

Awake Proning as an Adjunctive Therapy for Refractory Hypoxemia in Non-Intubated Patients with COVID-19 Acute Respiratory Failure: Guidance from an International Group of Healthcare Workers

Author(s)

Stilma, Willemke; Åkerman, Eva; Artigas, Antonio; Bentley, Andrew; Bos, Lieuwe D. ; Bosman, Thomas J. C. ; de Bruin, Hendrik; Brummaier, Tobias; Buiteman-Kruizinga, Laura A. ; Carcò, Francesco; Chesney, Gregg; Chu, Cindy; Dark, Paul; Dondorp, Arjen M. ; Gijsbers, Harm J. H. ; Gilder, Mary Ellen; Grieco, Domenico L. ; Inglis, Rebecca; Laffey, John G. ; Landoni, Giovanni; Lu, Weihua; Maduro, Lisa M. N. ; McGready, Rose; McNicholas, Bairbre; de Mendoza, Diego; Morales-Quinteros, Luis; Nosten, Francois; Papali, Alfred; Paternoster, Gianluca; Paulus, Frederique; Pisani, Luigi; Prud'homme, Eloi; Ricard, Jean-Damien; Roca, Oriol; Sartini, Chiara; Scaravilli, Vittorio; Schultz, Marcus J. ; Sivakorn, Chaisith; Spronk, Peter E. ; Sztajn bok, Jaques; Trigui, Youssef; Vollman, Kathleen M. ; van der Woude, Margaretha C. E.

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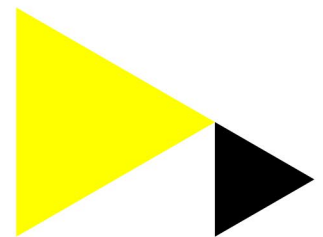
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Awake Proning as an Adjunctive Therapy for Refractory Hypoxemia in Non-Intubated Patients with COVID-19 Acute Respiratory Failure: Guidance from an International Group of Healthcare Workers

Willemke Stilma,^{1,2*} Eva Åkerman,^{3,4} Antonio Artigas,^{5,6} Andrew Bentley,^{7,8} Lieuwe D. Bos,¹ Thomas J. C. Bosman,¹ Hendrik de Bruin,¹ Tobias Brummaier,^{9,10} Laura A. Buiteman-Kruizinga,^{1,11} Francesco Carcò,¹² Gregg Chesney,¹³ Cindy Chu,^{9,10} Paul Dark,^{14,15,16} Arjen M. Dondorp,^{10,17} Harm J. H. Gijssbers,¹⁸ Mary Ellen Gilder,¹⁹ Domenico L. Grieco,^{20,21} Rebecca Inglis,²² John G. Laffey,^{23,24} Giovanni Landoni,^{12,25} Weihua Lu,²⁶ Lisa M. N. Maduro,¹⁸ Rose McGready,^{9,10} Bairbre McNicholas,²³ Diego de Mendoza,^{27,28,29} Luis Morales-Quinteros,^{27,30} Francois Nosten,^{9,10} Alfred Papali,^{31,32} Gianluca Paternoster,³³ Frederique Paulus,^{1,2} Luigi Pisani,^{1,17,34} Eloi Prud'homme,³⁵ Jean-Damien Ricard,^{36,37,38} Oriol Roca,³⁹ Chiara Sartini,¹² Vittorio Scaravilli,⁴⁰ Marcus J. Schultz,^{1,10,17} Chaisith Sivakorn,⁴¹ Peter E. Spronk,⁴² Jaques Sztajnbock,⁴³ Youssef Trigui,⁴⁴ Kathleen M. Vollman,⁴⁵ and Margaretha C. E. van der Woude⁴⁶

