T, Graham SM, Cherian MN, Ginsburg AS, English M, Howie S et al. Oxygen is an essential medicine: a call for international action. *Int J Tuberc Lung Dis*. 2010;14(11):1362-1368.
- Elharrar X, Trigui Y, Dols A, Touchon F, Martinez S, Prud'homme E et al. Use of prone positioning in nonintubated patients with COVID-19 and hypoxemic acute respiratory failure. *Research letter JAMA*. 2020;323(22):2336-2338 (<https://doi.org/10.1001/jama.2020.8255>, accessed 31 May 2021).
- Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med*. 2015;372(23):2185-96.
- Guerin C, Reignier J, Richard JC, Beuret P, Gacouin A, Boulain T et al. Prone positioning in severe acute respiratory distress syndrome. *NEJM*. 2013;368:2159-68 (<https://doi.org/10.1056/NEJMoa1214103>, accessed 31 May 2021).
- Jensen LA, Onyskiw JE, Prasad NG. Meta-analysis of arterial oxygen saturation monitoring by pulse oxymetry in adults. *Heart Lung*. 1998;27(6):387-408.
- McNicholas B, Cosgrave D, Giacomini C, Brennan A, Laffey JG. Prone positioning in COVID-19 acute respiratory failure: just do it? *BJA*. 2020;125(40):P440-443 (<https://doi.org/10.1016/j.bja.2020.06.003>, accessed 31 May 2021).
- Mikalsen IB, Davis P, Øymar K. High flow nasal cannula in children: a literature review. *Scand J Trauma Resusc Emerg Med*. 2016;24:93.
- OC₂. Compilation of oxygen planning resources. Open Critical care (Open Critical Care Compilation of oxygen forecasting tools - <https://opencriticalcare.org/resources/o2-planning-resource-compilation/>, accessed 31 May 2021).
- OC₂. Oxygen supply and delivery FAQ. Open Critical Care (<https://opencriticalcare.org/faq/>, accessed 31 May 2021).
- OC₂. Respiratory care pocket reference. Open Critical Care (<https://opencriticalcare.org/respiratory-care-card>, accessed 31 May 2021).
- O'Driscoll BR, Howard LS, Davison GA. BTS Guideline for emergency oxygen use in adult patients. *Thorax*. 2008;63(suppl 6):vi1-68.
- Potter VA. Pulse oximetry in general practice: how would a pulse oximeter influence patient management? *Eur J Gen Pract*. 2007;13(4):216-20.
- Rojas-Reyes MX, Granados Rugeles C, Charry-Anzola LP. Oxygen therapy for lower respiratory tract infections in children between 3 months and 15 years of age. *Cochrane Database Syst Rev*. 2014;(12):CD005975.
- Scaravilli V, Grasselli G, Castagna L, Zanelli A, Isgrò S, Lucchini A et al. Prone positioning improves oxygenation in spontaneously breathing nonintubated patients with hypoxemic acute respiratory failure: a retrospective study. *J Crit Care*. 2015;30(6):1390-1394 (<https://doi.org/10.1016/j.jcrc.2015.07.008>, accessed 31 May 2021).
- Thiessen, R. The impact of severe acute respiratory syndrome on the use of and requirements for filters in Canada. *Respir Care Clin N Am*. 2006;12(2):287-306.
- Thompson AE, Ranard BL, Wei Y, Jelic S. Prone positioning in awake, nonintubated patients with COVID-19 hypoxemic respiratory failure. *Research letter. JAMA Intern Med*. 2020;180(11):1573-1539 (<https://doi.org/10.1001/jamainternmed.2020.3030>, accessed 31 May 2021).
- WHO. Biomedical equipment for COVID-19 case management - inventory tool: interim guidance. Geneva: World Health Organization; 2020 (<https://www.who.int/publications/i/item/WHO-2019-nCoV-biomedical-equipment-inventory-2020.1>, accessed 31 May 2021).
- WHO. Guidelines on basic newborn resuscitation. Geneva: World Health Organization; 2012 (https://www.who.int/maternal_child_adolescent/documents/basic_newborn_resuscitation/en/, accessed 31 May 2021).
- WHO. IMAI district clinician manual: hospital care for adults and adolescents. Guidelines for the management of common illnesses with limited resources. Volume 1. Geneva: World Health Organization; 2011 (https://www.who.int/influenza/patient_care/IMAI_DCM/en/, accessed 31 May 2021).
- WHO. Oxygen access scale up. Geneva: World Health Organization; 2020 (<https://www.who.int/initiatives/oxygen-access-scale-up>, accessed 31 May 2021).
- WHO. Oxygen therapy for children. Geneva: World Health Organization; 2016 https://www.who.int/maternal_child_adolescent/documents/child-oxygen-therapy/en/, accessed 31 May 2021).

WHO. Patient safety pulse oximetry project [website]. Geneva: World Health Organization; 2019 ([http:// www.who.int/patientsafety/safesurgery/pulse_oximetry/en/](http://www.who.int/patientsafety/safesurgery/pulse_oximetry/en/), accessed 31 May 2021).

WHO. Pocket book of hospital care for children. Guidelines for the management of common illnesses with limited resources (second edition). Geneva: World Health Organization; 2013 (https://www.who.int/maternal_child_adolescent/documents/child_hospital_care/en/, accessed 31 May 2021).

WHO. Therapeutics and COVID-19: living guidance. Geneva: World Health Organization; 2021 (<https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.1>, accessed 31 May 2021).

WHO. WHO technical specifications for oxygen concentrators. Geneva: World Health Organization; 2015 (<https://www.who.int/publications/i/item/9789241509886>, accessed 31 May 2021).



7

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



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

Summary

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

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

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

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

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

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



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

Tools

- 7.1 Memory aid: treatment for acute respiratory infections according to severity (when COVID-19 and influenza are circulating)
- 7.2 COVID-19 and therapeutics
 - 7.2.1 Corticosteroids for COVID-19
 - 7.2.2 Interleukin-6 receptor blockers for COVID-19: tocilizumab, sarilumab
 - 7.2.3 Monoclonal antibodies for COVID-19: casirivimab and imdevimab
- 7.3 Memory aid: invasive fungal infections in patients with COVID-19
- 7.4 Treatment for influenza infection fact sheet

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

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

	Mild disease	Pneumonia	Severe pneumonia
Adults 	<p>Patients with uncomplicated upper respiratory tract viral infection may have <i>non-specific symptoms</i> such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnoea, nasal congestion or headache.</p> <p>Rarely, patients may also present with diarrhoea, nausea and vomiting.</p> <p>The elderly, immunosuppressed and pregnant women may present with atypical symptoms (mainly COVID-19).</p>	<p>Fever, cough, dyspnoea, fast breathing, but no signs of severe pneumonia, including SpO₂ ≥ 90% on room air.</p>	<p>Clinical signs of pneumonia (fever, cough, dyspnoea) plus one of the following:</p> <ul style="list-style-type: none"> • respiratory rate > 30 breaths/min • severe respiratory distress • SpO₂ < 90% on room air.
Children 	<p>Patients with uncomplicated upper respiratory tract viral infection may have <i>non-specific symptoms</i> such as fever, fatigue, cough (with or without sputum production), anorexia, malaise, muscle pain, sore throat, dyspnoea, nasal congestion or headache.</p> <p>Rarely, patients may also present with diarrhoea, nausea and vomiting.</p>	<p>Cough or difficulty breathing, plus fast breathing^a and/or chest indrawing but no signs of severe pneumonia.</p>	<p>Pneumonia plus at least one of the following signs of severe pneumonia:</p> <ul style="list-style-type: none"> • SpO₂ < 90% • Very severe chest wall indrawing, grunting, central cyanosis, or presence of any other general danger sign (inability to breastfeed or drink, lethargy or unconsciousness, or convulsions).
Treatment	<ul style="list-style-type: none"> • Isolation in hospital, community facility or home care (if required for highly infectious pathogen). • Give antipyretics for fever. <p>Monitor and refer immediately if signs of decompensation.</p> <p>If COVID-19 and risk factors: consider if therapies are required (see <i>Therapeutics and COVID-19: living guideline</i> (🔗)).</p> <p>If influenza circulating and risk factors for severe disease: consider if oseltamivir should be prescribed (see <i>Guidelines for the clinical management of severe illness from influenza virus infections</i> (🔗)).</p>	<ul style="list-style-type: none"> • Isolation in hospital, community facility or home care depending on risk factors (if required for highly infectious pathogen). • Give antipyretics for fever. • Give appropriate antibiotic if required if suspicion of bacterial source or co-infection. <p>Monitor (including saturation of oxygen with pulse oximeter twice daily for patients of high risk of severity) and refer immediately if signs of decompensation.</p> <p>If COVID-19 and risk factors: consider if therapies are required (see <i>Therapeutics and COVID-19: living guideline</i> (🔗)).</p> <p>If influenza circulating and risk factors for severe disease: consider if oseltamivir should be prescribed (see <i>Guidelines for the clinical management of severe illness from influenza virus infections</i> (🔗)).</p>	<ul style="list-style-type: none"> • Isolation and treatment in a hospital (if required for highly infectious pathogen), consider intensive care. • Give antipyretics for fever. • Give recommended antibiotic. • Manage airway as appropriate. • Give oxygen if: <ul style="list-style-type: none"> – SpO₂ < 90% and haemodynamically stable – SpO₂ < 94% and with any emergency signs (obstructed or absent breathing, severe respiratory distress, central cyanosis, shock, coma or convulsions) with or without respiratory distress – SpO₂ < 92-95% if pregnant. • If COVID-19 suspected, give steroids and IL-6 RB and/or other medications (see <i>Therapeutics and COVID-19: living guideline</i> (🔗)). • If influenza circulating treat (oseltamivir) (see <i>Guidelines for the clinical management of severe illness from influenza virus infections</i> (🔗)). <p>Monitor for signs of decompensation.</p>

Note:

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

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



Empiric antibiotics for severe pneumonia and sepsis in adults

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

Empiric antibiotic treatment for community-acquired bacterial pneumonia in adults

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

Notes:

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

^a Doxycycline is contraindicated in pregnant women.

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

All dosages are for normal renal function.

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

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

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

Notes:

IV: intravenous.

^a If the source of the infection is determined please follow infection-specific guidance.

^b Ceftriaxone or cefotaxime are alternative options. The choice can be made based on local availabilities.

^c Gentamicin and amikacin are alternative options. The choice can be made based on local availabilities. In addition, amikacin is still effective against isolates producing extended-spectrum β -lactamases (ESBL) and is considered an appropriate carbapenem-sparing option in settings where ESBL-producing isolates are very prevalent.

All dosages are for normal renal function.

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



Empiric antibiotics for SARI and severe bacterial pneumonia in children

	Children
Severe pneumonia (pneumonia with any danger sign, which requires referral to facility/hospital, admission and injectable therapy)	Ampicillin (IV/IM): 50 mg/kg dose given every 12 hours (1st week of life) 50 mg/kg dose given every 8 hours (> 1st week of life) and Gentamicin (IV/IM): <ul style="list-style-type: none"> • Neonates: 5 mg/kg dose given once a day • Children: 7.5 mg/kg dose given once a day Ampicillin can be replaced by Amoxicillin (IV/IM): 50 mg/kg dose given every 12 hours or Benzylpenicillin (IV/IM): 30 mg (50,000 IU)/kg given every 6 hours If no clinical response to ampicillin and gentamicin change to second line: Cefotaxime (IV/IM): 50mg/kg dose given every 8 hours or Ceftriaxone (IV/IM): 80 mg/kg dose given once a day

Note:

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

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

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

Notes:

VAP: ventilator-associated pneumonia.

^a Amoxicillin+clavulanic acid can be used within 5 days of hospital admission and if no prior antibiotic exposure or risk for resistance.

^b Piperacillin+tazobactam offers anti-pseudomonal coverage (which the other options do not). Risk of *Pseudomonas aeruginosa* is higher in patients with recent antibiotic exposure and especially in patients with known previous respiratory colonization and underlying lung diseases.

^c Where possible use dispersible tablets. Oral syrup must be refrigerated as clavulanic acid is rapidly metabolized in high ambient temperatures.

^d Reassess the diagnosis and consider longer treatment if the patient is not clinically stable at Day 7.

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

7.2 COVID-19 and therapeutics

Population

This recommendation applies only to people with these characteristics:



Interventions

Strong recommendations in favour

Weak or conditional recommendations in favour

Weak or conditional recommendations against

Strong recommendations against

Disease severity	
Non-severe	Severe
Absence of signs of severe or critical disease	Oxygen saturation <90% on room air Signs of pneumonia Signs of severe respiratory distress ⁱ
	Requires life sustaining treatment Acute respiratory distress syndrome Sepsis Septic shock
	Corticosteroids IL-6 receptor blockers or Baricitinib ⁱ
	Depending on availability as well as clinical and contextual factors
Molnupiravir ⁱ For those with highest risk of hospital admission	
Sotrovimab ⁱ For those with highest risk of hospital admission	
Casirivimab and imdevimab ⁱ For those with highest risk of hospital admission	Evidence of limited efficacy against Omicron BA1 variant
	Casirivimab and imdevimab ⁱ For those with seronegative status for SARS-CoV-2 antibodies
Corticosteroids	Ruxolitinib and tofacitinib Should be considered only if neither baricitinib nor IL-6 receptor blockers are available
	Remdesivir ⁱ Next update will incorporate important new evidence
	Ivermectin ⁱ Should be considered only in the context of a clinical trial
	Convalescent plasma ⁱ Should be considered only in the context of a clinical trial
Convalescent plasma	
	Hydroxychloroquine
	Lopinavir-ritonavir

Source: A living WHO guideline on drugs for COVID-19 (BMJ, 2020) (¹)

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

7.2.1 Corticosteroids for COVID-19

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

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

Indication: severe or critical COVID-19

Route^a	Systemic corticosteroids may be administered orally or intravenously.
Type^b	Daily regimen of dexamethasone 6 mg once daily is equivalent to: <ul style="list-style-type: none">• 150 mg of hydrocortisone daily (e.g. 50 mg every 8 hours) <u>or</u>• 40 mg of prednisone daily <u>or</u>• 32 mg of methylprednisolone daily (e.g. 8 mg every 6 hours or 16 mg every 12 hours).
Duration	Up to 5-14 days or until hospital discharge.
General monitoring	Monitor glucose levels (even if no diabetes diagnosed previously).
Special populations to monitor closely for complications	<ul style="list-style-type: none">• Patients receiving other immunosuppressants/immunomodulators.• Patients with these conditions:<ul style="list-style-type: none">– diabetes (specially with diabetic ketoacidosis)– severe immunodeficiency disorders– haematological and other malignancies– low number of white blood cells– organ transplantations– iron overload states– severe burns– injection drug use– malnutrition– open wound following trauma.
Examples of possible complications	<ul style="list-style-type: none">• Hyperglycaemia or decompensated diabetes• Immunosuppression• Superinfections: bacterial, fungal, viral, parasites• Poor wound healing.

Notes:

^a If intestinal dysfunction is suspected, clinicians must consider administering systemic corticosteroids intravenously rather than orally.

^b Different corticosteroid preparations have different potencies and doses vary for different steroids. Care should be taken not to confuse doses for different products.

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

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

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

Tocilizumab

Indication (patient criteria)

Patients with severe or critical COVID-19 requiring supplemental oxygen and/or mechanical ventilation AND corticosteroid treatment (see *Therapeutics and COVID-19: living guideline* ()). Treatment should be started as early as possible in the patient's critical illness.

Dose and route

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

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

Dose of tocilizumab (mg) to be given:	
Patient body weight	Band dose
< 30 kg	12 mg/kg
31-45 kg	8 mg/kg
46-55 kg	400 mg
56-65 kg	480 mg
66-80 kg	600 mg
81-90 kg	680 mg
> 91 kg	800 mg

Available formulations

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

Preparation of infusion and administration

1. Ensure area of preparation is well ventilated, clear and clean.
2. Ensure appropriate PPE is worn: gloves, mask and goggles.
3. Collect the appropriate numbers of tocilizumab vials from the fridge (between 2-8 °C) and a 100-mL bag of 0.9% sodium chloride for IV infusion.
4. Tocilizumab solution should be clear to opalescent, colourless to pale yellow and free of visible particles for administration.
5. Withdraw the volume of sodium chloride 0.9% from the 100-mL IV infusion bag equivalent to that which you will be injecting of tocilizumab, calculated as required for the patient dose (see table above).
** For patients < 30 kg, dilute to 50 mL in 0.9% or 0.45% sodium chloride Injection for intravenous infusion.*
6. Discard the withdrawn sodium chloride 0.9% inside the syringe and needle into a sharp bin.
7. Using an appropriate volume IV syringe, draw up the calculated mL of tocilizumab 20 mg/mL solution required from the vial(s) (see table above).
8. Slowly add the tocilizumab solution to the sodium chloride 0.9% IV infusion to make a final volume of 100 mL.
9. Dispose the tocilizumab needle and syringe in a sharp bin.
10. Mix the tocilizumab solution by gently inverting several times. Do not shake the solution.
11. Complete and apply an IV infusion label to the tocilizumab infusion.
12. Obtain second check for the IV tocilizumab infusion from a colleague and sign for preparation and administration.
13. Record baseline vital signs before, and saturation of oxygen (SpO₂) during and after administration: heart rate, blood pressure, temperature, respiratory rate.
14. Connect the tocilizumab IV infusion to the patient IV line and administer over 1 hour via volumetric infusion pump. Do not use the same IV line for other medications while the tocilizumab is being administered.
15. Complete patient observations again and monitor the patient for signs of hypersensitivity to tocilizumab during and after the administration.
16. Acute infusion reactions can occur during the administration of tocilizumab or within 24 hours of infusion.
17. For mild reactions (such as flushing or chills), the infusion rate can be slowed down and the patient continually monitored.
18. For severe reactions (such as hives, difficulty breathing, chest pain, high or low blood pressure, swelling of hand and face, fever, chills or anaphylaxis) or when mild reactions that do not disappear despite slowing infusion, stop the infusion and inform the doctor immediately for additional treatment.
19. Once tocilizumab infusion is complete, take down the infusion and flush the giving set with 20 mL of sodium chloride 0.9% over 15 minutes to ensure all the tocilizumab has been given.
20. Dispose of the infusion and giving set in a sharp bin.

Monitoring for potential serious adverse events

- Please refer to USPI, SmPC or local labelling for important safety issues and warnings.
- Monitor the patient for signs of hypersensitivity to tocilizumab during and after administration: 15 minutes after starting the infusion, then every 30 minutes during the infusion and for 1 hour after the end of the infusion (15 min, 45 min, 1 hr, 1 hr 15 min, 1 hr 45 min).
 - Laboratory monitoring is recommended due to potential consequences of treatment-related changes, at baseline, 72 hours, and after infusion of IL-6 RB:
 - **Neutrophil count** (it is not recommended to initiate treatment in patients with neutropenia).
 - **Platelets count** (it is not recommended to initiate treatment in patients with < 50 000/mL).
 - **Transaminases** (it is not recommended to initiate treatment in patients with elevated transaminases ALT or AST above 1.5× ULN. Discontinue infusion or do not give second dose in patients who develop persistent elevated ALT or AST above 3× ULN or who develop ALT or AST above 5× ULN).
 - **Lipid profile** (LDL, HDL cholesterol, triglycerides) (possibility of elevated lipid profile after treatment).
 - At baseline:
 - **Screening for HIV, Hep B (HBsAg, HBcAb) and C (HC Ab)*** (Discuss the results with microbiology or infectious diseases physicians if unsure how to interpret.) Individual clinical assessment of these patients is needed.
 - * *Delays in the result of these tests should not restrain clinicians from starting treatment when indicated.*
 - Before, during and after IL-6 receptor blockers infusion: patients should be regularly clinically assessed for bacterial infection. Monitor the appearance of sepsis produced by other pathogens different from COVID-19 (caution is recommended when considering the use in patients with a history of recurring or chronic infections or underlying conditions which may predispose patients to infections).
 - In areas of high prevalence of TB or immunosuppressed patients, monitoring and assessment for presumptive TB is important before and after administration.
 - Observe for hypersensitivity reactions during and after administration as mentioned in preparation and infusion section.

Safety profile/adverse effects

- The most common side-effects (occurring in up to 1 patient in 10) with tocilizumab are upper respiratory tract infections (nose and throat infection), nasopharyngitis (inflammation of the nose and throat), headache, hypertension (high blood pressure) and abnormal liver function tests. The most serious side-effects are serious infections, complications of diverticulitis and hypersensitivity (allergic) reactions.

High-risk groups that require special precautions for use

- Age > 70 years.
- Patients with recurring chronic infections or underlying conditions that predispose to infections, e.g. interstitial lung disease, diabetes, diverticulitis or patients taking steroids. Additionally there appears to be an increase risk of serious infections with increased body weight.
- Patients receiving IL-6 RB on long-term regimens for conditions other than COVID-19 (risk of fatal infections such as active TB, bacterial, viral and other opportunistic infections).
- Women of childbearing potential must use effective contraception during and up to 3 months after treatment.
- Pregnant women - only use in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Tocilizumab *continued*

Examples of possible complications

- Acute severe infections: TB, bacterial, invasive fungal, viral and other opportunistic superinfections.
- Immunosuppression.
- Elevated liver function tests and lipid profile.
- Gastrointestinal perforation.
- Hypersensitive reactions, anaphylaxis.
- Important risks include:
 - Serious infection
 - Complications of diverticulitis
 - Serious hypersensitivity reactions
 - Neutropenia
 - Hepatotoxicity
 - Thrombocytopenia and the potential risk of bleeding
 - Elevated lipid levels and the potential risk of cardiovascular and cerebrovascular events
 - Malignancies
 - Demyelinating disorders
 - Immunogenicity.

Not recommended

- On immunosuppressive therapy (excluding steroids)
- HIV with CD4 < 200.
- ANC < 200.
- Suspected active severe bacterial, viral, fungal or TB infection (other than COVID-19).
- Patients who may be at increased risk of gastrointestinal (GI) perforations: history of diverticulitis or bowel perforation.
- Patients with elevated ALT or AST above 10 times the upper limit of the reference range.
- Paediatric population < 2 years old.

Contraindications

- Tocilizumab is contraindicated in those with prior hypersensitivity to the medication or any known ingredient in it.

Notes:

Avoid concurrent use of live vaccines during treatment as clinical safety has not been established.

Further guidance for use can be obtained from the product information and training packages provided by the license holder.

Report all adverse events to the national pharmacovigilance centre or the manufacturer.

ALT - alanine aminotransferase; AST - aspartate aminotransferase; SmPC - Summary of Product Characteristics (European Union);

ULN - upper limit of normal; USPI- United States Prescribing Information.

Sarilumab

Indication (patient criteria)	Patients with severe or critical COVID-19 requiring supplemental oxygen and/or mechanical ventilation AND corticosteroid treatment (see <i>Therapeutics and COVID-19: living guideline</i> (1)) Treatment should be started as early as possible in the patient's critical illness.
Dose and route	Sarilumab will be administered as an IV infusion at a dose of 400 mg over at least 60 minutes using a dedicated IV line. <ul style="list-style-type: none"> • Avoid IV push or IV bolus. (Subcutaneous administration has not been studied for COVID-19.) • If a clinical response is determined to be inadequate after 12-48 hours, a second dose may be considered. • Renal dose adjustment is not warranted.
Available formulations	Single dose 200 mg pre-filled syringe 200 mg/1.14 mL. <ul style="list-style-type: none"> • Do not use sarilumab with autoinjector directly for SC injection, follow instructions to dilute them for IV infusion (see below).

Preparation of infusion and administration	1. Ensure area of preparation is well-ventilated, clear and clean.
Infusion instructions	2. Ensure appropriate PPE is worn: gloves, mask and goggles.
	3. Collect the contents of 2 pre-filled syringes (200 mg/1.14 mL) of sarilumab, which should be diluted in 100 mL of 0.9% sodium chloride to prepare 400 mg of sarilumab IV bag. Note: The needle attached to the sarilumab syringe is approx. 12.5 mm long (half of normal). Take care to ensure it fully penetrates the port and reaches the fluid.
	4. After mixing it is best practice to ensure the drug is not trapped in the injection port. A flush of 25 mL of normal saline can be given.
	5. Invert bag 10 times to mix, do not shake.
	6. Ensure the product solution is clear and free from any precipitation. Label as local policy.
	7. The infusion should be started within 4 hours of preparation and can be given via central line or peripheral line.
	8. Do not infuse concomitantly in the same IV line with other medications.
	9. The inline filter and the IV infusion pump must be able to deliver as little as 0.17 mL/min (10 mL/hr).
	10. Infusion speed must be set at 10 mL/h for 15 minutes, then increased to 130 mL/hr for the next 45 minutes. Infuse over 60 minutes.
	11. After completion of the infusion, 25 mL of 0.9% saline should be used to flush the drug through the giving set.
	12. IV infusion sets that have been evaluated in sarilumab compatibility include:

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

<p>Preparation of infusion and administration</p>	<p>13. Monitor for infusion-related reactions: chills, nausea, headache, wheezing, itching, flushing, pyrexia, dizziness. If infusion-related reactions are mild, stop infusion and treat symptoms. Reduce infusion rate by at least 50% when re-starting infusion.</p>
<p>Infusion instructions</p>	<p>14. For severe infusion-related reactions, stop the infusion and inform the doctor immediately. 15. Once the sarilumab infusion is complete, take down the infusion and flush the giving set with 20 mL of sodium chloride 0.9% at same rate as infusion. 16. Document the administration. 17. Dispose the infusion and giving set in a sharp bin.</p>
<p>Monitoring for potential serious adverse events</p>	<p>Please refer to USPI, SmPC or local labelling for important safety issues and warnings.</p> <ul style="list-style-type: none"> • Monitor the patient for signs of hypersensitivity to sarilumab during and after administration: 15 minutes after starting the infusion, then every 30 minutes during the infusion and for 1 hour after the end of the infusion (15 min, 45 min, 1 hr, 1 hr 15 min, 1 hr 45 min). • Laboratory monitoring is recommended due to potential consequences of treatment-related changes, at baseline, 72 hours, and after infusion of IL-6 RB: <ul style="list-style-type: none"> – Neutrophil count (it is not recommended to initiate treatment in patients with neutropenia). – Platelets count (it is not recommended to initiate treatment in patients with < 50 000/mL). – Transaminases (it is not recommended to initiate treatment in patients with elevated transaminases ALT or AST above 1.5x ULN. Discontinue infusion or do not give second dose in patients who develop persistent elevated ALT or AST above 3x ULN or who develop ALT or AST above 5x ULN. – SmPC recommends dose to be modified if ALT > 1-3 upper limit. – Lipid profile (LDL, HDL cholesterol, triglycerides) (possibility of elevated lipid profile after treatment). • At baseline: <ul style="list-style-type: none"> – Screening for HIV, Hep B (HBsAg, HBcAb) and C (HC Ab)* (Discuss the results with microbiology or infectious diseases physicians if unsure how to interpret.) <p><i>* Delays in the result of these tests should not restrain clinicians from starting treatment when indicated.</i></p> • Before, during and after IL-6 receptor blockers infusion: patients should be regularly clinically assessed for bacterial infection. Monitor the appearance of sepsis produced by other pathogens different from COVID-19 (caution is recommended when considering the use in patients with a history of recurring or chronic infections or underlying conditions which may predispose patients to infections). • In areas of high prevalence of TB or immunosuppressed patients, monitoring and assessment for presumptive TB is important before and after administration.
<p>Safety profile/adverse effects</p>	<ul style="list-style-type: none"> • Transient and/or reversible elevations in liver enzyme levels that appear to be dose dependent and rare occurrences of neutropenia and thrombocytopenia. Additional adverse effects, such as serious infections (e.g. TB, bacterial or fungal infections), and bowel perforation, have been reported, but only with long-term use of sarilumab.
<p>High-risk groups that require special precautions for use</p>	<ul style="list-style-type: none"> • Age > 70 years. • Patients with recurring chronic infections or underlying conditions that predispose to infections. • Patients receiving IL-6 RB on long-term regimens for conditions other than COVID-19 (risk of fatal infections such as active TB, bacterial, viral and other opportunistic infections). • Women of childbearing potential must use effective contraception during and up to 3 months after treatment. • Pregnant women - only use in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Sarilumab *continued*

Examples of possible complications	<ul style="list-style-type: none">• Acute severe infections: TB, bacterial, invasive fungal, viral and other opportunistic superinfections.• Immunosuppression• Elevated liver function tests and lipid profile.• Gastrointestinal perforation.• Hypersensitive reactions, anaphylaxis.
Not recommended	<ul style="list-style-type: none">• On immunosuppressive therapy (excluding steroids).• HIV with CD4 < 200.• ANC < 200.• Suspected active severe bacterial, viral, fungal or TB infection (other than COVID-19).• Patients who may be at increased risk of gastrointestinal (GI) perforations: history of diverticulitis or bowel perforation.• Patients with elevated ALT or AST above 10 times the upper limit of the reference range.• Paediatric population < 2 years old.
Contraindications	<ul style="list-style-type: none">• Sarilumab is contraindicated in those with prior hypersensitivity to the medication or any known ingredient in it.

Notes:

Avoid concurrent use of live vaccines during treatment as clinical safety has not been established.

Further guidance for use can be obtained from the product information and training packages provided by the license holder.

Report all adverse events to the national pharmacovigilance centre or the manufacturer.

ALT - alanine aminotransferase; AST - aspartate aminotransferase; SmPC - Summary of Product Characteristics (European Union);

ULN - upper limit of normal; USPI- United States Prescribing Information.

7.23 Monoclonal antibodies for COVID-19: casirivimab and imdevimab

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

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

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

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

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

Casirivimab and imdevimab

Indication (patient criteria)

1. **Patients with confirmed non-severe COVID-19 at highest risk for infection:**
 - Those with risk beyond 10% for being hospitalized with COVID-19. Those at highest risk for progression of infection:
 - Older age.
 - Risk factors: hypertension, diabetes, cardiac disease, chronic lung disease, cerebrovascular disease, dementia, mental disorders, chronic kidney disease, immunosuppression, obesity, cancer.
 - Not vaccinated.
2. **Severe or critical COVID-19:**
 - Seronegative for SARS-CoV-2.
 - Serologic testing should be conducted with tests that detect the presence of the SARS-CoV-2 spike protein antibodies and have performance characteristics similar to the reference standard test used to characterize seronegative patients in the RECOVERY trial (i.e. Oxford fluorescent-based ELISA assay for serum IgG against the SARS-CoV-2 spike protein), with an arbitrary cut-off determined by a panel of positive controls.
 - Some lateral flow assay may be suitable and can usually be performed in several minutes.
3. **No medical contraindication:**
 - No allergy to casirivimab and imdevimab or components: L-histidine, L-histidine monohydrochloride monohydrate, polysorbate 80, sucrose.

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

Dose and route

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

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

Casirivimab and imdevimab *continued*

Dose and route	<p><i>Notes:</i></p> <p>* If administered subcutaneously (SC), maximum total dose is 1200 mg. IV - intravenous infusion is preferred. SC - subcutaneous is an alternative route of administration. It can be given when intravenous infusion is not feasible and would lead to a delay in treatment.</p> <p>Preferred: Casirivimab and imdevimab intravenous single infusion using a dedicated IV line with a sterile low protein binding inline or add-on 0.2 micron filter via pump (preferred) or gravity + 1 hour post-infusion close monitoring (covered below in more detail).</p> <p>Alternative: Casirivimab and imdevimab by consecutive subcutaneous injections (syringes) + 1 hour post-injection close monitoring (covered below in more detail).</p> <p><i>Renal or hepatic dose adjustment is not currently warranted for either drug.</i></p>
Storage conditions	<ul style="list-style-type: none"> • Store in a refrigerator at 2-8 °C in the original carton to protect from light. • Do not freeze. • Do not shake.
Available formulations	<p>The vials of casirivimab and imdevimab come in two different sizes (20 mL or 6 mL).</p> <p>a) Each 20-mL vial contains 11.1 mL of product Concentration: 1332 mg per 11.1 mL (120 mg/mL).</p> <p>b) Each 6-mL vial contains 2.5 mL of product Concentration: 300 mg per 2.5 mL (120 mg/mL).</p>
Preparation of intravenous perfusion	<ol style="list-style-type: none"> 1. Wear PPE: gloves, gown, protective eyewear and respiratory mask. 2. Remove casirivimab and imdevimab vials from refrigerated storage. 3. Prepare in a well-ventilated area in clean room. 4. Allow to equilibrate to room temperature for approximately 20 minutes before preparation. Do not shake the vials or expose to direct heat. 5. Inspect the casirivimab and imdevimab vials to ensure there is no discolouration or particulate matter prior to administration. If either is observed, the vials should be discarded. The solution in each vial should be clear to slightly opalescent (colourless to pale yellow). 6. Obtain a prefilled intravenous infusion bag containing 50 mL, 100 mL, 150 mL or 250 mL of 0.9% of sodium chloride injection or 5% dextrose injection. 7. To allow for space in the infusion bag for the addition of the casirivimab and imdevimab, use a syringe and aseptic non-touch technique to withdraw the total volume dose equivalent from the infusion bag and discard. For example, if preparing a total dose of casirivimab and imdevimab of 1200 mg infusion, remove 10 mL of fluid from the infusion bag prior to injecting the monoclonal antibody (see Table 2 below). 8. Using a separate syringe for each vial, withdraw the appropriate amount of casirivimab and imdevimab from each respective vial and inject into a prefilled intravenous infusion bag containing either 0.9% of sodium chloride injection or 5% dextrose injection. If using one vial to prepare more than one bag, then prepare all bags at the same time. 9. Gently invert infusion bag by hand ten times to mix. Do not shake. 10. The product is preservative free, so the diluted infusion solution should be administered immediately. <i>If not possible to immediately administer, the diluted casirivimab and imdevimab infusion solution can be stored in the refrigerator at 2-8 °C for up to 36 hours or at room temperature up to 25 °C for no more than 4 hours. If refrigerated, remove approximately 30 minutes prior to patient infusion to allow for equilibration to room temperature.</i>

Casirivimab and imdevimab *continued*

Preparation of intravenous perfusion

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

Size of prefilled 0.9% sodium chloride or 5% dextrose infusion bag	Preparing casirivimab and imdevimab using individual vials
50 mL 100 mL 150 mL 250 mL	<p>Add:</p> <ul style="list-style-type: none"> • 5 mL of casirivimab (use two 6-mL vials of casirivimab <i>or</i> 5-mL of one 20-mL vial) <p><i>and</i></p> <ul style="list-style-type: none"> • 5 mL of imdevimab (use two 6-mL vials of imdevimab <i>or</i> 5-mL of one 20-mL vial) <p>Inject 5 mL of casirivimab + 5 mL of imdevimab into a prefilled 0.9% sodium chloride or 5% dextrose infusion bag and administer as instructed.</p>

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

Size of prefilled 0.9% sodium chloride or 5% dextrose infusion bag	Preparing casirivimab and imdevimab using individual vials
50 mL 100 mL 150 mL 250 mL	<p>Add:</p> <ul style="list-style-type: none"> • 10 mL of casirivimab (use four 6-mL vials of casirivimab <i>or</i> 10-mL from a 20-mL vial) <p><i>and</i></p> <ul style="list-style-type: none"> • 10 mL of imdevimab (use four 6-mL vials of imdevimab <i>or</i> 10-mL from a 20-mL vial) <p>Inject 10 mL of casirivimab + 10 mL of imdevimab into a prefilled infusion bag of 0.9% sodium chloride or 5% dextrose and administer as instructed.</p>

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

Size of prefilled 0.9% sodium chloride or 5% dextrose infusion bag	Preparing casirivimab and imdevimab using individual vials
150 mL 250 mL 500 mL	<p>Add:</p> <ul style="list-style-type: none"> • 33.3 mL of casirivimab (use three 20-mL vials of casirivimab) <p><i>and</i></p> <ul style="list-style-type: none"> • 33.3 mL of imdevimab (use three 20-mL vials of imdevimab) <p>Inject 33.3 mL of casirivimab + 33.3 mL of imdevimab into a prefilled infusion bag of 0.9% sodium chloride or 5% dextrose and administer as instructed.</p>

Casirivimab and imdevimab *continued*

Preparation of subcutaneous injections

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

Administration of intravenous infusion

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

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

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

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

Note: Infusion should not be administered > 4 hours.

Casirivimab and imdevimab *continued*

Administration of intravenous infusion

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

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

Note: Infusion should not be administered > 4 hours.

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

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

Note: Infusion should not be administered > 4 hours.

Administration of subcutaneous injection

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

General monitoring

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


Special populations to monitor closely for complications

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

Contraindications

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

Casirivimab and imdevimab *continued*

Examples of possible complications	<ul style="list-style-type: none">• Hypersensitivity reactions including anaphylaxis have been observed with casirivimab and imdevimab.• Infusion-related reactions (IV).• Injection site related reactions (SQ/SC).• <i>Hypersensitivity reactions occurring more than 24 hours after the infusion of casirivimab and imdevimab have been reported. If signs or symptoms of a clinically significant hypersensitivity reaction or anaphylaxis occur, immediately discontinue administration, and initiate appropriate medications and/or supportive therapy.</i>• <i>Infusion-related reactions occurring during infusion and up to 24 hours post infusion have been observed and may be severe or life threatening. These reactions may include: fever, difficulty breathing, reduced oxygenation, chills, fatigue, irregular heart beat, chest pain or discomfort, weakness, nausea, headache, angioedema, throat irritation, bronchospasm, hypertension, hypotension, throat irritation, rash, pruritis, muscle aches, pre-syncope, syncope, dizziness and diaphoresis.</i>• <i>If an infusion-related reaction occurs consider slowing or stopping the infusion and administer appropriate medications and/or supportive care.</i>
Reporting of adverse events	Report all adverse events to WHO and the manufacturer ( www.roche.com/products/local_safety_reporting.htm

Notes:

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

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

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

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

Mucormycosis

Risk factors	<ul style="list-style-type: none">• diabetes mellitus (<i>poorly controlled or complicated</i>) with or without diabetic ketoacidosis (DKA)• prolonged corticosteroid use• haematological malignancies• haematopoietic stem cell transplant• solid organ transplantation• iron chelation therapy• iron overload states• burns• other immunosuppressive conditions or medications (e.g. TNF- inhibitors or other immunosuppressive medication, cancer - chemotherapy, chronic immunosuppression - HIV).
Prevention	<p>Use the recommended dose and duration of corticosteroids based on WHO recommendations and clinical practice guidelines for the indication. See WHO <i>Therapeutics and COVID-19: living guideline</i> (). 📄</p> <p>Follow strict adherence to protocol of low-dose steroid and strict glycaemic control.</p> <p>Follow strict adherence to quality of oxygen humidification protocol and biosafety:</p> <ul style="list-style-type: none">• Appropriate hygiene should be followed when oxygen is being administered.• Use of sterile water for humidifiers during the oxygen therapy is recommended.• Disposable items should not be reused and where this avoidable they should be properly sterilized.• Use of medical masks.• Educate patients on early signs and symptoms of some of the most important secondary fungal infections in COVID-19 recovering patients (e.g. facial pain or orbital pain-diplopia, nasal blockage or excessive discharge of blood or brown/black discharge, loosening of teeth, etc. all could be signs of rhino-orbito-cerebral mucormycosis [ROCM]).• Include ENT surgeon and ophthalmologist in the post-COVID-19 clinic to pick up the cases early.• Environmental control in hospital. <p>Restrict antibiotics only when bacterial infection is suspected/proven, as the use of antibiotics also increases likelihood of fungal infection.</p>
Signs and symptoms	<ul style="list-style-type: none">• facial swelling (pain and numbness can be present)• nasal or sinus congestion• black lesions on nasal bridge or upper inside of mouth• blackish and foul-smelling nasal discharge• loosening of a tooth or a TMJ-like symptoms• eye pain-diplopia• headache or cranial nerve palsy• fever• for respiratory or gastrointestinal mucormycosis, there is no specific symptom or sign; however, suspect the disease if there is chest pain, shortness of breath, cough haemoptysis, blackish discolouration in the skin with necrosis, abdominal pain, nausea and vomiting, gastrointestinal bleeding, mental status changes or coma.
Diagnosis	<ul style="list-style-type: none">• early diagnosis is key!• imaging (CT or MRI)• endoscopic or bronchoscopic sample collection• histopathology or culture PLUS patient risk factors and clinical presentation.

Treatment

Primary regimen:

Liposomal (lipid) amphotericin B 5-10 mg/kg IV daily for 3-6 weeks:

- early administration is key - delay of 6 days was associated with two-fold increase in mortality in 12 weeks;
- monitor renal function regularly.

Surgical debridement:

- early aggressive surgical resection and debridement is key for local control of disease and can reduce morbidity and mortality.

Control underlying disease/risk (e.g. DM-DKA - discontinue corticosteroids, etc.).

Alternative regimens:

- amphotericin B deoxycholate 1-1.5 mg/kg IV daily (administered in at least 1000 mL of 5% dextrose over 2 hrs for 3-6 weeks):
 - during amphotericin B deoxycholate infusion, pre or peri-infusion normal saline and other symptomatic therapy may minimize the infusion related toxicity; monitor renal function regularly.
- posaconazole:
 - posaconazole IV 300 mg IV over 90 mins every 12h Day 1, then 300 mg IV daily;
 - delayed-release tablet 300 mg PO/12h on Day 1, then 300 mg PO daily;
 - suspension 200 mg QID, then 400 mg PO/12h after stabilization of disease;
- isavuconazonium sulfate (prodrug of isavuconazole) 372 mg PO/IV q8h x 6 doses, later 372 mg PO/IV daily.

Step-down or salvage therapy:

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

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

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

NOTE 3: Step-down or salvage therapy:

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

Candidemia

Risk factors	<ul style="list-style-type: none">• diabetes mellitus (<i>poorly controlled or complicated</i>)• prolonged corticosteroid use• haematological malignancies• active solid malignancy• recent chemotherapy• HIV infection• haemodialysis• long ICU stays• use of broad-spectrum antibiotics or antifungal agents• central venous catheters• parenteral nutrition• immunosuppressive agents• neutropenia• severe pancreatitis• <i>Candida</i> spp. colonization• recent abdominal surgery• extensive burns• COVID-19 infection.
Prevention	<p>Control of risk factors (above) mainly in nosocomial transmission.</p> <p>Use the recommended dose and duration of corticosteroids based on WHO recommendations and clinical practice guidelines. See WHO <i>Therapeutics and COVID-19: living guideline</i> ()📄</p> <p>Consider gradual withdrawal practices with corticosteroid regimens:</p> <ul style="list-style-type: none">• if a patient has received more than 3 weeks' treatment;• has recently received repeated courses of steroids;• has taken a short course within 1 year of stopping long-term therapy;• has other possible causes of adrenal suppression. <p>Follow strict adherence to protocol of low-dose steroid and strict glycaemic control.</p>
Clinical presentations	<ul style="list-style-type: none">• Sepsis.• Candidemia: one or more positive blood cultures for <i>Candida</i> spp.• Less frequent: infective endocarditis; endophthalmitis.
Diagnosis	<ul style="list-style-type: none">• One or more positive blood cultures for <i>Candida</i> spp. (they could be negative in 50% cases).• Beta-D-glucan (poor specificity).• Candida mannan and anti-mannan detection.• Clinical signs: suspected dissemination (e.g. fever, multiple colonized or infected sites, even if negative blood cultures).
Treatment	<p><i>First-line: echinocandins:</i></p> <ul style="list-style-type: none">• caspofungin: 70 mg IV × 1, then 50 mg/day IV;• micafungin: 100 mg/day IV;• anidulafungin: 100 mg/day IV; <p>Duration: 14 days timed from clearance of bloodstream and resolution of symptoms.</p> <p><i>Alternative regimens: amphotericin B, voriconazole, isavuconazole.</i></p> <ul style="list-style-type: none">• amphotericin B (lipid formulation): 3-5 mg/kg/day IV (especially if azole and echinocandin resistance or intolerance is of concern);• voriconazole, 6 mg/kg IV/PO × 2 doses on Day 1, then 3 mg/kg twice daily isavuconazole.

NOTE 1: The clinical presentation of candidemia is indistinguishable from most bacterial bloodstream infections - and the blood cultures can be falsely negative - this could lead to delays in appropriate therapy. Empiric treatment should be considered after consultation with infectious disease specialist if the patient is critically ill with unexplained sepsis and has some of the clinical risk factors, and/or colonized in non-sterile sites - or elevated markers (e.g. serum beta glucans levels, etc.).

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

Aspergillosis

Risk factors	<ul style="list-style-type: none">• prolonged neutropenia (acute leukaemia, myelodysplastic syndromes)• prolonged high-dose corticosteroids• allogenic stem cell transplant• solid organ transplant• haematologic malignancy• immunosuppressive medications• chronic granulomatous disease, e.g. TB, sarcoidosis• chronic lung diseases, e.g. asthma, cystic fibrosis• antimicrobial drug exposure• inherited immunodeficiencies• ICU care and mechanical ventilation• COVID-19 infection, especially those treated in ICU.
Prevention	<p>Use the recommended dose and duration of corticosteroids based on WHO recommendations and clinical practice guidelines. See WHO Therapeutics and COVID-19: living guideline ().</p> <p>Control of risk factors.</p> <p>Consider gradual withdrawal practices with corticosteroid regimens:</p> <ul style="list-style-type: none">• if a patient has received more than 3 weeks' treatment;• has recently received repeated courses of steroids;• has taken a short course within 1 year of stopping long-term therapy;• has other possible causes of adrenal suppression. <p>Follow strict adherence to protocol of low-dose steroid and strict glycaemic control.</p> <p>Follow strict adherence to quality of oxygen humidification protocol and biosafety:</p> <ul style="list-style-type: none">• appropriate hygiene should be followed when oxygen is being administered;• use of sterile water for humidifiers during the oxygen therapy is recommended;• disposable items should not be reused and where this avoidable it should be properly sterilized. <p>Restrict antibiotics only when bacterial infection is suspected/proven, as the use of antibiotics also increases likelihood of fungal infection.</p>
Signs and symptoms	<ul style="list-style-type: none">• Chest pain, fever, cough, shortness of breath, haemoptysis.• Invasive pulmonary infection - coronavirus disease-associated pulmonary aspergillosis (CAPA).• Dissemination can occur: CNS, skin, GI tract, etc.• Pulmonary deterioration - worsening respiratory status and need for increased respiratory support, hemoptysis, chest pain, sepsis (fever, tachycardia, tachypnoea, hypotension, change in mental status).
Diagnosis	<ul style="list-style-type: none">• Imaging - multiple nodule, thick-walled cavities; in immunosuppressed patients halo sign or air-crescent sign.• Histopathology or culture PLUS patient risk factors and clinical presentation.• Galactomannan antigen: serum, BAL fluid more sensitivity but reduced specificity for invasive disease.• Beta-D-glucan assay in serum.
Treatment	<p><i>Primary regimen:</i></p> <ul style="list-style-type: none">• voriconazole 6 mg/kg IV/PO every 12 hrs on Day 1, then 4 mg/kg IV/PO every 12 hrs. <p><i>Alternative regimens:</i></p> <ul style="list-style-type: none">• liposomal amphotericin B 3-5mg/kg IV daily.• posaconazole:<ul style="list-style-type: none">– delayed-release tablets 300 mg PO/12h on Day 1, then 300 mg PO daily;– suspension 200 mg QID, then 400 mg PO/12h after stabilization of disease;– posaconazole IV 300 mg IV over 90 mins every 12h Day 1, then 300 mg IV daily.• isavuconazonium sulfate (prodrug of isavuconazole) 372 mg PO/IV q8h × 6 doses, later 372 mg PO/IV daily.