¹Department of Intensive Care, Amsterdam University Medical Centers, Location 'AMC', Amsterdam, The Netherlands; ²Faculty of Health, Center of Expertise Urban Vitality, Amsterdam University of Applied Science, Amsterdam, The Netherlands; ³Division of Nursing, Department of Neurobiology, Care Sciences and Society, Karolinska Institute, Stockholm, Sweden; ⁴Function of Perioperative Medicine and Intensive Care, Department of Intensive Care, Karolinska University Hospital, Stockholm, Sweden; ⁵Department of Intensive Care, Hospital de Sabadell, CIBER Enfermedades Respiratorias, Sabadell, Barcelona, Spain; ⁶Autonomous University of Barcelona, Sabadell, Barcelona, Spain; ⁷Acute Intensive Care Unit, Manchester University NHS Foundation, Manchester, United Kingdom; ⁸Manchester Academic Health Science Centre, Faculty of Biology, Medicine and Health, University of Manchester, Manchester, United Kingdom; ⁹Shoklo Malaria Research Unit, Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Mae Sot, Thailand; ¹⁰Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom; ¹¹Department of Intensive Care, Reinier de Graaf Hospital, Delft, The Netherlands; ¹²Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute, Milan, Italy; ¹³Division of Emergency Medicine-Critical Care, Department of Emergency Medicine, NYU Grossman School of Medicine, New York, New York; ¹⁴Critical Care Medicine, NIHR Manchester Biomedical Research Centre, University of Manchester, Manchester, United Kingdom; ¹⁵Division of Infection, Immunity and Respiratory Medicine, NIHR Manchester Biomedical Research Centre, University of Manchester, Manchester, United Kingdom; ¹⁶Humanitarian and Conflict Response Institute, University of Manchester, Manchester, United Kingdom; ¹⁷Faculty of Tropical Medicine, Mahidol-Oxford Tropical Medicine Research Unit (MORU), Mahidol University, Bangkok, Thailand; ¹⁸Department of Rehabilitation Medicine, Amsterdam University Medical Centers, Location 'AMC', Amsterdam, The Netherlands; ¹⁹Department of Family Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand; ²⁰Department of Emergency, Intensive Care Medicine and Anesthesia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy; ²¹Department of Anesthesiology and Intensive Care Medicine, Catholic University of the Sacred Heart, Rome, Italy; ²²Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU), Mahosot Hospital, University of Oxford, Vientiane, Lao People's Democratic Republic; ²³Department of Anaesthesia and Intensive Care, Medicine Galway University Hospitals, Galway, Ireland; ²⁴School of Medicine, Disciplines of Anaesthesia and Intensive Care Medicine, National University of Ireland, Galway, Ireland; ²⁵School of Medicine, Vita Salute San Raffaele University, Milan, Italy; ²⁶Department of Critical Care Medicine, Yijishan Hospital of Wannan Medical College, Wuhu, China; ²⁷Intensive Care Department, Hospital Universitari Sagrat Cor. Grupo Quironsalud, Barcelona, Spain; ²⁸Emergency Department, Hospital Universitari Sagrat Cor. Grupo Quironsalud, Barcelona, Spain; ²⁹Ciber Enfermedades Respiratorias (CIBERES), Instituto de Salud Carlos III, Madrid, Spain; ³⁰Institut d'Investigació i Innovació Parc Taulí I3PT, Universidad Autónoma de Barcelona, Barcelona, Spain; ³¹Division of Pulmonary and Critical Medicine, Atrium Health, Charlotte, North Carolina; ³²School of Medicine, University of Maryland, Baltimore, Maryland; ³³Department of Cardiovascular Anaesthesia and ICU, San Carlo Hospital, Potenza, Italy; ³⁴Section of Operational Research, Doctors with Africa CUAMM, Padova, Italy; ³⁵Intensive Care Unit, D tresse Respiratoire Infections S v res, Assistance Publique H pitaux de Marseille, Marseille, France; ³⁶DMU ESPRIT-Enseignements et Soins de Proximit , Recherche, Innovation et Territoires, Universit  de Paris, Paris, France; ³⁷Infection, Antimicrobiens, Mod lisation, Evolution (IAME), Universit  de Paris, Paris, France; ³⁸Service de M decine Intensive R animation, H pital Louis Mourier, Assistance Publique – H pitaux de Paris, Colombes, France; ³⁹Servei de Medicina Intensiva, Hospital Vall d'Hebron, Barcelona, Spain; ⁴⁰Department of Anesthesia, Critical Care and Emergency, Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Milan, Italy; ⁴¹Department of Clinical Tropical Medicine, Mahidol University, Bangkok, Thailand; ⁴²Expertise Center for Intensive Care Rehabilitation Apeldoorn, Gelre Hospitals Apeldoorn, Apeldoorn, The Netherlands; ⁴³Intensive Care Unit, Instituto de Infectologia Emilio Ribas, S o Paulo, Brazil; ⁴⁴Service des Maladies Respiratoires, Centre Hospitalier D'Aix-en-Provence, Aix-en-Provence, France; ⁴⁵Clinical Nurse Specialist/Critical Care Consultant, Advancing Nursing LLC, Northville, Michigan; ⁴⁶Intensive Care Unit, Zuyderland Medisch Centrum, Location 'Heerlen', Heerlen, The Netherlands

Abstract. Non-intubated patients with acute respiratory failure due to COVID-19 could benefit from awake proning. Awake proning is an attractive intervention in settings with limited resources, as it comes with no additional costs. However, awake proning remains poorly used probably because of unfamiliarity and uncertainties regarding potential benefits and practical application. To summarize evidence for benefit and to develop a set of pragmatic recommendations for awake proning in patients with COVID-19 pneumonia, focusing on settings where resources are limited, international healthcare professionals from high and low- and middle-income countries (LMICs) with known expertise in awake proning were invited to contribute expert advice. A growing number of observational studies describe the effects of awake proning in patients with COVID-19 pneumonia in whom hypoxemia is refractory to simple measures of supplementary oxygen. Awake proning improves oxygenation in most patients, usually within minutes, and reduces dyspnea and work of breathing. The effects are maintained for up to 1 hour after turning back to supine, and mostly disappear after 6–12 hours. In available studies, awake proning was not associated with a reduction in the rate of intubation for invasive ventilation. Awake proning comes with little complications if properly implemented and monitored. Pragmatic recommendations including indications and contraindications were formulated and adjusted for resource-limited settings. Awake proning, an adjunctive treatment for hypoxemia refractory to supplemental oxygen, seems safe in non-intubated patients with COVID-19 acute respiratory failure. We provide pragmatic recommendations including indications and contraindications for the use of awake proning in LMICs.

* Address correspondence to Willemke Stilma, Department of Intensive Care, Amsterdam University Medical Centers, Location 'AMC', Meibergdreef 9, Amsterdam 1105 AZ, The Netherlands. E-mail: w.stilma@amsterdamumc.nl

INTRODUCTION

COVID-19 acute respiratory failure may cause severe hypoxemia.¹ Many patients need to be hospitalized for supplementary oxygen. If this fails, that is, when hypoxemia is refractory to oxygen therapy, invasive ventilation is often needed.

In intubated and invasively ventilated patients with moderate-to-severe acute respiratory distress syndrome, prone positioning can improve oxygenation and has been shown to improve survival.^{2,3} Benefit of prone positioning may not be restricted to invasively ventilated patients—at least in theory, non-intubated patients could also benefit from being placed in a prone position.^{4,5} The so-called awake proning is a cheap intervention, and thus very attractive from an economic viewpoint. Awake proning, however, could be or become uncomfortable if incorrectly performed, especially when it needs to be provided for many hours. It may also come with complications such as shoulder injuries,^{6,7} pressure ulcers,⁸ and aspiration of gastric content.⁹

We invited a group of healthcare professionals with known interest or expertise in awake proning or with practical knowledge regarding care for patients with acute respiratory failure in low- and middle-income countries (LMICs), to develop a set of pragmatic recommendations for use of this intervention. The goal was to develop a guidance enriched with illustrations for a better understanding and local training of healthcare professionals. Information on awake proning mainly originated in resource-rich settings in high-income countries—the group translated the available information into recommendations for use in resource-restricted settings in LMICs.

METHODS

An international group of healthcare professionals was invited by the study leads (W. S., L. D. B., L. P., M. J. S., and F. P.). Communication and writing within the group and three subgroups was merely by email correspondence and teleconferences, and a central shared online document was used to draft the current guidance.

Several literature searches in Medline were performed, using different combinations of search terms like “coronavirus disease,” “coronavirus disease 2019,” “COVID-19,” “SARS-CoV-2,” “prone positioning” and “awake proning,” “non-intubated,” “non-invasive,” “oxygen therapy,” “high flow nasal oxygen (HFNO),” “non-invasive ventilation (NIV),” “respiratory monitoring,” and “ratio of oxygen saturation (ROX) index.” Searches had to be updated several times, as publications continued to appear in the literature during the writing of this report. A final search in Medline was performed in late October 2020. In addition to these Medline searches, Internet searches, mainly through the Google search machine and using the comparable terms, were performed to explore the gray literature and search for webinars on awake proning.

Information was bundled and dealt within three subgroups regarding the following questions: 1) What is the evidence for benefit of awake proning for acute respiratory failure in general, and in COVID-19 pneumonia in particular? 2) What are the recommendations and suggestions for practical application of awake proning for acute respiratory failure in general, and in COVID-19 pneumonia? 3) Should recommendations for use of awake proning differ between high-income countries and

LMICs? Members could participate in more than one subgroup, by members' preferences.

Quality of evidence was scored from very high to very low, and the strength of each recommendation was given as strong or weak considering indirectness of evidence and magnitude of effects. For LMICs, the availability, affordability, safety, and feasibility of awake proning in patients with acute respiratory failure were used to refine the recommendations if necessary.¹⁰

RESULTS

Reports from the subgroups: Evidence for benefit. The number of studies investigating awake proning is rapidly increasing, but thus far, randomized clinical trials remain absent. Published studies were heterogeneous with regard to several aspects—for example, supplementary oxygen during awake proning was provided using diverse interfaces, from simple oxygen supplementation via a nasal prong or cannula^{11–14} or a Venturi mask¹⁴ to continuous positive airway pressure (CPAP),^{15–18} HFNO,^{4,12,19,20} and NIV²¹; the exact positions taken during awake proning also differed widely; thresholds for awake proning varied, from pulse oximetry as high as > 94%^{15,22} to as low as < 90%¹¹; duration of awake proning varied too, from 30 minutes to several hours^{4,5,11,15,21,23} or even longer,^{13,19,20,22,24} and proning could be applied more times per day,^{4,5,21} or until low oxygen saturations resolved.¹⁴