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

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

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

NOTE 4: Step-down or salvage therapy:

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




Cryptococcosis

Risk factors	<ul style="list-style-type: none">• conditions associated with reduced cell mediated immunity (e.g. lymphoma)• chronic corticosteroid use• HIV infection (CD4 cell count < 200)• allogenic stem cell transplant• solid organ transplantation.
Prevention	Control of risk factors.
Signs and symptoms	<ul style="list-style-type: none">• Meningoencephalitis (common presentation) with symptoms (fever, malaise, headache, meningism) but could be asymptomatic.<ul style="list-style-type: none">– Encephalopathic presentation: lethargy, seizure, dementia, personality changes or altered mental status.– Meningitis (fever, malaise, headache, meningism is seen in 25% of patients).• Less frequent: pulmonary (pneumonia presentation) or disseminated disease.
Diagnosis	<ul style="list-style-type: none">• Direct microscopy, culture, serology (CrAg, LAT, EIA, LFA), molecular identification (PCR).• Lumbar puncture: analysis of CSF: CrAg, India staining, culture.
Treatment	<p><i>Primary regimen:</i></p> <ul style="list-style-type: none">• <i>induction phase:</i> liposomal amphotericin B 3-4 mg/kg IV daily (or amphotericin B or amphotericin B lipid complex) AND fluconazole 800-1200 mg/day IV/PO for 2 weeks; or Duration > 2 weeks or until CSF sterilization achieved (if takes more than 2 weeks).• <i>consolidation phase:</i> fluconazole 800 mg/daily for 10 weeks. <p><i>Alternative regimens:</i></p> <ul style="list-style-type: none">• amphotericin B deoxycholate AND flucytosine followed by fluconazole• fluconazole AND flucytosine• amphotericin B deoxycholate AND fluconazole• flucytosine (5-FC) 25 mg/kg PO four times daily if no renal impairment.

7.4 Treatment for influenza infection fact sheet

- See *Guidelines for the clinical management of severe illness from influenza virus infections*, March 2022 (4).
- Oseltamivir is recommended to be used when influenza is suspected or known to be circulating.
- If testing for influenza is not possible, empiric treatment is indicated.
- Oseltamivir is not proven to be effective for COVID-19.

Treatment dosing

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

Note:

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

Safety considerations and side-effects

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

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

Side-effects: side-effects are generally minor:

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

Oral formulations

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

Note:

^a Preparation of oral oseltamivir suspension:

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

References and resources

- Arastehfar A, Carvalho A, van de Veerdonk FL, Jenks JD, Koehler P, Krause R et al. COVID-19-associated pulmonary aspergillosis (CAPA) - from immunology to treatment. *J Fungi*. 2020;6(2):91. doi: 10.3390/jof6020091.
- Bhatt K, Agolli A, Patel MH, Garimella R, Devi M, Garcia E et al. High mortality co-infections of COVID-19 patients: mucormycosis and other fungal infections. *Discoveries*. 2021;9(1):e126. doi: 10.15190/d.2021.5.
- Bradley JS, Byington CL, Shah SS, Alverson B, Carter ER, Harrison C et al. The management of community-acquired pneumonia in infants and children older than 3 months of age: clinical practice guidelines by the Pediatric Infectious Diseases Society and the Infectious Diseases Society of America. *Clin Infect Dis*. 2011;53(7):e25-76.
- CDC websites:
<https://www.cdc.gov/fungal/diseases/mucormycosis/risk-prevention.html>
<https://www.cdc.gov/fungal/diseases/mucormycosis/diagnosis.html>
<https://www.cdc.gov/fungal/diseases/mucormycosis/symptoms.html>
<https://www.cdc.gov/fungal/diseases/mucormycosis/health-professionals.html>
- Chamilos G, Lewis RE, Kontoyiannis DP. Delaying amphotericin B-based frontline therapy significantly increases mortality among patients with hematologic malignancy who have zygomycosis. *Clin Infect Dis*. 2008;47(4):503-509.
- Chan-Tack KM, Kim C, Moruf A, Birnkrant DB. Clinical experience with intravenous zanamivir under an Emergency IND program in the United States (2011-2014). *Antivir Ther*. 2015;20(5):561-4.
- Chu CM, Cheng VCC, Hung IFN, Wong MML, Chan KH, Chan KS et al. Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. *Thorax*. 2004;59(3):252-6
- de Jong MD, Ison MG, Monto AS, Metev H, Clark H, O'Neil B et al. Evaluation of intravenous peramivir for treatment of influenza in hospitalized patients. *Clin Infect Dis*. 2014;59(12):e172-85.
- Dobson J, Whitley RJ, Pocock S, Monto AS. Oseltamivir treatment for influenza in adults: a meta-analysis of randomised controlled trials. *Lancet*. 2015;385(9979):1729-37.
- Eccles S, Pincus C, Higgins B, Woodhead M, Guideline Development Group. Diagnosis and management of community and hospital-acquired pneumonia in adults: summary of NICE guidance. *BMJ*. 2014;349:g6722.
- EMA. CHMP assessment report on novel influenza (H1N1) outbreak, Tamiflu (oseltamivir), Relenza (zanamivir). (EMA/H/A-5.3/1172). London: European Medicines Agency; 7 May 2009 (https://www.ema.europa.eu/en/documents/other/chmp-assessment-report-novel-influenza-h1n1-outbreak-tamiflu-oseltamivir-relenza-zanamivir_en.pdf, accessed 25 July 2021).
- Goossens H, Merech M, Vander Stichele R, Elseviers M, ESAC Project Group. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet*. 2005;365(9459):579-87. Epub 2005/02/15.
- Harnett KP, Jackson BR, Perkins KM, Glowicz J, Kerins JL, Black SR et al. A guide to investigating suspected outbreaks of mucormycosis in healthcare. *J Fungi*. 2019;5(3):69. doi:10.3390/jof5030069.
- Hernandez JE, Adiga R, Armstrong R, Bazan J, Bonilla H, Bradley J et al. Clinical experience in adults and children treated with intravenous peramivir for 2009 influenza A (H1N1) under an Emergency IND program in the United States. *Clin Infect Dis*. 2011;52(6):695-706.
- Hoeningl M, Seidel D, Carvalho A, Rudramurthy SM, Arastehfar A, Gangneux JP et al. The emergence of COVID-19 associated mucormycosis: analysis of cases from 18 countries. SSRN. 12 May 2021 (<http://dx.doi.org/10.2139/ssrn.3844587>, accessed 25 July 2021).
- Hung IF, To KKW, Lee CK, Lee KL, Yan WW, Chan K et al. Hyperimmune IV immunoglobulin treatment: a multicenter double-blind randomized controlled trial for patients with severe 2009 influenza A(H1N1) infection. *Chest*. 144(2):464-73.
- Kalil AC, Metersky ML, Klompas M, Muscedere J, Sweeney DA, Palmer LB et al. Management of adults with hospital-acquired pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *CID*. 2016;63(5):e61-111 (<https://www.thoracic.org/statements/resources/tb-opi/hap-vap-guidelines-2016.pdf>, accessed 25 July 2021).
- Kim WY, Suh Gy, Huh JW, Kim SH, Kim MJ, Kim YS et al. Triple-combination antiviral drug for pandemic H1N1 influenza virus infection in critically ill patients on mechanical ventilation. *Antimicrob Agents Chemother*. 2011;55(12):5703-9.
- Kiselev OI, Maleev VV, Deeva EG, Leneva IA, Selkova EP, Osipova EA et al. [Clinical efficacy of arbidol (umifenovir) in the therapy of influenza in adults: preliminary results of the multicenter double-blind randomized placebo-controlled study ARBITR.] *Ter Arkh*. 2015;87(1):88-96.
- P Koehler, M Bassetti, A Chakrabarti, SCA Chen, AL Colombo, M Hoeningl. Defining and managing COVID-19-associated pulmonary aspergillosis: the 2020 ECMM/ISHAM consensus criteria for research and clinical guidance. *Lancet Infect Dis*. 2021;21(6):e149-e162. doi: 10.1016/S1473-3099(20)30847-1.
- Laidler MR, Thomas A, Baumbach D, Kirley PD, Meek J, Aragon D et al. Statin treatment and mortality: propensity score-matched analyses of 2007-2008 and 2009-2010 laboratory-confirmed influenza hospitalizations. *Open Forum Infect Dis*. 2015;2(1):ofv028.
- Langford BJ, So M, Raybardhan S, MacFadden DR, Sourcy JPR, Daneman N et al. Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. *CMI*. 2020;26(12):P1622-1629 ([https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X\(20\)30423-7/fulltext](https://www.clinicalmicrobiologyandinfection.com/article/S1198-743X(20)30423-7/fulltext), accessed 25 July 2021).
- Lee N, Chan PKS, Wong CK, Wong KT, Choi KW, Joynt GM et al. Viral clearance and inflammatory response patterns in adults hospitalized for pandemic 2009 influenza A(H1N1) virus pneumonia. *Antivir Ther*. 2011;16(2):237-47.

- Lee N, Leo YS, Cao B, Chan PKS, Kyaw WM, Uyeki TM et al. Neuraminidase inhibitors, superinfection and corticosteroids affect survival of influenza patients. *Eur Respir J*. 2015;45(6):1642-52.
- Lim WS, Baudouin SV, George RC, Hill AT, Jamieson C, Le Jeune I et al. BTS guidelines for the management of community acquired pneumonia in adults: update 2009. *Thorax*. 2009;64:iii1-iii55 (https://thorax.bmj.com/content/64/Suppl_3/iii1, accessed 25 July 2021).
- Llor C, Bjerrum L. Antimicrobial resistance: risk associated with antibiotic overuse and initiatives to reduce the problem. *Ther Adv Drug Saf*. 2014;5(6):229-41. Epub 2014/12/02.
- Machado M, Valerio M, Alvarez-Uria A, Olmedo M, Veintimilla C, Padilla B et al. Invasive pulmonary aspergillosis in the COVID-19 era: an expected new entity. *Mycoses*. 2021;64(20):132-143.
- Mandell LA, Wunderink RG, Anzueto A, Bartlett JG, Campbell GD, Dean NC et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. *Clin Infect Dis*. 2007;44(2):S27-72.
- Marr K, Platt A, Tornheim JA, Zhang SX, Datta K, Cardozo C et al. Aspergillosis complicating severe coronavirus disease. *Emerg Infect Dis*. 2021;27(1):18-25.
- Miller PE, Rambachan A, Hubbard RJ, Li J, Meyer AE, Stephens P et al. Supply of neuraminidase inhibitors related to reduced influenza A (H1N1) mortality during the 2009-2010 H1N1 pandemic: an ecological study. *PLoS One*. 2012;7(9):e43491.
- Musuuzza JS, Watson L, Parmasad V, Putman-Buehler N, Christensen L, Safdar N. Prevalence and outcomes of co-infection and superinfection with SARS-CoV-2 and other pathogens: A systematic review and meta-analysis. *PLoS One*. 2021 May 6;16(5):e0251170. doi: 10.1371/journal.pone.0251170. eCollection 2021.
- Muthuri SG, Venkatesan S, Myles PR, Leonardi-Bee J, Al Khuwaitir TSA, Al Mamum A et al. Effectiveness of neuraminidase inhibitors in reducing mortality in patients admitted to hospital with influenza A H1N1pdm09 virus infection: a meta-analysis of individual participant data. *Lancet Respir Med*. 2014;2(5):395-404.
- NICE. Pneumonia in adults: diagnosis and management. Clinical guideline. London: National Institute for Health and Care Excellence; 2014 (<https://www.nice.org.uk/guidance/cg191>, accessed 25 July 2021).
- Patel A, Agarwal R, Rudramurthy SM, Shevkani M, Xess I, Sharma R. Multicenter epidemiologic study of coronavirus disease-associated mucormycosis, India. *Emerg Infect Dis*. 2021;27(9).
- Rawson TM, Moore LSP, Zhu N, Ranganathan N, Skolimowska K, Gilchrist M et al. Bacterial and fungal coinfection in individuals with coronavirus: a rapid review to support COVID-19 antimicrobial prescribing. *Clin Infect Dis*. 2020;71(9):2459-2468. Epub 2020/05/03.
- Rodrigo C, Leonardi-Bee J, Nguyen-Van-Tam JS, Lim WS. Effect of corticosteroid therapy on influenza-related mortality: a systematic review and meta-analysis. *J Infect Dis*. 2015;212(2):183-94.
- SM Rudramurthy, M Hoenigl, JF Meis, OA Cornely, V Muthu, JP Gangneux et al. ECMM and ISHAMECM/ISHAM recommendations for clinical management of COVID-19 associated mucormycosis in low- and middle-income countries. *Mycoses*. 2021;64(9):1028-1037.
- Salmanton-Garcia J, Sprute R, Stemler J, Bartoletti M, Dupont D, Valerio M et al. COVID-19-associated pulmonary aspergillosis, March-August 2020. *Emerg Infect Dis*. 2021;27(4):1077-1086.
- South East Asia Infectious Disease Clinical Research Network. Effect of double dose oseltamivir on clinical and virological outcomes in children and adults admitted to hospital with severe influenza: double blind randomised controlled trial. *BMJ*. 2013;346:f3039.
- Vaughn VM, Gandhi TN, Petty LA, Patel PK, Prescott HC, Malani AN et al. Empiric antibacterial therapy and community-onset bacterial coinfection in patients hospitalized with coronavirus disease 2019 (COVID-19): a multi-hospital cohort study. *Clin Infect Dis*. 2021;72(10):e533-e541 (<https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa1239/5895253>, accessed 25 July 2021).
- Wang MZ, Cai BQ, Li LY, Lin JT, Su N, Yu HX et al. [Efficacy and safety of arbidol in treatment of naturally acquired influenza]. *Zhongguo Yi Xue Ke Xue Yuan Xue Bao*. 2004;26(3):289-93.
- WHO. Clinical management of human infection with pandemic (H1N1) 2009: revised guidance. Geneva: World Health Organization; 2009.
- WHO. COVID-19 Clinical management: living guidance. Geneva: World Health Organization; 2021 (<https://www.who.int/publications/i/item/WHO-2019-nCoV-clinical-2021-1>, accessed 25 July 2021).
- WHO. Guidelines for pharmacologic management of pandemic influenza A (H1N1) 2009 and other influenza viruses. Revised February 2010. Geneva: World Health Organization; 2010.
- WHO. IMAI district clinician manual: hospital care for adolescents and adults. Volume 2. Geneva: World Health Organization; 2012 (<https://apps.who.int/iris/handle/10665/77751>, accessed 25 July 2021).
- WHO. Pocket book of hospital care for children (second edition). Geneva: World Health Organization; 2013.
- WHO. R&D Blueprint and COVID-19 [website]. Geneva: World Health Organization; 2020 (<https://www.who.int/teams/blueprint/covid-19>, accessed 25 July 2021).
- WHO. Therapeutics and COVID-19: living guideline. Geneva: World Health Organization; 2021 (<https://www.who.int/publications/i/item/WHO-2019-nCoV-therapeutics-2021.2>, accessed 25 July 2021).
- WHO. WHO Living guideline: drugs to prevent COVID-19. Geneva: World Health Organization; 2021 (<https://www.who.int/publications/i/item/WHO-2019-nCoV-prophylaxes-2021-1>, accessed 25 July 2021).
- Zhang Y, Sun W, Svendsen ER, Tang S, MacIntyre RC, Yang P et al. Do corticosteroids reduce the mortality of influenza A (H1N1) infection? A meta-analysis. *Crit Care*. 2015;19(1):46.



8

Sepsis and septic shock



8 Sepsis and septic shock

Summary

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

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

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

Markers of tissue perfusion in adults and children

Capillary refill < 2 sec

Absence of skin mottling

Strong peripheral pulses

Warm and dry extremities

Regular urine output

Normal mental status

Normalization of lactate

In children: improved heart rate
(*tachycardia is an early sign of septic shock and low blood pressure is a late finding*)

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

Tools

- 8.1 Sepsis and septic shock definitions
- 8.2 Sequential Organ Failure Assessment (SOFA) score
- 8.3 Quick Sequential Organ Failure Assessment (qSOFA)
- 8.4 Paediatric Logistic Organ Dysfunction (PELOD-2) score
- 8.5 Algorithm on targeted resuscitation in adults with septic shock
- 8.6 Algorithms on initial resuscitation, and on fluid and vasoactive-inotrope management for children with septic shock
 - 8.6.1 Initial resuscitation algorithm for children
 - 8.6.2 Fluid and vasoactive-inotrope management algorithm for children
- 8.7 Guide to the use of vasopressors in septic shock for adults and children
- 8.8 Five rules for passive leg raise (PLR)

8.1 Sepsis and septic shock definitions

For further information see: Surviving Sepsis Campaign (October 2021) ([link](#))



Sepsis adults

Life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection

Signs of organ dysfunction include:

Altered mental status

Difficulty or fast breathing

Low oxygen saturation

Reduced urinary output

Fast heart rate

Weak pulse

Cold extremities

Low blood pressure

Skin mottling

Laboratory evidence of:

- coagulopathy
- thrombocytopenia
- acidosis
- high lactate
- hyperbilirubinaemia



Sepsis children

Suspected or proven infection and \geq two age-based systemic inflammatory response syndrome (SIRS) criteria, of which one must be abnormal temperature or white blood cell count

SIRS criteria include:

Abnormal temperature $< 36\text{ }^{\circ}\text{C}$ or $> 38.5\text{ }^{\circ}\text{C}$

Heart rate $> 2\text{ SD}$ above normal for age or bradycardia if < 1 year of age

Respiratory rate $> 2\text{ SD}$ above normal for age

Abnormal white blood cell count or $> 10\%$ immature neutrophils



Septic shock adults

Sepsis with circulatory and cellular/metabolic abnormalities profound enough to substantially increase mortality

Criteria:

Persisting hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥ 65 mmHg

or

Serum lactate level > 2 mmol/L (18 mg/dL)



Septic shock children

Sepsis with circulatory and cellular/metabolic abnormalities profound enough to substantially increase mortality

Criteria: two or three of the following

Altered mental status

Tachycardia or bradycardia

HR < 90 bpm or > 160 bpm in infants and

HR < 70 bpm or > 150 bpm in children

Prolonged capillary refill (> 2 sec) or feeble pulse

Tachypnoea

Mottled or cool skin or petechial or purpuric rash

High lactate

Oliguria

Hyperthermia or hypothermia

or

Any hypotension (SBP < 5th centile or 2 SD below normal for age)



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

Shock is the presence of all three clinical criteria:

Delayed capillary refill \geq 3 sec

Cold extremities

Weak and fast pulse

or

Frank hypotension for age:

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

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



8.2 Sequential Organ Failure Assessment (SOFA) score

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

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

- respiratory (hypoxaemia defined by low PaO₂/FiO₂);
- coagulation (low platelets);
- liver (high bilirubin);
- cardiovascular (hypotension);
- central nervous system (low level of consciousness defined by Glasgow Coma Scale [GCS]);
- renal (low urine output or high creatinine).

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

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

Notes:

bpm - beats per minute; FiO₂ - fraction of inspired oxygen; MAP - mean arterial pressure; PaO₂ - partial pressure of oxygen; SBP - systolic blood pressure; SOFA - sequential organ failure assessment.

^a Values are with respiratory support.

^b To convert bilirubin from mg/dL to μmol/L, multiply by 17.1.

^c Adrenergic agents administered for at least 1 hour (doses given are in μg/kg per minute).

^d To convert creatinine from mg/dL to μmol/L, multiply by 88.4.

8.3 Quick Sequential Organ Failure Assessment (qSOFA)

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


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

For further information see the latest Surviving Sepsis Campaign guidelines (October 2021) ([link](#)).


Altered mental status
 (Glasgow coma scale [GCS] < 15, AVPU scale: alert, verbal, pain, unresponsive - not alert)

Respiratory rate (RR)
 ≥ 22 breaths per minute


Systolic blood pressure (SBP)
 ≤ 100 mmHg



ALTERED MENTAL
STATUS



FAST RESPIRATORY
RATE



LOW BLOOD
PRESSURE

qSOFA Calculator		
Is the patient in the ICU	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Altered mentation	<input type="checkbox"/> Yes	<input type="checkbox"/> No
Respiratory rate (breaths per minute)	<input style="width: 50px;" type="text"/>	(0 to 60)
Systolic blood pressure (mmHg)	<input style="width: 50px;" type="text"/>	(0 to 300)

Source: Adapted from www.qsofa.org



8.4 Paediatric Logistic Organ Dysfunction (PELOD-2) score

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

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

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

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

Notes:

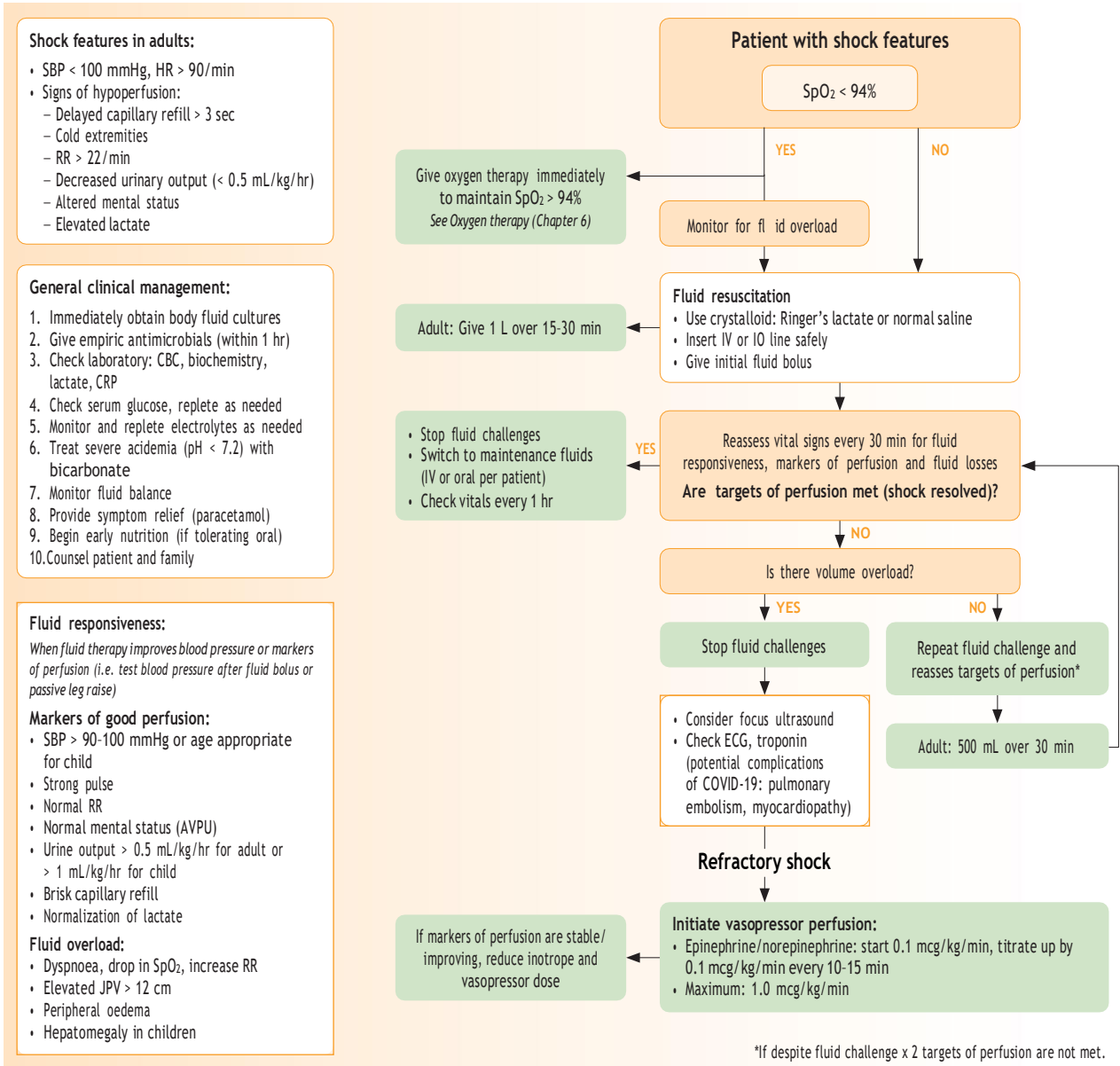
^a Neurologic dysfunction: Glasgow Coma Score: use the lowest value. If the patient is sedated, record the estimated Glasgow Coma Score before sedation. Assess only patients with known or suspected acute central nervous system disease. Pupillary reactions: nonreactive pupils must be > 3 mm. Do not assess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

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

^c Respiratory dysfunction: PaO₂ used: use arterial measurement only. PaO₂/FiO₂ ratio is considered normal in children with cyanotic heart disease. PaCO₂ can be measured from arterial, capillary or venous samples. Invasive ventilation; the use of mask ventilation is not considered invasive ventilation. FiO₂: fraction of inspired oxygen.



8.5 Algorithm on targeted resuscitation in adults with shock



Notes:

AVPU - alert, verbal, pain, unresponsive; HR - heart rate; JVP - jugular venous pressure; RR - respiratory rate; SBP - systolic blood pressure; SpO₂ - oxygen saturation.

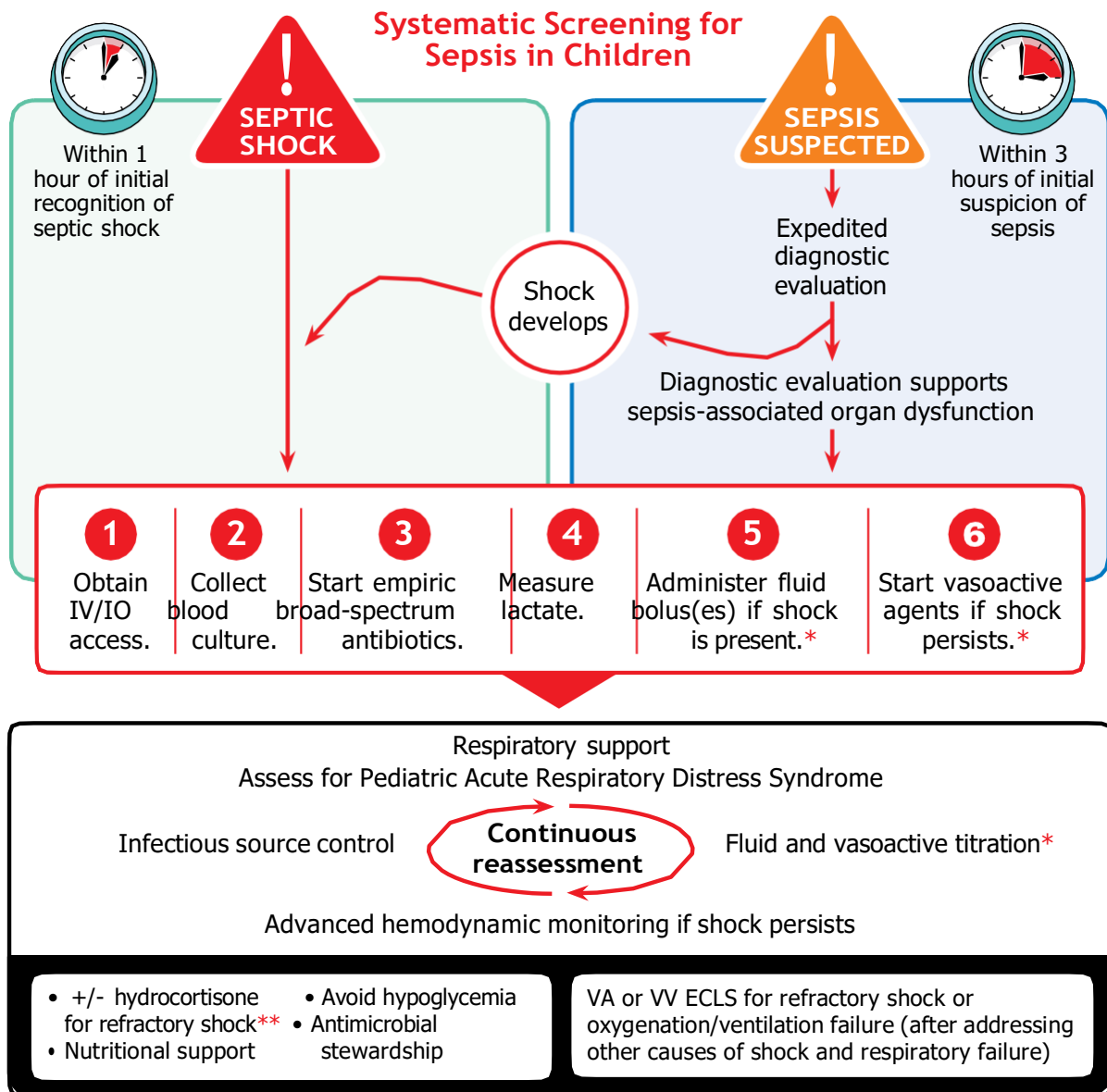
Source: Modified from *Optimized supportive care for Ebola virus disease (WHO, 2019)* ()



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

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

8.6.1 Initial resuscitation algorithm for children



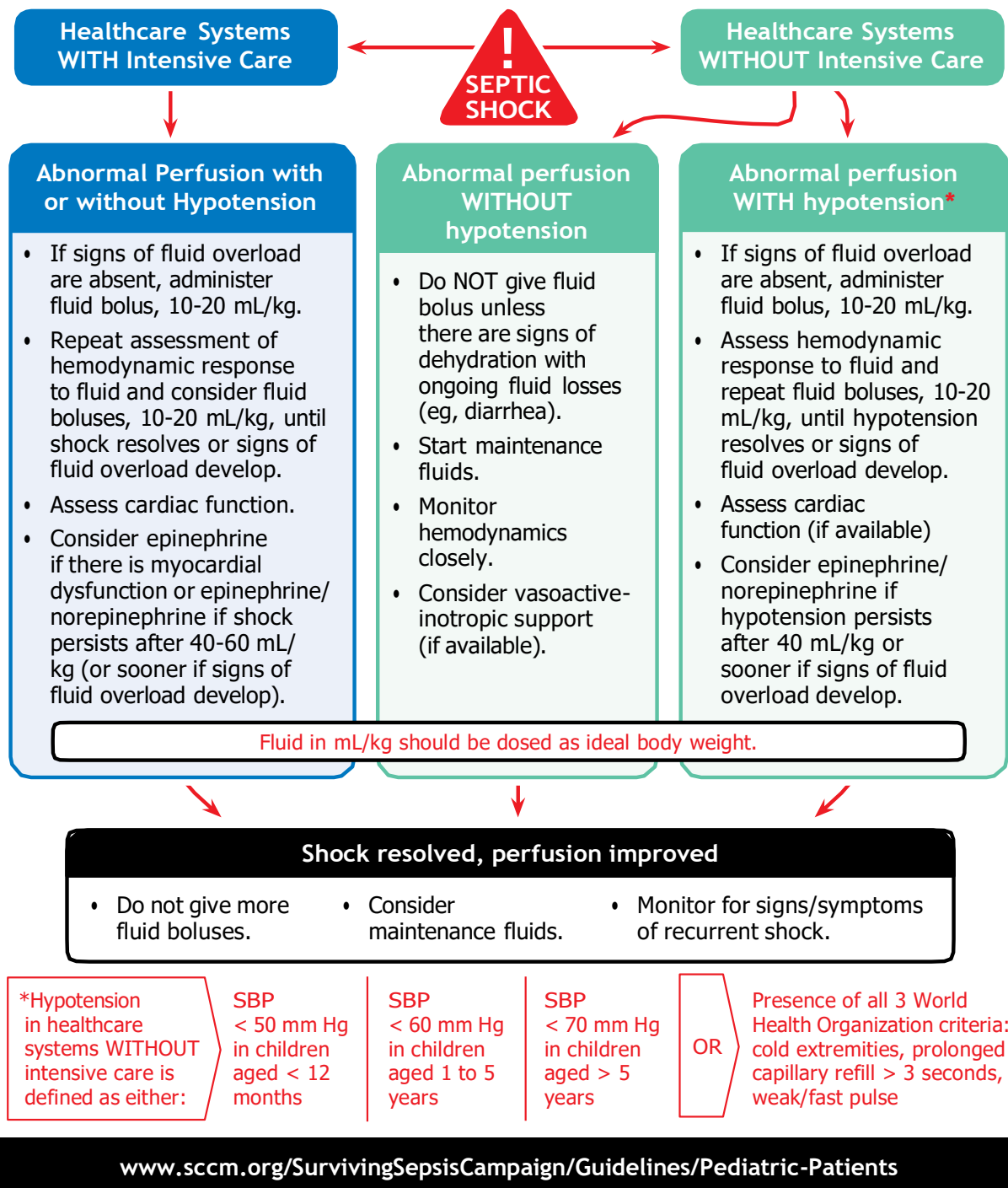
*See fluid and vasoactive algorithm. Note: Fluid bolus should be omitted from bundle if a) fluid overload is present or b) it is a low-resource setting without hypotension. Fluid in mL/kg should be dosed as ideal body weight.

**Hydrocortisone may produce benefit or harm.

Notes: ECLS - extracorporeal life support; VA - veno-arterial; VV - veno-venous.

Source: Surviving Sepsis Campaign paediatric patients ()

8.6.2 Fluid and vasoactive-inotrope management algorithm for children



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

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



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

Also, target other markers of perfusion such as:

Markers of tissue perfusion in adults and children

Capillary refill < 2 sec

Absence of skin mottling

Strong peripheral pulses

Warm and dry extremities

Regular urine output

Normal mental status

Normalization of lactate

In children: improved heart rate
(*tachycardia is an early sign of septic shock and low blood pressure is a late finding*)

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

Inotropes: dobutamine when there are persistent signs of hypoperfusion and clinical evidence of myocardial dysfunction (i.e. by ECHO, ScvO₂ < 70%) after adequate MAP and fluid status achieved.

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

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



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

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

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

Dosing of vasopressors in adults and children

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

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

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

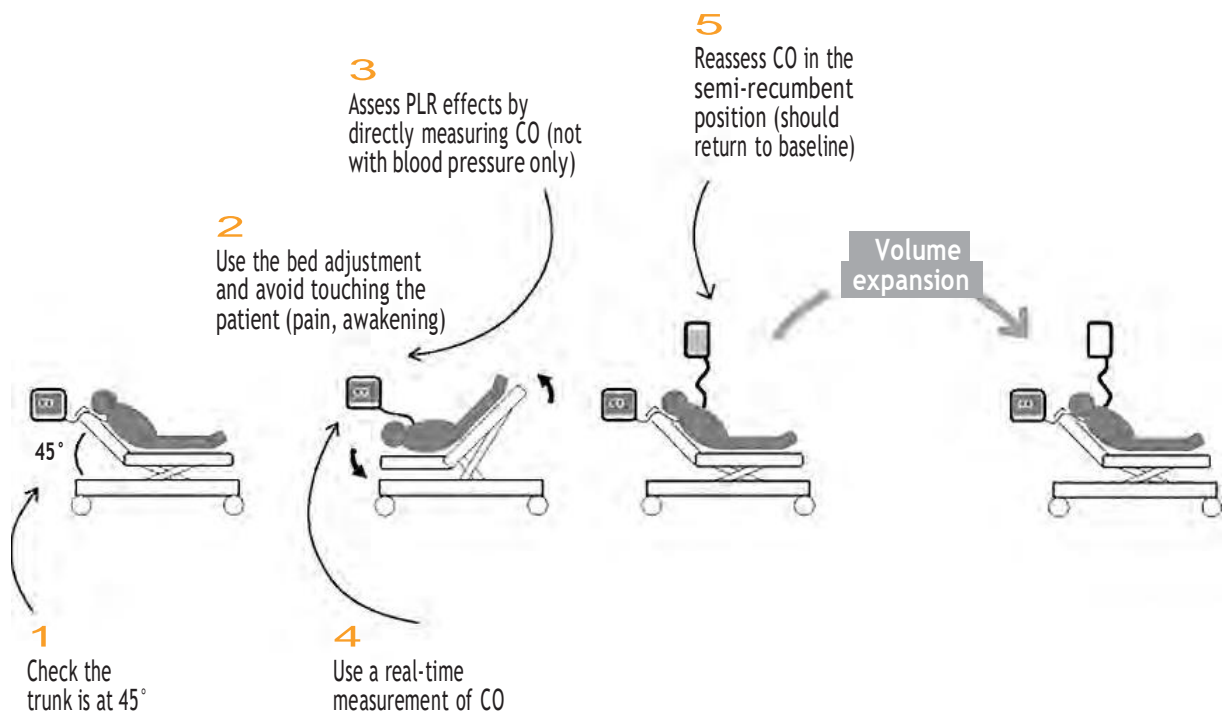
Side-effects of vasopressors and inotropes

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

8.8 The five rules for passive leg raise (PLR)

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

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



Notes: CO - cardiac output; PLR - passive leg raise.

Source: Monnet and Teboul (2015).

References and resources

- AnnaAnnane D, Bellissant E, Cavaillon JM. Septic shock. *Lancet*. 2005;365(9453):63-78.
- Annane D, Bellissant E, Bollaert PE, Briegel J, Keh D, Kupfer Y. Corticosteroids for treating sepsis. *Cochrane Database Syst Rev*. 2015;12: CD002243.
- Annane D, Vignon P, Renault A, Bollaert PE, Charpentier C, Martin C et al. Norepinephrine plus dobutamine versus epinephrine alone for management of septic shock: a randomised trial. *Lancet*. 2007;370(9588):276-684.
- The ARISE Investigators and the ANZICS Clinical Trials Group. Goal-directed resuscitation for patients with early septic shock. *N Engl J Med*. 2014;371:1496-1506.
- ASA. CPR and ECC guidelines. Part 12: Pediatric advanced life support. Dallas (TX): American Heart Association; 2018 (<https://eccguidelines.heart.org/index.php/circulation/cpr-ecc-guidelines-2/part-12-pediatric-advanced-life-support/>, accessed 1 July 2019).
- Brierley J, Carcillo JA, Choong K, Cornell T, Decaen A, Deymann A et al. Clinical practice parameters for haemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. *Crit Care*. 2009;37(2):666-88.
- Cecconi M, De Backer D, Antonelli M, Beale R, Bakker J, Hofer C et al. Consensus on circulatory shock and hemodynamic monitoring. Task Force of the European Society of Intensive Care Medicine. *Intensive Care Med*. 2014;40(12):1795-815.
- de Caen AR, Berg MD, Chameides L, Gooden CK, Hickey RW, Scott HF et al. Part 12: Pediatric advanced life support: 2015 American Heart Association Guidelines Update for Cardiopulmonary Resuscitation and Emergency Cardiovascular Care. *Circulation*. 2015;132(suppl 2):S526-S542.
- de Oliveira CF, De Oliveira DS, Gottschald AF, Moura JD, Costa GA, Ventura AC et al. ACCM/PALS haemodynamic support guidelines for paediatric shock: an outcomes comparison with and without monitoring central venous oxygen saturation. *Intensive Care Med*. 2008;34(6):1065-1075.
- Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM et al. Surviving Sepsis Campaign: guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med*. 2013;41(2):580-637.
- Fleischmann C, Scherag A, Adhikari NK, Hartog CS, Tsaganos T, Schlattmann P et al. Assessment of global incidence and mortality of hospital-treated sepsis. Current estimates and limitations. *Am J Respir Crit Care Med*. 2016;193(3):259-72.
- Grissom CK, Hirshberg EL, Dickerson JB, Brown SM, Lanspa MJ, Liu KD et al. Fluid management with a simplified conservative protocol for the acute respiratory distress syndrome. *Crit Care Med*. 2015;43(2):288-95.
- Holst LB, Haase N, Wetterslev J, Werneman J, Guttormsen AB, Karlsson S et al. Lower versus higher hemoglobin threshold for transfusion in septic shock. *N Engl J Med*. 2014;371(15):1381-1391.
- JAMA Network. Consensus definitions for sepsis and septic shock. 2021 (<https://sites.jamanetwork.com/sepsis/>, accessed 14 August 2021).
- Jones AE, Brown MD, Trzeciak S, Shapiro NI, Garrett JS, Heffner AC et al. The effect of a quantitative resuscitation strategy on mortality in patients with sepsis: a meta-analysis. *Crit Care Med*. 2008;36(10):2734-2739.
- Jones AE, Shapiro NI, Trzeciak S, Arnold RC, Claremont HA, Kline JA et al. Lactate clearance vs central venous oxygen saturation as goals of early sepsis therapy: a randomized clinical trial. *JAMA*. 2010;303(8):739-46.
- Kaukonen KM, Bailey M, Pilcher D, Cooper DJ, Bellomo R. Systemic inflammatory response syndrome criteria in defining severe sepsis. *N Engl J Med*. 2015;372(17):1629-38.
- Levy MM, Evans LE, Rhodes A. The Surviving Sepsis Campaign Bundle: 2018 update. *Crit Care Med*. 2018;46(6):997-1000.
- Magder S. Invasive intravascular hemodynamic monitoring: technical issues. *Crit Care Clin*. 2007;23(3):401-14.
- Maitland K, Kiguli S, Opoka RO, Engoru C, Olupot-Olupot P, Akech SO et al. Mortality after fluid bolus in African children with severe infection. *N Engl J Med*. 2011;364:2483-95.
- Marik J, Monnet X, Teboul JL. Hemodynamic parameters to guide fluid therapy. *Ann Intensive Care*. 2011;1:1.
- Monnet X, Teboul JL. Passive leg raising: five rules, not a drop of fluid! *Crit Care*. 2015;19(1):18.
- Myburgh JA, Finfer S, Bellomo R, Billot L, Cass A, Gattas D et al. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. *N Engl J Med*. 2012;367:1901-11.
- Perner A, Haase N, Guttormsen AB, Tenhunen J, Klemenzson G, Aneman A et al. Hydroxyethyl starch 130/0.42 versus Ringer's acetate in severe sepsis. *N Engl J Med*. 2012;367:124-34.
- ProCESS Investigators. A randomized trial of protocol-based care for early septic shock. *N Engl J Med*. 2014;370:1683-93.
- Rhodes A, Evans LE, Alhazzani W, Levy MM, Antonelli M, Ferrer R et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock: 2016. *Intensive Care Med*. 2017;43(3):304-377.
- Rivers E, Nguyen B, Havstad S, Ressler J, Muzzin A, Knoblich B et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med*. 2001;345(19):1368-77.
- Rudd KE, Johnson SC, Agesa KM, Shackelford KA, Tsoi D, Kievlan DR et al. Global, regional, and national sepsis incidence and mortality, 1990-2017: analysis for the Global Burden of Disease Study. *Lancet*. 2020;395(10219):P200-211 ([https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(19\)32989-7/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(19)32989-7/fulltext), accessed 18 March 2020).
- Russell JA. Management of sepsis. *N Engl J Med*. 2006;355(16):1699-1713.
- Seymour CW, Rosengart MR. Septic shock: advances in diagnosis and treatment. *JAMA*. 2015;314(7):708-17.

Siddiqui S, Razzak J. Early versus late pre-intensive care unit admission broad spectrum antibiotics for severe sepsis in adults. *Cochrane Database Syst Rev.* 2010;10:CD007081.

Singer M, Deutschman CS, Seymour CW. The Third International Consensus Definition for Sepsis and Septic Shock (Sepsis-3). *JAMA.* 2016;315(8):801-810 (<https://jamanetwork.com/journals/jama/fullarticle/2492881>, accessed 19 March 2020).

Surviving Sepsis Campaign (SSC). Guidelines on the management of critically ill adults with coronavirus disease 2019 (COVID-19). 2021 (<https://www.sccm.org/SurvivingSepsisCampaign/Guidelines/COVID-19>, accessed 14 August 2021).

Vasu TS, Cavallazzi R, Hirani A, Kaplan G, Leiby B, Marik PE. Norepinephrine or dopamine for septic shock: systematic review of randomized clinical trials. *J Intensive Care Med.* 2012;27(3):172-178.

Vincent JL, Marshall JC, Namendys-Silva SA, François B, Martin-Loeches I, Lipman J et al. Assessment of the worldwide burden of critical illness: the intensive care over nations (ICON) audit. *Lancet Respir Med.* 2014;2(5):380-6.

Weiss SL, Fitzgerald JC, Pappachan J, Wheeler D, Jaramillo-Bustamante JC, Salloo A et al. Global epidemiology of pediatric severe sepsis: the sepsis prevalence, outcomes, and therapies study. *Am J Respir Crit Care Med.* 2015;191(10):1147-57.

Weiss SL, Peters MJ, Waleed A, Agus MSD, Flori HR, Inwald DP et al. Surviving Sepsis Campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. *Pediatr Crit Care Med.* 2020;21(2):e52-e106 (https://journals.lww.com/pccmjournal/fulltext/2020/02000/surviving_sepsis_campaign_international_guidelines.20.aspx, accessed 18 March 2020).

WHO. Pocket book of hospital care for children (2nd edition). Geneva: World Health Organization; 2013.