Awake proning improves oxygenation^{4,5,11,12,15,19,25} and also reduces dyspnea.^{13,21,22} The improvements in oxygenation are seen within minutes after the start of awake proning.¹¹ The effects of awake proning on oxygenation are maintained for up to one hour after turning back to supine¹⁵ but disappear after 6–12 hours.^{12,26} Awake proning also reduces dyspnea sensation and work of breathing by improving ventilation–perfusion.^{14,19,21,22,25} Despite this benefit, awake proning is not always tolerated.^{5,12,14,21,27}

It remains uncertain whether awake proning can prevent invasive ventilation. Several studies show a low intubation rate with the use of awake proning.^{12,14,21} Two studies suggest prevention of intubation,^{20,22} but this is not confirmed in other investigations in invasively ventilated patients,^{15,28,29} nor in patients with severe hypoxemia receiving NIV,⁴ nor in patients receiving HFNO.³⁰ It is highly uncertain whether awake proning can be used as a rescue therapy, that is, to avoid intubation in patients who already fulfill the criteria for immediate intubation.

It remains unclear whether the effects of awake proning depend on the way supplemental oxygen is administered, albeit that improvements in oxygenation are described with all forms of oxygen supplementation, that is, via nasal cannula or oxygen mask,^{11–13,15,19,28,31} CPAP,^{15,21} HFNO,^{12,20,24,27,30,31} and NIV.^{4,21} Some studies suggest that “early” awake proning (i.e., when oxygen can still be supplied via a simple interface like a nasal cannula)^{11,12,22,28} could have a better effect than “late” awake proning (i.e., when oxygen needs to be supplied via HFNO or CPAP).^{15,21,24,32} A change in pulse oximetry readings or respiratory rate (RR) induced by awake proning could be useful parameters to define responders versus nonresponders. In one study, a rise of SpO₂ > 95% is associated with a lower intubation rate.²⁸

Persistent hypoxemia despite supplementary oxygen was used as an indication in all studies, albeit with considerable variation in the degree of hypoxia. Literature remains vague

regarding other indications, and also contraindications for awake proning. Based on the studies identified by the searches and consensus within the group, indications and (relative) contraindications for awake proning were formulated (Table 1). Consensus was not based on robust evidence, and may depend on various factors such as available resources, and local expertise—for example, in a hospital ward environment with a low nurse-to-patient ratio, it may be challenging to safely use light sedation in the management of a severely dyspneic patient who will receive awake proning.

Reports from the subgroups: Practical application of awake proning. Based on the studies identified by the searches and consensus within the group, recommendations and suggestions for practical application of awake proning in COVID-19 patients were formulated (Table 2). The group considers it essential to train local teams in terms of correct and safe use of awake proning, especially when light sedation is used. Ideally, an “awake proning team” consists of two healthcare professionals, including at least one doctor, and a nurse or a physical therapist. One professional should provide team leadership. The team will assist the patient to take the correct position and ascertain continuation of oxygenation supplementation—extra oxygen during positioning could be considered. The healthcare professional should assist in proper positioning of the limbs. Supporting materials, such as pillow blocks, cushions, or rolled blankets, should be closely at hand. To minimize the risks of awake proning, a practical checklist or “proning bundle” can be checked every time a patient is placed in the prone position³³ (Table 3).

For awake proning to be successful, the group thinks motivational support to the patient is one key to success. Before proning, why awake proning could work, what it is like to be in a prone position, and how to maintain a proper position should be explained to the patient and family members if present. A

potential increase on pulse oximetry readings and a reduction in dyspnea, coughing, and sputum production could increase following the position change—this is usually short-lasting. It can be useful to know if the patient normally sleeps face down (e.g., prone), to adjust this information. Patients could find awake proning uncomfortable, but this may be mitigated through supportive nursing care and noticing the marked improvements of pulse oximetry readings. Family can stay with patients who are proning, and use of mobile devices to spend time and communicate with relatives should be stimulated. If use of sedatives or anxiolytics is being considered to facilitate prone positioning in non-intubated patients, this should be undertaken in a closely monitored location, with access to continuous oxygen saturation, blood pressure, and electrocardiogram monitoring. Pain medication could be considered, as pain related to stiffness of shoulders and neck could develop.

Frequent assessment for tolerability, at least within 10 minutes after the start of proning, is considered important. In some patients, it may be necessary to start benzodiazepine, clonidine, or dexmedetomidine, but only if the setting allows; also, morphine in low dosages could be useful in a severely dyspneic patient. In those cases, proper monitoring, including continuous or intermittent pulse oximetry, blood pressure, and maybe electrocardiogram could be useful.

The vast majority of patients will receive supplemental oxygen through interfaces like a nasal prong or cannula, a face mask, CPAP via a mask, or a ventilation hood, HFNO, or NIV.^{15–17,19} There is no evidence as to which interface is best in patients who receive prone positioning. Nasal interfaces and masks seem more practical and better tolerated than hoods,⁵ especially in elderly patients.¹⁵ One current multicenter randomized clinical trial is testing the efficacy of different

TABLE 1
Indications and contraindications to apply awake proning

Indications
SpO ₂ /FI _O ₂ ratio < 315
Acute respiratory failure requiring any supplemental oxygen to maintain saturation > 90%
Able to follow instructions in their native language
Absolute contraindications in the ward and ICU setting
Anticipated difficult airway
Cardiogenic pulmonary edema as a cause for respiratory failure
Respiratory rate of above 40/min or accessory muscle use
Unreliable SpO ₂ tracing
Immobile or extremely limited mobility
Inability to tolerate proning due to anatomic concerns (e.g., injury or wound on the ventral surface of the body)
Spinal instability
Glaucoma or other condition with acutely elevated intraocular pressure
Severe head trauma with high ICP
Absolute contraindications in the ward, but relative contraindication in the ICU setting
Severe oxygenation problems defined as PaO ₂ /FI _O ₂ < 100 mmHg ⁴ or, alternatively, SpO ₂ /FI _O ₂ < 140 mmHg ⁶⁰
Altered mental status or inability to follow commands
Inability to communicate with care team or call for help verbally or with call bell
Hemodynamic instability defined as requiring vasopressor support (i.e., a systolic blood pressure < 90 mmHg or mean arterial pressure less than 65 mmHg despite appropriate volume resuscitation)
Inability to reposition self for comfort without assistance
Relative contraindications in the ward and ICU setting
Facial injury
Neurological issues (e.g., frequent seizures)
Morbid obesity (BMI > 40)
Pregnancy (2/3rd trimesters)
Pressure ulcers
Concomitant type II respiratory failure, unless chronic, stable, and compensated (pH > 7.36). If awake proning is considered, it should be trialed, and a blood gas should be taken within 30 minutes to ensure no deterioration in hypercapnia.

BMI: body mass index; FI_O₂: oxygen concentration; ICP: intracranial pressure; PaO₂: arterial blood oxygen concentration; SpO₂: peripheral oxygen saturation.

TABLE 2
Recommendations and suggestions for practical application of awake proning in COVID-19 patients (with grading)

Domain	Recommendation	Grading	Considerations for use in LMICs*
1	Indications	Suggest: Consider awake proning in patients with acute respiratory failure requiring supplemental oxygen to maintain saturation > 93%. ^{11,15,22}	Low-quality evidence Where pulse oximetry is not available, it would be reasonable to trial awake proning for COVID-19 patients with cyanosis, marked tachypnea, or other evidence of respiratory distress.
2	Indications	Suggest: Consider awake proning in patients able to follow instructions.	Expert opinion No additional considerations.
3	Indications	Recommend: Use awake proning during the 1st and 2nd trimesters in pregnant women with additional monitoring of the position and the fetus.	Expert opinion In settings without tocography and Doppler, fetal monitoring using clinical auscultation of the fetal heart rate should be performed.
4	Contra-indications	Suggest: Use awake proning in the 3rd trimester of pregnancy with additional monitoring with caution and on an individual risk–benefit basis.	Expert opinion In settings without tocography and Doppler, fetal monitoring using clinical auscultation of the fetal heart rate should be performed.
5	Contra-indications	Recommend against: Awake proning in patients with extreme respiratory distress requiring immediate intubation. ^{15,20,22,28,29}	Low-quality evidence Where mechanical ventilation is not available or affordable, a trial of awake proning may be performed as a rescue maneuver.
6	Contra-indications	Suggest against: Awake proning in patients with impaired consciousness.	Low-quality evidence No additional considerations.
7	Preparation	Strongly recommend: Preparing the patient and the family for what it is like to be in a prone position, what can be expected, and how to maintain this position.	Expert opinion Visual aids may be useful to illustrate the family what will happen. Caregivers will often become a key component of the proning team. Widely available fleece blankets can be used instead of pillows to reduce costs.
8	Preparation	Recommend: Preparation for complications (safe airway, suctioning, and pressure ulcers).	Expert opinion Examples of recommended preparations for complications include having the equipment necessary for emergency intubation prepared nearby in case it is required, having a functioning suction machine with a clean suction catheter available at all times, and ensuring careful padding of all pressure areas and daily pressure area surveillance.
9	Monitoring	Strongly recommend: Minimum monitoring of pulse rate and peripheral oxygen saturation.	Expert opinion Where available, a multiparametric monitor or a handheld or tabletop pulse oximeter is preferable to a fingertip pulse oximeter (not easily seen or heard from a distance and may automatically switch off after a certain time period). ⁶¹ Whatever device is used, the alarm should be set to alert staff if SpO ₂ drops below 90%. When there are insufficient pulse oximeters available for continuous monitoring, intermittent monitoring should be carried out as frequently as staffing and equipment allow.
10	Monitoring	Recommend: Monitoring respiratory rate, work of breathing (use of respiratory muscles), and dyspnea.	Expert opinion While safety is high, feasibility depends on the local level of staffing. ⁶²
11	Monitoring	Suggest: Possibility of monitoring respiratory status by using the ROX index.	Expert opinion Feasibility relies on the availability of pulse oximetry.
12	Monitoring	Recommend: Monitoring of hemodynamic parameters (MAP and SBP).	Expert opinion We recommend a noninvasive blood pressure measurement at least once an hour where possible (expert opinion).
13	Monitoring	Suggest: Visual care monitoring by open wards in event of high surge capacity.	Expert opinion This is a pragmatic measure that improves patient safety and makes efficient use of staff and PPE.
14	Monitoring	Suggest against: Awake proning in conventional hospital wards for patients with severe respiratory failure.	Expert opinion This recommendation may not apply in settings where no higher level of care is available.
15	Oxygen supply	Recommend: Use of any available method of oxygen delivery during awake proning.	Expert opinion Oxygen is a scarce resource in at least one-quarter of hospitals in LMICs. ⁵² The choice among oxygen concentrators, cylinders, or centralized