WHO. Optimized supportive care for Ebola virus Disease. Geneva: World Health Organization; 2019.

WHO/ICRC. Basic emergency care (BEC): approach to the acutely ill and injured. Geneva: World Health Organization and International Committee of the Red Cross; 2018 (<https://www.who.int/publications/i/item/basic-emergency-care-approach-to-the-acutely-ill-and-injured>, accessed 14 August 2021).

Wills BA, Nguyen MD, Ha TL, Dong TH, Tran TN, Le TT et al. Comparison of three fluid solutions for resuscitation in dengue shock syndrome. *N Engl J Med.* 2005;353:877-89.



9

Acute respiratory distress syndrome (ARDS)



9 Acute respiratory distress syndrome (ARDS)

Summary

When to suspect ARDS

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

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

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

- low tidal volumes (TV) (target 6 mL/kg predicted body weight or less);
- low plateau airway pressure (Pplat) (target $P_{plat} \leq 30$ cmH₂O);
- moderate positive end-expiratory pressure (PEEP) (8-14 cmH₂O needed in most ARDS cases);
- driving pressure ($P_{plat}-PEEP$) ≤ 15 cmH₂O to titrate TV when $PEEP \geq 15$ *and* $P_{plat} \geq 30$.

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



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

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

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

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

Tools

- 9.1 Memory aid: diagnosis and classification of ARDS in adults
- 9.2 Memory aid: diagnosis and classification of pARDS in children
- 9.3 Advanced non-invasive mechanical ventilation in ARDS: algorithm to escalate supportive respiratory therapy
- 9.4 Checklist for rapid sequence intubation procedure in adults and children
- 9.5 Considerations for intubation and mechanical ventilation in children
- 9.6 List of commonly used medicines and dosage in ICU with ventilated patients (adults, children)
- 9.7 Choice of induction agent in adults
- 9.8 Choice of induction agent in children
- 9.9 Protocol to deliver lung protective ventilation (LPV)
 - 9.10.1 ARDS-net PEEP FiO₂ grid to guide PEEP
 - 9.10.2 Goals of Pplat and pH in lung protective ventilation
- 9.10 Memory aid: comparison of normal waveforms during volume and pressure-limited ventilation
- 9.11 Memory aid: recognizing and interpreting abnormal pressure and flow waveforms during volume control ventilation
- 9.12 Guide to distinguishing between causes of high peak airway pressures: resistance versus compliance
- 9.13 Troubleshooting high peak airway pressures, low tidal volumes, desaturation or haemodynamic instability in ventilated patients
- 9.14 Respiratory care pocket card reference
- 9.15 Adult ventilation order set (ARDS)
- 9.16 Checklist for proning in severe ARDS
- 9.17 Ventilation circuit types, filter and humidifier locations for SARI



9.1 Memory aid: diagnosis and classification of ARDS in adults

Berlin definition of acute respiratory distress syndrome (ARDS), 2012

ARDS Definition Task Force et al. (2012).

Timing	Within 1 week of a known clinical insult or new or worsening respiratory symptoms
Chest imaging^a	Bilateral opacities - not fully explained by effusions, lobar/lung collapse or nodules
Origin of oedema	Respiratory failure not fully explained by cardiac failure or fluid overload Need objective assessment (e.g. echocardiography) to exclude hydrostatic oedema if no risk factor present
Oxygenation^b	
Mild	$200 < PaO_2 / FiO_2 \leq 300$ with PEEP or CPAP ≥ 5 cm H ₂ O ^c
Moderate	$100 < PaO_2 / FiO_2 \leq 200$ with PEEP ≥ 5 cm H ₂ O
Severe	$PaO_2 / FiO_2 \leq 100$ with PEEP ≥ 5 cm H ₂ O

Notes:

^a Chest radiograph or computed tomography scan;

^b If altitude is higher than 1000 m, the correction factor should be calculated as follows: $[PaO_2 / FiO_2 \times (\text{barometric pressure} / 760)]$;

^c This may be delivered non-invasively in the mild ARDS group;

CPAP - continuous positive airway pressure; FiO₂ - fraction of inspired oxygen; PaO₂ - partial pressure arterial oxygen; PEEP - positive end-expiratory pressure.

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

Kigali modifications of Berlin definition, 2016

Riviello et al. (2016).

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



9.2 Memory aid: diagnosis and classification of pARDS in children

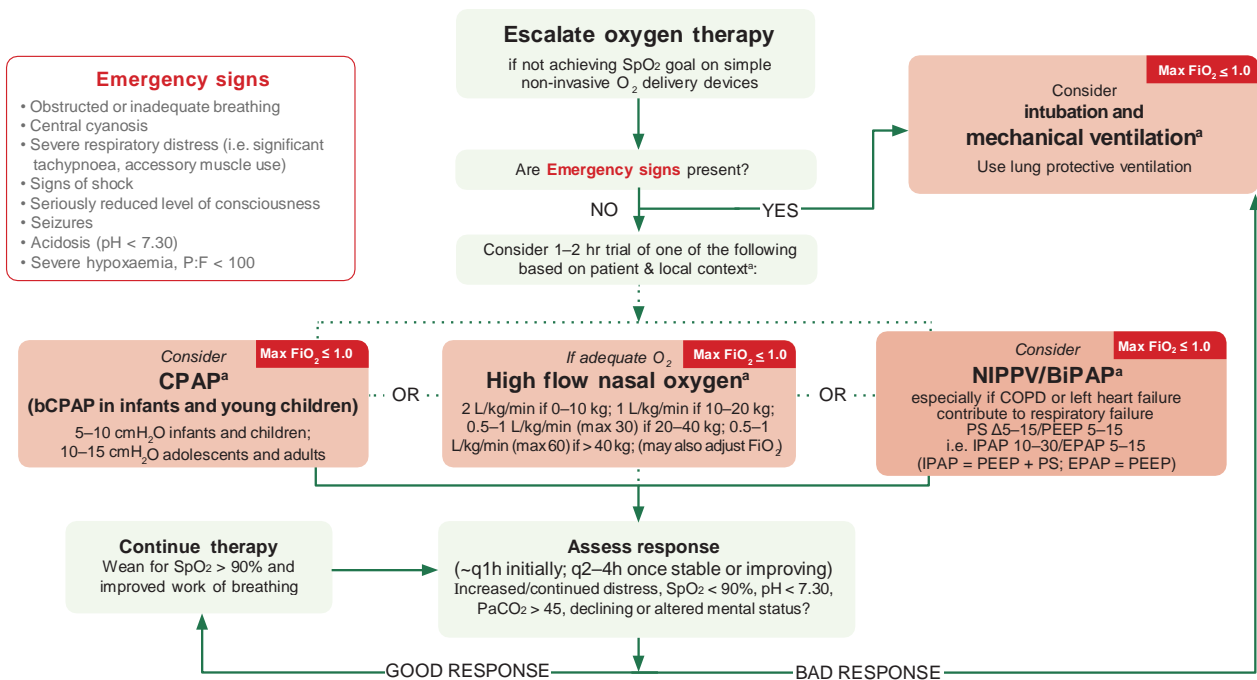
Paediatric acute respiratory distress syndrome (pARDS) definition

Pediatric Acute Lung Injury Consensus Conference Group (2015).

Age	Exclude patients with perinatal related lung disease			
Timing	Within 7 days of known clinical insult			
Origin of oedema	Respiratory failure not fully explained by cardiac failure or fluid overload			
Chest imaging	Chest imaging findings of new infiltrates(s) consistent with acute pulmonary parenchymal disease			
Oxygenation	Non-invasive mechanical ventilation	Invasive mechanical ventilation		
	pARDS (no severity stratification)	Mild	Moderate	Severe
	Full face mask bilevel ventilation of CPAP ≥ 5 cm H ₂ O	$4 \leq \text{OI} < 8$	$8 \leq \text{OI} < 16$	$\text{OI} \geq 16$
	PF ratio ≤ 300 , SF ratio ≤ 264	$5 \leq \text{OSI} < 7.5$	$7.5 \leq \text{OSI} < 12.3$	$\text{OSI} \geq 12.3$

Notes: CPAP - continuous positive airway pressure; OI - Oxygenation Index ($[\text{FiO}_2 \times \text{mean airway pressure} \times 100] / \text{PaO}_2$); OSI - oxygen saturation index ($[\text{FiO}_2 \times \text{mean airway pressure} \times 100] / \text{SpO}_2$); PF ratio - $\text{PaO}_2 / \text{FiO}_2$ ratio; SF ratio - $\text{SpO}_2 / \text{FiO}_2$ ratio.

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



^a Selection of optimal delivery device should be based on local clinician's judgment and risk-benefit assessment tailored to the individual patient, global and local outcomes data, as well as local resources including O₂ supply, skill of personnel, availability of consumables, monitoring and therapeutic adjuncts, among other factors.

^b Venturi/entrainment face masks deliver FiO₂ 24–60%, depending on flow rate and device setup

LPM (litres per minute), EPAP (expiratory positive airway pressure), PS (pressure support), COPD (chronic obstructive pulmonary disease), SpO₂ (oxygen saturation), PaCO₂ (arterial partial pressure of carbon dioxide), P:F (ratio between arterial partial pressure of oxygen and the fraction of inspired oxygen - FiO₂), CPAP (continuous positive airway pressure), bCPAP (bubble CPAP), NIPPV (non-invasive positive pressure ventilation), BiPAP (bi-level positive airway pressure); Δ - change.



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

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

✓ Predictive factors of success with non-invasive ventilation

- Absence of multiorgan failure
- Younger age
- Initial PaO₂/FiO₂ > 150 mmHg

✓ Early signs of success with non-invasive ventilation

- Improved oxygenation
- Decreased respiratory rate
- Stable PaO₂/FiO₂ > 150 mmHg

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



9.4 Checklist for rapid sequence intubation procedure in adults and children



- This tool can be used before performing endotracheal intubation. Intubation and IMV can be indicated, for adults and children, in case of hypoxaemia refractory to supplemental oxygen, depressed level of consciousness (AVPU) and severe shock.

1. Appropriate infection prevention precautions

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

2. Equipment needed

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

3. Drugs needed

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

4. Team role description

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

Note: See Gelb et al., 2018.

Rapid sequence intubation (RSI)

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

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

Technique: Quicker form of the process normally used to “induce” a state of general anaesthesia.

It uses drugs to rapidly allow an ETT to be placed between the vocal cords, by blocking the patient’s involuntary reflexes and muscle tone in the oropharynx and larynx. Once the ETT has been passed between the vocal cords, a cuff is inflated around the tube in the trachea and the patient can then be artificially ventilated. Correct ETT position can be verified by direct visualization through the vocal cords; capnography (persistent CO₂ return; may show CO₂ transiently if in esophagus); high SpO₂, bilateral breath sounds on chest auscultation; and correct position on X-ray.

5. Protocol

Pre-oxygenate for 5 minutes with 100% FiO₂

Ideally this is done with a device capable of reliably delivering 100% FiO₂ (HNFO, CPAP or BiPAP).

Note: Children, infants and obese patients have reduced functional residual capacity; they can desaturate quickly on induction.

Note: If the mask’s seal is broken, or for example the mask is removed so that the patient can speak clearly, the process must start again for an additional 5 minutes.

Anticipate shock

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

Anticipate instability and consider use ketamine for induction if available.

Anticipate instability by pre-loading with volume (10-20 mL/kg 0.9% isotonic crystalloid) and/or starting/increasing inotropic support.

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

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

Confirm correct ETT placement with end-tidal CO₂ as the gold standard. When end-tidal CO₂ measurement is not available, several additional signs and techniques are frequently used to assess endotracheal tube placement, including:

- direct visualization of cords
- improving SpO₂
- bilateral equal air on auscultation
- condensation in the endotracheal with exhalation
- external palpation of the endotracheal tube balloon in the trachea
- ultrasound of the endotracheal tube in the trachea
- chest X-ray position of ETT tip 1-2 cm above the carina (in adults), or T3 posterior.



9.5 Considerations for intubation and mechanical ventilation in children

Specifications for children

Decompress the stomach to prevent diaphragmatic splinting:

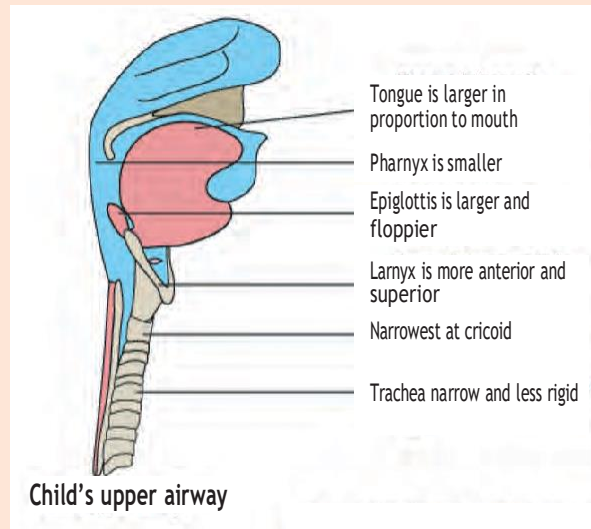
- use airway adjuncts to reduce stomach inflation;
- in bag-mask ventilation, place NG tube early and regularly aspirate with large bore syringe to decompress stomach.

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

Anatomical differences between children and adults

Anatomical differences between children and adults can make ventilation more difficult.

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



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

Choice of endotracheal tubes size for paediatric patients

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

Normal physiologic parameters and equipment

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

Neonatal and paediatric general estimates

Neonatal "1-2-3(kg)/7-8-9 (ETT@Lips) rule"

For preterm and term newborns: MAP equals the number of weeks post conceptual age (PCA)

By day of life 5, MAP = number of weeks PCA + 5

ETT size: (Age/4) + 4, or 5th finger size

ETT depth: [(height in cm)/10] + 5 or 3 × ETT size

Age +11 cm at lip

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

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

INDUCTION AGENT

NEUROMUSCULAR BLOCKING AGENT

SEDATIVE/HYPNOTIC

CARDIOVASCULAR SUPPORT AGENT

ANALGESIC

Medications

ACETAMINOPHEN	See Paracetamol
ADENOSINE	<i>Adult:</i> 6 mg IV push; then 12 mg IV q1min × 2 prn <i>Peds:</i> 0.1 mg/kg IV push (max 6 mg/dose), may repeat 0.2 mg/kg IV (max 12 mg/dose)
ADRENALINE (EPINEPHRINE)	<i>Adult:</i> Arrest: 1 mg q3-5min IV prn; ETT 2-2.5 mg q3-5min prn (dilute in 5-10 mL NS or sterile water) Anaphylaxis/hypotension: 0.05-0.1 mg IV q5min prn; 0.2-0.5 mg IM q5min prn; Infusion: 0.5-20 mcg/min IV Racemic 2.25% solut 0.5 mL via neb <i>Peds:</i> Arrest: 10 mcg/kg IV (max 1 mg) q3-5min prn; 100 mcg/kg ETT q3-5 min prn Anaphylaxis: Children > 6 mo < 30 kg: 10 mcg/kg IM; > 30 kg 300 mcg IM Severe Hypotension: 0.5-10 mcg/kg IV Infusion: 0.02-1 mcg/kg/min IV Racemic 2.25% solut 0.25-0.5 mL via neb
ALBUTEROL	<i>Adult & Peds:</i> (bronchodilation) Nebulized: 2.5 mg in 3 mL every 20 min or continuous (5-20 mg/hr)
AMIODARONE	<i>Adult:</i> 150-300 mg IV (dependent on rhythm) then 1 mg/min × 6hr, then 0.5 mg/min x18hr <i>Peds:</i> 5 mg/kg IV (max 300 mg) over 30 min, may repeat × 2; Infusion: 5-15 mcg/kg/min IV
ATRACURIUM	<i>Adult & Peds:</i> 0.4-0.5 mg/kg IV (t _{1/2} = ~20 min)
ATROPINE	<i>Adult:</i> Arrest/bradycardia: 0.5 mg IV q3-5min max 3 mg; ETT 1-2 mg q3-5min prn <i>Peds:</i> Arrest/brady: 0.02 mg/kg (max 0.5 mg) IV, repeat × 1 q5min prn; ETT 0.04-0.06 mg/kg; repeat × 1 prn
CALCIUM CHLORIDE	<i>Adult:</i> Arrest, CCB toxicity: 1-2 gm IV slowly; repeat q10min prn <i>Peds:</i> Arrest, CCB toxicity: 20 mg/kg IV (max 2 g); repeat q10min prn
CARBOPROST (HEMABATE)	<i>Adult:</i> 250 mcg IM, repeat q15min prn. Max 2 mg (see PPH for full details)
CISATRACURIUM	<i>Adult:</i> 0.1-0.2 mg/kg IV (t _{1/2} = ~ 25 min); Infusion 0.5-10 mcg/kg/min IV <i>Peds:</i> 0.1-0.15 mg/kg IV; Infusion 0.5-4 mcg/kg/min IV
CODEINE	<i>Adult:</i> 15-60 mg PO/IM/SQ; repeat q4h prn <i>Peds:</i> not recommended in children < 12 yr
DANTROLENE	<i>Adult & Peds:</i> 2.5 mg/kg IV, repeat 1 mg/kg prn (max of 10 mg/kg)
DEXMEDETOMIDINE	<i>Adult & Peds:</i> Load: 0.5-1 mcg/kg IV (over 10 min), Infusion: 0.2-1.5 mcg/kg/hr IV
DEXAMETHASONE	<i>Adult & Peds:</i> Airway oedema: 0.5 mg/kg IV q6hr PONV: Adults 4-8 mg IV; Peds 0.1 mg/kg IV
DIAZEPAM	<i>Adult:</i> 5-10 mg IV <i>Peds:</i> 0.2-0.3 mg/kg IV

DICLOFENAC	<i>Adult:</i> 50-100 mg PO <i>Peds:</i> 0.5 mg/kg IV/IM; 1 mg/kg PO/PR
DIPHENHYDRAMINE	<i>Adult:</i> 25-50 mg IV/IM/PO q4-6hr <i>Peds:</i> 0.5-1 mg/kg IV q4-6 hours; max 50 mg
DOBUTAMINE	<i>Adult & Peds:</i> 0.5-20 mcg/kg/min IV infusion
DOPAMINE	<i>Adult & Peds:</i> 0.5-20 mcg/kg/min IV infusion
EPINEPHRINE	See Adrenaline
EPHEDRINE	<i>Adult:</i> 5-10 mg IV prn <i>Peds:</i> 0.1-0.2 mg/kg (max 25 g/dose) IV prn
ERGOMETRINE	<i>Adult:</i> 0.5 mg IV/IM slow
ESMOLOL	<i>Adult & Peds:</i> Bolus: 0.5 mg/kg IV prn; Infusion: 50-300 mcg/kg/min IV
ETOMIDATE	<i>Adult & Peds:</i> 0.2-0.3 mg/kg IV
FENTANYL	<i>Adult:</i> Analgesia: 25-100 mcg IV prn; Infusion 25-200 mcg/hr (or higher) <i>Peds:</i> Analgesia: 0.5-1 mcg/kg IV prn; 1-2 mcg/kg intranasal prn; Infusion: 0.5-5 mcg/kg/hr IV
GLYCOPYRROLATE	<i>Adult:</i> Reversal: 0.1-0.2 mg IV <i>Peds:</i> Reversal: 0.015 mg/kg IV; Antisialagogue: 4 mcg/kg IM
HYDRALAZINE	<i>Adult:</i> 10-20 mg IV <i>Peds:</i> 0.1-0.2 mg/kg IV
HYDROCODONE	<i>Adult:</i> 20-40 mg PO <i>Peds:</i> 0.2 mg/kg PO
HYDROCORTISONE	<i>Adult:</i> 100 mg IV; stress dose 50 mg IV q6hr <i>Peds:</i> (stress dose) 1-2 mg/kg IV
HYDROMORPHONE	<i>Adult:</i> 0.5-2 mg IV prn <i>Peds:</i> IV: 5-10 mcg/kg IV prn PO/PR: 50-80 mcg/kg q3-6h prn
INTRALIPID	<i>Adult & Peds:</i> LAST: 1.5 mL/kg followed by infusion 0.25 mL/kg/min up to 0.5 mL/kg/min ; use ideal body weight; 12 mL/kg in peds
KETAMINE	<i>Adult:</i> Induction: 0.5-2 mg/kg IV, 4-10 mg/kg IM; Analgesia: 0.2-0.8 mg/kg IV, 2-4 mg/kg IM; Infusion 2-15 mcg/kg/min IV <i>Peds:</i> Induction: 1-3 mg/kg IV, 5-8 mg/kg IM, 5-10 mg/kg PR; Analgesia: 0.2-0.5 mg/kg IV, 2-4 mg/kg IM; Infusion: 2-10 mcg/kg/min IV
KETOROLAC	<i>Adult:</i> 30-60 mg IV/IM, then 15-30 mg IV/IM q6h prn <i>Peds:</i> 0.5 mg/kg (max 30 mg) IV q6h prn; 1 mg/kg IM
LABETALOL	<i>Adult:</i> 10-20 mg IV, double dose q15min prn to max 300 mg; Infusion 0.5-2 mg/min (or higher) <i>Peds:</i> 0.1 mg/kg IV q5-10min
LIDOCAINE	<i>Adult:</i> Arrest: 1-1.5 mg/kg IV, 0.5-0.75 mg/kg q5-10min prn (max 3 mg/kg), ETT 2-3.75 mg/kg, infusion 1-4 mg/min; analgesia: 1-2 mg/kg IV, infusion: 0.5-3 mg/kg/hr IV <i>Peds:</i> Arrest: 1 mg/kg IV, repeat x1 prn, ETT 2-3 mg/kg infusion 20-50 mcg/kg/min IV; Analgesia: 1 mg/kg IV; infusion: 1.5-2 mg/kg/hr IV
LORAZEPAM	<i>Adult:</i> 1-4 mg IV prn <i>Peds:</i> 0.1 mg/kg IV prn (max 4 mg/dose)

MAGNESIUM SULFATE	<i>Adult:</i> Asthma: 2 gm IV over 20 min; eclampsia/pre-eclampsia: load 4-6 gm IV, infusion 1-2 gm/hr IV; torsade de pointes: 1-2 gm IV, infusion 0.5-1 gm/hr IV <i>Peds:</i> Asthma: 25-75 mg/kg (max 2 gm) IV over 20 min; torsade de pointes: 25-50 mg/kg/dose (max 2 gm) IV
MEPERIDINE	See Pethidine
METARAMINOL	<i>Adult & Peds:</i> 0.5 mg IV bolus, repeat q2-3min prn (avoid in children < 12)
METHADONE	<i>Adult:</i> Analgesia: 2.5-10 mg PO/IM/IV/SQ (based on opioid tolerance), repeat q8-12h prn <i>Peds:</i> Analgesia: 0.05-0.1 mg/kg PO/IM/IV/SQ; (t _{1/2} = 18-24 hrs)
METHOHEXITAL	<i>Adult:</i> Induction: 1-1.5 mg/kg IV <i>Peds:</i> Induction: 1-3 mg/kg IV, 20-30 mg/kg PR
METHYLER-GONOVINE/ METHERGINE	<i>Adult:</i> 0.2 mg IM; repeat q5-10min max 2 doses
METHYLPREDNISOLONE	<i>Adult:</i> Asthma: 40-80 mg IV; anaphylaxis: 125 mg IV <i>Peds:</i> Asthma: 1 mg/kg IV; anaphylaxis: 1-2 mg/kg IV
METOCLOPRAMIDE	<i>Adult:</i> 10-20 mg IV/PO, repeat 5-10 mg q6h prn <i>Peds:</i> 0.1-0.15 mg/kg IV/PO q6h prn
MIDAZOLAM	<i>Adult:</i> 0.5-4 mg IV <i>Peds:</i> 0.1-0.2 mg/kg IV, 0.5 mg/kg PO/PR
MISOPROSTOL	<i>Adult:</i> 1 mg PR
MORPHINE SULFATE	<i>Adult:</i> 2.5-10 mg IV/IM <i>Peds:</i> 0.05-0.1 mg/kg IV/IM
NALOXONE	<i>Adult:</i> Excessive sedation: 0.02-0.2 mg q4-8; opioid overdose: 0.1-2 mg IV/IM q2-3min prn, 2 mg nebulized, 4 mg intranasal <i>Peds:</i> Excessive sedation: 0.5-1 mcg/kg IV q2-3min prn; opioid overdose: 10 mcg/kg IV/IM q2-3min prn; 4 mg intranasal
NEOSTIGMINE	<i>Adult & Peds:</i> 0.03-0.07 mg/kg IV (max 5 mg) Add atropine IV 0.5-1 mg (adults), 20 mcg/kg (peds) or glycopyrrolate (see “glycopyrrolate”)
NITROGLYCERIN	<i>Adult:</i> Infusion: 10-200 mcg/min IV <i>Peds:</i> 0.5-20 mcg/kg/min IV infusion IV
NOREPINEPHRINE	<i>Adult:</i> Infusion: 0.05-2 mcg/kg/min or 0.5-20 mcg/min IV <i>Peds:</i> Infusion: 0.05-2 mcg/kg/min IV
ONDANSETRON	<i>Adult:</i> 4-8 mg IV, repeat q4-8h prn <i>Peds:</i> 0.15 mg/kg IV; repeat q6-8h prn
OXYCODONE	<i>Adult:</i> 5-15 mg (or higher depending on opioid tolerance), repeat q3-4h prn <i>Peds:</i> 0.1 mg/kg PO; repeat q3-4h prn
OXYTOCIN (PITOCIN)	<i>Adult:</i> 3 U stat IV over 30 sec, consider repeat dosing and infusion
PANCURONIUM	<i>Adult:</i> 0.04-0.1 mg/kg IV <i>Peds:</i> 0.05-0.15 mg/kg IV (t _{1/2} = ~110 min)
PARACETAMOL (ACETAMINOPHEN)	<i>Adult:</i> 500-1000 mg IV/PO, repeat q4-6 prn (max 2-4 gm/day) <i>Peds:</i> PO/IV: 10-15 mg/kg, repeat q6h prn, PR: 40 mg/kg × 1, max: 75 mg/kg/24 hr
PETHIDINE (MEPERIDINE)	<i>Adult:</i> Shivering/analgesia: 12.5-50 mg IV <i>Peds:</i> 0.5-1 mg/kg IV, max 400 mg daily
PHENOBARBITAL/ PHENOBARBITONE	<i>Adult & Peds:</i> Status epilepticus: 15-20 mg/kg IV, may repeat 5-10 mg/kg in 10 min prn x 1

PHENYLEPHRINE	<i>Adult:</i> 40-100 mcg IV q1-2min prn; infusion 10-200 mcg/min
PITOCIN	See Oxytocin
PROCHLORPERAZINE	<i>Adult:</i> 5-10 mg IV/IM/PO q3-6h prn (max 40 mg/day) <i>Peds:</i> 0.1-0.15 mg/kg PO/IM/IV q6-8h prn (max 10 mg/dose)
PROMETHAZINE	<i>Adult:</i> 12.5-25 mg PO/PR q4-6h prn <i>Peds:</i> 0.2-0.5 mg/kg PO/PR q6-8h Max 25 mg/dose (do not give if < 2 yr)
PROPOFOL	Induction: Dose variable, Adults: 1-2.5 mg/kg; Children 2-4 mg/kg Infusion: 10-250 mcg/kg/min
RANITIDINE	<i>Adult:</i> 50 mg IV; 150-300 mg PO <i>Peds:</i> 1 mg/kg IV; 2.5 mg/kg PO
REMIFENTANIL	<i>Adult & Peds:</i> Bolus: 0.5-1 mcg/kg IV; Infusion: 0.05-0.5 mcg/kg/min IV
ROCURONIUM	<i>Adult:</i> 0.6-1.2 mg/kg IV (t _{1/2} = ~60 min) <i>Peds:</i> 0.9-1.2 mg/kg IV
SCOPOLAMINE	<i>Adult & Adolescents:</i> 1 patch q72h <i>Peds:</i> 6 mcg/kg IV (max 0.3 mg)
SODIUM CITRATE (Bicitra)	<i>Adult:</i> 15-30 mL PO q6h prn <i>Peds</i> ≥ 2 yr: 1-1.5 mL/kg q6-8h prn (max 30 mL/dose)
SODIUM BICARBONATE	<i>Adult:</i> 50-100 mEq IV prn (1 “amp” of 50 mL 8.4% = 50 mEq) <i>Peds:</i> 1-2 mEq/kg IV
SUCCINYLCHOLINE/ SUXAMETHONIUM	<i>Adult:</i> (induction) 0.6-2 mg/kg IV (high end for RSI) IM: 3-4 mg/kg; max 5 mL at injection site (t _{1/2} = ~6-8 min) <i>Peds:</i> 1-2 mg/kg IV; 3-4 mg/kg IM
SUFENTANIL	<i>Adult:</i> Analgesia: 0.5-2 mcg/kg IV Infusion: 0.05-2 mcg/kg/hr
SUGAMMADEX	<i>Adult:</i> 2 TOF twitches: 2 mg/kg; 0 TOF, 1-2 PTC: 4 mg/kg; Immediate emergent reversal: 16 mg/kg
TERBUTALINE	<i>Adult:</i> (tocolysis) 5-10 mcg/kg IV q15min (max 250 mcg)
THIOPENTAL/ THIOPENTONE	<i>Adult:</i> (induction) 3-6 mg/kg
TRAMADOL	<i>Adult:</i> 25-100 mg PO q4-6h prn <i>Peds:</i> not recommended in children < 12 yr
TRANEXAMIC ACID	<i>Adult:</i> 1 g IV over 10 min, repeat × 1 after 30 min prn
VASOPRESSIN	<i>Adult:</i> (shock) 0.03-0.05 units/minute drip <i>Peds:</i> (shock) Infusion: 0.0002-0.002 units/kg/min IV
VECURIONIUM	<i>Adult & Peds:</i> (induction) 0.1 mg/kg IV (t _{1/2} = ~65 min) 0.8- 1.7 mcg/kg/min drip

Notes: CCB - calcium channel blocker; ETT- endotracheal tube; IV- intravenous; IM - intramuscular; min - minute; PO - per os/oral; PONV - post-operative nausea and vomiting; PR - per rectal; prn - pro re nata; PTC - post-tetanic count; SQ - subcutaneous; TOF - train of four.

Source: Adapted from USAID-STAR-UCSF Project ()



9.7 Choice of induction agents in adults

Choice of induction agents in adult patients

		Intravenous dose	Notes
Opiates	Fentanyl	50-250 mcg	Can cause ↓ blood pressure May cause chest stiffness
	Morphine	2.5-10 mg	Takes long time to be effective ~10 mins
Sedative/hypnotic	Midazolam	0.5-4 mg	Can cause delirium Accumulates in liver failure
	Lorazepam	1-4 mg	Can cause delirium Accumulates in liver failure
	Diazepam	5-10 mg	Can cause delirium Accumulates in renal failure
Induction agent	Ketamine	0.5-2 mg/kg	Can cause ↑ intracranial pressure
	Etomidate	0.2-0.3 mg/kg	Can cause adrenal suppression with multiple doses
	Propofol 1%	1-2.5 mg/kg ^a	Can cause ↓ blood pressure
	Thiopental	3-6 mg/kg	
Neuromuscular blockers	Suxamethonium	0.6-2 mg/kg	Avoid if hyperkalaemia, neuromuscular patients, recent burn or renal failure
	Rocuronium	0.6-1.2 mg/kg	First-line RSI paralytic
	Vecuronium	0.1 mg/kg	
	Atracurium	0.4-0.5 mg/kg	
	Pancuronium	0.04-0.1 mg/kg	Prolonged block if renal failure

Note:

^a Consider dose reduction for critically ill patients or selecting alternate agents if haemodynamically unstable.



9.8 Choice of induction agents in children

Choice of induction agents in paediatric patients

		Intravenous dose	Notes
Opiates	Atropine	20 mcg/kg (min. dose 100 mcg); > 12 years 300-600 mcg	
	Fentanyl	2-5 mcg/kg	Can cause ↓ blood pressure
	Morphine	0.1-0.2 mg/kg	Relatively prolonged onset: ~10 mins
Sedative/hypnotic	Midazolam	0.1-0.2 mg/kg	Can cause delirium Accumulates in liver failure
	Lorazepam	0.1 mg/kg	Can cause delirium Accumulates in liver failure
	Diazepam	0.2-0.3 mg/kg	Can cause delirium Accumulates in renal failure
Induction agent	Ketamine	1-3 mg/kg	Can cause ↑ intracranial pressure
	Etomidate	0.2-0.3 mg/kg	Can cause adrenal suppression with multiple doses
	Propofol 1% (induction only)	2-4 mg/kg ^a (> 3 years)	Can cause ↓ blood pressure
Neuromuscular blockers	Suxamethonium	3 mg/kg/dose (neonate); 1-2 mg/kg all other ages	Avoid if hyperkalaemia, neuromuscular patients, recent burn or renal failure
	Rocuronium	0.9-1.2 mg/kg	First-line RSI paralytic
	Vecuronium	0.1 mg/kg	
	Atracurium	0.4-0.5 mg/kg	
	Pancuronium	0.05-0.15 mg/kg	Vastly prolonged block in renal failure

Note:

^a Consider dose reduction for critically ill patients or selecting alternate agents if haemodynamically unstable.

9.9 Protocol to deliver lung protective ventilation (LPV)

This protocol to deliver lung protective ventilation (LPV) was used in the low tidal volume (TV) trial published in 2000 (ARDS Network et al., 2000).

Ventilator set up and adjustment

- Calculate predicted body weight (PBW):
Males = $50 + 1.1 [\text{height (cm)} - 152]$
Females = $45.5 + 1.1 [\text{height (cm)} - 152]$.
- Select any ventilator mode.
- Set ventilator settings to achieve initial tidal volume (TV) = 6 mL/kg PBW (range 4-8 mL/kg).
- Reduce TV by 1 mL/kg at intervals ≤ 2 hrs until achieve pressure goals.
- Set initial rate to approximate baseline minute ventilation (MV) (not > 35 breaths/min in adults).
 $MV = \text{Tidal volume (TV)} \times \text{Respiratory rate (RR)}$
- Set I:E ratio (ratio of the duration of inspiration and expiration phases):
 - set high inspiratory flow rates
 - monitor for intrinsic PEEP
 - in severe ARDS I:E ratios of 1:1 or inverse ratios may be needed.
- Set inspiratory flow rate above patient demand (commonly > 60 L/min).
- Set FiO₂ at 1.0 and titrate down.
- Set PEEP 5-10 cmH₂O or higher for severe ARDS.
- Adjust TV and RR to achieve pH and Pplat goals below.



Note: Principles are the same for children except that children younger than 8 years require a lower maximum PEEP - 15 cmH₂O and the peak Pplat should be < 28 cmH₂O.

9.9.1 ARDS-net PEEP FiO₂ grid to guide PEEP

See [\(3\)](#)

Set PEEP corresponding to severity of oxygen impairment:

Oxygenation goal: PaO₂ 55-80 mmHg or SpO₂ 88-95%

- Use a minimum PEEP of 5 cmH₂O
- Consider incremental PEEP/FiO₂ combinations such as shown below to achieve goal
- PEEP levels > 15 should not be used in children < 8 years

There are two PEEP/FiO₂ grids - the second one can be used for more severe hypoxaemia.

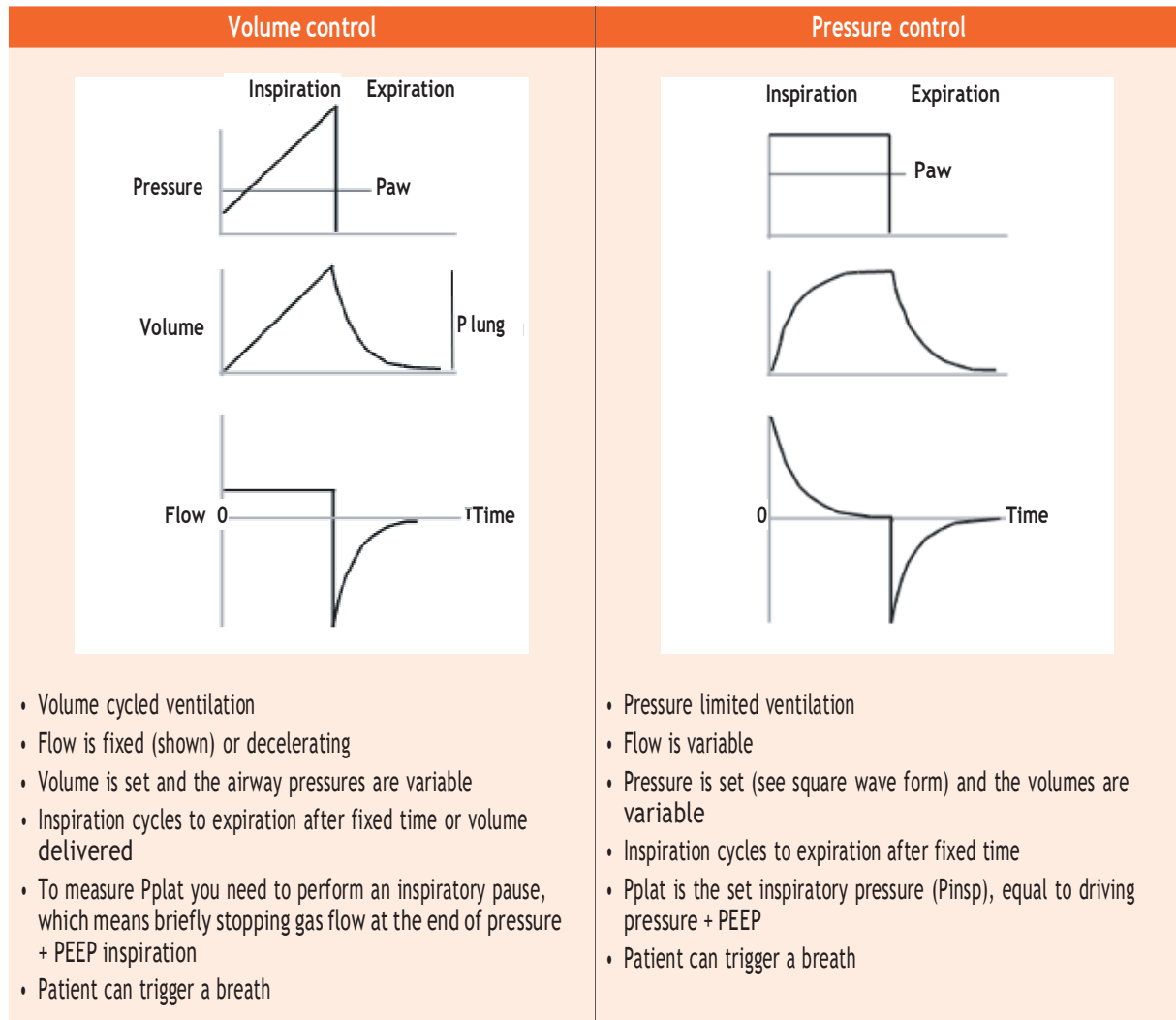
Lower PEEP/higher FiO ₂														
FiO ₂	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	0.9	1.0
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18	18-24
Higher PEEP/lower FiO ₂ for more severe hypoxaemia														
FiO ₂	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5	0.5-0.8	0.8	0.9	1.0	1.0
PEEP	5	8	10	12	14	14	16	16	18	20	22	22	22	18-24

9.9.2 Goals of Pplat and pH in lung protective ventilation

Pplat goal: ≤ 30 cmH₂O	<p>Check Pplat using 0.5 second inspiratory pause, at least every 4 hours and after each change in PEEP or TV</p> <ul style="list-style-type: none"> • If Pplat > 30 cmH₂O or > 28 cmH₂O in children: decrease TV by 1 mL/kg steps (minimum = 4 mL/kg). • If Pplat < 25 cmH₂O and TV < 6 mL/kg: increase TV by 1 mL/kg until Pplat > 25 cmH₂O or TV = 6 mL/kg. • If Pplat < 30 cmH₂O and breath stacking or asynchrony occurs: may increase TV in 1 mL/kg increments to 7-8 mL/kg if Pplat remains ≤ 30 cmH₂O.
pH goal: 7.30-7.45	<p>Acidosis management: (pH < 7.30)</p> <ul style="list-style-type: none"> • If pH 7.15-7.30: increase RR until pH > 7.30 or PaCO₂ < 25 (maximum set RR = 35). • If pH < 7.15: increase RR to 35. • If pH remains < 7.15, TV may be increased in 1 mL/kg steps until pH > 7.15 (Pplat target of 30 may be exceeded). • May give NaHCO₃ to act as a transient buffer.
Alkalosis management: pH > 7.45	Decrease ventilator rate if possible.
Inspiration to expiration ratio goal	Recommend that duration of inspiration be less than duration of expiration.

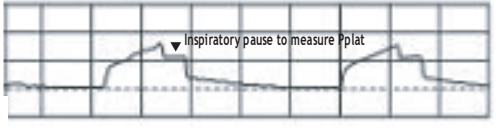
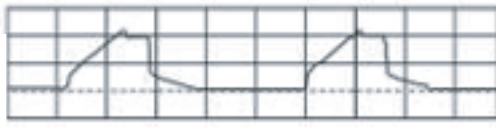



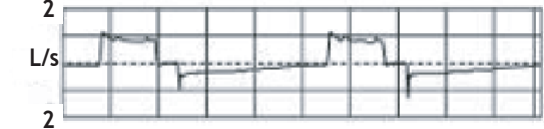
Notes: Paw - airway pressure; PEEP - positive end-expiratory pressure; Pplat - plateau airway pressure.

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



Notes: Paw - airway pressure; PEEP - positive end-expiratory pressure; Pplat - plateau airway pressure.

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

Pressure curves		Characteristics	Interpretation
60 cm H ₂ O  -20 P A W	Normal pressure curve	Normal	
90 cm H ₂ O  -30 P A W	Increased peak airway pressure Increased Pplat	Reduced compliance	
60 cm H ₂ O  -20 P A W	Increased peak airway pressure Normal Pplat Intrinsic PEEP	Increased resistance	
Flow curves		Characteristics	Interpretation
2  L/s 2 · V	Normal flow pattern	Normal	
3  L/s 3 · V	High expiratory peak flow rate flow rate expiratory flow is shorter	Reduced compliance	
2  L/s 2 · V	Prolonged expiratory flow Intrinsic PEEP	Increased resistance	

Source: Hess DR (2005).

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

Abnormal airway pressure(s)	High peak with high plateau airway pressure	High peak with normal plateau airway pressure
Main physiologic problem	Reduced respiratory system compliance (C _{rs})	High resistance (R)
Formula	$C_{rs} = \frac{\text{Tidal volume}}{P_{\text{plat}} - \text{PEEP}}$	$R = \frac{P_{\text{peak}} - P_{\text{plat}}}{\text{Flow}}$
Normal	60-100 mL/cm H ₂ O	5-10 cm H ₂ O/L/sec for intubated adult
Problems that can be treated quickly	<ul style="list-style-type: none"> • mainstem bronchus intubation • tension pneumothorax • pleural effusion • abdominal distension • congestive heart failure • atelectasis • hyperinflation 	<p>Patient problems:</p> <ul style="list-style-type: none"> • patient biting, coughing, fighting ventilator • secretions • bronchospasm <p>Ventilator problems:</p> <ul style="list-style-type: none"> • tube kinked • circuit filled with water • small endotracheal tube
Other problems that may improve over the time	<ul style="list-style-type: none"> • ARDS • consolidation • fibrosis • chest wall oedema • thoracic deformity 	<ul style="list-style-type: none"> • asthma • chronic obstructive pulmonary disease (COPD)

Factors influencing peak airway pressure

P airway = P resistance + P compliance

Airflow resistance	Respiratory system compliance	Chest wall compliance
<ul style="list-style-type: none"> • size of airway • lower airway obstruction • mechanical obstruction 	<ul style="list-style-type: none"> • chest wall • tidal volume • lung elasticity 	<ul style="list-style-type: none"> • chest wall • patient position • external compression of chest from abdomen

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



Is the endotracheal tube in the trachea?

- Large cuff leak or no chest rise with inspiration suggest that ETT is dislodged: assess with direct laryngoscopy and re-intubate.

Is there a problem with the ventilator circuit or oxygen supply?

- Take the patient off the ventilator and hand ventilate with 100% oxygen while checking equipment.

Can you pass a suction catheter through the endotracheal tube?

- If no, ETT may be kinked: straighten or insert bite block to prevent patient from biting.
- If no, ETT may be blocked with secretions: reintubate with new ETT.
- If yes, suction ETT to remove sputum/mucus plugs.

Are there breath sounds bilaterally?

- Unilaterally absent breath sounds: evaluate for mainstem intubation/lobar collapse versus pneumothorax by assessing mediastinal shift and by chest X-ray or ultrasound if patient not in extremis.
- Suspicion of tension pneumothorax mandates immediate needle decompression followed by chest tube placement, without a chest X-ray.
- Mainstem intubation may be suspected clinically if ETT further in patient than previously. Withdraw to previous position; can confirm with bronchoscopy if available.
- Lobar collapse or atelectasis may respond to aggressive suctioning and can be confirmed with chest X-ray.
- Bilateral wheezing: consider bronchospasm; give bronchodilators.
- Bilateral crackles: consider pulmonary oedema; give diuretic or more PEEP depending on full clinical evaluation of volume status.

Are there other problems causing low compliance?

- Abdominal distension: drain stomach with NG tube.
- Auto-PEEP: diagnose by examining ventilator waveforms. Treat with bronchodilators, sedation; may require temporary disconnection from positive pressure.

Is there haemodynamic instability?

- Restore haemodynamic stability with fluid or vasopressors while determining and treating primary cause.
- If severe hypotension, evaluate for tension pneumothorax or severe auto-PEEP (often in patients with asthma or COPD).
- Other causes include high airway pressures reducing venous return, vasodilation due to sedative and analgesic medications or a new problem (sepsis, bleeding, pulmonary embolism, myocardial infarction).

Is the patient agitated and asynchronous with the ventilator?

- May be secondary to any other problem or may be primary problem and causing asynchrony: treat cautiously with sedation.



9.14 Respiratory care pocket card reference

The following respiratory care pocket card reference is intended to serve as a tool to learn about the fundamentals of oxygen delivery, including mechanical ventilation, ARDS management and ventilator liberation (6).