(continued)

TABLE 2
Continued

Domain	Recommendation	Grading	Considerations for use in LMICs*	
			systems will depend on local availability and option assessment. ⁶³ Reservoir masks may represent feasible and affordable option. Attention should be paid to ensuring the tubing is not kinked in the prone position and in the case of a reservoir mask that the bag is fully inflated.	
16	Oxygen supply	Suggest: Use of CPAP or HFNO for delivery of higher FiO ₂ , depending on the locally available expertise.	Low-quality evidence	Availability and affordability of CPAP and HFNO systems is variable but generally low. ⁶⁴ Feasibility of HFNO is low because of high oxygen demands.
17	Position	Suggest: Train multidisciplinary proning teams in approaches on awake and sedated proning with one person having the lead.	Expert opinion	Where insufficient staff are available, care givers can also provide support. ⁶⁵
18	Position	Suggest: Have a slightly lateral position to turn the face.	Expert opinion	Some patients prefer to keep their head central rather than turned to the side (see Figure 2 for a configuration of padding to accommodate this).
19	Position	Suggest: Avoid a closed packed shoulder by keeping the shoulder of the raised arm around 80° abduction. ³⁵	Expert opinion	No additional considerations.
20	Position	Suggest: Full flexion of the knees if possible and maximum range ankle motion.	Expert opinion	Extra pillows may be needed. Widely available fleece blankets can be used instead of pillows to reduce costs.
21	Position	Suggest: Use analgesia when low back pain becomes a problem.	Expert opinion	
22	Position	Recommend: Supportive padding above and below the gravid uterus when pregnant women are prone (Figure 1).	Expert opinion	Folded fleece blankets can be used for this purpose.
23	Position	Suggest: A semi-lateral prone position in pregnant woman in the 2nd/3rd trimester as an alternative (Figure 1).	Expert opinion	No additional recommendations.
24	Hydration and nutrition	Recommend: Maintain normovolemia.	Expert opinion	No additional recommendations.
25	Hydration and nutrition	Suggest: Allow oral intake unless there is a high risk of intubation.	Expert opinion	No additional recommendations.
26	Hydration and nutrition	Suggest: Stay in the supine position for one hour after oral feeding in the supine position.	Expert opinion	No additional recommendations.
27	Risk management	Recommend: Have equipment for endotracheal intubation nearby and frequently checked.	Expert opinion	This only applies to centers where mechanical ventilation is available.
28	Risk management	Recommend: Have an intravenous port available for sudden clinical deterioration.	Expert opinion	No additional recommendations.
29	Risk management	Recommend: Have materials for (endotracheal or nasal) suctioning standby.	Expert opinion	Where electrical suction devices are not available, a manual suction pump or bulb suction can be used.
30	Risk management	Suggest: Start reverse CPR until a team is ready to get the patient in the supine position.	Expert opinion	CPR should only be commenced once staff attending the patient are wearing N95 respirators/masks or equivalent.

CPAP = continuous positive airway pressure; CPR = cardiopulmonary resuscitation; HFNO = high-flow nasal oxygen; LMICs = low- and middle-income countries; MAP = mean arterial pressure; NIV = noninvasive ventilation; PPE = personal protective equipment; SBP = systolic blood pressure.

* Considerations regarding feasibility, availability, safety and affordability.¹⁰

interfaces for supplemental oxygen during awake proning in patients with COVID-19 acute respiratory failure.³⁴

In patients with mild hypoxemia, “self-proning” could be possible, eventually with the help of a family member. In patients with severe hypoxemia, “assisted proning” is likely to be superior to “self-proning,” as patients may need all of their energy to breathe, and thus need help. Assistance also prevents dislocation of the interfaces for supplemental oxygen and any indwelling catheter. Assistance may prevent an increase in oxygen consumption induced by changing the position, especially in older, frail, pregnant, and obese patients.

Some refinements could increase safety of awake proning and may allow acceptance for a longer period of time. Suggested positions are illustrated in Figures 1 and 2. A slightly lateral prone position allows a patient to turn the face to one side, which can be supported by a pillow or rolled blanket placed under one side of the chest, and a raised arm embracing the pillow (the “front crawl” or “swimmers position”). While in the prone position, the patient faces the armpit of the raised arm of which the elbow is flexed at ~90°, and the contralateral arm remains aligned with the body. A maximum closed packed position of the shoulder is avoided by keeping the shoulder of the raised arm at ~80° abduction, or even lower

TABLE 3
Safe awake proning checklist

Preparation	Proning	After turning/during proning
Patient Identity Explanation procedure Document duration of procedure Consent Materials Pillows and slide sheet Crash cart Oxygen available Suction equipment available Monitoring: pulse oximetry if available Check Vital signs: SpO ₂ , RR, HR, and BP IV access Nurse call system Baby monitor in case of pregnancy Emergencies Emergency team for the supine position Crash cart (intubation equipment) available	Patient Self-proning Assisted proning Materials Sufficient room between the head and shoulders for oxygen supply In pregnant women, special attention to alleviate pressure on the gravid uterus Oxygen supply continued Emergencies Emergency team for the supine position Crash cart (intubation equipment) available	Patient Comfort Document chosen position (prone and lateral) Document position of arms Materials Provide emergency buzzer, mobile phone, and improvised rattle Check Vital signs: SpO ₂ , RR, HR, and BP IV access Nurse call system Additional external fetal monitoring Medication Pain: paracetamol 4 dd 1 g Anxiety: low-dose benzodiazepine Oxazepam 10 mg po Midazolam 1–2 mg po Emergencies Emergency team for the supine position Crash cart (intubation equipment) available and know where to find

BP = blood pressure; HR = heart rate; IV = intravenous; RR = respiratory rate; SpO₂ = peripheral oxygen saturation. Based on the WHO surgical checklist and Safe prone checklist.⁶⁶

if possible.³⁵ The upper arm and shoulder blade are positioned in a straight horizontal line to protect the shoulder, and arm repositioning is encouraged, if pain or stiffness occurs. Slight adjustments or repositioning of the legs and hip should be encouraged to prevent pressure ulcers and meralgia paresthetica. The latter complication is a result of compression injury of the lateral femoral cutaneous nerve.³⁶ The side of the swimmers position changes frequently, preferably every 2 or 3 hours. Full flexion of the knees should be possible, with a maximum range of ankle motion to prevent stiffness and pointed feet. In patients with lower back pain, a semi-prone or lateral position could be taken. If this does not provide relief for the lower back pain, pain medication could be considered.

As patients in prone position may need urgent intubation, they should remain fasting. Fasting is also advisable because of an increased risk for aspiration when in a prone position. Patients should thus be encouraged to take oral feeds in supine,

head-up position, between the sessions, if allowed, and should not be placed in a prone position for at least 1 hour after oral intake. Fluids should be given intravenously, if needed. However, sips of water could be taken with the bed in a more upright position.

Direct visual care and monitoring of patients during awake proning is facilitated by designated areas for cohorts of patients. Monitoring of RR, accessory muscle use, and work of breathing could help identifying patients who need escalation of care. The ROX index,³⁷ defined as the ratio of SpO₂/FiO₂ to RR, has been proposed for monitoring. This index combines three parameters that assess a patient's respiratory status. Improvement in the ROX index during awake proning could indicate a lesser likelihood for intubation,³⁸ but experience with the ROX index in patients with COVID-19 acute respiratory failure is still very limited.

In case of cardiac arrest in a prone position, "reverse cardiopulmonary resuscitation (CPR)"^{39,40} can and must be