The card, which can be printed or saved to your mobile device, is available in:

- English
- French
- Portuguese
- Spanish.

Source: USAID-STAR-UCSF Open Critical Care Project (6).

Respiratory Care Pocket Reference

v2022.2



By collaborators & with support from multiple institutions, including:



Oxygen Sources & Delivery Devices

<p>Nasal Cannula (NC)</p>	<p>Pros: Ubiquitous; commonly used up to 6LPM Cons: Requires humidification if >4LPM (risk of epistaxis); no work of breathing support O₂: works with any pressure source via flow meter; FiO₂ increases 2-4% per LPM; variable FiO₂ delivery based on patient's minute ventilation & flow rate</p>
<p>Non-Rebreather/Face mask (NRB/FM)</p>	<p>Pros: -High FiO₂ Cons: Limited FiO₂ if high respiratory drive; no work of breathing support O₂: works with any pressure source via flow meter; simple FM 5-10 LPM (-FiO₂ 35-50%); NRB 10-15 LPM (-FiO₂ 60-95%); enough flow to prevent bag collapse</p>
<p>High Flow Nasal Cannula (HFNC)</p>	<p>Pros: High FiO₂ even with high minute ventilation; can titrate flow and FiO₂; heated and humidified for comfort; may improve outcomes in acute hypoxemic respiratory failure compared to NIPPV or low-flow O₂; small amount positive pressure may help with recruitment; high flow = deadspace washout, may help with work of breathing Cons: Requires special device; consumes massive amounts of oxygen O₂: Requires high pressure/flow source; - >90% FiO₂ (variable with minute ventilation, entraining room air around cannula) 3 types: 1) With blender to mix compressed air + O₂; 2) With port/Venturi effect to entrain room air and mix with compressed O₂; or 3) Without blender. Initial Settings: infant <1year = 8LPM; child 1-4 years = 10LPM; Child > 4 years = 20LPM; adolescents/adults = 40LPM flow and 100% FiO₂; can titrate flow and/or FiO₂ (max flow depends on cannula size; up to 60 LPM for adults and 100% FiO₂) if tolerated and O₂ source adequate.</p>
<p>Non-invasive Ventilation (NIV) or Positive Pressure Ventilation (NIPPV) Trade name "BiPAP"</p>	<p>Pros: May avoid intubation in some patients (COPD, cardiogenic pulmonary edema, upper airway obstruction) by decreasing work of breathing and adding PEEP Cons: Risk of infectious aerosol generation (possibly less if helmet NIPPV); risk of aspiration if patient not alert / unable to protect airway or if inspiratory pressures >20cm H₂O; pt must be alert enough to remove mask if uncomfortable; skin breakdown with prolonged use; confusing terminology: IPAP (inspiratory pressure) = PS + PEEP; EPAP (expiratory pressure) = PEEP; PS of "5 over 5" is the same as PS Δ 5 over 5, is the same as IPAP 10/EPAP 5 O₂: requires high pressure/flow source to achieve high FiO₂ Initial Settings: PS Δ5-8/PEEP (EPAP) 5-10; titrate ΔP up to 15 to reduce inspiratory work; use higher initial IPAP with obese patients; higher pressures may require sedation in pediatric patients</p>
<p>Continuous Positive Airway Pressure (CPAP)</p>	<p>Pros: Delivered via face mask or multiple other potential interfaces to splint open the upper airway, increase lung volume & intrathoracic pressure Cons: Prolonged use is uncomfortable & causes skin breakdown; limited unloading of inspiratory muscles or provide complete respiratory support O₂: requires high flow/pressure source to achieve high FiO₂ Initial Settings (adults/peds): CPAP or PEEP 5-10; adults: titrate as needed up to 15; peds ≤12; higher pressures may require sedation in peds</p>

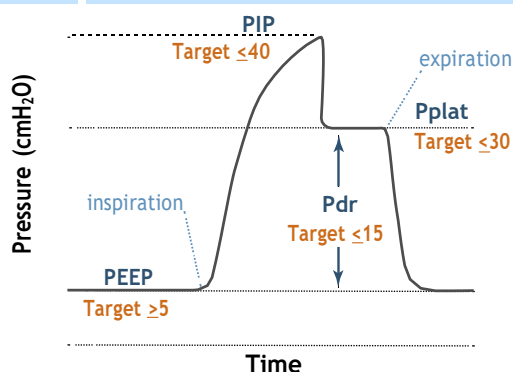
[Oxygen Delivery Device & Supply FAQ](#)



[Oxygen Supply & Demand Calculator](#)

Respiratory Mechanics

<p>Positive End Expiratory Pressure (PEEP)</p> <p>Pressure_{Peak Inspiratory} (PIP)</p>	<ul style="list-style-type: none"> Pressure within respiratory circuit at end of expiration Must be ≥ 5 cmH₂O in IMV to prevent derecruitment of alveoli This value is always set by ventilator operator <ul style="list-style-type: none"> Reflects pressure generated by airway/ETT resistance and compliance Range 10-40cmH₂O; target <40cmH₂O
<p>Pressure_{Plateau} (Pplat)</p> <p>Pressure_{Driving} (Pdr)</p> <p>I:E and Inspiratory Time (T_i)</p>	<ul style="list-style-type: none"> Reflects pressure in alveoli only If in volume control, perform inspiratory pause (when there is no flow, there is no effect of resistance; Pplat = Pressure at alveoli) Target <30cmH₂O (adults); <28 (peds); optimal ≤ 25 cmH₂O <ul style="list-style-type: none"> Pdr = Pplat - PEEP Tidal stress (lung injury and mortality risk) if elevated Target ≤ 15cmH₂O; mortality risk if ≥ 20cmH₂O <ul style="list-style-type: none"> I:E = ratio of Inspiration to Expiration Normal 1:2 or 1:3, 1:1 is only tolerated when paralyzed (and rarely indicated), 1:4 or 1:5 may be better in asthma or COPD Normal T_i ~ 1-1.5s in non ARDS; Consider T_i 0.7-1 for ARDS
<p>Minute Ventilation (MV)</p> <p>Peak Flow</p>	<ul style="list-style-type: none"> MV = V_T x RR; where V_T is the tidal volume (i.e. volume of each breath) and RR is the respiratory rate (breaths per minute) Normal 4-6 LPM; -lower if obtunded, hypothermic, deeply sedated; -higher 8-14 LPM in hypoxemic respiratory failure Adjust for pCO₂ goal (e.g. permissive hypercarbia if ARDS); -6-8 L/min in most intubated adults, may be ≥ 10-15 L/min in ARDS <ul style="list-style-type: none"> Highest flow delivered by ventilator during inspiration 40-60 LPM common; -50-80 LPM if patient triggered mode Sometimes increasing flow can improve patient-ventilator synchrony; caution this may cause elevation in PIP
<p>Compliance (C)</p> <p>Inspiratory Resistance (R)</p>	<ul style="list-style-type: none"> C = $\Delta V / \Delta P$ = Tidal volume of breath / Pdr Dynamic compliance (VT/PIP-PEEP) or static compliance (VT/Pplat-PEEP) measured at end inspiratory pause Range is 60-80mL/cmH₂O in intubated patients; ARDS ≤ 40 <ul style="list-style-type: none"> R = PIP - Pplat/inspiratory flow Must be measured during constant flow Normal <10cmH₂O/L/sec; concern if ≥ 15cmH₂O/L/sec

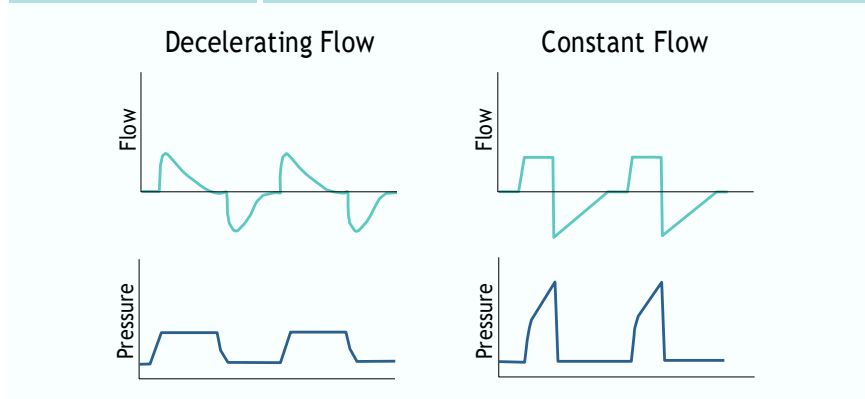


Choosing a Ventilator Mode

- Assist Control (AC) Volume Mode is default for non-spontaneous breathing patients or ARDS
- AC Pressure Mode & Dual Modes can be used for non-spontaneous breathing patients or ARDS
- PSV if spontaneous breathing and non-ARDS; SIMV and APRV have no data to support regular use

Volume Control

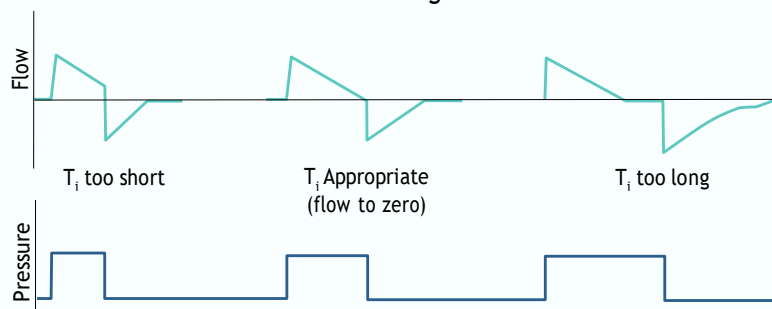
Other Names	AC-VC; Assist Control Volume Control; VCV; -CMV (controlled mandatory ventilation = all modes with RR and fixed T_i); (S)CMV
Controlled Variables	RR, V_T , PEEP, FiO_2 , Trigger level, Flow pattern, I:E (either directly or via peak flow, T_i settings)
Initial Settings Adult & Pediatric (More details on next page)	<ol style="list-style-type: none"> Set V_T at 6-8 mL/kg predicted body weight (PBW) Set RR: Adults: set at pt's most recent RR (do not exceed 35); Peds: set at most recent RR (do not exceed 60 bpm in infants, 40 bpm in toddlers/preschoolers, 35 bpm in school-aged children or adolescents) Set T_i: Adults 0.70-1 sec; Peds based on RR to maintain a minimum ratio of 1:2 Select FiO_2 and PEEP (use ARDSnet grid if applicable; see next page)
Flow	Square wave/constant/fixe; or Variable/decreasing ramp (potentially more physiologic); 40LPM healthy, 60LPM ARDS
I:E	<ul style="list-style-type: none"> I:E of 1:2 or 1:3 is best for most patients; Normal T_i ~ 1-1.5s in non ARDS patients; Consider T_i 0.7-1 for ARDS I:E of 1:1 or >1:1 associated with PEEPi, decreased cardiac output (CO) and oxygen delivery Process for setting I:E may vary by ventilator make; commonly by changing T_i, inspiratory flow and flow pattern
Pros	Guaranteed MV regardless of changing respiratory system mechanics; precise control of V_T to limit volutrauma
Cons	Will overcome high resistance or compliance to deliver set V_T (must set pressure limit & alarm); breath stacking (i.e. next breath T_i delivered before exhalation of prior breath); fixed flow and T_i can increase asynchrony when V_T & flow demand > vent settings
Breath Initiation	Control: Time trigger (60s/set RR): fixed VE Assist: Pt effort triggers full breath at set T_i , V_T , and flow rate
If No Patient Trigger	Delivers full set V_T at set rate (i.e. guaranteed VE)
Breath Termination	Time cycled = breath ends at set T_i ; alarms if V_T not achieved; flow is set, breath ends once V_T delivered Pressure cycled = safety mechanism; breath termination by clinician set high-pressure limit (10-15cmH ₂ O>avg PIP); "pop-off"
Notes	<ul style="list-style-type: none"> Inspiratory pause (-0.3s) can be built into each breath, will increase mean airway pressure; can measure P_{plat} Alarms: high pressure 5-10 > PIP, VE 50% above+below actual Trigger: 2-5 Lpm for flow; -2 cmH₂O for pressure



Pressure Control

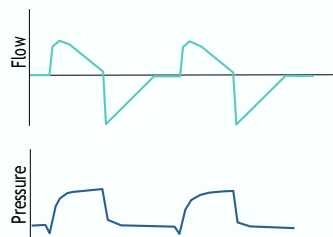
Other Names	AC-PC; Assist Control Pressure Control; -CMV - PC
Controlled Variables	RR, P_{insp} (or PC level) , PEEP, FiO ₂ , Flow trigger, Rise time, I:E (set directly or by Inspiratory time, T _i)
Initial Settings Adult & Pediatric (More details on next card)	<ol style="list-style-type: none"> 1. Set inspiratory pressure (P_{insp}) at 8-20cmH₂O, or set equal to previous P_{dr}, P_{plt} or -1/2 of PIP if transitioning from VC (goal 6-8 mL/Kg PBW) 2. Set RR: Adults: set at pt's most recent RR (do not exceed 35); Peds: set at most recent RR (do not exceed 60 bpm in infants, 40 bpm in toddlers/preschoolers, 35 bpm in school-aged children or adolescents) 3. Set T_i : Adults 0.70-0.85 sec; Peds based on RR to maintain a minimum ratio of 1:2 4. Select FiO₂ & PEEP (use ARDSnet grid if applicable; see next page)
Flow	<ul style="list-style-type: none"> • Variable/decreasing ramp (potentially more physiologic) • Peak Flow determined by: 1) P_{insp} level, 2) R, 3) T_i (shorter = more flow), 4) Pressure rise time (↓ Rise time → ↑ Peak flow), 5. Pt effort (↑ Effort → ↑ Peak flow)
I:E	<ul style="list-style-type: none"> • I:E of 1:2 or 1:3 is best for most patients; T_i 0.7-1s for ARDS • I:E 1:1 or >1:1 associated with PEEPi, decreased CO & O₂ delivery Determined by set T _i and RR (Volume and flow variable)
Pros	<ul style="list-style-type: none"> • Avoids high PIPs • Variable flow (↑ pt effort causes ↑flow to maintain constant airway pressure = potentially better synchrony: ↑ pt effort → ↑ flow and ↑ V_T) • "Automated/active expiratory valves" (transiently opens expiratory valve to vent off pressure with coughing, asynchrony); ↑ comfort and ↓ barotrauma risk
Cons	V _T and MV not guaranteed; V _T determined by C and R (might be bigger or smaller than is optimal)
Breath Initiation	Control: Time trigger - (60s/set RR) Assist: Pt trigger delivers P _{insp} for inspiratory time cycle
If No Patient Trigger	Delivers P _{insp} at set rate and T _i
Breath Termination	Time cycled = I:E or T _i set, breath ends at set time
Notes	<ul style="list-style-type: none"> • P_{plat} is the set inspiratory pressure • Alarms: high pressure 5-10 > PIP, VE 50% above/below actual • Trigger: 2-5 Lpm for flow; -2 cmH₂O for pressure • Unlike in VC, in PC the ventilator cannot compensate for volume lost to circuit compliance (i.e. V_T delivered may be less than V_T measured and may be significant especially in pediatrics)

Decelerating Flow



Pressure Support

Other Names	PS; PSV; Spontaneous
Controlled Variables	P_{insp} (PS), PEEP, FiO ₂ , Flow trigger, Rise time
Initial Setting Adult & Pediatric (More details on next card)	Use for Spontaneous Breathing Trial (SBT): 1. Set P _{insp} Δ5-10 cmH ₂ O accounting for ETT size (3.0/3.5mm = 10 cmH ₂ O; 4.0/4.5mm = Δ8 cmH ₂ O; ≥5mm = Δ5 cmH ₂ O) 2. Set PEEP 5-8 cmH ₂ O 3. FiO ₂ ≤0.40 (<u>Peds</u>) or ≤0.50 (<u>Adults</u>) per SBT initiation criteria
Flow	<ul style="list-style-type: none"> Decreasing ramp (potentially more physiologic) Determined by 1) PS level; 2) Airway resistance (R_{aw}); 3), Rise time (↑ Rise time --> ↓ Peak flow) and 4) Pt effort
I:E	Determined by patient effort and flow termination ("E _{sens} " - see below "Breath Termination")
Pros	Synchrony: allows pt to determine peak flow, V _T , and T _i
Cons	<ul style="list-style-type: none"> No guaranteed MV; V_T determined by pt (big or small); high PS and/or low E_{sens} in COPD can incr air-trapping asynchrony; muscle weakness/fatigue: ↓ effort or ability to sustain effort --> hypoventilation, ↑ fatigue
Breath Initiation	Pt flow or pressure triggered; Flow (3-5LPM) more sensitive than pressure trigger (~2cmH ₂ O)
If No Patient Trigger	Apnea (Most vents will have backup rate; all have alarm)
Breath Termination	Flow cycled: Delivers P _{insp} until flow drops to predetermined % of initial peak flow -E_{sens} (Standard setting ~25%; ~40-50% if obstructive pulmonary disease to prevent air trapping)
Notes	PS mode is not necessarily equivalent to a spontaneous breathing trial (SBT); must know if PS is relative to PEEP or ambient



Dual (Control) Mode

Other Names & Function	<ul style="list-style-type: none"> Pressure regulated volume control (PRVC); VC+, AutoFlow -PC with a target V_T & variable P_{insp} (Δ1-3cmH₂O per breath) to meet goal V_T despite changing C and R;
Pros	<ul style="list-style-type: none"> ↓ likelihood of hypo/hyperventilation associated with PC. If R or C changes, P_{insp} automatically adjusts to keep target V_T Active expiratory valve (unlike AC-VC) promotes synchrony
Cons	<ul style="list-style-type: none"> C & R can change significantly without notification Vent can't discern if V_T>target is due to ↑ pt effort or ↑ C; vent response to both = ↓ P_{insp}; Can lead to closed-loop "runaway" (↓ P_{insp}--> ↑ Pt Effort--> ↓ P_{insp})= ↑ Pt work; must carefully set alarms

Respiratory Care, Setup, & Monitoring

Ventilator Setup (prior to connecting patients)	<ul style="list-style-type: none"> Inspect all equipment for cleanliness or damage Review circuit orientation, filters, & heat & humidification system Ensure gas supply connected Perform machine self-test with new patient and per manufacture (ensure leak test included) Confirm initial settings and alarms
Ventilator Performance	<ul style="list-style-type: none"> Perform Full Status Check q4h: (PIP, Pplat, V_T, FiO₂, auto-PEEP, Alarms, SpO₂, ETCO₂ in addition to routine ICU monitoring) Evaluate vent & patient within -1h of ventilator settings changes Wipe down ventilator with approved disinfection qShift
Pulmonary, Endotracheal Tube & Circuit Hygiene	<ul style="list-style-type: none"> Check cuff pressure and auscultate q12h to avoid over-inflation/leak (<25 cmH₂O); consider 'minimal occluding volume' in peds Check inflation of pilot balloon to ensure it remains inflated Reposition & secure endotracheal tube with skin checks q12h Check ventilator circuit qShift for moisture accumulation (drainage); change circuit only if damaged or gross contamination (Ventilator Associated Pneumonia Prophylaxis -VAP PPx) Head of bed 30 degrees elevated for pneumonia prophylaxis (VAP PPx) Oral hygiene with mouthwash & suctioning TID (VAP PPx) Consider continuous subglottic suctioning or q12h oropharyngeal suctioning (VAP PPx)
Filters	<ul style="list-style-type: none"> All external filters should be inspected <u>≥</u>daily (and after nebs) Replace viral filters as frequently as supplies allow in accord with the manufacturer's recommendations or if damaged/soiled (may last >1 week) For turbine & compressor ventilators, external inlet filters & fan filters must be cleaned at least monthly. For ventilators that allow, bacterial/viral filters should be placed proximal to external intake filters Minimize instrumental/filter deadspace
Heat & Humidification	<ul style="list-style-type: none"> Active system: must use distilled or sterile water (->500mL daily) to avoid infectious risk and device damage; can be made on site or purchased; check H₂O supply q12-24h Passive heat moisture exchanger (HME): Only some HME include pathogen filter capability; Many manufacturers suggest change q24h, but studies show that an unsoiled HME in some circumstances can be used for 3-7 days. Nebs decrease lifespan (and must be given via bypass or with HME removed from circuit). Monitor for signs of an increased resistance (e.g. increase in PIP but no change in Pplat, or a prolonged exp flow). Ensure at least 28-30 mgH₂O/L efficiency
Respiratory Specific Monitoring	<ul style="list-style-type: none"> Continuous pulse oximetry, if unable then spot check as frequently as possible Continuous capnography, if unable then spot check as frequently as possible, especially after major ventilator settings changes Auscultation performed routinely with checks Skin/Mucosal Assessments qShift
Contingency Planning	<ul style="list-style-type: none"> Ensure manual (i.e. bag valve resuscitator) ventilation device is operational and at beside along with a face mask and PEEP valve

Disclaimer: This card is intended to be educational in nature and is not a substitute for clinical decision making based on the medical condition presented. It is intended to serve as an introduction to terminology. It is the responsibility of the user to ensure all information contained herein is current and accurate by using published references. This card is a collaborative effort by representatives of multiple academic medical centers.

Lung-Protective Ventilation (LPV)

<p>When to Use LPV?</p> <p>Acute Respiratory Distress Syndrome (ARDS)</p>	<p>All ARDS patients and most intubated non-ARDS patients will benefit from LPV, though there are some instances where departures from LPV are justified.</p> <p>ARDS Berlin Definition for Adult ARDS with Kigali Modification</p> <ol style="list-style-type: none"> 1) Acute (within 1 week of new symptoms or insult) 2) Bilateral opacities on CXR or Chest CT or chest US 3) P:F \leq300 or S:F $<$315 with or without \geq5 cmH₂O PEEP 4) Not fully explained by cardiac failure or fluid overload on exam <p>Pediatric ARDS (pARDS) Definition</p> <ol style="list-style-type: none"> 1) Acute (within 1 week of new symptoms or insult) 2) Infiltrate(s) on chest imaging consistent with acute lung disease 3) <u>Non-Invasive Ventilation</u>: P:F \leq300 or S:F \leq264 with CPAP \leq5 cmH₂O <u>Invasive Ventilation</u>: Oxygen Index (OI) \geq4 or Oxygen Saturation Index (OSI) \geq5 4) Not fully explained by cardiac failure or fluid overload on exam; exclude perinatal related lung disease <table border="1" data-bbox="611 757 1233 920"> <thead> <tr> <th colspan="3">Severity Grading of ARDS (Correct for altitude)</th> </tr> <tr> <th></th> <th>Adult: P:F (PaO₂ ÷ FiO₂)</th> <th>Peds: OI & OSI</th> </tr> </thead> <tbody> <tr> <td>Mild</td> <td>P:F 200-300, ~27% mortality</td> <td>OI 4-7.9; OSI 5-7.4</td> </tr> <tr> <td>Moderate</td> <td>P:F 100-200, ~32% mortality</td> <td>OI 8-15.9; OSI 7.5-12.2</td> </tr> <tr> <td>Severe</td> <td>PF: $<$100, ~45% mortality</td> <td>OI$>$16; OSI$>$12.3</td> </tr> </tbody> </table> <p>If P:F $<$150 and worsening ARDS, consider adjunctive therapies</p>	Severity Grading of ARDS (Correct for altitude)				Adult: P:F (PaO ₂ ÷ FiO ₂)	Peds: OI & OSI	Mild	P:F 200-300, ~27% mortality	OI 4-7.9; OSI 5-7.4	Moderate	P:F 100-200, ~32% mortality	OI 8-15.9; OSI 7.5-12.2	Severe	PF: $<$ 100, ~45% mortality	OI $>$ 16; OSI $>$ 12.3																																																																					
Severity Grading of ARDS (Correct for altitude)																																																																																					
	Adult: P:F (PaO ₂ ÷ FiO ₂)	Peds: OI & OSI																																																																																			
Mild	P:F 200-300, ~27% mortality	OI 4-7.9; OSI 5-7.4																																																																																			
Moderate	P:F 100-200, ~32% mortality	OI 8-15.9; OSI 7.5-12.2																																																																																			
Severe	PF: $<$ 100, ~45% mortality	OI $>$ 16; OSI $>$ 12.3																																																																																			
<p>Tidal Volume (V_T)</p> <p>(Goal 4-6 mL/Kg PBW)</p>	<ul style="list-style-type: none"> • Measure height & calculate predicted body weight (PBW) (See table) • Set initial V_T 6 mL/kg PBW_V(AC-VC) • Check V_T at least every 4h (PC or if weaning PS mode) • Titrate V_T by pressure goals & pH (below) • If pH $<$ 7.15 consider increase V_T toward 8mL/kg regardless of Pplat 																																																																																				
<p>Pressures</p> <p>(Adults Goals: Pplat$<$30cmH₂O and Pdr $<$15 cmH₂O) ₂</p> <p>(Pediatric Goal: Pplat$<$28cmH₂O)</p>	<p>Check Pplat (0.5s inspiratory pause) & Pdr (deltaP=Vt/C_{RS} = Pplat-PEEP) ~q4-6h and after each change in PEEP or V_T</p> <ul style="list-style-type: none"> • If adult Pplat $>$30 cmH₂O ($>$28 Pediatrics), optimize sedation (\pmparalysis) and decreasing V_T by 0.5-1 cc/kg toward ~4 mL/kg • If Pplat $<$30 cmH₂O and severe patient-ventilator dyssynchrony that cannot be addressed pharmacologically, consider increase V_T in 1 mL/kg steps up to 8 mL/kg • If Pplat $<$25 cm H₂O and V_T $<$6 mL/kg, increase V_T to 6 mL/kg • If PEEP \geq20 then use Pdr goal $<$15 (rather than Pplat goal) 																																																																																				
<p>Respiratory Rate (RR) & Inspiratory Time (Ti)</p> <p>(Goal based on pH)</p>	<p>Set RR at ~pre-intubation RR don't exceed ~35 breaths/minute (Adults)</p> <p>Set Ti 0.70-0.85 sec (may be longer if low RR) (avoid Ti $<$0.70 sec)</p> <ul style="list-style-type: none"> • When changing V_T, adjust RR to keep target VE by goal pH (-8-12 L/min in acute ARDS) • Consider lower RR if evidence of obstructive ventilatory defect • Increase RR if pH $<$7.30 and decrease RR if pH $>$7.45 • Keep duration of inspiration \leq expiration 																																																																																				
<p>PEEP & FiO₂</p> <p>(Goal to minimize)</p>	<ul style="list-style-type: none"> • Start at 5 cmH₂O PEEP for 2min, if stable hemodynamics, then • Select one of the following PEEP / FiO₂ titration strategies for goal PaO₂ 55-80 mmHg or SpO₂ 88-95% (In ARDS, PEEP usually ~10-14 cmH₂O). • When \uparrow PEEP, if Pplat \uparrow more than Δ PEEP, think over-distension <table border="1" data-bbox="352 1839 1238 1921"> <thead> <tr> <th colspan="14">Lower PEEP/higher FiO₂ Strategy (*Default - May consider if low Pdr or pediatrics)</th> </tr> </thead> <tbody> <tr> <td>FiO₂</td> <td>0.3</td> <td>0.4</td> <td>0.4</td> <td>0.5</td> <td>0.5</td> <td>0.6</td> <td>0.7</td> <td>0.7</td> <td>0.7</td> <td>0.8</td> <td>0.9</td> <td>0.9</td> <td>1.0</td> </tr> <tr> <td>PEEP</td> <td>5</td> <td>5</td> <td>8</td> <td>8</td> <td>10</td> <td>10</td> <td>10</td> <td>12</td> <td>14</td> <td>14</td> <td>14</td> <td>16</td> <td>18-24</td> </tr> </tbody> </table> <table border="1" data-bbox="352 1928 1238 2011"> <thead> <tr> <th colspan="14">Higher PEEP/lower FiO₂ Strategy (May consider if PaO₂/FiO₂ is $<$100, high Pdr, or BMI$>$40)</th> </tr> </thead> <tbody> <tr> <td>FiO₂</td> <td>0.3</td> <td>0.3</td> <td>0.3</td> <td>0.3</td> <td>0.3</td> <td>0.4</td> <td>0.4</td> <td>0.5</td> <td>0.5 - 0.8</td> <td>0.8</td> <td>0.9</td> <td>1.0</td> <td>1.0</td> </tr> <tr> <td>PEEP</td> <td>5</td> <td>8</td> <td>10</td> <td>12</td> <td>14</td> <td>16</td> <td>16</td> <td>18</td> <td>20</td> <td>22</td> <td>22</td> <td>22</td> <td>24</td> </tr> </tbody> </table>	Lower PEEP/higher FiO ₂ Strategy (*Default - May consider if low Pdr or pediatrics)														FiO ₂	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	1.0	PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18-24	Higher PEEP/lower FiO ₂ Strategy (May consider if PaO ₂ /FiO ₂ is $<$ 100, high Pdr, or BMI $>$ 40)														FiO ₂	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5 - 0.8	0.8	0.9	1.0	1.0	PEEP	5	8	10	12	14	16	16	18	20	22	22	22	24
Lower PEEP/higher FiO ₂ Strategy (*Default - May consider if low Pdr or pediatrics)																																																																																					
FiO ₂	0.3	0.4	0.4	0.5	0.5	0.6	0.7	0.7	0.7	0.8	0.9	0.9	1.0																																																																								
PEEP	5	5	8	8	10	10	10	12	14	14	14	16	18-24																																																																								
Higher PEEP/lower FiO ₂ Strategy (May consider if PaO ₂ /FiO ₂ is $<$ 100, high Pdr, or BMI $>$ 40)																																																																																					
FiO ₂	0.3	0.3	0.3	0.3	0.3	0.4	0.4	0.5	0.5 - 0.8	0.8	0.9	1.0	1.0																																																																								
PEEP	5	8	10	12	14	16	16	18	20	22	22	22	24																																																																								

Adjunctive Therapies for ARDS Hypoxemia

Fluid Management	<ul style="list-style-type: none"> • Concentrate IV medications and consider diuresis once hemodynamically tolerated with goal of euvolemia • FACTT Trial of conservative vs. liberal fluid strategy showed conservative fluid strategy improved oxygenation, more ventilator-free & ICU-free days, no increased shock. However, no mortality benefit.
Paralysis	<ul style="list-style-type: none"> • May be considered in severe ARDS if high PEEP and FiO₂, especially if asynchrony present; requires adequate sedation and train of four monitoring • Choice of agent (each with pros & cons, may vary by setting): cisatracurium, atracurium, rocuronium, pancuronium, or vecuronium • ACURASYS Trial showed mortality benefit; PETAL Trial did not • Short term paralysis eliminates work of breathing and can be helpful to accurately assess respiratory mechanics & asynchronies associated w/ ARDS
Prone Positioning	<ul style="list-style-type: none"> • Prone patient for ~12-16h at a time, continue proning until P:F >150 with PEEP remaining <10 cmH₂O while patient is supine for >4h • Alternate with supine positioning which allows for patient care • Do not need special bed; manually proning requires a team • If unable to prone, could put less diseased lung down to improve V/Q match • PROSEVA Trial showed mortality benefit

Additional LPV Reference Calculations

Predicted Body Weight (PBW) (kg)

Males = 50 + 2.3 [height (inches) - 60]

Females = 45.5 + 2.3 [height (inches) - 60]

[Scan for PBW Calculator](#)

Height	PBW f/m	4mL/Kg f/m	5mL/Kg f/m	6mL/Kg f/m	7mL/Kg f/m	8mL/Kg f/m
58" (147cm)	40.9/45.4 kg	164/182	205/227	245/272	286/318	327/363
60" (152cm)	45.5/50 kg	182/200	228/250	273/300	319/350	364/400
62" (157cm)	50.1/54.6 kg	200/218	251/273	301/328	351/382	401/437
64" (163cm)	54.7/59.2 kg	219/237	274/296	328/355	383/414	438/474
66" (168cm)	59.3/63.8 kg	237/255	297/319	356/383	415/447	474/510
68" (173cm)	63.9/68.4 kg	256/274	320/342	383/410	447/479	511/547
70" (178cm)	68.5/73 kg	274/292	343/365	411/438	480/511	548/584

Imputed Values for P:F Ratio

- Use when blood gas analysis unavailable ([Link to source data](#))

[Scan for Imputed P:F Calculator](#)



SpO₂ Values Corresponding to P:F ≤150:

Measured SpO ₂	Imputed PaO ₂	FiO ₂	Imputed P:F
96%	82 mmHg	≥0.6	≤137
95%	76 mmHg	≥0.5	≤152
94%	71 mmHg	≥0.5	≤142
93%	67 mmHg	≥0.5	≤134
92%	64 mmHg	≥0.5	≤128
91%	61 mmHg	≥0.4	≤153
90%	59 mmHg	≥0.4	≤148
<89%	≤57 mmHg	≥0.4	≤150

9.15 Adult ventilation order set (ARDS)

Last updated March 10, 2021

Hospital Name/Logo		Adult Ventilator (ARDS) Order Set																							
Surname/Family Name		Name		Attending/Team																					
Today's Date / /		Patient MRN/Registration #		Age	Sex	Predicted Weight (kg):	Height(cm)																		
Mode:		<input type="checkbox"/> AC-VC	<input type="checkbox"/> AC-PC	<input type="checkbox"/> PRVC	<input type="checkbox"/> _____																				
Tidal Volume:		<ol style="list-style-type: none"> 1. Initiate at 6-8 mL/kg predicted body weight (PBW). Titrate down in 0.5-1 mL/kg steps Q 1-2hrs if needed to prevent acute acidosis. 2. If EIP > 30 cm H2O, ↓ VT to as low as 4 mL/kg. 3. pH < 7.15, ↑ VT 1 mL/kg steps to 8 mL/kg regardless of EIP until pH = 7.20. 4. When severe asynchrony occurs and sedation cannot be increased, then ↑VT 1 mL/kg to upper limit of 8mL/kg. 5. If EIP<25 and VT<6mL/kg, ↑ VT to 6mL/kg. 6. When using AC-PC adjust PIP for VT=6mL/kg 																							
Plateau Pressure:		<ol style="list-style-type: none"> 1. 25-30 cm H2O. 2. EIP > 30 cm H2O allowed if PEEP > 20 cm H2O or pH < 7.20 																							
Respiratory Rate:		<ol style="list-style-type: none"> 1. Set Rate 6-35 (Typical starting rate 20, consider >25 if profound acidosis or markedly increased preintubation RR; consider lower if signs of obstructive pulmonary physiology) 2. Adjust RR to target Minute Ventilation (prior to intubation), though be cautious for possible air trapping if set too fast and/or too large of tidal volumes. (Typical minute ventilation requirements for adult ARDS ~8-12 LPM, 130-190 mL/kg PBW) 3. ↑RR when pH < 7.30 (Max ~35) 4. ↓ RR when pH > 7.45. 																							
Inspiratory Time:		0.70-0.85 sec. Avoid T _{insp} < 0.70. Upper I:E Limit of 1:1 (T _{insp} of 0.85 @ RR of 35)																							
Peak Flow Rate:		60-75 L/min for comfort. Avoid peak flow rate < 50 L/min																							
Arterial pH:		<ol style="list-style-type: none"> 1. Target: 7.30-7.45 2. pH < 7.25 and PaCO₂ < 25: Consider Buffer Rx 3. pH < 7.15: Modify VT/EIP goals to achieve pH = 7.20. Buffer Rx indicated to maintain lung-protective ventilation. 																							
PEEP FiO2 Titration:		Maintain PaO ₂ of 55-80 mm Hg (SpO ₂ 88-95%). Select one of the PEEP FiO ₂ Tables below: <input type="checkbox"/> ARDS Net ARMA Trial Low PEEP Table (Default for most patients)																							
		<table border="1"> <tr> <td>FiO₂</td> <td>0.3</td> <td>0.4</td> <td>0.5</td> <td>0.6</td> <td>0.7</td> <td>0.8</td> <td>0.9</td> <td>1.0</td> </tr> <tr> <td>PEEP</td> <td>5</td> <td>5-8</td> <td>8-10</td> <td>10</td> <td>10-14</td> <td>14</td> <td>14-18</td> <td>18-26</td> </tr> </table>						FiO ₂	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0	PEEP	5	5-8	8-10	10	10-14	14	14-18	18-26
FiO ₂	0.3	0.4	0.5	0.6	0.7	0.8	0.9	1.0																	
PEEP	5	5-8	8-10	10	10-14	14	14-18	18-26																	
		<input type="checkbox"/> ARDS Net Modified from ALVEOLI Trial High PEEP Table (May consider if PaO ₂ /FiO ₂ is <100, or BMI>40)																							
		<table border="1"> <tr> <td>FiO₂</td> <td>0.3</td> <td>0.4</td> <td>0.5</td> <td>0.60 - 0.70</td> <td>0.8</td> <td>0.9</td> <td>1.0</td> </tr> <tr> <td>PEEP</td> <td>5-14</td> <td>14-16</td> <td>16-18</td> <td>16-20</td> <td>20-22</td> <td>22</td> <td>22-24</td> </tr> </table>						FiO ₂	0.3	0.4	0.5	0.60 - 0.70	0.8	0.9	1.0	PEEP	5-14	14-16	16-18	16-20	20-22	22	22-24		
FiO ₂	0.3	0.4	0.5	0.60 - 0.70	0.8	0.9	1.0																		
PEEP	5-14	14-16	16-18	16-20	20-22	22	22-24																		
Free Form PEEP:		Maintain PEEP at _____ cm H2O and Titrate FiO ₂ for Protocol PaO ₂ /SpO ₂ range.																							
Alternative Arterial:		For patients concurrently managed on the traumatic brain injury protocols, or patients with/at risk for myocardial or gastrointestinal ischemia: PaO ₂ range: _____ PaCO ₂ Range: _____ pH Range: _____																							
Arterial Blood Gas:		<ol style="list-style-type: none"> 1. Protocol initiation and/or immediately after intubation 2. Every day, first 7 days of protocol 3. Severe acidosis (pH < 7.15) after VT ↑ to 7 and 8 mL/Kg 4. Every PEEP ↑ > 10 cm H2O 5. Check SpO₂ at least Q4h and < 30 min after adjustments in PEEP/FiO₂ 																							
VD/VT (deadspace):		When volumetric capnography available (or by crude estimation with time-based capnography - i.e., PaCO ₂ -end tidal CO ₂ /PaCO ₂), check on protocol initiation, after PEEP titrations and daily.																							
Routine Care:		<input type="checkbox"/> Head of bed 30 degrees <input type="checkbox"/> Mouthwash oral solution (15 mL) swish and suction orally q12h white intubated <input type="checkbox"/> Oropharyngeal suctioning q 12h <input type="checkbox"/> Perform full status check ~q4h (PIP, Pplat, VT, FiO ₂ , RR)																							

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



TO PRINT MORE forms scan here

TO LEARN MORE on calculating PBW and for lung protective ventilation [scan or click here](#)



Source: Adapted with permission from San Francisco General Hospital, San Francisco (CA) and USAID-STAR-UCSF Open Critical Care Project (🇺🇸).

9.16 Checklist for proning in severe ARDS

This checklist is adapted from Messerole et al. (2002) and the most recent randomized control trial by Guérin et al. (2013). These studies found an improved mortality in patients treated with LPV plus prone position.

Prone ventilation should be carried out by four to five team members using a protocol rehearsed in advance. It is easier to perform in children. See the following article and video ()

Timing and duration of prone position

The most recent clinical trial (Guérin et al., 2013) observed mortality benefit in patients with severe ARDS. Patients were turned prone within 24 hours of recognition and kept prone for at least 12-16 consecutive hours a day.

Contraindications

- Elevated intracranial pressure > 30 mmHg or cerebral perfusion pressure < 60 mmHg
- Massive haemoptysis
- Recent tracheal surgery or sternotomy
- Serious facial trauma or facial surgery
- Deep venous thrombosis treated for less than 2 days
- Cardiac pacemaker inserted in the last 2 days
- Unstable spine, femur or pelvic fractures
- MAP < 65 mmHg
- Pregnancy
- Single anterior chest tube with air leaks.

Preparation of the patient for proning while IMV

1	Check for contraindications.
2	Consider possible adverse effects of prone positioning (e.g. if on chest tube drainage).
3	Whenever possible, explain the manoeuvre to the patient or their family.
4	Confirm from a recent chest X-ray that the tip of the endotracheal tube is located 2-4 cm above the main carina.
5	Inspect and confirm that the endotracheal tube and all central and large bore peripheral catheters are firmly secured.
6	Consider exactly how the patient's head, neck and shoulder girdle will be supported after they are turned prone. Assemble all needed pillows, foam pads or other supports that might be needed.
7	Stop tube feeding, check for residual, fully evacuate the stomach, and cap or clamp the feeding and gastric tubes.
8	Prepare endotracheal suctioning equipment, and review what the process will be if copious airway secretions abruptly interfere with ventilation.
9	Decide whether the turn will be rightward or leftward.
10	Prepare all IV tubing and other catheters and tubing for connection when the patient is prone: <ul style="list-style-type: none">• Assure sufficient tubing length.• If chest drainage: relocate all drainage bags on the opposite side of the bed, move chest tube drains between the legs.• Reposition IV tubing toward the patient's head, on the opposite side of the bed.

Turning procedure

1	Place one (or more) people on both sides of the bed (to be responsible for the turning processes) and another at the head of the bed (to assure the central lines and the endotracheal tube do not become dislodged or kinked).
2	Increase the FiO_2 to 1.0 and note the mode of ventilation, the tidal volume, the minute ventilation, and the peak and plateau airway pressures.
3	Pull the patient to the edge of the bed furthest from whichever lateral decubitus position will be used while turning.
4	Place a new draw sheet on the side of the bed that the patient will face when in this lateral decubitus position. Leave most of the sheet hanging.
5	Turn the patient to the lateral decubitus position with the dependent arm tucked slightly under the thorax. As the turning progresses the nondependent arm can be raised in a cocked position over the patient's head. Alternatively, the turn can progress using a log-rolling procedure.
6	Remove ECG leads and patches. Suction the airway, mouth and nasal passages if necessary.
7	Continue turning to the prone position.
8	Reposition in the centre of the bed using the new draw sheet.
9	If the patient is on a standard hospital bed, turn their face toward the ventilator. Assure that the airway is not kinked and has not migrated during the turning process. Suction the airway if necessary.
10	Support the face and shoulders appropriately avoiding any contact of the supporting padding with the orbits or the eyes.
11	Position the arms for patient comfort. If the patient cannot communicate avoid any type of arm extension that might result in a brachial plexus injury.
12	Auscultate the chest to check for right mainstem intubation. Reassess the tidal volume and minute ventilation.
13	Adjust all tubing and reassess connections and functions.
14	Reattach ECG patches and leads to the back.
15	Tilt the patient into reverse Trendelenburg. Slight, intermittent lateral repositioning ($20\text{-}30^\circ$) should also be used, changing sides at least every 2 hours.
16	Document a skin assessment every shift, specifically inspecting weight bearing, ventral surfaces.

Criteria for stopping proning in severe ARDS:

- Oxygenation improvement defined as $\text{PaO}_2/\text{FiO}_2 \geq 150$ mmHg with $\text{PEEP} \leq 10$ cmH₂O and $\text{FiO}_2 \leq 0.6$; in the prone group, these criteria had to be met in supine at least 4 hours after the end of the last prone session.
- $\text{PaO}_2/\text{FiO}_2$ ratio deterioration by more than 20% relative to supine before two consecutive prone sessions.
- Complications occurring during a prone session such as:
 - non-scheduled extubation
 - mainstem bronchus intubation
 - endotracheal tube obstruction
 - haemoptysis, $\text{SpO}_2 < 85\%$
 - $\text{PaO}_2 < 55$ mmHg for more than 5 minutes under $\text{FiO}_2 1.0$
 - cardiac arrest
 - HR < 30 beats per minute for more than 1 minute
 - SBP < 60 mmHg for more than 5 minutes
 - or any other life-threatening reason for which the clinician decided to stop.

9.17 Ventilator circuit types, filter and humidifier locations for SARI

When managing a patient with infectious SARI, careful consideration must be given to the placement of adequate bacterial-viral (BV) filters to protect health care workers and patients from potential exposure to infectious particles.

Filters may be placed at the air intake, inspiratory limb, patient wye, expiratory limb and/or exhaust port; however, placement at each of these sites does not provide equivalent function.

Ideally a two-filter setup should be used:

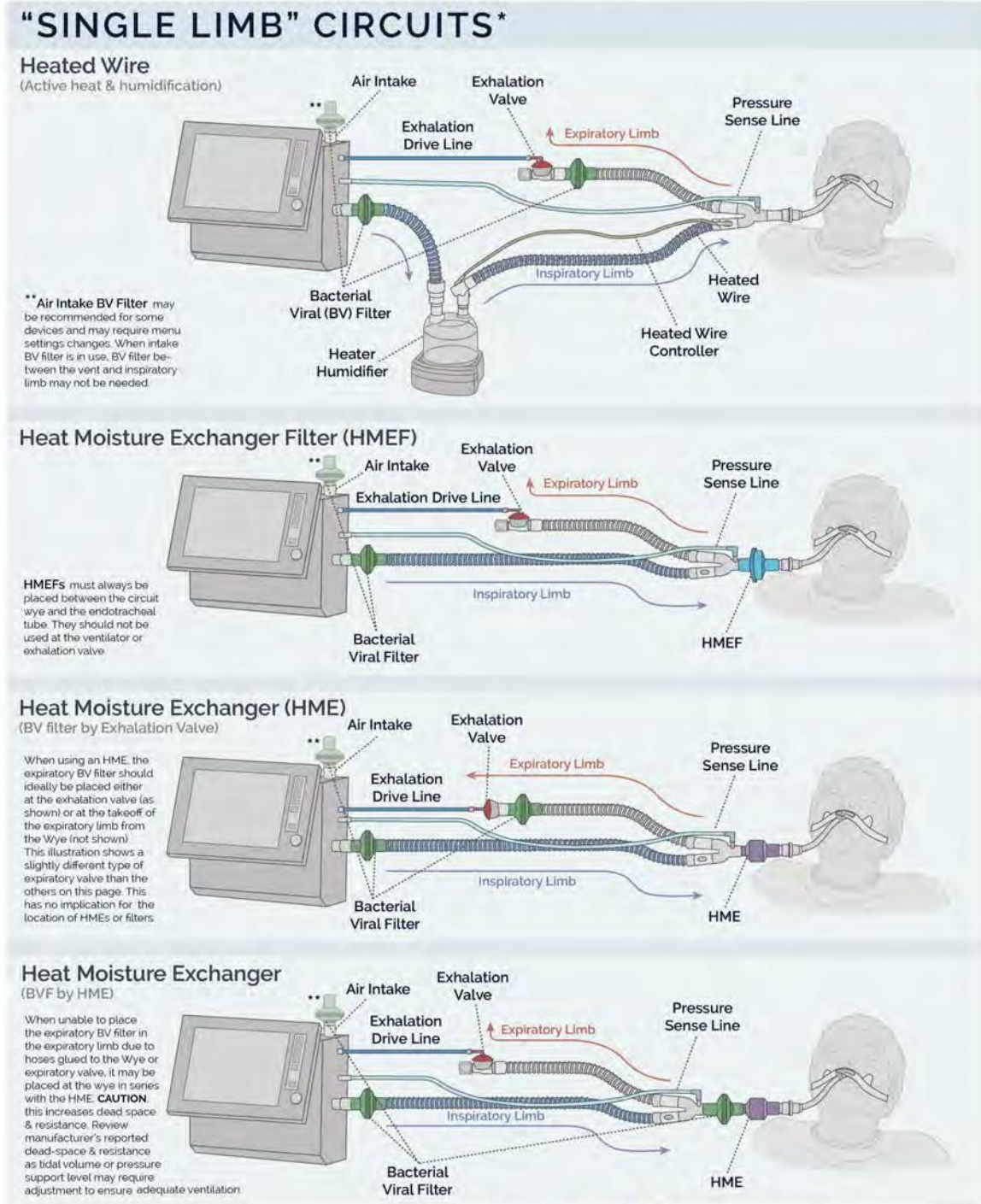
- **Inspiratory/patient filter:** The first BV filter should be placed between the patient and the inspiratory limb take off from the ventilator. This filter is often placed between the inspiratory limb and the ventilator or between the circuit wye connector and the patient. The inspiratory/patient filter has two purposes: 1) to protect the ventilator from exhaled gases from an infected patient; and 2) to protect a non-infected patient from a possibly contaminated ventilator.
- **Expiratory filter:** A second BV filter should be placed between the patient and the exhalation valve on the expiratory limb of the circuit. This filter is intended to protect the room environment and health care staff from aerosolized particles, and to protect the device in a dual limb circuit setup.

If using an active heat and humidification system, then the inspiratory filter should be a BV filter, without heat-moisture exchange (HME) function. If not using an active heat and humidification system, then the circuit must include either: 1) an HME with BV filter function (also known as an HMEF) between the wye and patient; or 2) an HME without BV filter function placed at the wye, in addition to an inspiratory and expiratory BV filter.

Placement of HME, BV or HMEF filters between the circuit wye and the patient's endotracheal tube can add significant dead space to the circuit, especially for paediatric patients, and must always be accounted for when using this setup.

Ventilator Circuit Setup

Filter Placement & Humidification Types



* The term "single limb" is a commonly used misnomer to describe the circuits shown here. These circuits do have a second (expiratory) limb, and thus may be considered functionally similar to "dual limb circuits".

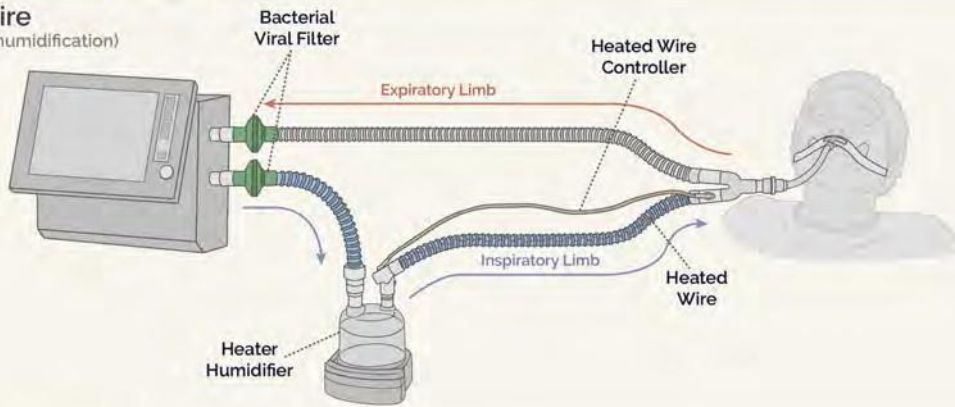


Source: USAID-STAR-UCSF Open Critical Care Project ([link](#))

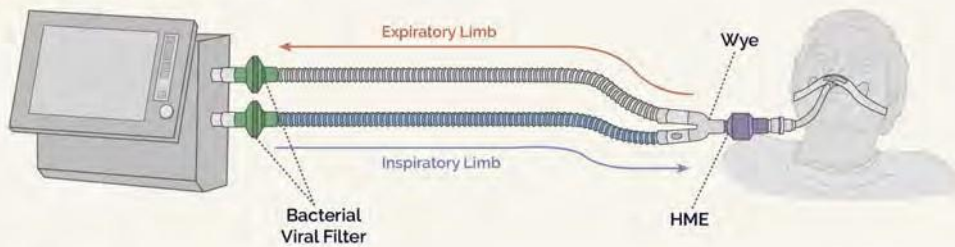
DUAL LIMB CIRCUITS

Heated Wire

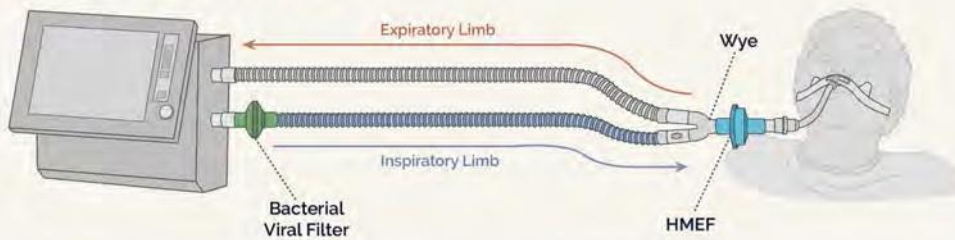
(Active heat & humidification)



Heat Moisture Exchanger (HME)

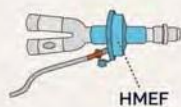


Heat Moisture Exchange Filter (HMEF)

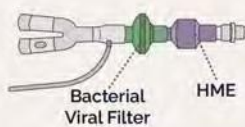


END TIDAL CO₂ PLACEMENT

Sidestream CO₂
Sampling HMEF with
integrated sampling port



Sidestream CO₂
Sampling HME and
Bacterial Viral Filter



Mainstream CO₂
Monitoring HME

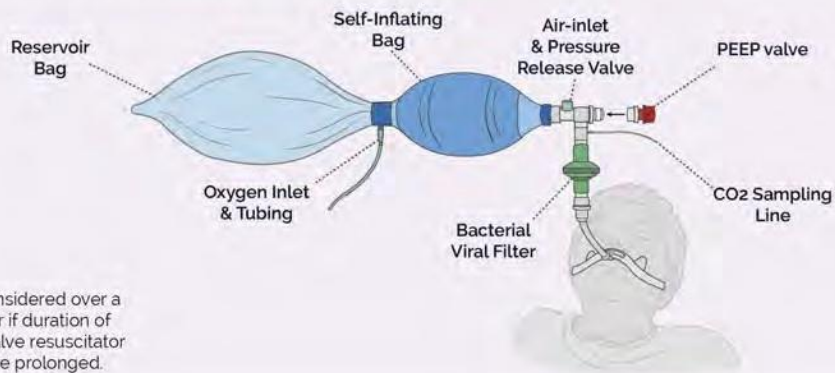


Deadspace and resistance are increased by the addition of any filters or other adapters, including end tidal CO₂. Read manufacturers' specifications to quantify potential impact on ventilator strategy.



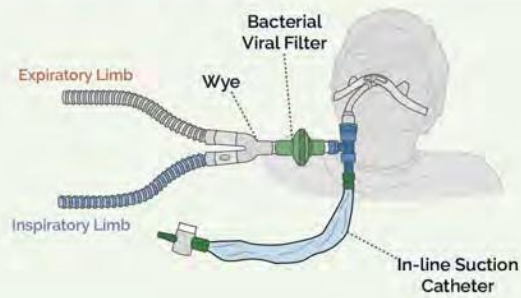
Source: USAID-STAR-UCSF Open Critical Care Project ([link](#))

Bag valve resuscitator setup



HMEF may be considered over a bacterial viral filter if duration of use on the bag valve resuscitator is anticipated to be prolonged.

In-line suction catheter setup



This illustration shows the location of the in-line suction catheter in relation to the patient circuit. There are other potential configurations not shown here, but in all, the in-line suction catheter is placed on the endotracheal tube.



Source: USAID-STAR-UCSF Open Critical Care Project ([link](#))

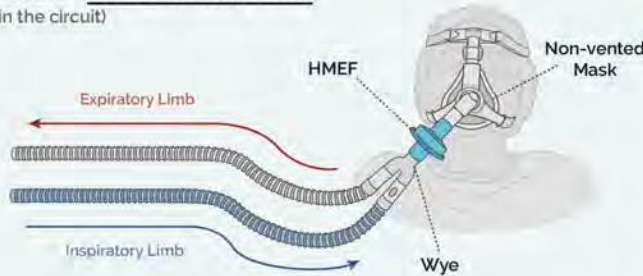
Non-invasive mechanical ventilation

CPAP/NIPPV Circuit Setup

Mask types, filter and humidification placement

Dual Limb Circuit + Non-Vented Mask

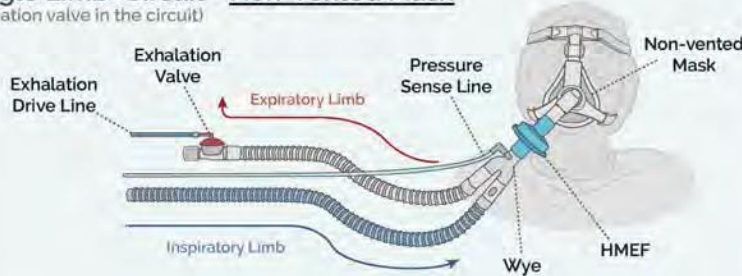
(Exhalation valve in the circuit)



- Because this setup has an **expiratory valve** at or in the ventilator (not shown), a **non-vented mask** must be used for CPAP/NIPPV
- See Figure "Ventilator Circuit Setup" for alternative humidification & filter setups. An HMEF is shown here but may not be the optimal setup depending on local resources.
- The addition of filters between the circuit Wye and the patient introduce dead space.

"Single Limb" Circuit + Non-Vented Mask

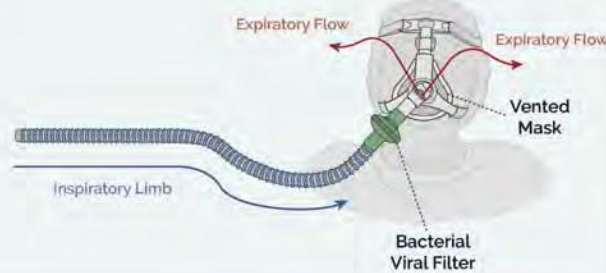
(Exhalation valve in the circuit)



- The term 'single limb' circuit is a commonly used misnomer when referring to the type of circuit shown here. The setup shown has a short expiratory limb and expiratory valve and functions similarly to a dual limb circuit.
- Because this setup has an **expiratory valve**, a **non-vented mask** must be used for CPAP/NIPPV
- See Figure "Ventilator Circuit Setup" for alternative humidification & filter setups.

True Single Limb Circuit + Vented Mask

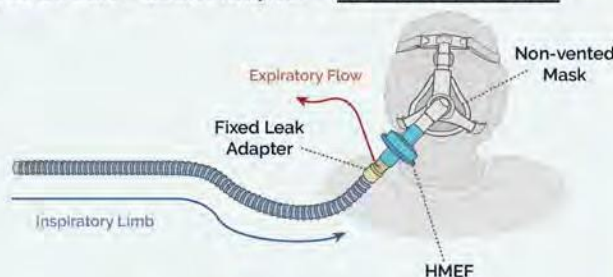
(No exhalation valve)



- The 'true' single limb circuit is commonly found in home CPAP/NIPPV machines and has **no expiratory valve**.
- Exhaled breath must leave through intentional leak ports - in this setup a **vented mask** is used
- The BV filter in this scenario protects the patient from a potentially contaminated device/circuit but does not protect personnel from potentially infectious aerosolized particles in the exhaled gas.

True Single Limb Circuit + Leak Adapter + Non-Vented Mask

(No exhalation valve)



- This 'true' single limb circuit is commonly found in home CPAP/NIPPV machines and has **no expiratory valve**.
- Exhaled breath must leave through intentional leak ports - in this setup, a non-vented mask is used and the leak occurs via a specialized **fixed leak adapter** in the circuit.
- Either a bacterial viral filter (if active heated humidification is being used) or HMEF (if no active heated humidification) should be placed between the leak adapter & the patient.

CPAP - continuous positive airway pressure
NIPPV - non-invasive positive pressure ventilation (e.g. bilevel positive airway pressure)



Open Critical Care



UCSF



Source: USAID-STAR-UCSF Open Critical Care Project ([link](#))

References and resources

- Amato MB, Meade MO, Slutsky AS, Brochard L, Costa EL, Schoenfeld DA. Driving pressure and survival in the acute respiratory distress syndrome. *N Engl J Med*. 2015;372(8):747-55.
- Antonelli M, Conti G, Moro ML, Esquinas A, Gonzalez-Diaz G, Confalonieri M et al. Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic respiratory failure: a multi-center study. *Intensive Care Med*. 2001;27(11):1718-1728.
- ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E et al. Acute respiratory distress syndrome: the Berlin definition. *JAMA*. 2012;307(23):2526-33.
- ARDS Network, Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT et al. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*. 2000;342(18):1301-1308.
- Bellani G, Grasselli G, Cecconi M, Antonini L, Borelli M, De Giacomo F et al. Noninvasive ventilatory support of COVID-19 patients outside the intensive care units (ward-COVID). *Ann Am Thorac Soc*. 2021. doi: 10.1513/AnnalsATS.202008-1080OC.
- Bellani G, Laffey JG, Pham T, Fan E, Brochard L, Esteban A et al. Epidemiology, patterns of care, and mortality for patients with acute respiratory distress syndrome in intensive care units in 50 countries. *JAMA*. 2016;315(8):788-800.
- Bellani G, Laffey JG, Pham T, Madotto F, Fan E, Brochard L et al. Noninvasive ventilation of patients with acute respiratory distress syndrome. Insights from the LUNG SAFE Study. *Am J Respir Crit Care Med*. 2017;195(1):67-77.
- Carteaux G, Millan-Guilarte T, De Prost N, Razazi K, Abid S, Thille AW et al. Failure of noninvasive ventilation for de novo acute hypoxemic respiratory failure: role of tidal volume. *Crit Care Med*. 2016;44(2):282-290.
- Diaz JV, Brower R, Calfee CS, Matthay MA. Therapeutic strategies for severe acute lung injury. *Crit Care Med*. 2010;38(8):1644-1650.
- Egan J. Acute lung injury in the child. *Paediatr Resp Rev*. 2010;11:171-176.
- Ekhuagere OA, Mairami AB, Kirpalani H. Risk and benefits of bubble continuous positive airway pressure for neonatal and childhood respiratory diseases in low- and middle-income countries. *Paediatr Respir Rev*. 2019;29:31-6. Epub 2018/06/17. doi: 10.1016/j.prrv.2018.04.004. PubMed PMID: 29907334.
- Ferguson ND, Fan E, Camporota L, Antonelli M, Anzueto A, Beale R et al. The Berlin definition of ARDS: an expanded rationale, justification, and supplementary material. *Intensive Care Med*. 2012;38(10):1573- 82.
- Gelb A, Morriss WW, Johnson W, Merry A, on behalf of the International Standards for a Safe Practice of Anesthesia Workgroup. WHO-WFSA International standards for a safe practice of anesthesia. *Anesth Analg*. 2018;126(1):2047-2055 (https://journals.lww.com/anesthesia-analgesia/Fulltext/2018/06000/World_Health_Organization_World_Federation_of.39.aspx, accessed 13 December 2021).
- Goligher EC, Kavanagh BP, Rubenfeld GD, Adhikari NK, Pinto R, Fan E et al. Oxygenation response to positive end-expiratory pressure predicts mortality in acute respiratory distress syndrome. A secondary analysis of the LOVS and ExPress trials. *Am J Respir Crit Care Med*. 2014;190(1):70-6.
- Grissom CK, Hirshberg EL, Dickerson JB, Brown SM, Lanspa MJ, Liu KD et al. Fluid management with a simplified conservative protocol for the acute respiratory distress syndrome. *Crit Care Med*. 2015;43(2):288-95.
- Guérin C, Reigner J, Richard J-C, Beuret P, Gacouin A, Boulain T et al. Prone positioning in severe acute respiratory distress syndrome. *N Engl J Med*. 2013;368:2159-2168.
- Hess DR. Using the ventilator to probe physiology: monitoring graphics and lung mechanics during mechanical ventilation (course). Boston (MA): Massachusetts General Hospital; 2005.
- Hess DR. Ventilator waveforms and the physiology of pressure support ventilation. *Respir Care*. 2005;50(2):166-186.
- Khemani RG, Smith LS, Zimmerman JJ, Ericson S, for the Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: definition, incidence, and epidemiology: proceedings from the Pediatric Acute Lung Injury Conference. *PCCM*. 2015;16(5):S23-S40.
- Laffey JG, Bellani G, Pham T, Fan E, Madotto F, Bajwa EK et al. Potentially modifiable factors contributing to outcome from acute respiratory distress syndrome: the LUNG SAFE study. *Intensive Care Med*. 2016;42(12):1865-1876.
- Lee MK, Choi J, Park B, Kim B, Lee SJ, Kim SH et al. High flow nasal cannulae oxygen therapy in acute- moderate hypercapnic respiratory failure. *Clin Respir J*. 2018;12(6):2046-56. Epub 2018/02/03. doi: 10.1111/crj.12772. PubMed PMID: 29392846.
- Lichtenstein D, Goldstein I, Mourgeon E, Cluzel P, Grenier P, Rouby JJ. Comparative diagnostic performances of auscultation, chest radiography, and lung ultrasonography in acute respiratory distress syndrome. *Anesthesiology*. 2004;100:9-15.
- Luo Y, Ou R, Ling Y, Qin T. [The therapeutic effect of high flow nasal cannula oxygen therapy for the first imported case of Middle East respiratory syndrome to China]. *Zhonghua Wei Zhong Bing Ji Jiu Yi Xue*. 2015;27(10):841-4. Epub 2016/05/03. PubMed PMID: 27132449.
- Malhotra A. Low-tidal-volume ventilation in the acute respiratory distress syndrome. *N Engl J Med*. 2007;357(11):1113-1120.
- Meade M, Cook DJ, Guyatt GH, Slutsky AS, Arabi YM, Cooper DJ et al. Ventilation strategy using low tidal volumes, recruitment maneuvers, and high positive end-expiratory pressure for acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA*. 2008;299(6):637-645.
- Mercat A, Richard JC, Vielle B, Jaber S, Osman D, Diehl JL et al. Positive end-expiratory pressure setting in adults with acute lung injury and acute respiratory distress syndrome: a randomized controlled trial. *JAMA*. 2008;299(6):646-655.

- Messerole E, Peine P, Wittkopp S, Marini JJ, Albert RK. The pragmatics of prone positioning. *Am J Respir Crit Care Med.* 2002;165(10):1359-1363.
- Murray JF, Matthay MA, Luce JM, Flick MR. An expanded definition of the adult respiratory distress syndrome. *Am Rev Respir Dis.* 1988;138(3):720-3.
- National Heart, Lung, and Blood Institute ARDS Clinical Trials Network. Comparison of two fluid-management strategies in acute lung injury. *N Engl J Med.* 2006;354:2564-2575.
- Papazian L, Aubron C, Brochard L, Chiche JD, Combes A, Dreyfuss D et al. Formal guidelines: management of acute respiratory distress syndrome. *Ann Intensive Care.* 2019;9(1):69. doi:10.1186/s13613-019-0540-9.
- Pediatric Acute Lung Injury Consensus Conference Group. Pediatric acute respiratory distress syndrome: consensus recommendations from the Pediatric Acute Lung Injury Consensus Conference. *Pediatr Crit Care Med.* 2015;16(5):428-439.
- Randolph AG. Management of acute lung injury and acute respiratory distress syndrome in children. *Crit Care Med* 2009; 37:2448-2454.
- Riviello ED, Kiviri W, Twagirumugabe T, Mueller A, Banner-Goodspeed VM, Officer L et al. Hospital incidence and outcomes of ARDS using the Kigali modification of the Berlin definition. *Am J Respir Crit Care Med.* 2016;193(1):52-9.
- Rochweg B, Brochard L, Elliott MW, Hess D, Hill NS, Nava S et al. Official ERS/ATS clinical practice guidelines: noninvasive ventilation for acute respiratory failure. *Eur Respir J.* 2017;50(2). Epub 2017/09/02. doi: 10.1183/13993003.02426-2016. PubMed PMID: 28860265.
- Sehgal IS, Chaudhuri S, Dhooria S, Agarwal R, Chaudhry D. A study on the role of noninvasive ventilation in mild-to-moderate acute respiratory distress syndrome. *Indian J Crit Care Med.* 2015;19(10):593-599.
- Slutsky AS. Neuromuscular blocking agents in ARDS. *N Engl J Med.* 2010;363(12):1176-80.
- Slutsky AS, Ranieri VM. Ventilator-induced lung injury. *N Engl J Med.* 2014;370(10):980.
- Sud S, Fredrich JO, Taccone P, Polli F, Adhikari NK, Latini R et al. Prone ventilation reduces mortality in patients with acute respiratory failure and severe hypoxemia: systematic review and meta-analysis. *Intensive Care Med.* 2010;36(4):585-599.
- Suttapanit K, Boriboon J, Sanguanwit P. Risk factors for non-invasive ventilation failure in influenza infection with acute respiratory failure in emergency department. *Am J Emerg Med.* 2020;38(9):1901-1907.
- Taccone P, Presenti A, Latini R, Polli F, Vagginelli F, Mietto C et al. Prone positioning in patients with moderate and severe acute respiratory distress syndrome: a randomized controlled trial. *JAMA.* 2009;302(18):1977-1984.
- Thille AW, Contou D, Fragnoli C, Cordoba-Izquierdo A, Boissier F, Brun-Buisson C. Non-invasive ventilation for acute hypoxemic respiratory failure: intubation rate and risk factors. *Crit Care.* 2013;17(6):R269.
- Tobin M. Advances in mechanical ventilation. *N Engl J Med.* 2001;344(26):1986-1996.
- Wheeler AP, Bernard GR. Acute lung injury and the acute respiratory distress syndrome: a clinical review. *Lancet.* 2007;369(9572):1553-1565.
- Writing Group for the Alveolar Recruitment for Acute Respiratory Distress Syndrome Trial (ART) Investigators, Cavalcanti AB, Suzumura EA et al. Effect of lung recruitment and titrated positive end-expiratory pressure (PEEP) vs low PEEP on mortality in patients with acute respiratory distress syndrome: a randomized clinical trial. *JAMA.* 2017;318(14):1335-1345. doi:10.1001/jama.2017.14171.



10

Manage pain, sedation and delirium



10

Manage pain, sedation and delirium

Summary

In critically ill patients, comfort and safety should be the goals when managing pain control, anxiolysis and prevention and treatment of delirium.

Implementation of a protocolized management approach to pain, agitation and delirium (**PAD protocol**) improves patient outcomes

Short-term outcomes

- Fewer days of delirium
- Fewer days of IMV (quicker time to extubation)
- Fewer days in ICU
- Lower hospital costs
- More mobilization during ICU stay
- Increased survival

Long-term outcomes

- Better cognitive function
- Better physical mobility
- Fewer psychiatric conditions (e.g. PTSD, depression, anxiety)
- Increased survival

Steps to develop a PAD protocol adapted to the health facility

Step 1 Assess and recognize pain, agitation and delirium using standardized and reproducible scales (i.e. VAS, RASS, CAM-ICU).

Step 2 **Manage pain first:** prevention and treatment (treat pain with a multimodal approach using opioids and non-opioids to minimize the harmful effects of sedatives).

Step 3 **Manage agitation:** choice of targeted sedation (treat anxiety using non-benzodiazepines sedatives and target light sedation). Evaluate patients daily for potential reductions of sedation, anxiolytics, and analgesics as well as for sedation interruptions in intubated patients when criteria are met.

Step 4 **Manage delirium:** prevention and treatment (prioritize non-pharmacologic interventions to prevent or treat delirium, over pharmacologic treatments).

Step 5 Special situations that may need deep sedation and neuromuscular blockade (i.e. severe ARDS).

Step 6 **Monitor-record-interpret-respond.**

Step 7 **Deliver quality care:** implementation as part of ABCDEF bundle.

Tools

- 10.1 Numerical pain assessment scales
- 10.2 Behavioural pain assessment scales
 - 10.2.1 Behavioural Pain Scale (BPS)
 - 10.2.2 Critical-Care Pain Observation Tool (CPOT)
 - 10.2.3 COMFORT-B Scale
 - 10.2.4 FLACC Behavioural Pain Assessment Scale
- 10.3 Richmond Agitation-Sedation Scale (RASS)
- 10.4 Flowchart and worksheet for the Confusion Assessment Method of the ICU for adults (CAM- ICU)
- 10.5 Flowchart and worksheet for the Confusion Assessment Method of the ICU for children (pCAM- ICU)
- 10.6 Procedure for assessing attention: attention screening exam (ASE) for adults
- 10.7 Guide to commonly used sedatives in adults
- 10.8 Guide to commonly used opioid analgesics in adults
- 10.9 Guide to using neuromuscular blockers in adults
- 10.10 Guide to commonly used antipsychotics (haloperidol) in adults
- 10.11 Guide to paediatric analgesics, sedatives and neuromuscular blockers

10.1 Numerical pain assessment scales

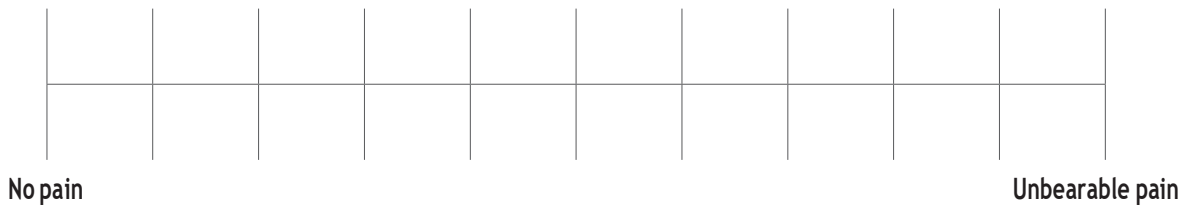
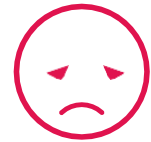


Visual analogue scale

The visual analogue scale (VAS) for pain assessment in adults and adolescents is a validated and widely used method of monitoring the subjective level of pain experienced by patients. It is a 10 cm long scale, which ranges from 0 (no pain) to 10 (the worst pain that one can imagine). It is flexible, in that patients can make verbal or visual responses (i.e. if verbal communication is not possible, the patient can be shown a 10 cm scale and can point to the region which corresponds to their pain).

A major limitation of the VAS is that it requires an awake patient who grasps the concept of a scale. These conditions are frequently not satisfied in ICU patients.

The lower the VAS score, the higher the quality of the analgesia. However, a low VAS score with excessive sedation must be avoided, if possible. The level of sedation must be also closely monitored (see the Richmond Agitation-Sedation Scale tool).



Wong-Baker Faces Scale

The Wong-Baker Faces Scale can be used in younger children - they are asked to point to the face that reflects their pain level.



Source: Wong and Hockenberry (2001).

10.2 Behavioural pain assessment scales

There are two validated behavioural pain assessment scales that can be used to assess pain in non-communicative or sedated patients (e.g. mechanical ventilation); these are recommended to use instead of physiological indicators alone. The sedation and pain levels of children in intensive care should be assessed at least 4 hourly in intensive care.

- **BPS:** Behavioural Pain Scale
- **CPOT:** Critical-Care Pain Observation Tool
- In children: **Comfort-B Scale** and **FLACC** Behavioural Pain Assessment Scale

10.2.1 Behavioural Pain Scale (BPS)

BPS score ranges from 3 (no pain) to 12 (maximum pain).

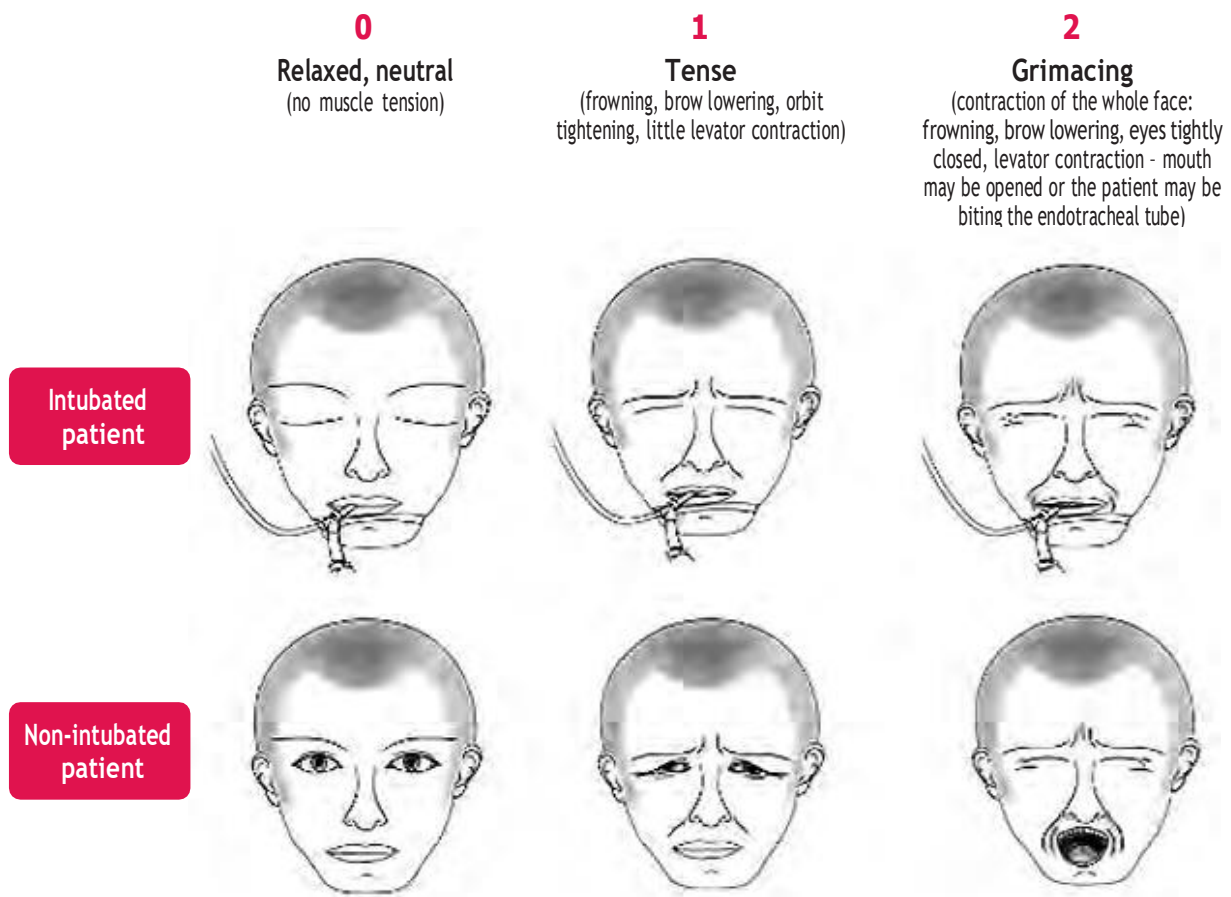
Item	Description	Score
Facial expression	Relaxed	1
	Partially tightened (e.g. brow lowering)	2
	Fully tightened (e.g. eyelid closing)	3
	Grimacing	4
Upper limb movements	No movement	1
	Partially bent	2
	Fully bent with finger flexion	3
	Permanently retracted	4
Compliance with mechanical ventilation	Tolerating movement	1
	Coughing but tolerating ventilation most of the time	2
	Fighting ventilator	3
	Unable to control ventilation	4

10.2.2 Critical-Care Pain Observation Tool (CPOT)

Indicator	Score		Description
Facial expressions	Relaxed, neutral	0	No muscle tension
	Tense	1	Presence of frowning, brow lowering, orbit tightening and levator contraction or any other change (e.g. opening eyes or tearing during nociceptive procedures)
	Grimacing	2	All previous facial movements plus eyelid tightly closed (the patient may present with mouth open or biting endotracheal tube)
Body movements	Absence of movements or normal position	0	Does not move at all (doesn't necessarily mean absence of pain) or normal position (movements not aimed toward the pain site or not made for the purpose of protection)
	Protection	1	Slow, cautious movements, touching or rubbing the pain site, seeking attention through movements
	Restlessness/agitation	2	Pulling tube, attempting to sit up, moving limbs/thrashing, not following commands, striking at staff, trying to climb out of bed
Compliance with the ventilator (intubated patients) or	Tolerating ventilator or movement	0	Alarms not activated, easy ventilation
	Coughing but tolerating	1	Coughing, alarms may be activated but stop spontaneously
	Fighting ventilator	2	Asynchrony; blocking ventilation, alarms frequently activated
Vocalization (extubated patient)	Talking in normal tone or no sound	0	Talking in normal tone or no sound
	Sighing, moaning	1	Sighing, moaning
	Crying out, sobbing	2	Crying out, sobbing
Muscle tension Evaluation by passive flexion and extension of upper limbs when patient is at rest or evaluation when patient is being turned	Relaxed	0	No resistance to passive movements
	Tense, rigid	1	Resistance to passive movements
	Very tense or rigid	2	Strong resistance to passive movements or incapacity to complete them
Total		(_ /8)	

Source: Adapted from Gélinas et al (2006).

Facial expressions



Source: Adapted from Payen et al (2001).

Note: A score of 1 may be attributed when a change in the patient's facial expression is observed compared with rest (e.g. opening or weeping).

How to use the Critical-Care Pain Observation Tool

1. The patient must be observed at rest for 1 minute to obtain a baseline value of the CPOT.
2. Then, the patient should be observed during nociceptive procedures known to be painful (e.g. turning, wound care) to detect any changes in the patient's behaviours to pain.
3. The patient should be evaluated before and at the peak effect of an analgesic agent to assess whether the treatment was effective or not in relieving pain.
4. For the rating of the CPOT, the patient should be attributed the highest score observed for each item during the observation period.
5. The patient should be attributed a score for each behaviour included in the CPOT and muscle tension should be evaluated last, especially when the patient is at rest because the stimulation of touch alone (when performing passive flexion and extension of the arm) may lead to behavioural reactions.

Free teaching CPOT video available from the Society of Critical Care Medicine ([🔗](#))

Observation of patient at rest (baseline)

The nurse looks at the patient's face and body to note any visible reaction for an observation period of 1 minute. She/he gives a score for all items except for muscle tension. At the end of the 1-minute period, the nurse holds the patient's arm in both hands - one at the elbow, and one to hold the patient's hand. Then she/he performs and passive flexion and extension of the upper limb, and feels any resistance the patient may exhibit. If the movements are performed easily, the patient is found to be relaxed with no resistance (score 0). If the movements can still be performed but with more strength, then it is concluded that the patient is showing resistance to movement (score 1). Finally, if the nurse cannot perform the movement, strong resistance is felt (score 2). This can be observed in patients who are spastic.

Observation of patient during turning

Even during the turning procedure, the nurse can still assess the patient's pain. While she/he is turning the patient on one side, she/he looks at the patient's face to note any reactions such as frowning or grimacing. These reactions may be brief or can last longer. The nurse also looks out for body movements. For instance, she/he looks for protective movements like the patient trying to reach or touching the pain site (e.g. surgical incision, injury site). In the mechanically ventilated patient the nurse pays attention to alarms and if they stop spontaneously or require that she/he intervenes (reassurance, administering medication). According to muscle tension, the nurse can feel if the patient is resisting to the movement or not. A score of 2 is given when the patient is resisting against the movement and attempts to get on his/her back.



10.2.3 COMFORT-B Scale

It cannot be used in children who are receiving muscle relaxant drugs or children with severe neurological impairment. The child should be observed for 2 minutes and six behaviours are scored as below (score either respiratory response or crying, depending on the child's intubation status).

Children scoring 11-22 are in the optimal range of sedation; children scoring < 10 may be oversedated (consider weaning); and children > 23 are undersedated.

COMFORT-B Scale

Item	Description	Score
Alertness	1. Deeply asleep	
	2. Lightly asleep	
	3. Drowsy	
	4. Fully awake and alert	
	5. Hyperalert	
Calmness/agitation	1. Calm	
	2. Slightly anxious	
	3. Anxious	
	4. Very anxious	
	5. Panicky	

COMFORT-B Scale

Item	Description	Score
Respiratory response (ventilated children)	1. No coughing and no spontaneous respiration	
	2. Spontaneous respiration with little or no response to ventilation	
	3. Occasional cough or resistance to ventilator	
	4. Actively breathes against ventilator or coughs regularly	
	5. Fights ventilator, cough or choking	
Cry (non-ventilated children)	1. Quiet breathing, no crying	
	2. Sobbing or gasping	
	3. Moaning	
	4. Crying	
	5. Screaming	
Physical movement	1. No movement	
	2. Occasional, slight movements	
	3. Frequent, slight movements	
	4. Vigorous movement limited to extremities	
	5. Vigorous movements including torso and head	
Muscle tone	1. Muscles totally relaxed, no muscle tone	
	2. Reduced muscle tone	
	3. Normal muscle tone	
	4. Increased muscle tone and flexion of fingers and toes	
	5. Extreme muscle rigidity and flexion of fingers and toes	
Facial tension	1. Facial muscle totally relaxed	
	2. Facial muscle tone normal; no facial muscle tension evident	
	3. Tension evident in some facial muscles	
	4. Tension evident throughout facial muscles	
	5. Facial muscles contorted and grimacing	
Total score		_____

Source: Adapted from Ambuel et al (1992).



10.24 FLACC Behavioural Pain Assessment Scale

The FLACC scale is a measurement used to assess pain for children between 2 months and 7 years or for individuals who are unable to communicate their pain.

FLACC Behavioural Pain Assessment Scale

Categories	Scoring		
	0	1	2
Face	No particular expression or smile	Occasional grimace or frown; withdrawn, disinterested	Frequent to constant frown, clenched jaw, quivering chin
Legs	Normal position or relaxed	Uneasy, restless, tense	Kicking or legs drawn up
Activity	Lying quietly, normal position, moves easily	Squirming, shifting back and forth, tense	Arches, rigid or jerking
Cry	No cry (awake or asleep)	Moans or whimpers, occasional complaint	Crying steadily, screams or sobs, frequent complaints
Consolability	Content, relaxed	Reassured by occasional touching, hugging or being talked to, distractible	Difficult to console or comfort

Source: Merkel et al (1997).

How to use the FLACC

In patients who are awake: observe for 1 to 5 minutes or longer. Observe legs and body uncovered. Reposition patient or observe activity. Observe body for tenseness and tone. Initiate consoling interventions if needed.

In patients who are asleep: observe for 5 minutes or longer. Observe legs and body uncovered. If possible, reposition the patient. Touch the body and observe for tenseness and tone.

Face

- Score 0 if the patient has a relaxed face, makes eye contact, shows interest in surroundings.
- Score 1 if the patient has a worried facial expression, with eyebrows lowered, eyes partially closed, cheeks raised, mouth pursed.
- Score 2 if the patient has deep furrows in the forehead, closed eyes, an open mouth, deep lines around nose and lips.

Legs

- Score 0 if the muscle tone and motion in the limbs are normal.
- Score 1 if the patient has increased tone, rigidity, or tension; if there is intermittent flexion or extension of the limbs.
- Score 2 if the patient has hypertonicity, the legs are pulled tight, there is exaggerated flexion or extension of the limbs, tremors.

Activity

- Score 0 if the patient moves easily and freely, normal activity or restrictions.
- Score 1 if the patient shifts positions, appears hesitant to move, demonstrates guarding, a tense torso, pressure on a body part.
- Score 2 if the patient is in a fixed position, rocking; demonstrates side-to-side head movement or rubbing of body part.

Cry

- Score 0 if the patient has no cry or moan, awake or asleep.
- Score 1 if the patient has occasional moans, awake or asleep.
- Score 2 if the patient has frequent or continuous moans, cries, grunts.

Consolability

- Score 0 if the patient is clam and does not require consoling.
- Score 1 if the patient responds to comfort by touching or talking in 30 seconds to 1 minute.
- Score 2 if the patient requires constant comforting or is inconsolable.

Interpreting the Behavioural Score

Each category is scored on the 0-2 scale, which results in a total score of 0-10; 0 = Relaxed and comfortable; 1-3 = Mild discomfort; 4-6 = Moderate pain; 7-10 = Severe discomfort or pain or both.

10.3 Richmond Agitation-Sedation Scale (RASS)

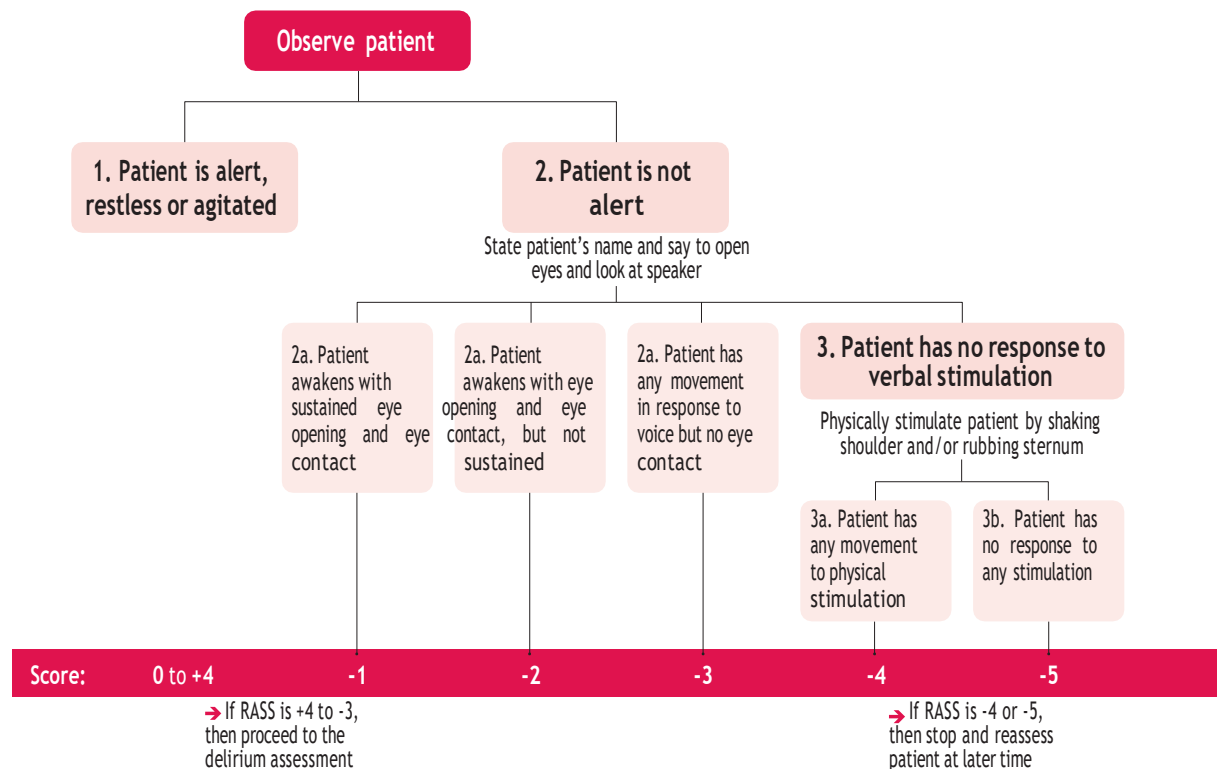
Assess agitation, anxiety and sedation levels on a regular basis using a standardized scale and set a daily sedation target based on clinical condition and management plans for the day. Consider the use of the Richmond Agitation-Sedation Scale (RASS). This has been validated in many clinical trials and can be easily taught to staff.

Score	Term	Description	
+4	Combative	Overtly combative, violent, immediate danger to staff	
+3	Very agitated	Pulls or removes tube(s) or catheter(s); aggressive	
+2	Agitated	Frequent non-purposeful movement, fights ventilator	
+1	Restless	Anxious but movements not aggressive vigorous	
0	Alert and calm		
-1	Drowsy	Not fully alert, but has sustained awakening (eye-opening/eye contact) to voice (> 10 seconds)	Verbal stimulation
-2	Light sedation	Briefly awakens with eye contact to voice (< 10 seconds)	
-3	Moderate sedation	Movement or eye opening to voice (but no eye contact)	Physical stimulation
-4	Deep sedation	No response to voice, but movement or eye opening to physical stimulation	
-5	Unarousable	No response to voice or physical stimulation	

Source: Adapted from Sessler et al (2002).

Algorithm for RASS assessment

In most patients, this assessment is very quick and takes only 30 seconds (only 10% take a few minutes).



Source: Adapted from Sessler et al (2002).

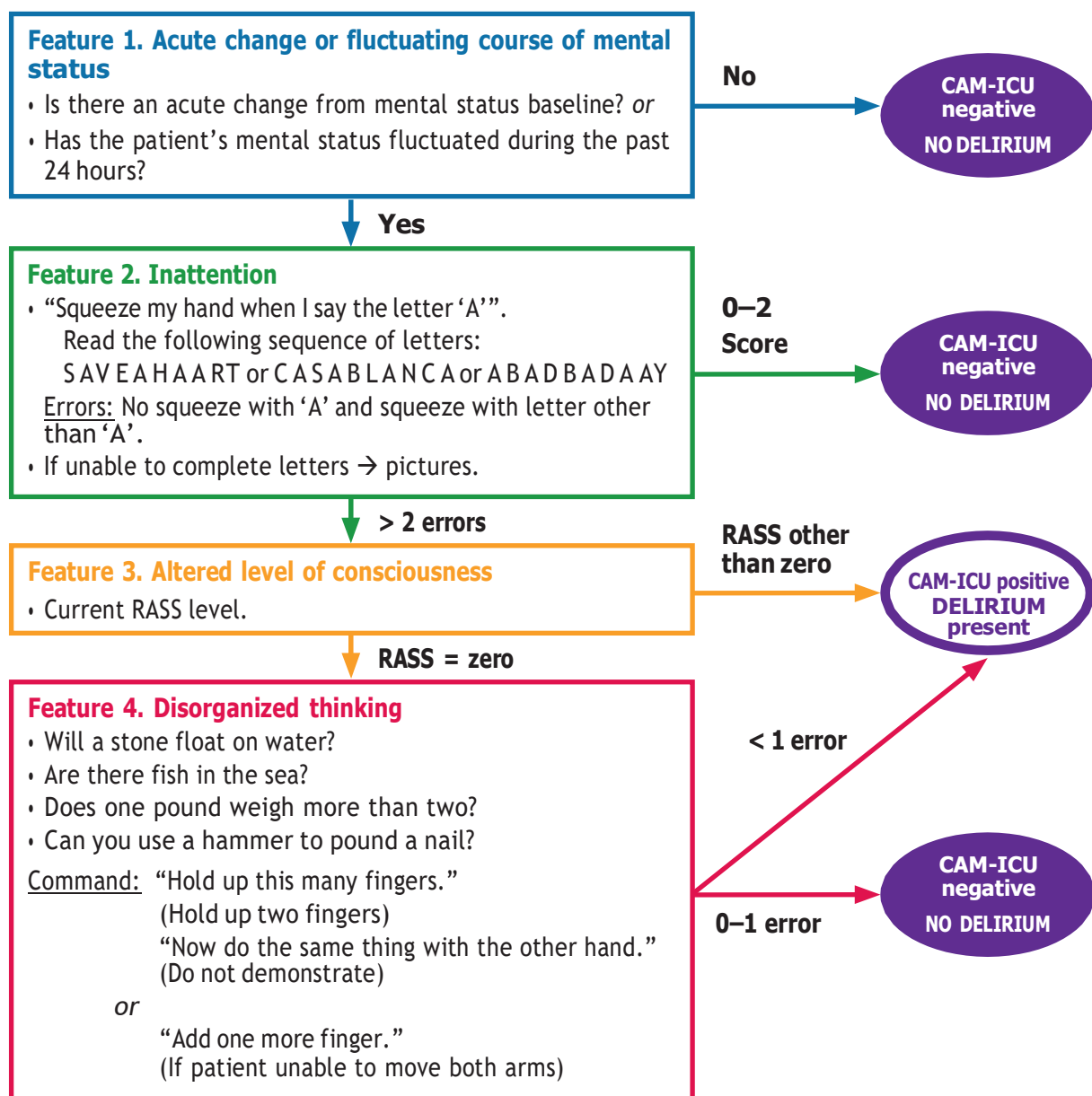


10.4 Flowchart and worksheet for the Confusion Assessment Method of the ICU for adults (CAM-ICU)

Use the CAM-ICU flowsheets and worksheet (4) reproduced below, to assess delirium in conjunction with the RASS scale. Additional training materials on how to do the CAM-ICU and train staff can also be found at the same link.

CAM-ICU flowchart

The flowchart can be used as a pocket card or wall poster to easily reference the procedure to assess for the presence of delirium.



Source: Ely et al (2001).

CAM-ICU worksheet

	Score	Check here if present
Feature 1: Acute onset or fluctuating course		
Is the patient different than his/her baseline mental status? or Has the patient had any fluctuation in mental status in the past 24 hours as evidenced by fluctuation on a sedation/level of consciousness scale (i.e. RASS/SAS, GCS or previous delirium assessment)?	Either question Yes →	<input type="checkbox"/>
Feature 2: Inattention		
Letters attention test: <u>Directions:</u> Say to the patient, "I am going to read you a series of 10 letters. Whenever you hear the letter 'A', indicate by squeezing my hand." Read the letters from the following list in a normal tone 3 seconds apart. SAVEAHAART or CASABLANCA or ABADBADAAY Errors are counted when patient fails to squeeze on the letter "A" and when the patient squeezes on any letter other than "A". If unable to complete letters attention test → use pictures (see Tool 10.6)	Number of errors > 2 →	<input type="checkbox"/>
Feature 3: Altered level of consciousness		
Present if actual RASS score is anything other than alert and calm (zero)	RASS anything other than zero →	<input type="checkbox"/>
Feature 4: Disorganized thinking		
Yes/No questions: Will a stone float on water? Are there fish in the sea? Does one pound weigh more than two? Can you use a hammer to pound a nail? Errors are counted when the patient incorrectly answers a question. <u>Command:</u> Say to the patient, "Hold up this many fingers." (Hold up two fingers in front of the patient) "Now do the same thing with the other hand." (Do not repeat the number of fingers) <i>Note:</i> If patient is unable to move both arms, for second part of command ask patient to "Add one more finger". An error is counted if patient unable to complete entire command.	Combined number of errors > 1 →	<input type="checkbox"/>
Overall CAM-ICU CAM-ICU positive = Feature 1 _____ + Feature 2 _____ + either Feature 3 _____ or Feature 4 _____	Criteria met →	<input type="checkbox"/> CAM-ICU positive (DELIRIUM present)
	Criteria not met →	<input type="checkbox"/> CAM-ICU negative (NO DELIRIUM)

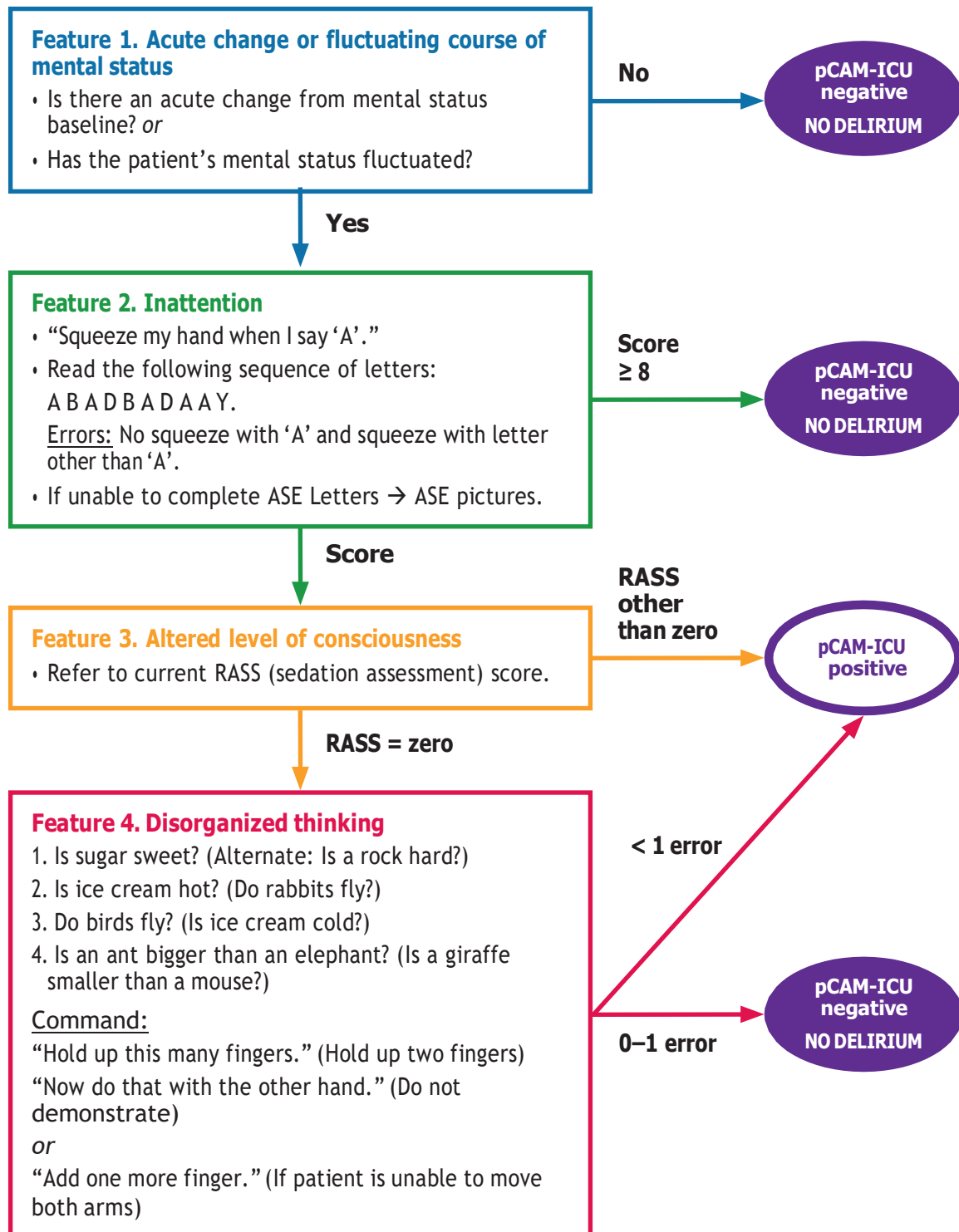
Source: Ely et al (2001).



10.5 Flowchart and worksheet for the Confusion Assessment Method of the ICU for children (pCAM-ICU)

This tool is adapted from Smith et al (2011) (see References and resources).

pCAM-ICU flowchart



pCAM-ICU worksheet

Feature 1: Acute change or fluctuating course of mental status		
<p>A. Is there an acute change from mental status baseline? Yes or No</p> <p>B. Has my patient's mental status fluctuated during the past 24 hours? Yes or No Evidenced by fluctuation on a sedation scale (RASS), SAS, GCS or previous delirium assessment.</p>	<p>If either answer YES then circle + →</p>	<p>+ / -</p>
Feature 2: Inattention →FEATURE POSITIVE if SCORE 0-7 on Vigilance "A" test or ASE picture test		
<p>Vigilance "A" test:</p> <p>I want my patient to squeeze my hand when I say ONLY the letter "A". I will read the 10-letter sequence in the same order every day, with my normal voice, saying each letter once every second.</p> <p><u>Directions to patient:</u> "Squeeze my hand when I say the letter 'A'. Let's practise, 'A'".</p> <p><u>To score:</u> When I say the letter "A" and the patient does not squeeze my hand, I subtract 1 point. When I say the other letters and the patient squeezes my hand, I subtract 1 point.</p> <p>A _ B _ A _ D _ B _ A _ D _ A _ A _ Y _</p>	<p>If the SCORE is 0-7 then circle + →</p>	<p>+ / -</p>
or		
<p>ASE picture test:</p> <p>I will show the patient "5 memory pictures". I want the patient to remember the 5 "memory pictures" when shown a larger "deck" of 10 pictures.</p> <p><u>Directions to patient:</u> "I am going to show you 5 pictures that I want you to remember". (Show 1 picture every 3 seconds and state object's name.)</p> <p><u>Directions if patient can verbalize:</u> "Say yes when you see 1 of those 5 pictures again". (Show all pictures from deck and state object's name.)</p> <p><u>Directions to intubated patient:</u> "Nod your head yes when you see 1 of those 5 pictures again".</p> <p><u>To score:</u> If the patient nods or says "yes" to ONLY the 5 memory pictures they have completed the task successfully - SCORE 10/10. If patient does not nod or say "yes" to 1 of the 5 memory pictures, I will subtract 1 point. If the patient nods or says "yes" to the other pictures in the deck, I will subtract 1 point.</p> <p>Memory picture: _____ / 5 Deck pictures: _____ / 5</p>	<p>If the SCORE is 0-7 then circle + →</p>	<p>+ / -</p>
Feature 3: Altered level of consciousness →FEATURE POSITIVE if the current RASS score is anything other than 0		
<p>At the time of sedation assessment the RASS score was _____</p>		<p>+ / -</p>

Feature 4: Disorganized thinking

Directions if patient can verbalize: "I am going to ask you 4 questions, say 'yes' or 'no' to answer".

Directions to intubated patient: "I am going to ask you 4 questions, nod your head yes or no to answer".

Set A:

1. Is sugar sweet?
2. Is ice cream hot?
3. Do birds fly?
4. Is an ant bigger than an elephant?

Set B:

1. Is a rock hard?
2. Do rabbits fly?
3. Is ice cream cold?
4. Is a giraffe smaller than a mouse?
5. Directions to patient: "Hold up this many fingers." (Examiner hold up two fingers for patient to see)
Directions to patient: "Now do the same thing with the other hand." (Do not show fingers again to patient)
Directions to patient if unable to move both arms: "Now, add one more finger." (Do not show fingers again to patient)

To score:

If the patient answers a question incorrectly, I will subtract 1 point.
If the patient is not able to complete the command no. 5, I will subtract 1 point.

If the SCORE is 0-3 then circle +
→

+ / -

Paediatric delirium = Feature 1 _____ + Feature 2 _____ + either Feature 3 _____ or Feature 4 _____



10.6 Procedure for assessing attention: attention screening exam (ASE) for adults

This procedure is to be used to assess for feature 2 (**inattention** - a cardinal feature of delirium), when the patient is unable to complete the letters attention test (SAVEAHAART). This happens in only about 10% of patients.

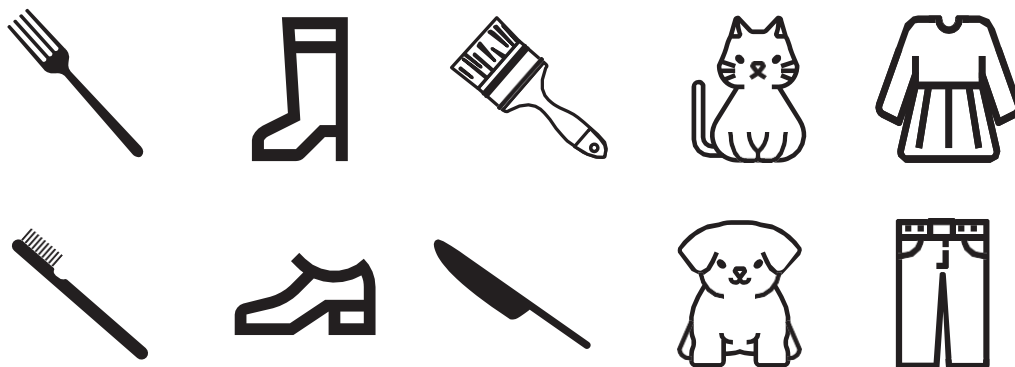
Step 1

- Say to the patient: *“Mr or Mrs ..., I am going to show you pictures of some common objects. Watch carefully and try to remember each picture because I will ask what pictures you have seen.”*
- Present five pictures: naming them and showing them each for 3 seconds.



Step 2

- Say to the patient: *“Now I am going to show you some more pictures. Some of these you have already seen and some are new. Let me know whether or not you saw the picture before by nodding your head yes (demonstrate) or no (demonstrate).”*
- Present ten pictures (five new, five repeated): naming them and showing them each for 3 seconds.



Scoring

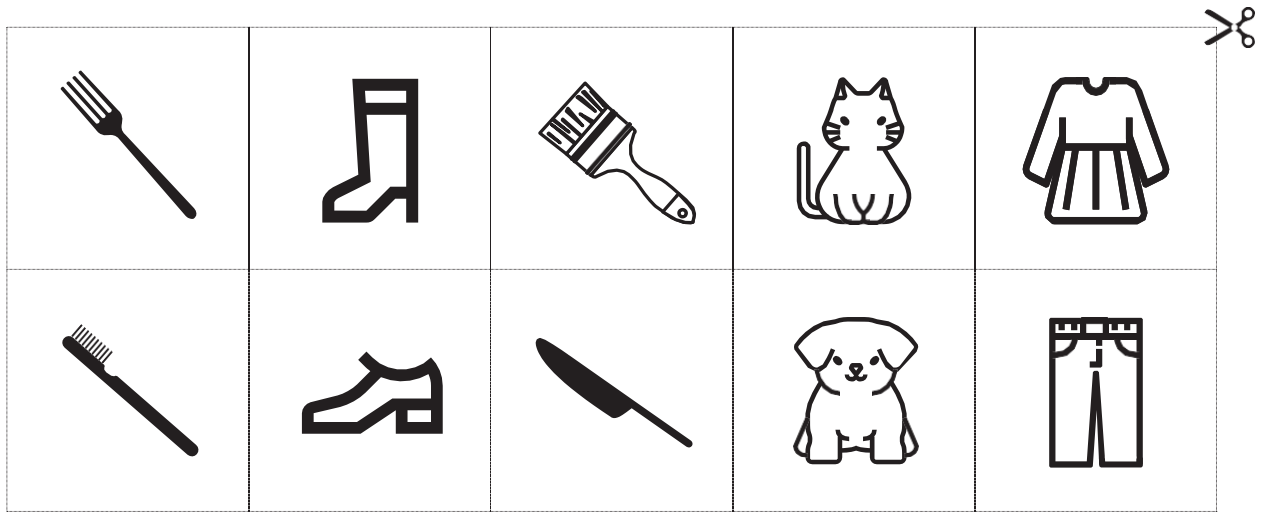
This test is scored by the number of correct “yes” or “no” answers during Step 2 (out of a possible 10).



Important: Alternate daily between Forms A and B (see next tool) if repeat measures are taken. If a patient wears glasses make sure they have them on when attempting the ASE.

Source: Adapted from Ely and Vanderbilt University (2002).

Form A



Source: Adapted from Ely and Vanderbilt University (2002).

Form B



Source: Adapted from Ely and Vanderbilt University (2002).



10.7 Guide to commonly used sedatives in adults

There are many sedative medications available to treat agitation and anxiety. You will need to see which medications your hospital currently has and consider which medications you may want to use in the future. It is important to familiarize yourself with the basic pharmacokinetics and side-effects of any drug you use. The goal is to reach the sedation target with the lowest possible sedative medication to minimize toxicity. The doses provided below are intended to be used for adult patients who are intubated and receiving mechanical ventilation. Continuous infusions of benzodiazepines should be avoided in adult patient if safe alternatives are to reduce the risks of oversedation, prolonged days of IMV and delirium.

	Propofol	Midazolam	Lorazepam	Diazepam	Dexmedetomidine ^a	Ketamine
Onset	< 1 minute	1-5 minutes	5-20 minutes	2-5 minutes	1-3 minutes	< 1 minute
Infusion	10-80 µg/kg/min	0.04-0.2 mg/kg/hr	0.01-0.1 mg/kg/hr	Not used	0.2-1.5 µg/kg/hr	0.2-0.5 mg/kg/hr
Time to arousal	10-15 minutes	1-2 hours	2-6 hours	2-4 hours	6-10 minutes	1-2 hours
Risks	Respiratory depression Hypotension Idiosyncratic rhabdomyolysis and acidosis and cardiovascular collapse (Propofol Infusion Syndrome, PRIS) Raised triglycerides	Respiratory depression Hypotension Prolonged sedation with infusions due to active metabolite Reduce dose in renal and liver failure Delirium	Respiratory depression Hypotension Propylene glycol carrier may irritate veins and cause metabolic acidosis with prolonged administration Delirium	Respiratory depression Hypotension Oversedation with repeated boluses with accumulation of drug and active metabolite Delirium	Hypotension Bradycardia More pronounced in elderly	Laryngospasm Emergence delirium Respiratory depression (especially in neonates or when used concurrently with opiates) Porphyria Genitourinary symptoms

Note:

^a Less commonly available.



Early in severe ARDS, however, deep sedation targets may be needed to safely achieve LPV targets and reduce asynchrony. In cases when NMB are administered, remember to also give a continuous sedative for amnesia and analgesic for pain.



10.8 Guide to commonly used opioid analgesics in adults

There are several opioids available to treat pain. You will need to see which medications your hospital currently has and consider which medications you may want to use in the future. Familiarize yourself with the basic pharmacokinetics and side-effects of any drug you use. Be sure to set a therapeutic analgesia plan and communicate to all caregivers for a consistent approach.

These considerations are adapted from the *Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult* (Jacobi et al., 2002) (see References and resources).

The doses provided below are suggestions and will need adjustment based on the amount of pain and whether the patient is receiving mechanical ventilation.

	Morphine	Hydromorphone	Fentanyl
Intermittent dose IV	0.01-0.15 mg/kg every 1-2 hr	10-30 µg/kg every 1-2 hr	0.35-1.5 µg/kg every 0.5-1 hr
Infusion	0.07-0.5 mg/kg/hr	7-15 µg/kg/hr	0.7-10 µg/kg/hr
Half-life	3-7 hr	2-3 hr	1.5-6 hr
Equianalgesic IV dose ^a	10 mg	1.5 mg	200 µg
Situations where drug is preferred	Intermittent dosing	Intermittent dosing Haemodynamic instability Renal failure	Rapid onset in acutely distressed patients Haemodynamic instability Renal failure
Risks ^b	Histamine release causing hypotension Prolonged effect in renal failure due to metabolite		Rigidity with high doses Repeated dosing may cause accumulation and prolonged effects

Notes:

^a These doses produce approximately the same analgesic effects;

^b Side-effects common to all agents include respiratory depression, coma and delirium, hypotension (especially with morphine) and ileus.



Meperidine (pethidine), tramadol and codeine may be available at many hospitals; however, each drug has noteworthy limitations and thus are not optimal for critically ill patients. Meperidine has variable efficacy for analgesia, has an active metabolite that causes neuroexcitation (apprehension, tremors, delirium and seizures) and may interact with antidepressants (contraindicated with monoamine oxidase inhibitors and best avoided with selective serotonin-reuptake inhibitors), so it is not recommended for repetitive use. Tramadol is generally considered inferior to many other analgesics and can cause adverse reactions when used with other serotonin re-uptake inhibiting medications. Codeine has markedly different pharmacodynamics across different patients due to variability in drug metabolizing rates.



10.9 Guide to using neuromuscular blockers in adults

WHO suggests that in moderate-severe ARDS ($\text{PaO}_2/\text{FiO}_2 < 150$), neuromuscular blockade by continuous infusion should not be routinely used.

A trial found that neuromuscular blockade improved survival in adult patients with severe ARDS without causing significant weakness (Papazian et al., 2010), but results of a recent larger trial found that use of neuromuscular blockade with high PEEP strategy was not associated with a survival benefit when compared with a light sedation strategy without neuromuscular blockade (NHLBI PCTN et al., 2019). Continuous neuromuscular blockade may still be considered in patients with ARDS, both adults and children, in certain situations: ventilator dyssynchrony despite sedation, such that tidal volume limitation cannot be reliably achieved; or refractory hypoxaemia or hypercapnia. Neuromuscular blockade may also be useful to ascertain accurate pulmonary mechanics (e.g. plateau pressure measurements), but this alone is not an indication for neuromuscular blockade infusion.

Suxamethonium (ie succinylcholine) is a depolarizing muscle relaxant used most commonly for rapid sequence induction for intubation. This medication can cause bradycardia (especially in infants or children < 5 years of age) and life-threatening hyperkalaemia. Because of this latter concern, suxamethonium is contraindicated in chronic skeletal muscle disease, denervating events or neuromuscular disease, recent burns, rhabdomyolysis, history of malignant hyperthermia or concurrent hyperkalaemia.

	Pancuronium	Vecuronium	Cisatracurium	Rocuronium
IV dose	Intermittent: 0.08-0.1 mg/kg Infusion: 0.2-0.6 µg/kg/min (usually 1-2.5 mg/hr)	Intermittent: 0.08-0.1 mg/kg Infusion: 0.2-0.8 µg/kg/min (usually 1-4 mg/hr)	Intermittent: 0.15-0.20 mg/kg Infusion: 3 mcg/kg/min for first 20 minutes then reduce to 1-2 mcg/kg/min (range: 0.5-10 mcg/kg/min)	Intermittent: 0.6-1.2 mg/kg Infusion: 0.5-0.7 mg/kg/hr
Common points on dosing	Tailor intermittent dose to patient response. Titrate infusion dose clinically or to achieve one or two twitches with train of four stimulation on peripheral nerve stimulator, if available			
Onset	< 4 minutes	2-3 minutes	2-3 minutes	2-3 minutes
Specific risks	Long duration of activity: ~90-160 minutes Accumulation in hepatic and renal dysfunction Dose-dependent increased HR and blood pressure (due to vagolytic and weak sympathomimetic effects)	Intermediate duration of activity: ~30-45 minutes. Accumulation in hepatic and renal dysfunction	Duration of action: ~45-75 minutes Slight accumulation in hepatic and renal dysfunction	Intermediate duration of activity: ~30-45 minutes. Accumulation in hepatic and renal dysfunction Can be reversed completely by sugammadex when available
Common risks	Appropriate sedation and analgesia should be administered concurrently. HR and blood pressure should be routinely monitored; increases may indicate inadequate sedation or analgesia. ICU-acquired weakness if used for prolonged period			



10.10 Guide to commonly used antipsychotics (haloperidol) in adults

Antipsychotic agents can be used to keep actively delirious patients safer. Haloperidol is a typical antipsychotic that has been available for many years. Atypical antipsychotics can also be used (e.g. quetiapine, olanzapine and risperidone). Dexmedetomidine is a newer agent that has both sedative and anti-delirium effects.

Haloperidol	
Loading dose	Begin with 2-5 mg IV Double dose every 15 minutes until desired effect is achieved Do not exceed total of 20 mg/day
Onset	10-20 minutes
Risks	Torsade de pointes arrhythmia, do not use if the QTc interval on ECG is prolonged to > 460 milliseconds Suspect neuroleptic malignant syndrome if patient develops hyperthermia, muscle rigidity and rhabdomyolysis

Dosing recommendations	
Quetiapine	Begin with 25-50 mg po twice or three times daily Increase up to 200 mg po total daily dose (halve dose in elderly)
Olanzapine	Begin with 5-10 mg IV/IM/po Repeat dose in 2 hours to maximum of 30 mg/day
Risperidone	Begin with 1-2 mg po daily Increase to maximum of 6 mg po daily



Side-effects of atypical antipsychotics are prolonged QTc interval and extrapyramidal effects (less common than with typical antipsychotic agents).



10.11 Guide to paediatric analgesics, sedatives and neuromuscular blockers

There are several agents available for analgesia, sedation and neuromuscular blockade. You will need to see which medications your hospital currently has and consider which medications you may want to use in the future. Familiarize yourself with the basic pharmacokinetics and side-effects of any drugs you use. The doses provided below are suggestions and will need titration in individual patients based on the amount of pain and whether the patient is receiving mechanical ventilation. Appropriate sedation and analgesia should be administered concurrently with neuromuscular blockade, which has no sedative or analgesic properties.



Propofol is contraindicated for sedation in children < 16 years old in the ICU because of the risk of propofol infusion syndrome (acidosis and rhabdomyolysis).

	Drug	Enteral dose	Bolus IV dose	IV infusion
Analgesia	Paracetamol	10-15 mg/kg/6hr	10mg/kg q6-8hr	N/A
	Oxycodone	0.05-0.2 mg/kg/4-6hr	N/A	N/A
	Ibuprofen	5-10 mg/kg/6-8hr	N/A	N/A
	Morphine	0.2-0.4 mg/kg/6hr	0.1-0.2 mg/kg	0-40 µg/kg/hr
	Fentanyl	N/A	1-2 µg/kg	0-8 µg/kg/hr
Sedation	Hydromorphone	0.03-0.06 mg/kg/4hr	0.01-0.015 mg/kg	0.003-0.005 mg/kg/hr
	Midazolam	N/A	0.05-0.2 mg/kg	0-4 µg/kg/min
	Diazepam		0.1-0.2 mg/kg	N/A
	Chloral hydrate	30-50 µg/kg/6hr	N/A	N/A
	Triclofos	30-50 µg/kg/6hr	N/A	N/A
	Allmemazine	1 mg/kg/6hr	N/A	N/A
	Ketamine	6-8 mg/kg	0.5-2 mg/kg	0.3-1.22 mg/kg/hr
	Dexmedetomidine	N/A	1 mcg/kg over 10 minutes	0.2-0.7 mcg/kg/hr
	Clonidine	4-5 mcg/kg	1-2 mcg/kg	0.18-3.16 mcg/kg/hr
Neuromuscular blockade	Vecuronium	N/A	0.1 mg/kg as required	0-4 µg/kg/min
	Cisatracurium	N/A	0.1-0.15 mg/kg	0.5-10 µg/kg/min
	Rocuronium	N/A	0.6 mg/kg	0.12 µg/kg/min
	Pancuronium	N/A	0.04-0.1 mg/kg	0.1 mg/kg/h
	Suxamethonium	N/A	1-2 mg/kg	0.3-0.6 mg/kg q5-10min PRN

References and resources

- Ambuel B, Hamlett KW, Marx CM, Blumer JL. Assessing distress in pediatric intensive care environments: the COMFORT scale. *J Pediatr Psychol.* 1992;17(1):95-109.
- Balas MC, Vasilevskis EE, Olsen KM, Schmid KK, Shostrom V, Cohen MZ et al. Effectiveness and safety of the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle. *Crit Care Med.* 2014;42(5):1024-36.
- Bar J, Fraser GL, Puntillo K, Ely EW, Gélinas C, Dasta GF et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. *Crit Care Med.* 2013;41(1):263-306.
- Barnes-Daly MA, Phillips G, Ely EW. Improving hospital survival and reducing brain dysfunction at seven California community hospitals: implementing PAD guidelines via the ABCDEF bundle in 6,064 patients. *Crit Care Med.* 2017;45(2):171-178.
- Bradt J, Dileo C. Music interventions for mechanically ventilated patients. *Cochrane Database Syst Rev.* 2014;12:CD006902. doi: 10.1002/14651858.CD006902.pub3.
- Davidson JE, Harvey MA, Bemis-Dougherty A, Smith JM, Hopkins RO. Implementation of the Pain, Agitation, and Delirium Clinical Practice Guidelines and promoting patient mobility to prevent post-intensive care syndrome. *Crit Care Med.* 2013;41(9 suppl 1):S136-145.
- Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM et al. Surviving Sepsis Campaign: guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med.* 2013;41(2):580-637.
- Ely EW. The ABCDEF bundle: science and philosophy of how ICU liberation serves patients and families. *Crit Care Med.* 2017;45(2):321-330.
- Ely EW, Inouye SK, Bernard GR, Gordon S, Francis J, May L et al. Delirium in mechanically ventilated patients: validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *JAMA.* 2001;286(21):2703-2710.
- Ely EW, Truman B, Shintani A, Thomason JW, Wheeler AP, Gordon S et al. Monitoring sedation status over time in ICU patients: the reliability and validity of the Richmond Agitation-Sedation Scale (RASS). *JAMA.* 2003;289(22):2983-2991.
- Ely EW and Vanderbilt University. The confusion assessment method for the ICU (CAM-ICU) training manual. Nashville, TN: Vanderbilt University Medical Center; 2002.
- Gélinas C, Fillion L, Puntillo KA, Viens C, Fortier M. Validation of the critical-care pain observation tool in adult patients. *Am J Crit Care.* 2006;15(4):420-427.
- Girard TD, Jackson JC, Pandharipande PP, Pun BT, Thompson JL, Shintani AK et al. Delirium as a predictor of long-term cognitive impairment in survivors of critical illness. *Crit Care Med.* 2010;38(7):1513-20.
- Girard TD, Kress JP, Fuchs BD, Thomason JW, Schweickert WD, Pun BT et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. *Lancet.* 2008;371(9607):126-134.
- Ista E, van Dijk M, Tibboel D, de Hoog M. Assessment of sedation levels of paediatric intensive care patients can be improved using the COMFORT "behavior" scale. *Pediatr Crit Care Med.* 2005;6(1):58-63.
- Iwashyna T. Survivorship will be the defining challenge of critical care in the 21st century. *Ann Intern Med.* 2010;153(3):204-205.
- Iwashyna TJ, Ely EW, Smith DM, Langa KM. Long-term cognitive impairment and functional disability among survivors of severe sepsis. *JAMA.* 2010;304(16):1787-94.
- Jacobi J, Fraser GL, Coursin DB, Riker RR, Fontaine D, Wittbrodt ET et al. Clinical practice guidelines for the sustained use of sedatives and analgesics in the critically ill adult. *Crit Care Med.* 2002;30(1):119-141.
- Johansson M, Kokinsky E. The COMFORT behavioural scale and the modified FLACC scale in paediatric intensive care. *Nurs Crit Care.* 2009;14(3):122-130.
- Loneragan E, Britton AM, Luxenberg J, Wyller T. Antipsychotics for delirium. *Cochrane Database Syst Rev.* 2007;2:CD005594.
- Merkel SI, Voepel-Lewis T, Shayevitz JR, Malviya S. The FLACC: a behavioral scale for scoring postoperative pain in young children. *Pediatr Nurs.* 1997;23(3):293-297.
- National Heart, Lung, and Blood Institute (NHLBI) PCTN, Moss M, Huang DT, Brower RG, Ferguson ND, Ginde AA et al. Early neuromuscular blockade in the acute respiratory distress syndrome. *N Engl J Med.* 2019;380(21):1997-2008. Epub 2019/05/22. doi: 10.1056/NEJMoa1901686. PubMed PMID: 31112383; PMCID: PMC6741345.
- Pandharipande PP, Pun BT, Herr DL, Maze M, Girard TD, Miller RR et al. Effect of sedation with dexmedetomidine vs lorazepam on acute brain dysfunction in mechanically ventilated patients: the MENDS randomized controlled trial. *JAMA.* 2007;298(22):2644-2653.
- Papazian L, Forel J-M, Gacouin A, Penot-Ragon C, Perrin G, Loundou A et al. Neuromuscular blockers in early acute respiratory distress syndrome. *N Engl J Med.* 2010;363:1107-16.
- Payen JF, Bru O, Bosson JL, Lagrasta A, Novel E, Deschaux I et al. Assessing pain in critically ill sedated patients by using a behavioral pain scale. *Crit Care Med.* 2001;29(12):2258-2263.
- Rijkenberg S, Stilma W, Endeman H, Bosman RJ, Oudemans-van Straaten HM. Pain measurement in mechanically ventilated critically ill patients: Behavioral Pain Scale versus Critical-Care Pain Observation Tool. *J Crit Care.* 2015;30(1):167-72.
- Sessler CN, Gosnell MS, Grap MJ, Brophy GM, O'Neal PV, Keane KA et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care patients. *Am J Respir Crit Care Med.* 2002;166(10):1338-1344.
- Smith HAB, Boyd J, Fuchs C, Melvin K, Berry P, Shintani A et al. Diagnosing delirium in critically ill children: validity and reliability of the Pediatric Confusion Assessment Method for the intensive care unit. *Crit Care Med.* 2011;39(1):150-157.
- Umunna P, Tekwani K, Barounis D, Kettaneh N, Kulstad E. Ketamine for continuous sedation of mechanically ventilated patients. *J Emerg Trauma Shock.* 2015;8(1):11-15.
- Wong DL, Hockenberry MJ. Wong's essentials of pediatric nursing (sixth edition). St Louis, MO: Elsevier (Mosby); 2001.

11

Liberation from invasive mechanical ventilation



11

Liberation from invasive mechanical ventilation

Summary

Use a daily coordinated spontaneous awakening trial (SAT) with spontaneous breathing trial (SBT) protocol to liberate patients from mechanical ventilation as soon as possible as this improves patient outcomes. In patients who fail SBT, recognize and treat the reason for failure, and try again the next day. In patients who pass SBT, consider extubation after evaluating their ability to protect the airway and clear secretions. After extubation, monitor the patient closely for signs of respiratory failure and the need for prompt re-intubation.

Steps for liberation from invasive mechanical ventilation (IMV)

Step 1	Daily assessment for patient readiness to breath spontaneously
Step 2	Conduct the SBT safely
Step 3	Evaluate patient's performance on the SBT
Step 4	Assess safety for extubating
Step 5	Extubate
Step 6	Monitor-record-interpret-respond
Step 7	Deliver quality care: implement as part of ABCDEF protocol

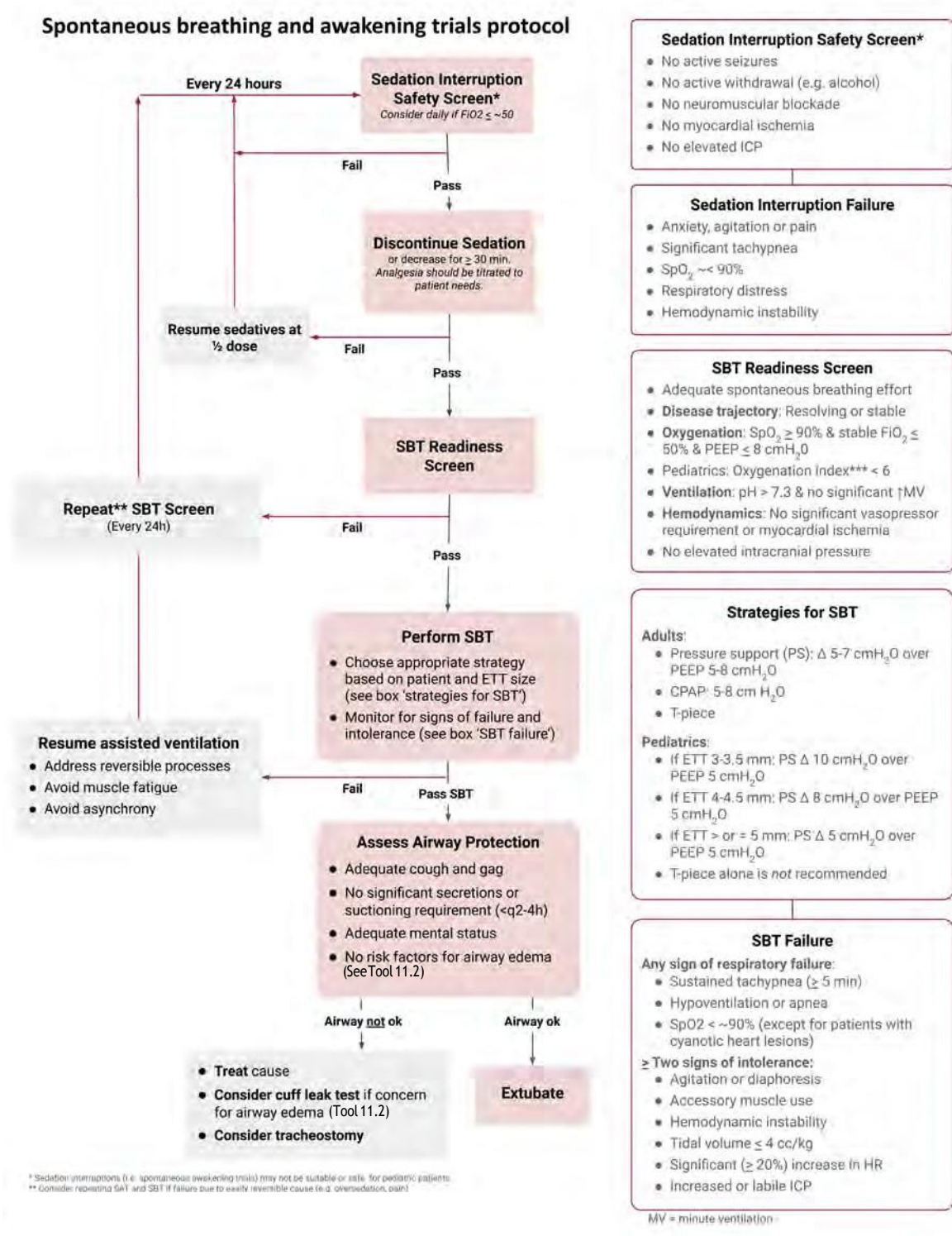
There are limited data to guide the timing of tracheostomy, though routinely this is considered at 10-14 days if the need for prolonged mechanical ventilation persists. During the COVID-19 pandemic, the optimal timing of tracheostomy has been debated. These debates have included arguments to perform tracheostomy as early as possible to assist with early mobilization, reduced sedation requirements, easier pulmonary hygiene and less potential risk for tube malposition. The debates have also included arguments to perform tracheostomy considerably later than routine in order to decrease the chance of health care worker exposure to aerosolized particles during the procedure.

Tools

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

11.1 Algorithm for daily sedation interruption and daily spontaneous breathing trial (SBT)

This protocol outlines the steps for daily consideration of sedation interruption, spontaneous breathing trial, and extubation - modified by the OpenCriticalCare.org Project from Girard et al. (2008) and MacIntyre (2007).



Source: USAID-STAR-UCSF Open Critical Care Project ([link](#))

11.2 How to perform a cuff leak test

Performing a cuff leak test may help to determine that the airway is patent, without swelling.

When an adequate cuff leak is present, it signifies that the patient's airway is unlikely to be profoundly edematous, and the patient is less likely to have post-extubation stridor (PES). Of note, studies of the predictive value of cuff leak tests vary, and generally the cuff leak test is considered to have higher specificity than sensitivity. The presence of a cuff leak does not ensure that the patient's airway will remain open after extubation.

***When an adequate cuff leak is not present*, consider steroids and elevating the head of the bed to reduce swelling; check again in 12–24 hours.**

The lack of a cuff leak makes it more likely that the patient could have post-extubation stridor if steroids are not given prior (Kuriyama et al., 2020; Miller and Cole, 1996).

The American Thoracic Society recommends checking a cuff leak in patients with high risk of post-extubation stridor.

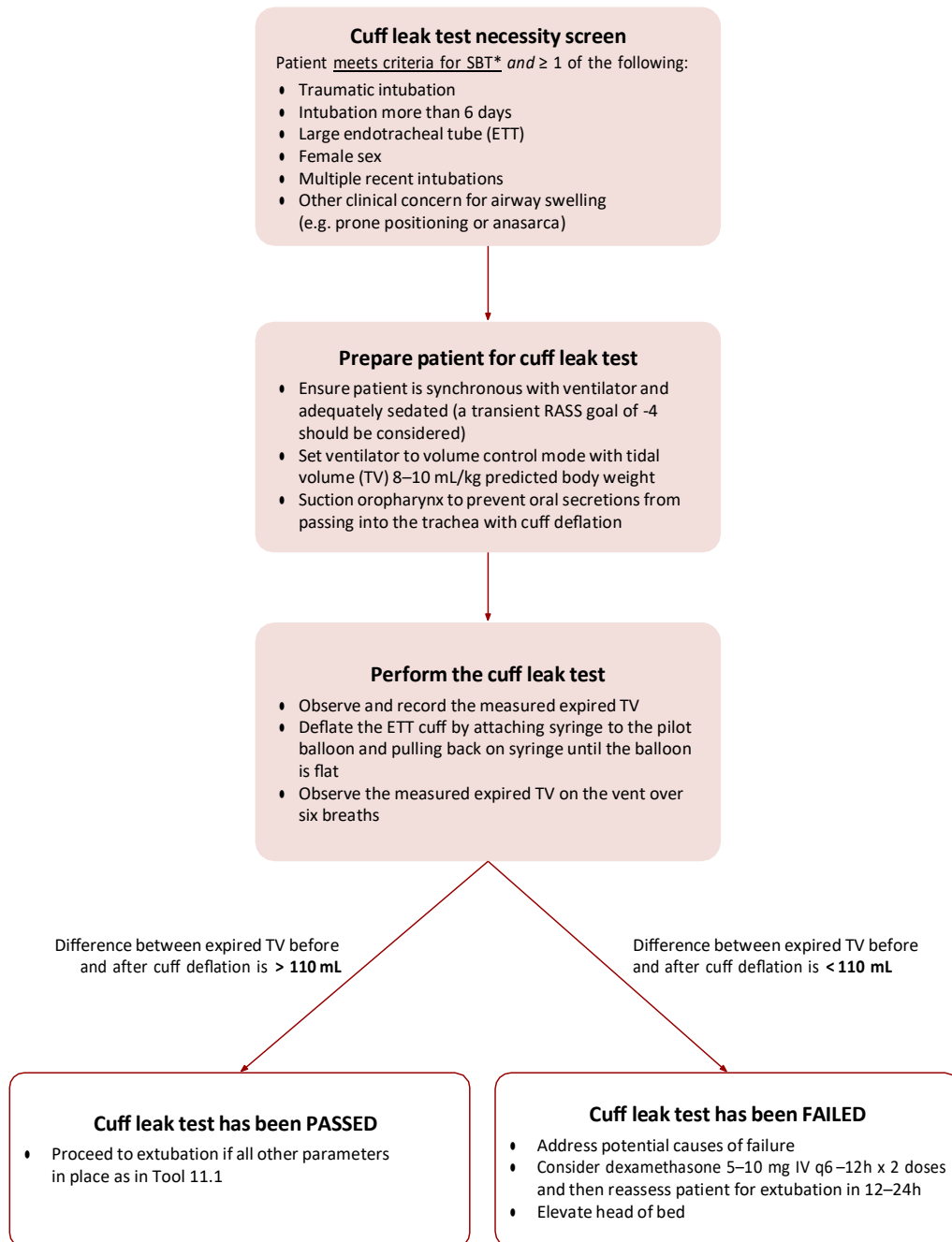
Risk factors for post-extubation stridor

neck trauma
prone positioning
anasarca
multiple recent intubations
intubation for > 6 days

Protocol to perform a cuff leak test

1. Ensure proper PPE and IPC for providers as the leak test is an aerosol-generating procedure.
2. Patient should be sedated, or the test done when the patient is asleep (to prevent measurement artifacts).
3. Standard vent settings; volume-controlled ventilation with:
 - TV: 8-10 mL/kg
 - RR: 10-12
 - flow rate: 50-60 L/min.
4. Suction oropharynx (to prevent secretions from passing into the trachea when the ETT cuff is deflated).
5. Measure the expired TV.
6. Deflate the ETT cuff.
7. Re-measure the expired TV over six breaths:
 - cuff leak is the difference in TV with cuff inflated and deflated;
 - > 110 mL difference in expiratory TV before and after cuff down has negative predictive value (NPV) 98% for post-extubation stridor.
8. Re-inflation of the cuff.

Cuff leak protocol



*SBT – spontaneous breathing trial criteria (see Tool 11.1).

Source: USAID-STAR-UCSF Open Critical Care Project ([link](#))

11.3 Respiratory care pocket card reference

The card, which can be printed or saved to your mobile device, ( is available in:

- English
- French
- Portuguese
- Spanish.

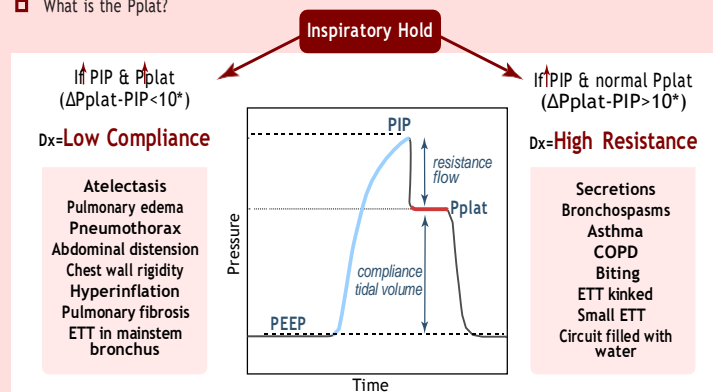
High Pressures, Desaturations & Dyssynchrony

General Considerations

- ❑ Is the ventilator set to FiO₂ 100% while you troubleshoot?
- ❑ Is the patient hemodynamically unstable? If so, consider pressors & urgent evaluation for pneumothorax or severe auto-PEEP.
- ❑ Is the ventilator circuit connected & set correctly?
- ❑ Are breath sounds bilateral? If unilateral, consider mainstem ETT, lobar collapse, atelectasis, and pneumothorax.

High Pressures

- ❑ Is the patient agitated or asynchronous?
- ❑ Can a suction catheter pass easily through the endotracheal tube? If no, consider kinked tube, biting/bite block, secretions/suction, or replace ETT.
- ❑ What is the Pplat?



Troubleshooting low compliance: Decrease V_T & evaluate for breath stacking (auto-PEEP). Consider ↓ PEEP or adjunct therapies for hypoxemia if decrease in PEEP causes desaturations.

Troubleshooting high resistance: Work outside (machine) to inside (alveoli); circuit problem, ETT kink/occlusion/biting, ETT obstructed/mainstem, large airway obstruction (mucous plug), small/medium airway obstruction (bronchospasm); auscultation & passing a suction catheter can quickly eliminate many of these.

Desaturations

- ❑ Is the endotracheal tube in good position? (consider CXR)
- ❑ Is the pulse oximetry waveform good quality?
- ❑ Is there acute hypotension? Evaluate for tension pneumothorax, air trapping and pulmonary embolism
- ❑ Is the source of oxygen faulty or is there an air leak? Check each connection/element sequentially from source of oxygen to the patient.
- ❑ Are there concomitant pressure elevations? If so, see "High Pressures" (next column)
- ❑ Is P:F < 150 in setting of worsening ARDS? If so, consider adjunct therapies (above).
- ❑ Are there signs of infection? Consider ventilator-associated pneumonia.

Patient-Ventilator Dyssynchrony

- Detect signs of dyssynchrony: coughing, paradoxical breathing, ventilator alarms (low tidal volumes or high pressures), breath stacking.
- Treat underlying causes: 1) Ineffective triggering (patient or ventilator); 2) Inappropriate triggering (patient inspires while ventilator expires); 3) Auto-triggering (non-respiratory muscle movement triggers ventilator); 4) Flow dyssynchrony (too fast or too slow)

General Approach

- Treat pain or anxiety if present
- If ineffective ventilator triggering change trigger sensitivity, decrease VT or pressure
- Increase V_T to 8 mL/kg and increase flow rate if pressures allow. Consider change to decelerating flow delivery if setting available.
- If still dyssynchronous, paralyze patient (and sedate patient to RASS goal -5)

Discomfort & Delirium

Discomfort (pain, agitation, anxiety) & Delirium

- Ensure appropriate analgesia & sedation to minimize ICU/IMV duration & risk of long-term neuropsychiatric impact.
- **Reassess every ≤ 4 hours using a standardized scale**
 - Goal RASS -4 to 0 in intubated patients
 - If RASS -4 to -5 consider lightening sedation unless patient is paralyzed or dyssynchronous with ventilator.
 - Target RASS -5 for paralyzed patients. Never paralyze without sedation
- Perform Daily Sedation Interruptions (DSIs) in non-paralyzed patients to reassess sedation & analgesia needs, which can guide weaning these medications.

Delirium: Prevention & treatment of delirium reduces mortality and ICU/IMV duration

- Screen every 12h using standardized tool (i.e. CAM-ICU)
- Treat delirium by addressing underlying causes (pain, agitation, anxiety, or physiologic derangements)

[Richmond Agitation Sedation Scale \(RASS\)](#)



[Confusion Assessment Method for the ICU \(CAM-ICU\)](#)



Ventilator Weaning & Extubation

Spontaneous Breathing Trial (SBT) Initiation Criteria & Considerations

- Patient likely to trigger ventilator, stable $FiO_2 \leq 0.50$ adults (≤ 0.40 pediatrics) and PEEP ≤ 8
- pH > 7.30 . VE < 15 L/min
- -MAP > 60 mmHg (minimal pressors)
- ICP: non-labile and < 20 mmHg w/ CPP > 60 mmHg
- No MI in previous -48hr

Weaning Strategies

- Once daily SBT PS $\Delta 5-7$ cmH₂O if ETT size > 5 ($\Delta 8$ cmH₂O if ETT 4-4.5; $\Delta 10$ cmH₂O if ETT 3-3.5) in addition to PEEP 5-8 cmH₂O (2nd daily trial ok if failure sedation-related or due to transient issue); Consider additional $\Delta 3-5$ cmH₂O of PS if HME used
- SBT x 30min -probably as good as SBT x 2hr or longer for most adult patients
- If adult with cardiogenic pulmonary edema risk: Consider 15min T-piece (i.e. no PS or PEEP)
- RSBI (rapid Shallow Breathing Index) = f/V_T ; RSBI is unreliable; < 80 goal for extubation; sensitive, not specific (if > 105 , good predictor of failure)
- Coupling daily sedation interruption, early mobility, & SBT is associated with faster extubation

Extubation Criteria

- Have you fixed the original problem and **no upcoming procedures?**
- Adequate **oxygenation?** ($PaO_2 > -60$ on PEEP ≤ 8 cmH₂O, $FiO_2 \leq 0.50$)
- Adequate **ventilation** without excessive **work of breathing?** ($\Delta PaCO_2 \uparrow$ of < 10 mmHg with remaining pH > 7.30 during SBT)
- **Secretions?** (assess cough strength, suction frequency & secretion volume)
- **Airway protection?** (assess gag, spontaneous cough and GCS)
 - Assess **risk of post-extubation airway obstruction**:
 - Consider cuff leak test if: intubation $> 6d$, trauma, multiple intubations, prolonged prone, flat, volume overload, head/neck trauma, among others
- **Cuff Leak Test:** 1. pt must be sedated (interaction with vent = incr PIP= incr leak = false reassurance); 2. Suction oropharynx; 3. Initiate AC-VC V_T 8 mL/kg, RR 12, Ti: 1.5sec, Flow 50 LPM; 4. Measure expired V_T ; 5. Deflate cuff and wait 6 breaths; 6. Measure expired V_T (should \downarrow by > 110 mL to predict low risk of stridor post extubation); 7. Reinflate cuff
 - Decrease aspiration risk by holding tube feeds for safe interval (-6-8h)
 - Extubation criteria/goals for neuro patients may be different (e.g. visual tracking, swallowing, GCS > 10 , $< 40yo$)
- **Hemodynamics** - re-intubation of an unstable patient can be lethal

Source: USAID-STAR-UCSF Open Critical Care Project ()

11.4 Spontaneous breathing trial (SBT) order set

Last updated December 2021

Spontaneous Breathing Trial (SBT) Order Set					
Surname/Family Name		Name		Attending/Team	
Today's Date / /		Patient MRN/Registration #	Age	Sex	Predicted Weight (kg) Height(cm)
SBT Initiation Criteria:		- FiO ₂ ≤ 0.50 and PEEP ≤ 8 or OI < 6 in pediatrics patients - No ↑ in PEEP/FiO ₂ requirements over past 24hrs - pH > 7.30 and no significant IMV required		- MAP: no significant vasopressor requirement - ICP: non-labile and in normal range - No myocardial infarction in previous <48hr	
Tube Feeds During SBT: <input type="checkbox"/> Continue Tube Feeds <input type="checkbox"/> Hold tube feedings _____ hours prior to SBT. If patient fails SBT, resume immediately.					
Standard SBT Strategy:		<ul style="list-style-type: none"> - Daily SBT until patient is extubated, or until at least 3 consecutive failed trials (see below). - If failure is sedation related can repeat SBT later on same day - When possible, coordinate with Daily Sedation Interruption/Spontaneous Awakening Trial (adults only) - Suspend SBT on days when weaning readiness criteria are not met (see protocol for details). - May withhold SBT for pending special procedures / surgery. 			
Mode:		<input type="checkbox"/> Default if ETT size > 5mm, Pressure Support (PS) = delta 5-7 cmH ₂ O above PEEP of 5-8 cmH ₂ O; FiO ₂ ≤ 0.50 <input type="checkbox"/> Default if ETT size 4-4.5mm, Pressure Support (PS) = delta 8 cmH ₂ O above PEEP of 5 cmH ₂ O; FiO ₂ ≤ 0.50 <input type="checkbox"/> Default if ETT size 3-3.5mm, Pressure Support (PS) = delta 10 cmH ₂ O above PEEP of 5 cmH ₂ O; FiO ₂ ≤ 0.50 <input type="checkbox"/> T-piece Trial (Consider if resolving cardiogenic pulmonary edema - <i>Adults only</i>) <input type="checkbox"/> CPAP (Consider when VT > 10 mL/kg - <i>Adults only</i>) <input type="checkbox"/> PS = _____ PEEP= _____ FiO ₂ = _____			
Duration:		<input type="checkbox"/> 30 minutes <input type="checkbox"/> 2 hours <ul style="list-style-type: none"> - Initial intolerance of SBT: PS can be titrated down from PS of 15-20 to SBT settings over 5-30 min. - Evaluation: RT at bedside for initial 5 min until a 30 min SBT is passed. Full Vent check @ 30 min or 2 hrs. - Failure Criteria Met: Return to previous ventilator settings (or new written orders for post-SBT). When ARDS Net protocol is in place resume previous ARDS Net settings. 			
After SBT Passed: <input type="checkbox"/> Notify ICU team to evaluate for extubation <input type="checkbox"/> Extended SBT as tolerated <input type="checkbox"/> Return to prior settings					
When Tracheostomy tube is present:		Follow orders as written above. When patient passes a 2hr SBT, then: <ul style="list-style-type: none"> <input type="checkbox"/> Extend SBT as tolerated if failure criteria met, then return to prior settings <input type="checkbox"/> Tracheostomy Mask Trials at FiO₂ ≤ 0.50 as tolerated. If failure criteria met, then return to SBT PS settings. If these PS settings also are not tolerated then return to prior or newly ordered vent settings. 			
Difficult to Wean:		Initiate only after 3 consecutive SBT failures PS Range: delta PS 5-20 cmH ₂ O above PEEP 5-8 cm H ₂ O; FiO ₂ ≤ 0.50 Titrate PS as needed to maintain spontaneous RR 25-35 (1-1.5x age adjusted normal) and VT 5-8 mL/kg Daily Routine: After 2 hrs of stable breathing pattern at a stable PS level, then: <ul style="list-style-type: none"> <input type="checkbox"/> PS Decrement challenge: reduce by 3-5 CmH₂O every 2-4 hrs <input type="checkbox"/> Trial Duration: not to exceed _____ hrs/day <input type="checkbox"/> Notify ICU team when patient passes 2 hr SBT at standard PS settings to evaluate for extubation 			
Cuff Leak Check:		Consider if: intubation > 6 days, neck trauma, multiple intubations, prolonged prone positioning, volume overload <ul style="list-style-type: none"> <input type="checkbox"/> Perform cuff leak PRIOR TO SBT <input type="checkbox"/> No cuff leak necessary <div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <ol style="list-style-type: none"> 1. Pt must be sedated (interaction with vent can incr PIP which can incr leak = false reassurance) 2. Suction oropharynx 3. Initiate AC-VC VT 8 mL/kg, RR 12, Ti: 1.5sec, Flow 50 LPM 4. Measure expired VT 5. Deflate cuff and wait 6 breaths 6. Measure expired VT expired VT (goal is ↓ by >110mL in measure expired VT for adults) 7. Re-inflate cuff </div> <div style="width: 45%;"> <p><i>Alternative approach (pediatrics):</i></p> <ol style="list-style-type: none"> 1. Sedate patient and suction oropharynx 2. Connect patient to resuscitation bag 3. Place stethoscope over larynx and listen 4. Slowly deflate ETT cuff completely w/cuff manometer 5. Give a breath by slowly squeezing the bag, increasing pressure until audible leak is heard 6. If pressure reaches 30 cmH₂O without a leak = failure; if pressure <12 cmH₂O with leak = pass; if pressure >20 cm H₂O then patient likely to fail 7. Reinflate cuff and resume prior settings </div> </div>			
Date (time): _____		Name: _____		Signature: _____ Contact #: _____	



TO PRINT MORE
Forms scan here

TO LEARN MORE
check out [this algorithm](#)
for SBT, SAT and cuff leak



Source: USAID-STAR-UCSF Open Critical Care Project ([link](#))

References and resources

- Acute Respiratory Distress Syndrome Network, Brower RG, Matthay MA, Morris A, Schoenfeld D, Thompson BT et al. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. *N Engl J Med*. 2000;342(18):1301-1308.
- American Thoracic Society. Slideshow on ventilator waveforms (<https://www.thoracic.org/professionals/clinical-resources/critical-care/clinical-education/mechanical-ventilation/ventilator-waveform-analysis.php> (accessed 12 August 2019).
- Bice T, Nelson JE, Carson SS. To trach or not to trach: uncertainty in the care of the chronically critically ill. *Semin Respir Crit Care Med*. 2015;36(6):851-8.
- Blackwood B, Alderdice F, Burns KE, Cardwell CR, Lavery G, O'Halloran P. Protocolized versus non-protocolized weaning for reducing the duration of mechanical ventilation in critically ill adult patients. *Cochrane Database Syst Rev*. 2010;5:CD006904.
- Brochard L, Rauss A, Benito S, Conti G, Mancebo J, Rkik N et al. Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. *Am J Respir Crit Care Med*. 1994;150(4):896-903.
- Brooks AD, Ahrens TS, Schaiff R, Prentice D, Sherman G, Shannon W et al. Effect of a nursing-implemented sedation protocol on the duration of mechanical ventilation *Crit Care Med*. 1999;27(12):2609-2615.
- Cabello B, Thille AW, Roche-Campo F, Brochard L, Gómez FJ, Mancebo J. Physiological comparison of three spontaneous breathing trials in difficult-to-wean patients. *Intensive Care Med*. 2010;36(7):1171-9. doi: 10.1007/s00134-010-1870-0. Epub 2010 Mar 30. PMID: 20352189.
- Epstein S. Decision to extubate. *Intensive Care Med*. 2002;28(5):535-546.
- Esteban A, Frutos F, Tobin MJ, Alía I, Solsona JF, Vallverdú I et al. A comparison of four methods of weaning patients from mechanical ventilation. Spanish Lung Failure Collaborative Group. *N Engl J Med*. 1995;332(6):345-350.
- Esteban A, Alía I, Gordo F, Fernández R, Sonsona JF, Vallverdú I et al. Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. Spanish Lung Failure Collaborative Group. *Am J Respir Crit Care Med*. 1997;156(2 Pt 1):459-465.
- Esteban A, Alía I, Tobin MJ, Gil A, Gordo F, Vallverdú I et al. Effect of spontaneous breathing trial duration on outcome of attempts to discontinue mechanical ventilation. Spanish Lung Failure Collaborative Group. *Am J Respir Crit Care Med*. 1999;159(2):512-8. doi: 10.1164/ajrccm.159.2.9803106. PMID: 9927366.
- Fan E, Zakhary B, Amaral A, McCannon J, Girard TD, Morris PE et al. Liberation from mechanical ventilation in critically ill adults. An official ATS/ACCP clinical practice guideline. *Ann Am Thorac Soc*. 2017;14(3):441-443.
- Girard TD, Kress GP, Fuchs BD, Thomason JW, Schweickert WD, Pun BT et al. Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): a randomised controlled trial. *Lancet*. 2008;371(9607):126-133.
- Klompas M, Anderson D, Trick W, Babcock H, Kerlin MP, Li L et al. The preventability of ventilator-associated events. The CDC Prevention Epicenters Wake Up and Breathe Collaborative. *Am J Respir Crit Care Med*. 2015;191(3):292-301.
- Kuriyama A, Jackson JL, Kamei J. Performance of the cuff leak test in adults in predicting post-extubation airway complications: a systematic review and meta-analysis. *Crit Care*. 2020;24(1):640. (<https://pubmed.ncbi.nlm.nih.gov/33160405/>, accessed 23 August 2021).
- Lemaire F, Teboul JL, Cinotti L, Giotto G, Abrouk F, Steg G et al. Acute left ventricular dysfunction during unsuccessful weaning from mechanical ventilation. *Anesthesiology*. 1988;69(2):171-9. doi: 10.1097/0000542-198808000-00004. PMID: 3044189.
- Levine S, Nguyen T, Taylor N, Friscia ME, Budak MT, Rothenberg P et al. Rapid disuse atrophy of diaphragm fibers in mechanically ventilated humans. *N Engl J Med*. 2008;358(13):1327-1335.
- MacIntyre N. Discontinuing mechanical ventilatory support. *Chest*. 2007;132(3):1049-1056.
- MacIntyre NR, Cook DJ, Ely EW Jr, Epstein SK, Fink JB, Heffner JE et al. Evidence-based guidelines for weaning and discontinuing ventilatory support: a collective task force facilitated by the American College of Chest Physicians; the American Association for Respiratory Care; and the American College of Critical Care Medicine. *Chest*. 2001;120(6 suppl):375S-95S.
- MacIntyre PE, Schug SA. Acute pain management: a practical guide. Taylor & Francis; 2021.
- Maggiore SM, Idone FA, Vaschetto R, Festa R, Cataldo A, Antonicelli F et al. Nasal high-flow versus Venturi mask oxygen therapy after extubation. Effects on oxygenation, comfort, and clinical outcome. *Am J Respir Crit Care Med*. 2014;190(3):282-8.
- Manthous CA, Schmidt GA, Hall JB. Liberation from mechanical ventilation. *Chest*. 1998;114(3):886-901.
- Miller RL, Cole RP. Association between reduced cuff leak volume and postextubation stridor. *Chest*. 1996;110(4):1035-40.
- Newth CJ, Venkataraman S, Willson DF, Meert KL, Harrison R, Dean JM et al. Weaning and extubation readiness in pediatric patients. *Pediatr Crit Care Med*. 2009;10(1):1-11.
- Nilsestuen Jo, Hargett KN. Using ventilator graphics to identify patient-ventilator asynchrony. *Respir Care*. 2005;50(2):202-234.
- Perren A, Domenighetti G, Mauri S, Genini F, Vizzardi N. Protocol-directed weaning from mechanical ventilation: clinical outcome in patients randomized for a 30-min or 120-min trial with pressure support ventilation. *Intensive Care Med*. 2002;28:1058-1063.
- Rothaar RC, Epstein SK. Extubation failure: magnitude of the problem, impact on outcomes, and prevention. *Curr Opin Crit Care*. 2003;9(1):59-66.
- Subirà C, Hernández G, Vázquez A, Rodríguez-García R, González-Castro A, García C et al. Effect of pressure support vs T-piece ventilation strategies during spontaneous breathing trials on successful extubation among patients receiving mechanical ventilation: a randomized clinical trial. *JAMA*. 2019;321(22):2175-2182. doi:10.1001/jama.2019.7234.



12

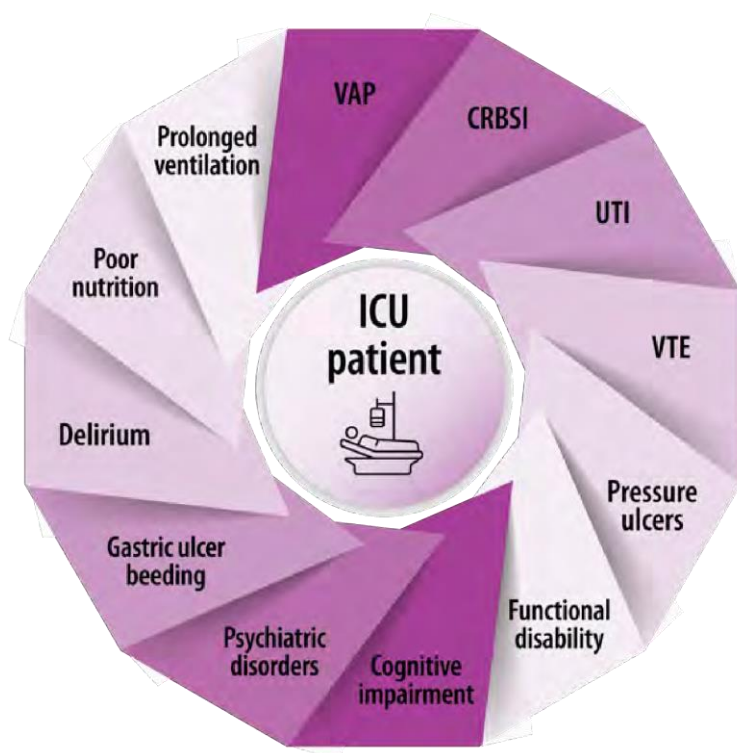
Best practices to prevent complications



12 Best practices to prevent complications

Summary

ICU patients are at high risk for complications. This chapter provides tools for implementation of key interventions to reduce the risk of complications in the ICU which include:



Notes: CRBSI - catheter-related bloodstream infection; UTI - urinary tract infection; VAP - ventilator-associated pneumonia; VTE - venous thromboembolism.

Tools

- 12.1 Interventions to prevent complications in hospitalized and critically ill patients with COVID-19
- 12.2 Checklist for central venous catheter (CVC) insertion
- 12.3 Checklist for preventing ventilator-associated pneumonia (VAP)
- 12.4 Checklist for preventing urinary tract infections (UTI)
- 12.5 Procedure for providing enteral nutrition (EN) for adults
- 12.6 Procedure for providing enteral nutrition (EN): paediatric considerations
- 12.7 Algorithm for early mobility in the ICU
- 12.8 Thromboembolic prophylaxis in COVID-19
- 12.9 ABCDE bundle

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

See WHO COVID-19 Clinical management: living guidance (2021) ([↗](#))

Anticipated outcome	Interventions
Reduce days of invasive mechanical ventilation	<ul style="list-style-type: none"> • Use weaning protocols that include daily assessment for readiness to breathe spontaneously • Minimize continuous or intermittent sedation, targeting specific titration endpoints (light sedation unless contraindicated) or with daily interruption of continuous sedative infusions • Early mobilization • Implementation as a bundle of care
Reduce incidence of ventilator-associated pneumonia (VAP)	<ul style="list-style-type: none"> • Oral intubation is preferable to nasal intubation in adolescents and adults • Keep patient in semi-recumbent position (head of bed elevation 30-45°) • Use a closed suctioning system; periodically drain and discard condensate in tubing • Use a new ventilator circuit for each patient; once patient is ventilated, change circuit if it is soiled or damaged, but not routinely • Change heat moisture exchanger when it malfunctions, when soiled, or every 5-7 days
Reduce incidence of catheter-related bloodstream infection (CRBSI)	<ul style="list-style-type: none"> • 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	<ul style="list-style-type: none"> • Turn patient every 2 hours
Reduce incidence of stress ulcers and GI bleeding	<ul style="list-style-type: none"> • 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: <ul style="list-style-type: none"> – mechanical ventilation for ≥ 48 hours – coagulopathy – renal replacement therapy – liver disease – multiple comorbidities – higher organ failure score
Reduce the development of antimicrobial resistance	Utilize de-escalation protocols as soon as patient is clinically stable and there is no evidence of bacterial infection
Reduce the development of adverse drug effects	Expose patient to empiric antimicrobial therapy for the shortest time possible, to prevent nephrotoxicity, cardiac and other side-effects from unnecessary antimicrobial use
Promote appropriate antimicrobial prescribing and use during the COVID-19 pandemic	Do not prescribe antibiotics to suspected or confirmed COVID-19 patients with low suspicion of a bacterial infection, to avoid more short-term side-effects of antibiotics in patients and negative long-term consequences of increased antimicrobial resistance

12.2 Checklist for central venous catheter (CVC) insertion

- In the literature, a research collaborative found that **using a central line checklist** as a reminder for the inserter **significantly reduced the incidence of central venous catheter-related blood stream infections**. This checklist is adapted from *An intervention to decrease catheter-related blood stream infections in the ICU* (Provonost et al., 2006).

- Patient verification, allergies and informed consent.

- Hand hygiene before the procedure.

- Wear maximal barrier precautions on insertion: full
 - sterile gown
 - face mask
 - face shields
 - sterile gloves
 - hair cover
 - cover the patient in a full sterile sheet from head to toe.

- Use chlorhexidine 2% in 70% isopropyl alcohol for skin preparation and apply in a back and forth friction rub motion for 30 seconds.

- Let dry completely before puncturing site. It should not be blotted dry.

- Choose the optimal site: subclavian or internal jugular vein preferred in adults; internal jugular or femoral vein preferred in children depending on age.

- Once in place, evaluate the continuing need for the central line on a daily basis.

- Remove line immediately when no longer needed or when non-functional.

12.3 Checklist for preventing ventilator-associated pneumonia (VAP)

- In order to prevent VAP, a complication of endotracheal intubation and invasive mechanical ventilation, consider the following procedures, when possible:
 - Oral intubation instead of nasal intubation.
 - Keep the patient in a semi-recumbent position (head of bed elevated up to $\geq 30\text{-}45^\circ$).
 - Use a closed suctioning system.
 - Periodically drain and remove condensation in tubing.
 - Use a new ventilator circuit for each patient. Change if soiled or damaged.
 - Do not routinely change ETT or ventilator circuit, only if they malfunction.
 - Change heat and moisture exchanger when malfunctions, soiled, or every 5-7 days.
 - Perform regular antiseptic oral care with chlorhexidine gel or mouthwash.
 - Discontinue invasive ventilation in a safe and prompt manner: Daily
 - sedation interruption of continuous sedative infusions. Daily evaluation for SBT readiness (see Chapter 11).
 - Extubation to non-invasive ventilation when appropriate (i.e. primarily for patients ventilated because of a COPD exacerbation, and only in centres with sufficient expertise in non-invasive ventilation).
 - ABCDE bundle.



Note: Note: Heat and moisture exchangers (HME) are not routinely used in infants and small children as they significantly increase dead space. Use heated humidifiers instead.

When HMEs are used, ensure the size of the selected filter is appropriate for the size of the patient to minimize dead space and calculate/account for increased dead space in the circuit when choosing ventilator settings (and target minute ventilation).

12.4 Checklist for preventing urinary tract infections (UTI)

- Prevention of UTI requires an appropriate technique for catheter insertion as well as appropriate management of indwelling catheters. Consider the following procedures when possible:

Catheter insertion

- Insert catheter only when necessary.
- Hand hygiene before procedure.
- Use aseptic technique and sterile equipment.
- Use as small a catheter as possible, consistent with proper drainage.

Catheter management

- Maintain unobstructed urine flow.
- Empty collection bag regularly:
 - Separate collecting container for each patient.
 - Do not allow draining spigot to touch collecting container.
- Keep collecting bag below level of bladder at all times.
- Cleaning urethral meatus with antiseptic is unnecessary. Routine cleaning is adequate.
- Secure catheter to prevent movement and urethral traction.
- Sterile, continuously closed drainage system.
 - Do not disconnect catheter and drainage tube unless catheter must be irrigated.
 - Replace collecting system aseptically and after disinfecting catheter-tubing junction if the following occur:
 - break in aseptic technique
 - disconnection
 - leakage.
- Daily check and remove as soon as there is no indication.

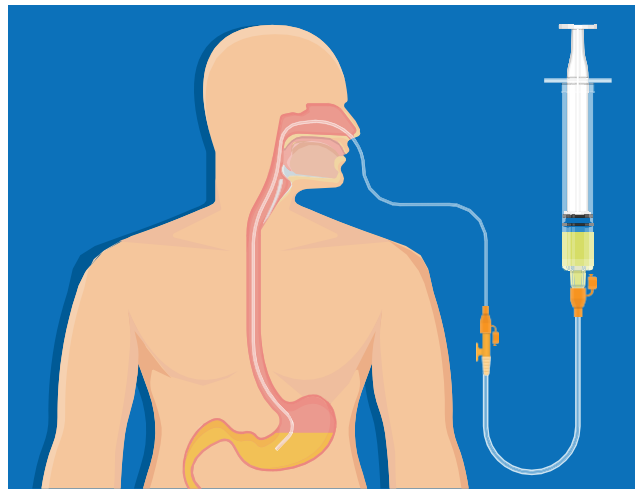


12.5 Procedure for providing enteral nutrition (EN) for adults

The goal is to start enteral nutrition, even in small volumes, as soon as the patient is stable.

This tool can be used to start enteral nutrition.

1. Place a feeding tube.
2. Confirm placement with radiograph (gastric [NG] or small bowel [NJ] feeding are acceptable).
3. Once the feeding tube has been confirmed, start with an infusion of up to **30 mL/hr of clear fluid or feed**.
4. Aspirate the NG tube every 4 hours.
5. Gradually increase the volume of feed with the aim of building up to full feeding within 48 hours.



Feeding intolerance

Intolerance of feeding may result from poor gastric emptying and lead to high residual gastric volumes.

The absolute value that is too high and should prompt cessation of tube feeds is not clear.

Stop feeding when:

- volumes high (between 250-500 mL)
- clinical signs of intolerance (abdominal pain, abdominal distension and diarrhoea).

None of the features are specific for feed intolerance.

Possible treatments include advancing the feeding tube into the small bowel (can be done at the bedside) or adding prokinetic medications (e.g. metoclopramide intravenously).

Note: With an NJ tube, only continuous feeds can be delivered (no bolus) and residuals cannot be checked.

Set caloric target and aim to reach this within a few days

Estimate the patient's daily caloric needs, or basal energy expenditure (BEE). Adjust for fever and stress:

- $BEE \text{ (kcal/day)} = 25 \times \text{body weight (kg)}$
- fever: $BEE \times 1.1$ (for each degree above the normal body temperature)
- mild to moderate stress: $BEE \times 1.2-1.4$
- moderate to severe stress: $BEE \times 1.4-1.6$.

Estimate your patient's daily protein requirements:

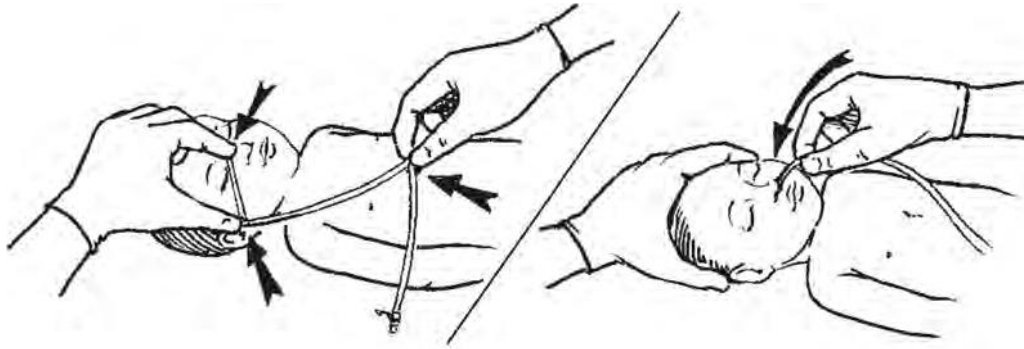
- normal 1.2- 2.0 g/kg
- hypercatabolism: 2-3 g/kg
- ratio of non-protein calories to nitrogen (70:1-100:1).

Note: Hypocaloric feeding (40-60% of non-protein caloric needs) may be as beneficial as full caloric feeds (> 70%).



12.6 Procedure for providing enteral nutrition (EN): paediatric considerations

Enteral feeding via NG tube is the preferred method of providing maintenance fluid.



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

Initial fitting

1. Measure the distance from the nose to the ear and then to the epigastrium.
2. Insert NG tube to the measured distance.
3. Check correct placement of tube:
 - check the pH of aspirate using pH indicator strips
 - position can be seen on chest X-ray
 - if in doubt remove and replace.
4. Secure the NG tube by taping to the cheek avoiding upwards pressure on the nares.
5. Once correct placement has been confirmed, flush the tube with water. It is now safe to use the tube for administration of feed and medication.
6. Flush the NG tube with sterile water after administration of NG drugs otherwise it will block.

Ongoing checks

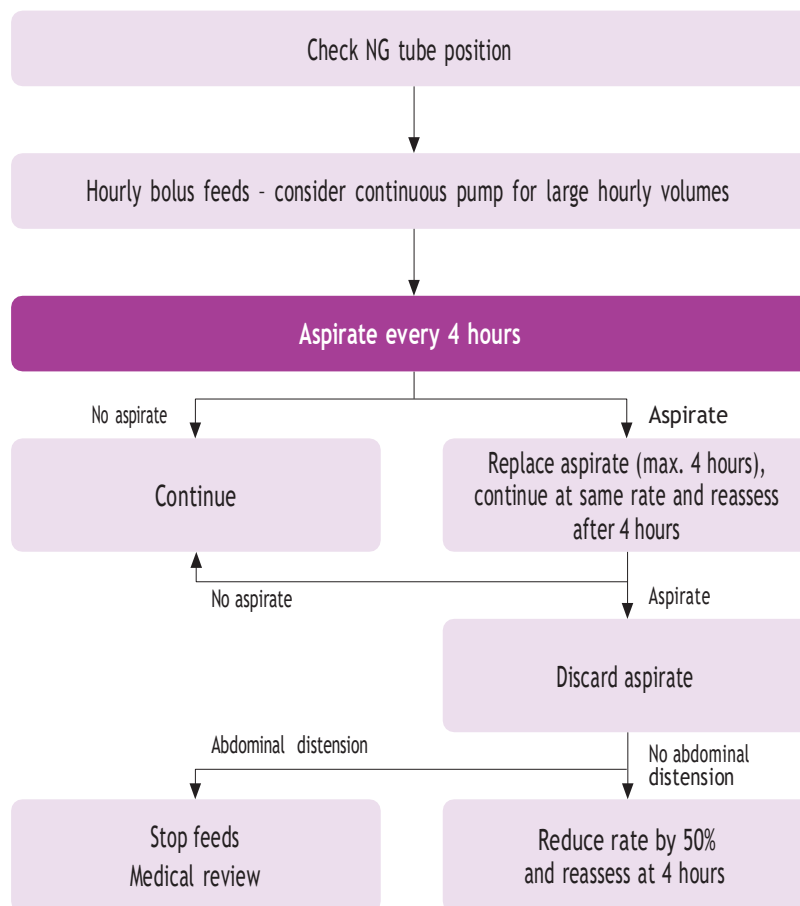
Check the position of the NG tube:

- before each use
- every 6 hours if continuous feeds
- after episodes of vomiting or retching, increased respiratory distress or excessive coughing
- if the tube looks dislodged (i.e. with more tubing visible).

NG tube sizes

This is only a rough guide; the bore of tube must fit easily in the child's nostril.

Description of patient	Tubes sizes
< 2 kg, preterm	4 Fr
2-4 kg	6 Fr
Term to 1 year	8 Fr
Younger children	10 Fr
Older children and adolescents	12 Fr
Small adult	14 Fr
Large adult	16 Fr



12.7 Algorithm for early mobility in the ICU

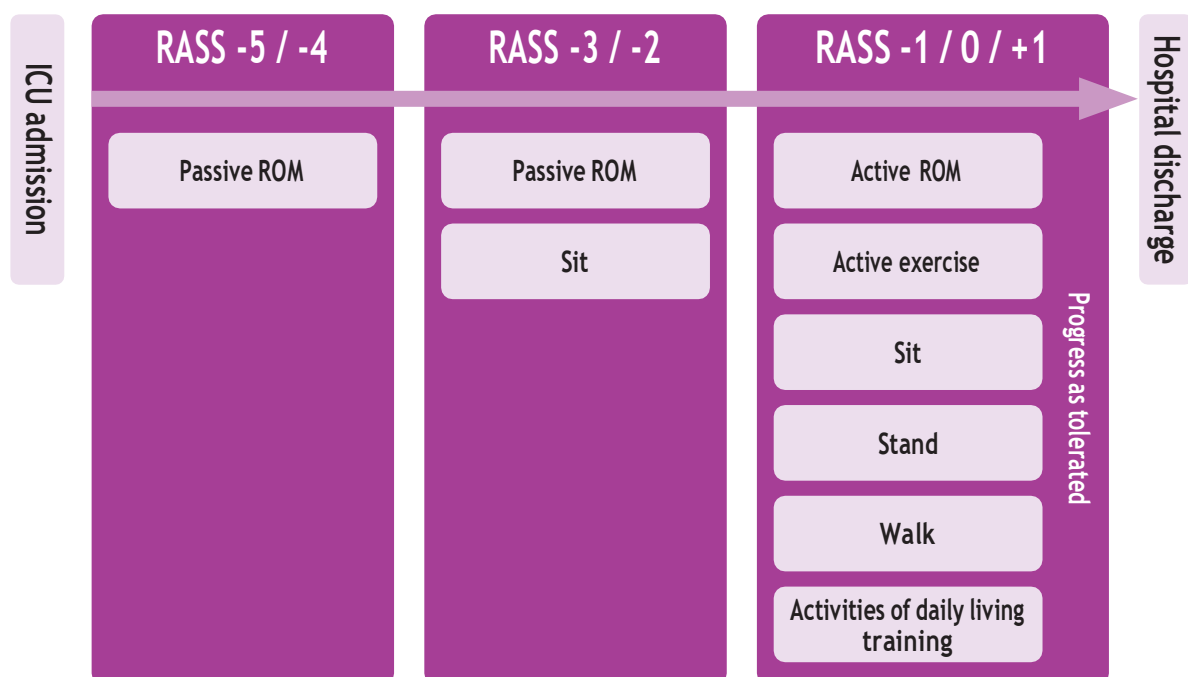
An adapted early mobility algorithm is presented below. It is adapted from Balas et al. (2014).

The patient's level of consciousness will be determined prior to the daily physical rehabilitation session using the Richmond Agitation-Sedation Scale.

- **A patient who is only arousable to physical stimulation (RASS -4/-5)** will undergo passive range of motion (ROM) exercises.
- **Once a patient can open their eyes to voice (RASS -2/-3)**, passive ROM exercises will be performed, and the patient will be placed in the chair position in bed.
- Finally, **once a patient is alert and calm (RASS -1/+1)**, they will progress from active ROM up through ambulation as they are able.

Sessions will continue until hospital discharge or a patient meets certain functional milestones. Early mobility in select intubated patients is feasible when adequate staff are available and safety assessment has been completed.

Physical rehabilitation protocol



12.8 Thromboembolic prophylaxis in COVID-19

Coagulopathy is common in patients with severe COVID-19, and both venous and arterial thromboembolism have been reported.

Monitor patients with COVID-19 for signs or symptoms suggestive of thromboembolism, such as stroke, deep vein thrombosis, pulmonary embolism or acute coronary syndrome. If these are clinically suspected, proceed immediately with appropriate diagnosis and management pathways.

In hospitalized patients with COVID-19 without an established indication for higher dose anticoagulation, WHO recommends to administer standard thromboprophylaxis dosing of anticoagulation (rather than therapeutic or intermediate dosing).

Type of heparin	Dose	Comments
Enoxaparin	40 mg/day SC	Clinical observation if < 45 kg (women) or < 57 kg (men): risk of bleeding BMI > 40 mg/m ² or weight >120 kg: 40 mg/12h SC
Unfractionated heparin (UFH)	5000 units/12h or 8h SC	BMI > 40 mg/m ² or weight >120 kg: 7500 units/12h or 5000 units/8h
Tinzaparin	4500 units/day SC	BMI > 40 mg/m ² or weight >120 kg: 9000 units/day
Dalteparin	5000 units/day SC	BMI > 40 mg/m ² or weight >120 kg: 5000 units/12h
Fondaparinux	2.5 mg/day SC	

Notes:

SC - subcutaneous injection.

In renal failure, reduce dose of low molecular weight heparin (LMWH) (except dalteparin).

Patients on thromboprophylaxis dosing of anticoagulation do not require monitoring, except for platelet count monitoring after 5-7 days if UFH is used.

Dosing should be adjusted according to body weight/BMI and renal function according to local protocols.

Use mechanical prophylaxis if moderate VTE risk, in patient at risk of bleeding:

- intermittent pneumatic compression devices;
- graduated compression stockings.

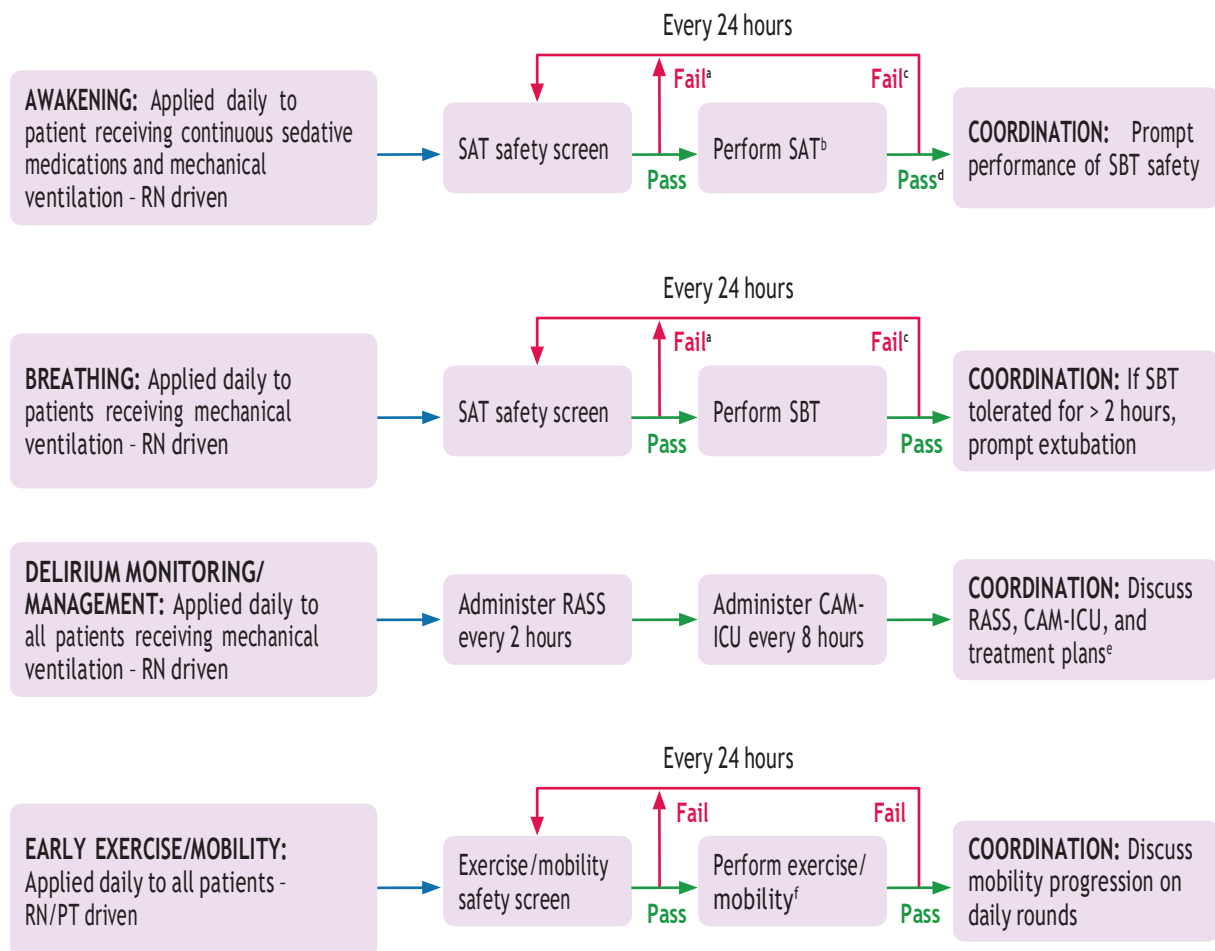
Switch to pharmacologic agent once risk of bleeding has decreased.

12.9 ABCDE bundle

This algorithm is adapted from Balas et al. (2014). Implementing this bundle reduced the time patients spent on invasive mechanical ventilation by 3 days. Additionally, patients experienced less delirium and were more likely to be mobilized.

Adapt this bundle to fit your ICU and implement using a quality improvement mechanism.

ABCDE bundle algorithm



Notes:

- ^a Continuous sedative medications maintained at previous rate if spontaneous awakening trial (SAT) safety screen failure. Mechanical ventilation continued, and continuous sedative medications restarted at half the previous dose only if needed due to SBT safety screen failure.
 - ^b Continuous sedative infusions stopped, and sedative boluses held. Bolus doses of opioid medications allowed for pain. Continuous opioid infusions maintained only if needed for active pain.
 - ^c Continuous sedative medications restarted at half the previous dose, and then titrated to sedation target if SAT failed. Interdisciplinary team determines possible causes of SAT/STB failure during rounds. Mechanical ventilation restarted at previous settings, and continuous sedative medications restarted at half the previous dose only if needed if SBT failed.
 - ^d SAT pass if the patient can open their eyes to verbal stimulation without failure criteria (regardless of trial length) or does not display any of the failure criteria after 4 hours of shutting off sedation.
 - ^e Each day on interdisciplinary rounds, the RN will inform the team of the patient's target RASS score, actual RASS score, CAM-ICU status, and sedative and analgesic medications the patients is receiving. If delirium is detected, team will discuss possible causes, eliminate risk factors, and employ non-pharmacologic management strategies.
 - ^f Each eligible patient is encouraged to be mobile at least once a day, with the specific level of activity geared to their readiness. Patients progress through a three-step process, embarking on the highest level of physical activity they can tolerate. Progress includes sitting on edge of bed, standing at bedside and sitting in chair, and walking a short distance. Use of the protocol ends when the patient is discharged from the ICU.
- CAM-ICU = confusion assessment method for the intensive care unit; PT - physical therapist; RASS - Richmond Agitation-Sedation Scale; RN - registered nurse; RT - respiratory therapist; SAT - spontaneous awakening trial; SBT - spontaneous breathing trial.

ABCDE bundle safety screen questions and success/fail criteria

ABCDE bundle component	Safety screen criteria: conditions for exclusion	Pass/fail criteria: conditions denoting failure
Spontaneous awakening trial	<ol style="list-style-type: none"> 1. Active seizures 2. Alcohol withdrawal 3. Neuromuscular blockade 4. Control of increased ICP 5. ICP > 20 mmHg 6. Receiving ECMO 7. Documentation of MI in past 24 hours 8. Current RASS > 2 	<ol style="list-style-type: none"> 1. RASS score > 2 for ≥ 5 minutes 2. Pulse oximetry < 88% for ≥ 5 minutes 3. Respirations > 35 BPM for ≥ 5 minutes 4. Acute cardiac arrhythmia 5. ICP > 20 mmHg 6. Two or more of the following: (heart rate increase ≥ 20 BPM, heart rate < 55 BPM, use of accessory muscles, abdominal paradox, diaphoresis or dyspnoea)
Spontaneous breathing trial	<ol style="list-style-type: none"> 1. Chronic ventilator dependence 2. Pulse oximeter reading < 88% 3. FiO₂ > 50% 4. Set PEEP > 7 5. ICP > 20 mmHg 6. Receiving mechanical ventilation in attempt to control ICP 7. Documentation of MI in past 24 hours 8. Increasing doses of vasopressor medications 9. Lack of inspiratory effort 	<ol style="list-style-type: none"> 1. RR > 35 BPM for ≥ 5 minutes 2. RR < 8 3. Pulse oximetry < 88% > 5 minutes 4. ICP > 20 mmHg 5. Mental status changes 6. Acute cardiac arrhythmia 7. Two or more of the following: <ul style="list-style-type: none"> • use of accessory muscles • abdominal paradox diaphoresis • dyspnoea
Early exercise/mobility	<ol style="list-style-type: none"> 1. RASS -3 2. FiO₂ > 0.6 3. Set PEEP > 10 cmH₂O 4. Increasing doses of vasopressor infusions in the last 2 hours 5. Evidence of active MI 6. Administration of a new antiarrhythmic agent 7. Receiving therapies that restricted mobility (e.g. ECMO, open-abdomen, etc.) 8. Injuries in which mobility is contraindicated (e.g. unstable fractures, etc.) 	<ol style="list-style-type: none"> 1. Symptomatic drop in mean arterial pressure 2. Heart rate < 50 or > 130 BPM ≥ 5 minutes 3. RR < 5 or > 40 BPM ≥ 5 minutes 4. Systolic blood pressure > 180 mmHg ≥ 5 minutes 5. Pulse oximetry < 88% ≥ 5 minutes 6. Marked ventilator dyssynchrony 7. Patient distress 8. New arrhythmia or evidence of active MI 9. Concern for airway device integrity or endotracheal removal 10. Fall to knees

Notes: ABCDE - Awakening and Breathing Coordination, Delirium Monitoring/Management and Early Mobility Bundle; BPM - beats per minute; ECMO - extracorporeal membrane oxygenation; FiO₂ - fraction of inspired oxygen; ICP - intracranial pressure; MI - myocardial ischaemia; PEEP - positive end-expiratory pressure; RASS - Richmond Agitation-Sedation Scale; RR - respiratory rate.

Bedside checklist for ABCDE protocol

Date: ____ / ____ / ____

ABC

Awakening and Breathing Coordination

	Check if yes or indicate reasons
SAT screen passed? If not, why?	
SAT done? If not, why?	
SBT screened passed? If not, why?	
SBT done? If not, why?	
SAT and SBT coordinated/paired?	

D

Delirium nonpharmacologic interventions

Intervention	Check if done
Pain assessment/management	
Orientation	
Sensory (eyes/ears)	
Sleep (nonpharm)	
Check any intervention that was performed during your shift (including night shift)	

E

Early Exercise and mobility

Intervention	Check if done
Active ROM	
Sitting up on side of bed	
Standing	
Walking	
Check any level of activity the patient performed during your shift (including night shift)	

Notes: ROM - range of motion; SAT - spontaneous awakening trial; SBT - spontaneous breathing trial.

References and resources

- Arabi YM, Aldawood AS, Haddad SH, Al-Dorzi HM, Tamim HM, Jones G et al. Permissive underfeeding or standard enteral feeding in critically ill adults. *N Engl J Med*. 2015;372(25):2398-408.
- Balas MC, Vasilevskis EE, Olsen KM, Schmid KK, Shostrom V, Cohen MZ et al. Effectiveness and safety of the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle. *Crit Care Med*. 2014;42(5):1024-36.
- Barnes-Daly MA, Phillips G, Ely EW. Improving hospital survival and reducing brain dysfunction at seven California community hospitals: implementing PAD guidelines via the ABCDEF bundle in 6,064 patients. *Crit Care Med*. 2017;45(2):171-178.
- Brummel NE, Girard TD, Ely EW, Pandharipande PP, Morandi A, Hughes CG et al. Feasibility and safety of early combined cognitive and physical therapy for critically ill medical and surgical patients: the Activity and Cognitive Therapy in ICU (ACT-ICU) trial. *Intensive Care Med*. 2014;40(3):370-379.
- Buendgens L, Bruensing J, Matthes M, Dückers H, Luedde T, Trautwein C et al. Administration of proton pump inhibitors in critically ill medical patients is associated with increased risk of developing *Clostridium difficile*-associated diarrhea. *J Crit Care*. 2014;29(4):696.e11-5.
- CHECKLIST-ICU Investigators and BRICNet, Machado F, Bozza F, Ibrain J, Salluh F, Campagnucci VP et al. A cluster randomized trial of a multifaceted quality improvement intervention in Brazilian intensive care units: study protocol. *Implement Sci*. 2015;10:8.
- Coffin SE, Klompas M, Classen D, Arias KM, Podgomy K, Anderson DJ et al. Strategies to prevent ventilator-associated pneumonia in acute care hospitals. *Infect Control Hosp Epidemiol*. 2008;29(suppl 1):S31-40.
- Cohen AT, Tapson VF, Bergmann JF, Goldhaber SZ, Kakkar AK, Deslandes B et al. Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): a multinational cross-sectional study. *Lancet*. 2008;371(9610):387-94. Erratum in: *Lancet*. 2008;371(9628):1914.
- Geerts WH, Bergqvist D, Pineo GF, Helt JA, Samama CM, Lassen MR et al. Prevention of venous thromboembolism. American College of Chest Physicians Evidence-Based Clinical Practice Guidelines (8th edition). *Chest*. 2008;133(suppl 6):381S-453S.
- Herridge MS, Tansey CM, Matté A, Tomlinson G, Diaz-Granados N, Cooper A et al. Functional disability 5 years after acute respiratory distress syndrome. *N Engl J Med*. 2011;7;364(14):1293-304.
- IHI. Implement the Central Line Bundle [website resource]. Boston (MA): Institute of Healthcare Improvement; 2019 (<http://app.ihl.org/imap/tool/processpdf.aspx?processGUID=e876565d-fd43-42ce-8340-8643b7e675c7>, accessed 2 July 2019).
- Lo E, Nicolle L, Classen D, Arias KM, Podgomy K, Anderson DJ et al. Strategies to prevent catheter-associated urinary tract infections in acute care hospitals. *Infect Control Hosp Epidemiol*. 2008;29(suppl 1):S41-S50.
- Klompas M, Anderson D, Trick W, Babcock H, Kerlin MP, Li L et al. The preventability of ventilator-associated events. The CDC Prevention Epicenters Wake Up and Breathe Collaborative. *Am J Respir Crit Care Med*. 2015;191(3):292-301.
- MacLaren R, Reynolds PM, Allen RR. Histamine-2 receptor antagonists vs proton pump inhibitors on gastrointestinal tract hemorrhage and infectious complications in the intensive care unit. *JAMA Intern Med*. 2014;174(4):564-74.
- McClave SA, Martindale RG, Verek VW, McCarthy M, Roberts P, Taylor B et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient. *J Parenter Enteral Nutr*. 2009;33(3):277-316.
- Muscledere J, Dodek P, Keenan S, Fowler R, Cook D, Heyland D et al. Comprehensive evidence-based clinical practice guidelines for ventilator-associated pneumonia: prevention. *J Crit Care*. 2008;23(1):126-137.
- Pronovost P, Needham D, Berenholtz S, Sinopoli D, Chu H, Cosgrove S et al. An intervention to decrease catheter-related bloodstream infections in the ICU. *N Engl J Med*. 2006;355:2725-2732.
- Schweickert WD, Kress JP. Implementing early mobilization interventions in mechanically ventilated patients in the ICU. *Chest*. 2011;140(6):1612-1617.
- Schweickert WD, Pohlman MC, Pohlman AS, Nigos C, Pawlik AJ, Esbrook CL et al. Early physical and occupational therapy in mechanically ventilated, critically ill patients: a randomised controlled trial. *Lancet*. 2009;373(9678):1874-82.
- Waters B, Muscedere J. A 2015 update on ventilator-associated pneumonia: new insights on its prevention, diagnosis, and treatment. *Curr Infect Dis Rep*. 2015;17(8):496.
- WHO. Pocket book of hospital care for children. Guidelines for the management of common illnesses with limited resources (second edition). Geneva: World Health Organization; 2013 (https://www.who.int/maternal_child_adolescent/documents/child_hospital_care/en/, accessed 26 June 2019).



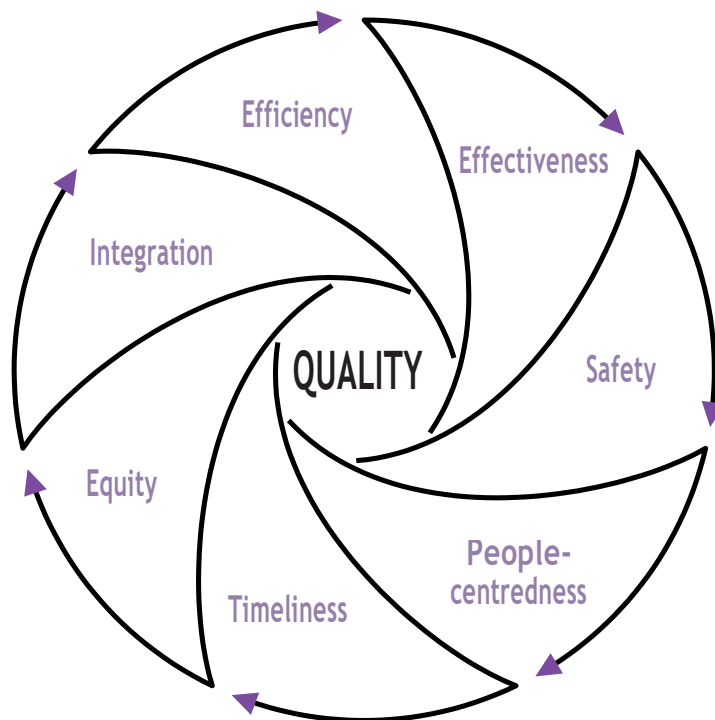
13

Quality in critical care



13 Quality in critical care

Summary



Quality elements	Description
Safety	Avoiding harm to people for whom the care is intended.
Timeliness	Reducing waiting times and sometimes harmful delays for both those who receive and those who give care.
Effectiveness	Providing evidence-based health care services to those who need them.
Efficiency	Maximizing the benefit of available resources and avoiding waste.
Equity	Providing care that does not vary because of age, sex, gender, race, ethnicity, geography, religion, socio-economic status, linguistic or political affiliation.
Patient-centredness	Providing care that responds to individual preferences, needs and values in health services that are organized around the needs of people.

Systematic and continuous quality improvement work is essential because health care delivery is complex and imperfect, even with the best efforts. Quality measures are related to ICU resources/structure, processes of care and patient outcomes. The focus should be on processes of care, instead of hard-to-measure outcomes.

Use the iterative, real-time, **plan-do-act-check** cycle to test changes/improvement.

Create an inclusive team and culture of change for a successful and sustainable quality improvement programme.

See further information on quality interventions see the WHO *Handbook for national quality policy and strategy*).

Tools

- 13.1 Checklist for ICU daily best practices
- 13.2 Surviving Sepsis Campaign bundles
- 13.3 Checklist for high-quality use of invasive mechanical ventilation for ARDS
- 13.4 Process for selecting problem to focus on in the ICU and quality improvement process
- 13.5 Checklist for initiating, improving, evaluating and sustaining a quality improvement programme

13.1 Checklist for ICU daily best practices

ICU Daily Rounding Checklist			
Can sedation be reduced?	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Can analgesia be reduced?	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Is delirium being assessed, addressed and prevented?	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Spontaneous awakening trial and/or Spontaneous breathing trial candidate?	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Total fluid balance goal reviewed? And targeting: _____ [12h] [24h]	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Is the patient at goals for lung protective ventilation ?	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Head of bed elevation (30 degrees)	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Skin breakdown assessment (prevention) completed	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Is enteral nutrition at goal?	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Is blood glucose at goal?	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Deep venous thrombosis prophylaxis?	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Gastric ulcer prophylaxis? <small>If coagulopathy (INR>1.5, PTT>2x normal, Plt < 50k), mechanical ventilation > 48h, history of GI bleed/ulcer within past year, TBI, SCI or burn, or if ≥2 minor risk factors (sepsis, ICU stay >1 week, occult GI bleed > 6 days, glucocorticoid therapy, NSAID use, antiplatelet use)</small>	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Can Antibiotics be narrowed or discontinued?	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Early mobility candidate and physical therapy consulted?	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Is foley catheter needed?	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Is central venous/arterial catheter needed?	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Has the family been updated?	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No
Are the patient's goals of care and code status current?	<input type="checkbox"/> Yes	<input type="checkbox"/> NA	<input type="checkbox"/> No

TBI = traumatic brain injury; SCI = spinal cord injury; GI = gastrointestinal; PT = physical therapy; Plt = platelet; NSAID = non-steroidal anti-inflammatory drugs.

DISCLAIMER: This tool is intended to serve as a framework for local modification in accordance with local resources, standards and guidelines. This is intended to be educational in nature and is not a substitute for clinical decision making based on the medical condition presented. It is the responsibility of the user to ensure all information contained herein is current and accurate by using published references. Table based in part on [ABCDEF Guidelines – Critical Care Medicine, 2018](#)

Source: Open Critical Care Project ([🌐](#))

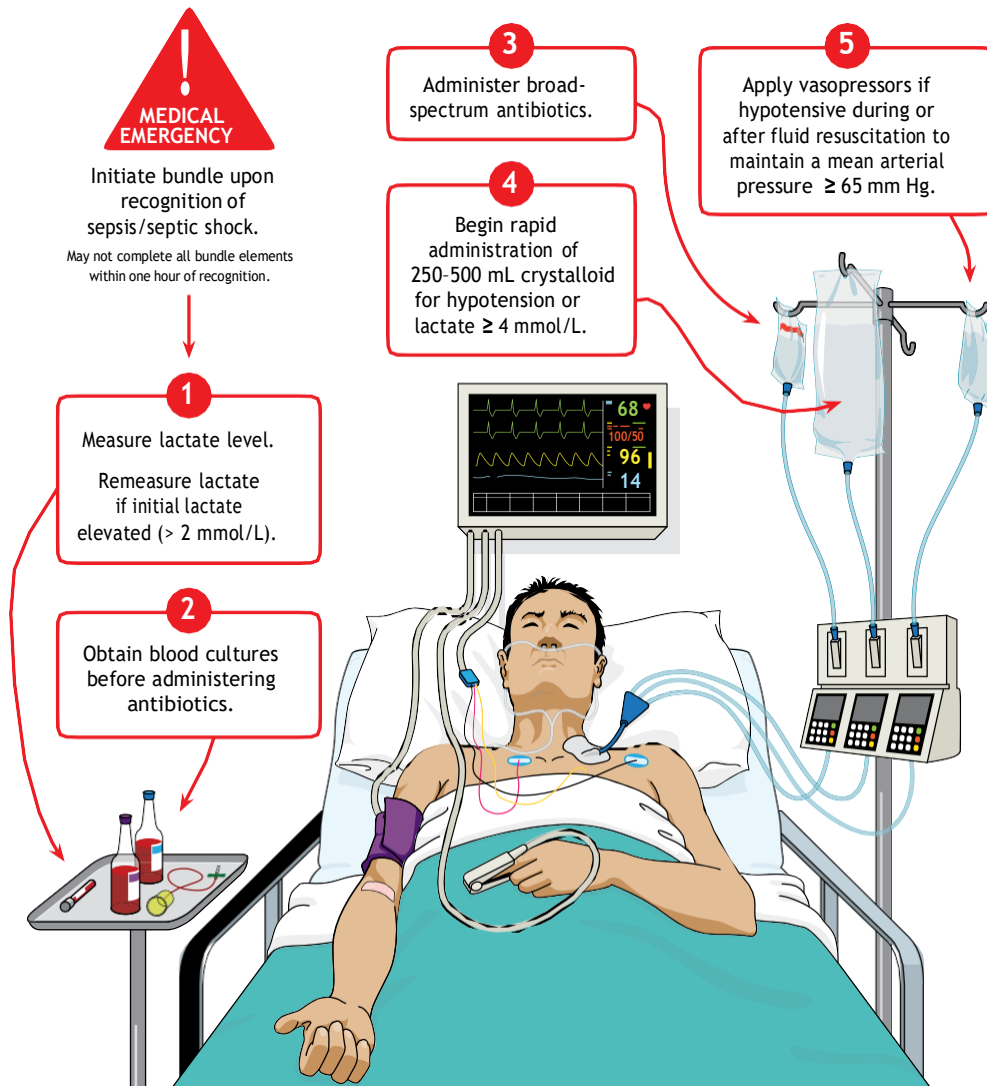
To **DOWNLOAD** or
PRINT more



13.2 Surviving Sepsis Campaign bundles

Hour-1 bundle: initiate bundle upon recognition of sepsis/septic shock

May not complete all elements within first hour.



Remember

1. Act quickly upon sepsis and septic shock recognition;
2. Minimize time to treatment - sepsis and septic shock are medical emergencies;
3. Monitor closely for response to interventions;
4. Communicate sepsis status in hand-offs.



Consider using an adapted version of this tool to monitor performance for sepsis care. This bundle was recently revised based on the most recent version of these tools. See the Surviving Sepsis Campaign - adult patients website for full details ([link](#)).



The Paediatric Surviving Sepsis Campaign Bundle can be found in Chapter 8 (Tool 8.6) or on the Surviving Sepsis - paediatric patients website ([link](#)).

13.3 Checklist for high-quality use of invasive mechanical ventilation for ARDS

- Consider using this tool if you are using IMV to deliver quality care to your patients with ARDS.

Technical competence

- Type of mechanical ventilator available.
- Able to deliver internal PEEP 5-20 cmH₂O.
- Able to measure plateau airway pressure.
- Able to deliver FiO₂ 100%.
- Able to titrate FiO₂.
- Able to titrate tidal volumes from 4-10 mL/kg.
- Intubation equipment readily available. See full WHO specifications for mechanical ventilators ([🔗](#))
- Infection prevention materials readily available (airborne precautions). Skilled person to intubate available.
- Skilled personnel to use and troubleshoot IMV. Arterial blood gas analyser available and working. Pulse oximeter available and working.
- Supply chain for ventilator consumables (circuits, filters).
- Skilled personnel and equipment for biomedical/ventilator troubleshooting and preventive maintenance.

Safety

- Protocols and equipment for difficult airway (e.g. backup personnel, equipment and plan - e.g. cricothyrotomy).
- Plan for IMV complications (e.g. chest tube for pneumothorax, sedation for agitation).
- Protocols for prevention while on IMV (e.g. daily SBT evaluation, daily sedation interruption, VAP prevention).
- Protocols for lung protective ventilation. See OpenCritical Care Respiratory care order set (protocol) templates [🔗](#)).

Process measures

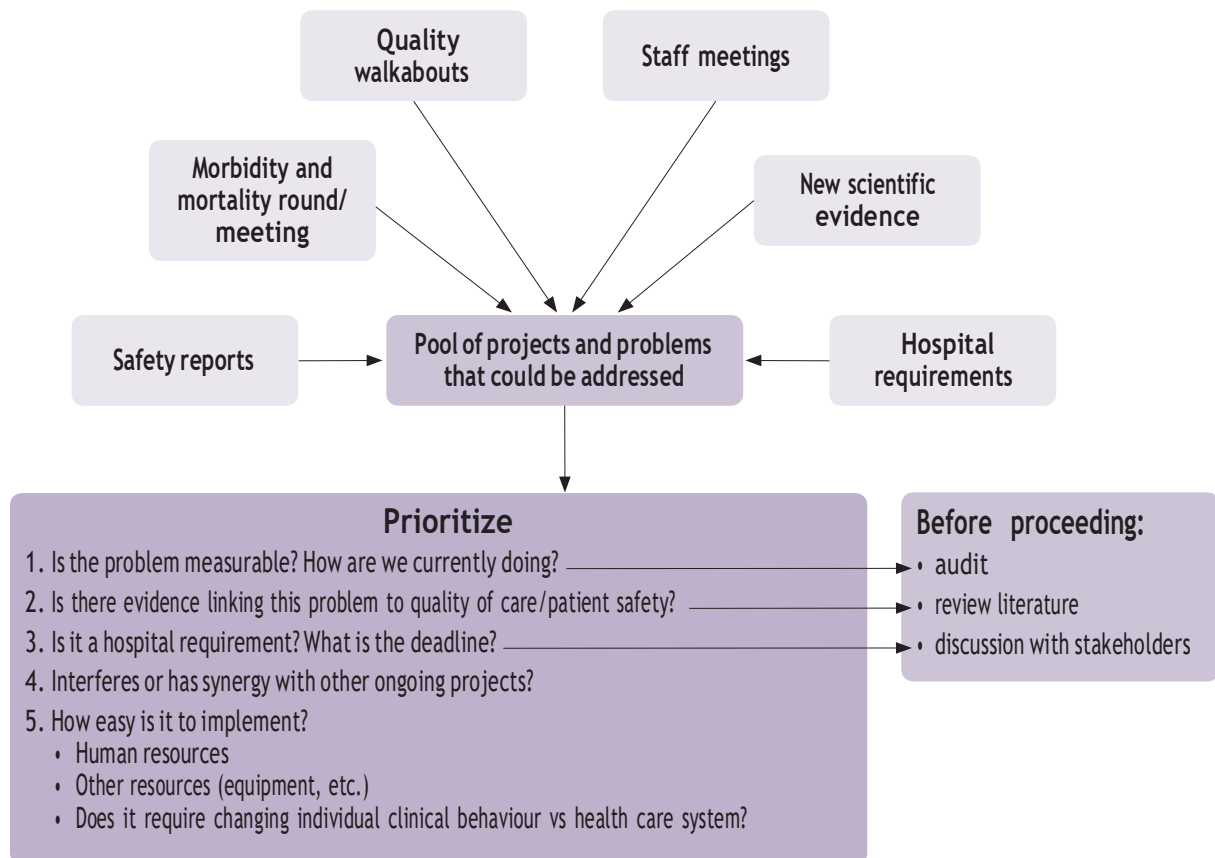
- Process measures (e.g. lung protective targets met).

Outcome measures

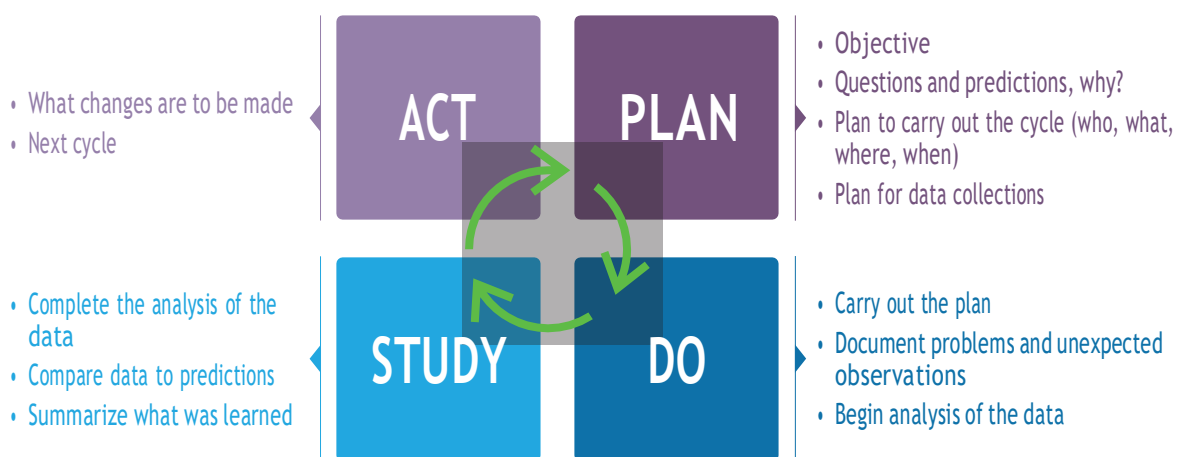
- Complications (e.g. VAP, pneumothorax).

13.4 Process for selecting problem to focus on in the ICU and quality improvement process

This flowchart provides a framework for selecting a problem to focus on for quality improvement among the many that might be considered.



Essential steps in the **plan-do-study-act** cycle:



Source: Adapted from Dr Andre Amaral, Sunnybrook Health Sciences Centre and University of Toronto, Canada.

13.5 Checklist for initiating, improving, evaluating and sustaining a quality improvement programme

- This checklist provides steps for initiating, improving, evaluating and sustaining a quality improvement programme in the ICU (adapted from Curtis et al., 2006).

Initiating or improving a quality improvement programme

- Do background work: identify motivation, support team and develop strong leadership. Prioritize potential projects and choose the projects to begin.
- Prepare for the project by operationalizing the measures, building support for the project and developing a business plan.
- Do an environmental scan to understand the current situation (structure, process or outcome), the potential barriers, opportunities and resources for the project.
- Create a data collection system to provide accurate baseline data and document improvement.
- Create a data reporting system that will allow clinicians and other stakeholders to see and understand the problem and the improvement.
- Introduce strategies to change clinician behaviour and create the change that will produce improvement.

Evaluating and sustaining a quality improvement programme

- Determine whether the target is changing with ongoing observation, periodic data collection and interpretation.
- Modify behaviour change strategies to improve, regain or sustain improvements.
- Focus on sustaining interdisciplinary leadership and collaboration for the quality improvement programme.
- Develop and sustain support from the hospital leadership.

Common ICU quality indicators

- Deep venous thrombosis prophylaxis - number of patients receiving prophylaxis per eligible day.
- Stress ulcer prophylaxis - percentage of patients receiving prophylaxis per eligible day.
- Ventilator-associated pneumonia prevention strategies - percentage of patients receiving VAP bundle per eligible day.
- Central venous catheter blood stream infection prevention strategies - percentage of patients receiving checklist per eligible central venous catheter insertion.

References and resources

AHQR. Quality measure tools and resources [website]. Rockville (MD): Agency for Healthcare Research and Quality (<http://www.ahrq.gov/professionals/quality-patient-safety/quality-resources/index.html>, accessed 3 July 2019).

Bion JF, Heffner JE. Challenges in the care of the acutely ill. *Lancet*. 2004;363(9413):970-977.

Brown L, Franco LM, Rafeh N, Hatzell T. Quality assurance of health care in developing countries. *Quality Assurance Methodology Refinement Series*. Bethesda (MD): Quality Assurance Project; 2000.

Campbell H, Duke T, Weber M, English M, Carai S, Tamburlini G et al. Global initiatives for improving hospital care for children: state of the art and future prospects. *Pediatrics*. 2008;121(4):e984-994.

Curtis JR, Cook DJ, Wall RJ, Angus DC, Bion J, Kacmarek R et al. Intensive care unit quality improvement: a "how-to" guide for the interdisciplinary team. *Crit Care Med*. 2006;34(1):211-8.

Hales BM, Pronovost P. The checklist - a tool for error management and performance improvement. *J Crit Care*. 2006;21(3):231-235.

Hales BM, Terblanche M, Fowler R, Sibbald W. Development of medical checklists for improved quality of patient care. *Int J Qual Health Care*. 2008;20(1):22-30.

HMD. Health and Medicines Division, National Academies of Sciences, Engineering and Medicine, United States of America [website]. Washington (DC) (<http://www.nationalacademies.org/hmd/>, accessed 12 August 2019).

IHI. How to improve [website]. Boston (MA): Institute for Healthcare Improvement; 2019 (<http://www.ihl.org/resources/Pages/HowtoImprove/ScienceofImprovementSettingAims.aspx>, accessed 25 August 2021).

Kuzniewicz MW, Vasilevskis EE, Lane R, Dean ML, Trivedi NG, Rennie DJ et al. Variation in ICU risk-adjusted mortality impact of methods of assessment and potential confounders. *Chest*. 2008;133(6):1319-1327.

Langley GL, Moen RD, Nolan KM, Nolan TW, Norman CL, Provost LP. *The improvement guide: a practical approach to enhancing organizational performance* (2nd edition). San Francisco (CA): Jossey-Bass Publishers; 2009.

Murthy S, Wunsch H. Clinical review: international comparisons in critical care - lessons learned. *Crit Care*. 2012;16(2):218. doi: 10.1186/cc11140.

WHO. *Assessing and tackling patient harm: a methodological guide for data-poor hospitals*. Geneva: World Health Organization; 2010 (<https://apps.who.int/iris/handle/10665/77100>, accessed 25 August 2021).

WHO. *Handbook for national quality policy and strategy: a practical approach for developing policy and strategy to improve quality of care*. Geneva: World Health Organization; 2018 (<https://www.who.int/publications/i/item/9789241565561>, accessed 25 August 2021).



14

Ethical considerations



14 Ethical considerations

Summary

During a pandemic, the need for critical care services can exceed available resources. Triage decisions may need to be made on how to allocate scarce resources and prioritize patients.

Before patients are prioritized, allocation planners need to prioritize among often mutually exclusive substantive values and principles.

Key values and principles include: maximizing the number of lives or life-years saved; first come, first served; allocating in ways that reduces, rather than maintains or increases inequities; however, there is neither international nor, typically, national consensus on which values and principles to include and/or how to rank them.

Public engagement in pandemic preparedness is essential to develop a prioritization strategy that is fair, transparent and builds trust.

Tools

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

14.1 Ethical values and principles

Ethical analysis involves identifying relevant principles, applying them to a particular situation, and making judgements about how to weigh competing principles when it is not possible to satisfy them all.

The fundamental ethical challenge in triage is how to justify who to initially allocate a ventilator to when there are insufficient resources for all patients who require one, and under what circumstances patients might be removed from ventilators.

Ethical triage requires:

- first, identifying relevant substantive and procedural principles;
- second, processes to apply these principles in a transparent way to particular situations; and
- third, monitoring that triage accomplishes its goals and that there are no unintended consequences.

While there is international agreement on the need for transparent processes, consensus on substantive principles is elusive at the international level and typically also at national level.

Historically, the dominant trend underlying triage frameworks has been to focus on maximizing benefits; and allocation frameworks comprised clinical measures such as prognosis that help ensure that triage saves the most lives, or the most life-years. However, drawing on such frameworks in the COVID-19 pandemic made clear that maximizing benefits has a tendency to exacerbate existing inequities due to the social and political determinants of health. For example, considering prior comorbidities, remaining life expectancy, or even seemingly objective measures such as the Sequential Organ Failure Assessment (SOFA) score, tend to favour economically and otherwise privileged population groups, while simultaneously disadvantage less privileged groups. A major challenge is, therefore, how to weigh competing principles when it is not possible to satisfy them all.

Key ethical principles and descriptions (in alphabetical, not lexical, order)

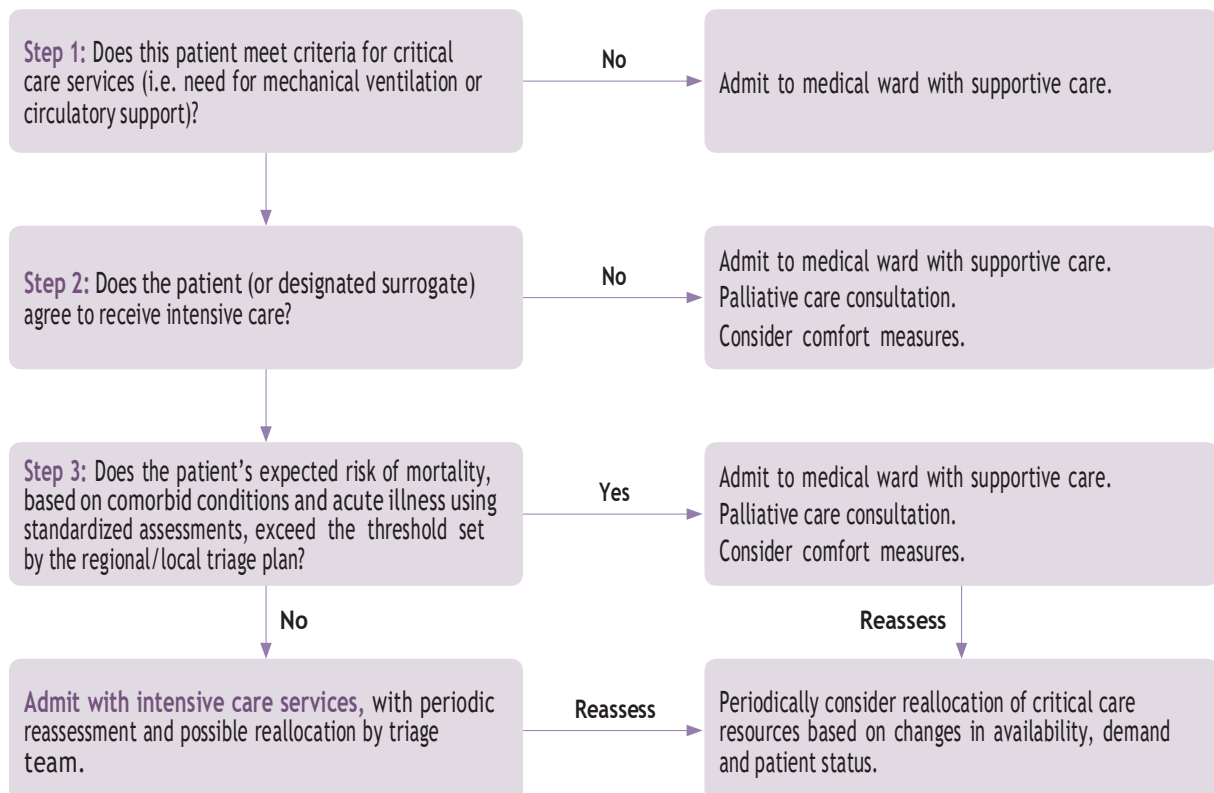
Ethical principle	Description
Autonomy	Enabling, and letting individuals make their own choices based on their values and preferences.
Equity	<ul style="list-style-type: none"> • Treating the same those who have the same needs, and treating differently those with different needs, which usually requires reducing, rather than maintaining, or worse, exacerbating, avoidable unfair differences in opportunities or health outcomes. • Equity important if policies appear to systematically disadvantage groups already experiencing disproportionate discrimination, injustice or other forms of disadvantage.
First come, first served	Allocates resources by respecting the temporal sequence of requests. Typically this assumes that all those requesting resources are reasonably equal in their ability to access services.
Informed consent	Process in which a competent individual authorizes a course of action based on sufficient relevant information, without coercion or undue inducement.
Instrumental value	Giving priority to those who have made, or are likely to make, relevant contributions, for example, essential key health care staff.
Justice	Encompasses <i>equity</i> - fairness in the distribution of resources, opportunities and outcomes - and procedural justice - a fair process for making important decisions.
Liberty	Includes a broad range of social, religious and political freedoms (e.g. freedom of movement, peaceful assembly, speech), many of which are protected as fundamental human rights.
Life cycle	Captures the notion that it is desirable that everyone should be able to live a life of normal length, and that, while all deaths are tragic, deaths of individuals who are younger are more tragic than those of people near the end of normal life expectancy.
Maximizing benefits	Actions or policies are right insofar as they maximize benefits. Most commonly this is understood to require policies that save the most lives or life-years.
Procedural justice	Includes: <ul style="list-style-type: none"> • Due process - acknowledgement of people and give opportunity to be heard. • Transparency - clear, accurate information about the basis for decisions and the decision-making process. • Inclusiveness/community engagement - ensuring all relevant stakeholders participate. • Accountability - allocating and enforcing responsibility for decisions. • Oversight - ensuring appropriate mechanisms for monitoring and review.
Respect for persons	Treating individuals in recognition of our common humanity, dignity and inherent rights. Key aspects include: autonomy; informed consent; privacy; confidentiality; social, religious and cultural beliefs; important relationships (e.g. family); and transparency and truth telling in public health and research.
Random selection	Assumes that everyone is equal irrespective of factors such as age, comorbidities, prognosis or other factors and should have an equal chance that can be implemented through a lottery, coin-toss or similar methods. Sometimes proposed as a secondary principle, for example, for patients with similar prognosis.
Solidarity	Social relations in which a group, community, nation or global community stands together. Justifies collective action in the face of common threats and supports efforts to overcome inequalities that undermine the welfare of minorities and groups that suffer discrimination.

Source: Adapted from *Guidance for managing ethical issues in infectious disease outbreaks* (WHO, 2016); *WHO SAGE values framework for the allocation and prioritization of COVID-19 vaccination*, 14 September 2020 (WHO, 2020).

14.2 Triage decision process flow

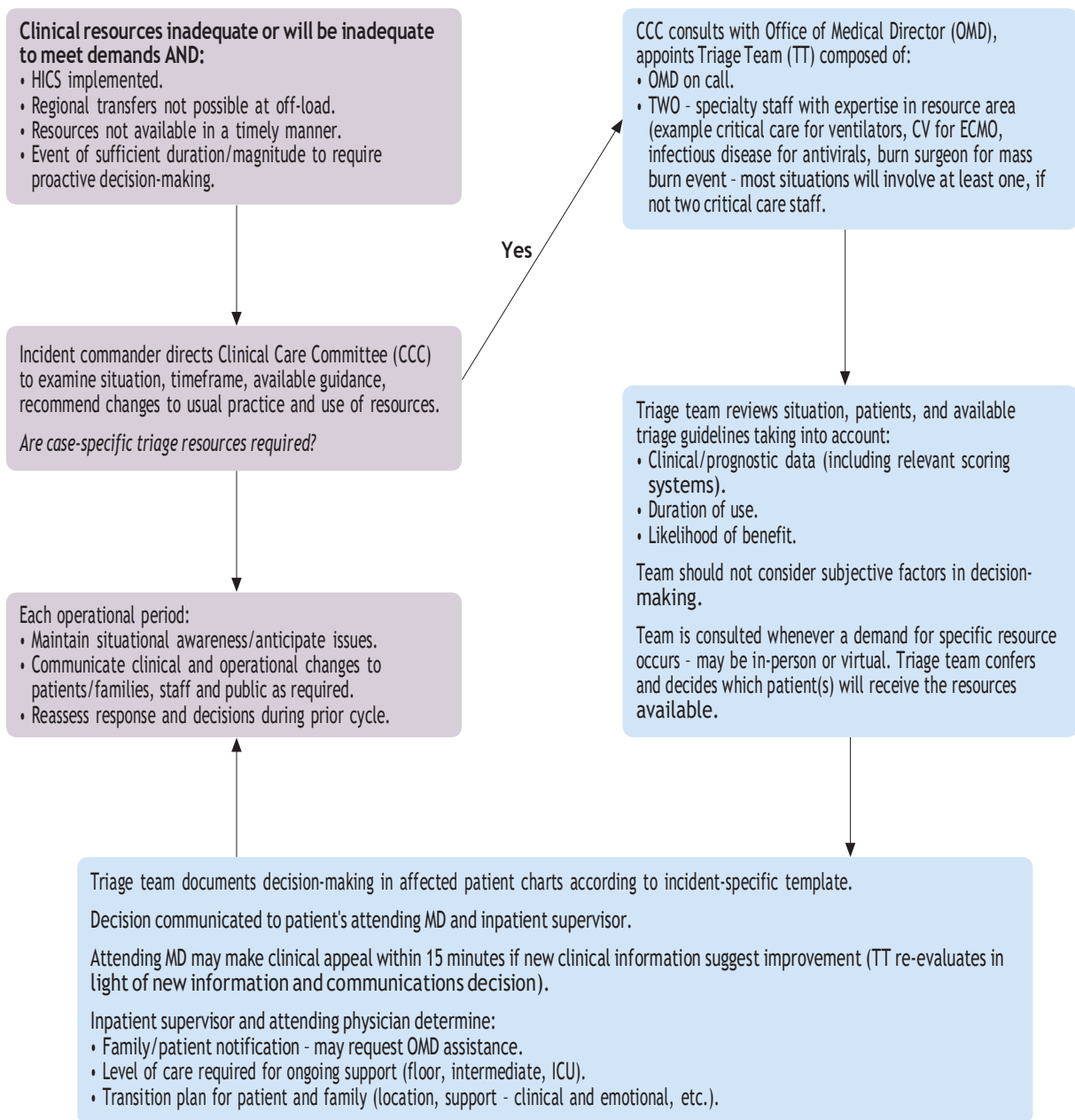
This is adapted from the 2020 *Triage of scarce critical care resources in COVID-19 an implementation guide for regional allocation* (Expert Panel Report of the Task Force for Mass Critical Care and the American College of Chest Physicians) (Maves et al., 2020). It is presented as a framework only, and has not been validated in any population.

Triage decision algorithm



Source: Maves et al. (2020).

14.3 Hospital scarce resource decision-making



Notes: Algorithm and plan does not apply to immediate, reactive triage decisions in the early phase of a disaster (e.g. ED, trauma surgery) or to non-emergency circumstances (specialty providers will engage colleagues in decision-making). This algorithm is a summary of select actions in the HCMC Crisis Care Annex which should be referred to for further details.
 CCC = clinical care committee; CV = cardiovascular specialist; ECMO = extracorporeal membrane oxygenation; HICS = hospital incident command system; MD = medical doctor; OMD = office of medical director; TT = triage team.

Source: Maves et al. (2020).

References and resources

- Ashana DC, Anesi GL, Liu VX, Escobar GJ, Chesley C, Eneanya ND et al. Equitably allocating resources during crises: racial differences in mortality prediction models. *Am J Respir Crit Care Med*. 2021;204(2):178-186.
- Antommaria AH, Sweney J, Poss WB. Critical appraisal of: triaging pediatric critical care resources during a pandemic: ethical and medical considerations. *Pediatr Crit Care Med*. 2010;11(3):396-400.
- Cardona M, Dobler CC, Koreshe E, Heyland DK, Nguyen RH, Sim JP et al. A catalogue of tools and variables from crisis and routine care to support decision-making about allocation of intensive care beds and ventilator treatment during pandemics: scoping review. *J Crit Care*. 2021;66:33-43.
- Emanuel EJ, Persad G, Upshur R, Thome B, Parker M, Glickman A et al. Fair allocation of scarce medical resources in the time of Covid-19. *N Engl J Med*. 2020;382:2049-2055.
- Institute of Medicine. Crisis standards of care: a systems framework for catastrophic disaster response: Volume 1: Introduction and CSC framework. Washington, DC: The National Academies Press; 2012 (<https://doi.org/10.17226/13351>, accessed 8 September 2021).
- Kerr W, Schmidt H. COVID-19 ventilator rationing protocols: why we need to know more about the views of those with most to lose. *J Med Ethics*. 2021;47(3):133-6.
- Maves RC, Downar J, Dichter JR, Hick JL, Devereaux A, Geiling JA et al. Triage of scarce critical care resources in COVID-19. An implementation guide for regional allocation. *CHEST*. 2020;158(1):212-225 ([https://journal.chestnet.org/article/S0012-3692\(20\)30691-7/fulltext?_ga=2.38446883.1829816982.1631011515-343769087.1631011515](https://journal.chestnet.org/article/S0012-3692(20)30691-7/fulltext?_ga=2.38446883.1829816982.1631011515-343769087.1631011515), accessed 8 September 2021).
- Piscitello GM, Kapania EM, Miller WD, Rojas JC, Siegler M, Parker WF. Variation in ventilator allocation guidelines by US state during the coronavirus disease 2019 pandemic: a systematic review. *JAMA Netw Open*. 2020;3(6):e2012606.
- Scheidegger D, Fumeaux T, Hurst S, Salathé M. COVID-19 pandemic: triage for intensive-care treatment under resource scarcity. *Swiss Med Wkly*. 2020;150:w20229.
- Schmidt H, Roberts DE, Eneanya ND. Rationing, racism and justice: advancing the debate around 'colourblind' COVID-19 ventilator allocation. *J Med Ethics*. 2021;medethics-2020-106856. doi: 10.1136/medethics-2020-106856.
- Smith MJ, Silva DS. Ethics for pandemics beyond influenza: Ebola, drug-resistant tuberculosis, and anticipating future ethical challenges in pandemic preparedness and response. *Monash Bioeth Rev*. 2015;33(2-3):130-47.
- White DB, Lo B. Mitigating inequities and saving lives with ICU triage during the COVID-19 pandemic. *Am J Respir Crit Care Med*. 2021;203(3):287-95.
- WHO. Ethical considerations in developing a public health response to pandemic influenza. Geneva: World Health Organization; 2007.
- WHO. Addressing ethical issues in pandemic influenza planning. Discussion papers. Geneva: World Health Organization; 2008.
- WHO. Guidance for managing ethical issues in infectious disease outbreaks. Geneva: World Health Organization; 2016 (<https://apps.who.int/iris/bitstream/handle/10665/250580/9789241549837-eng.%20%20pdf?sequence=1>, accessed 8 September 2021).



For more information, please contact:

Emerging Diseases Clinical Assessment and Response Network
World Health Organization
Avenue Appia 20
CH-1211 Geneva 27
Switzerland

Email: COVID_ClinPlatform@who.int
Website: www.who.int/groups/edcarn