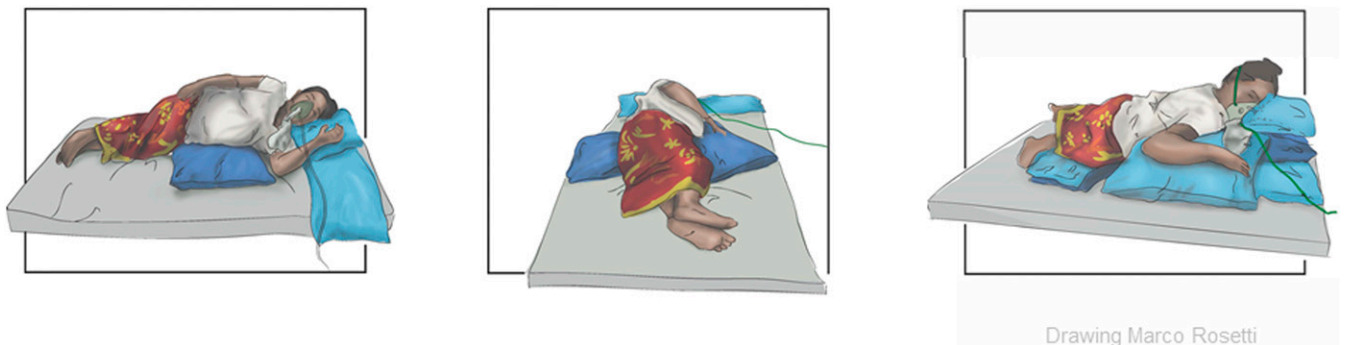


FIGURE 1. Awake proning in a 9-month pregnant woman. Both $\frac{3}{4}$ prone and full prone options are shown. Suggested position is an indication and could be adapted based on patient preferences. This figure appears in color at www.ajtmh.org.

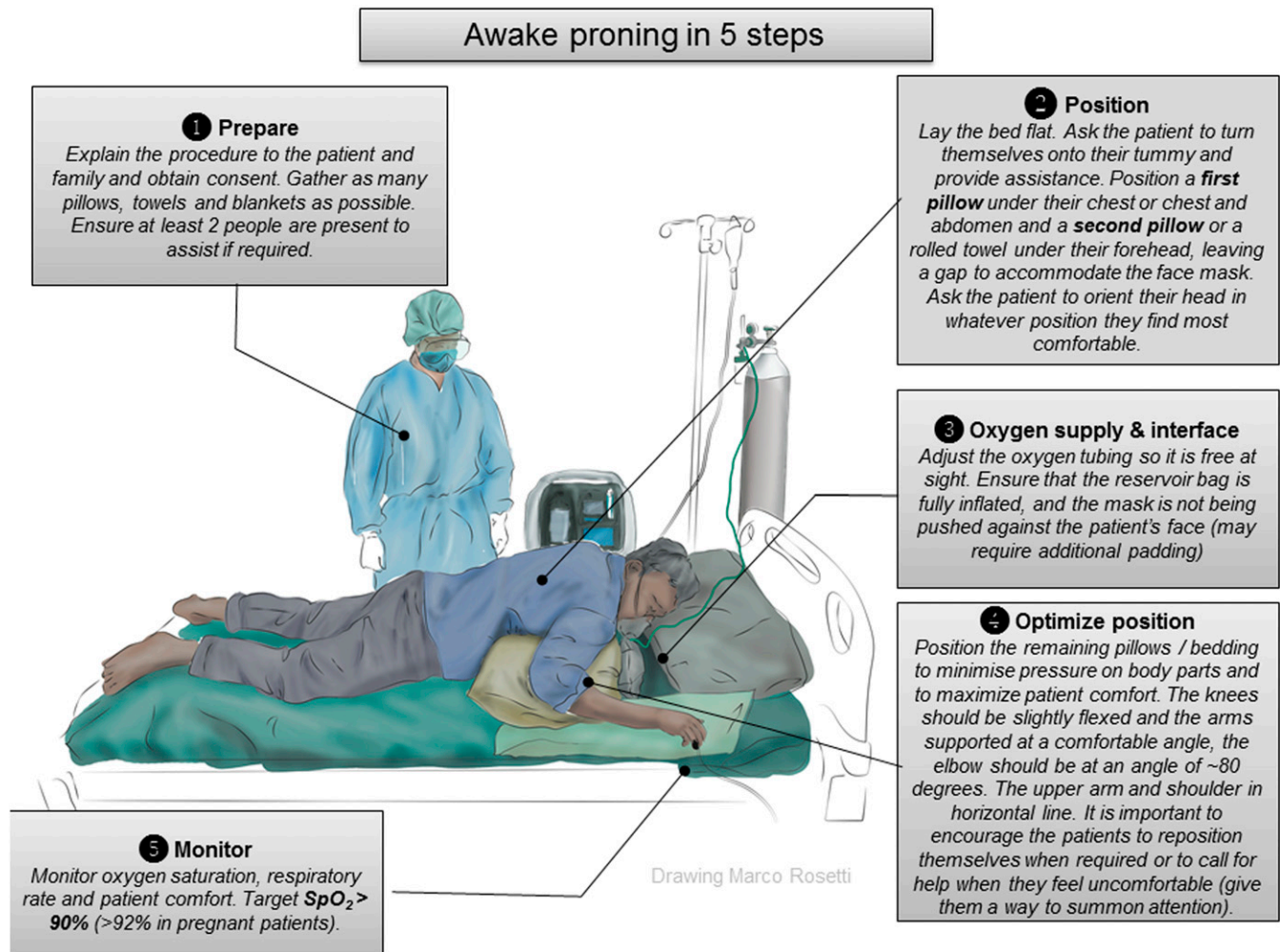


FIGURE 2. Visual aid to facilitate awake proning implementation in a resource-limited setting. Suggested position is an indication and could be adapted based on patient preferences. Adapted with permission from a prone positioning checklist developed by Dr. Rebecca Inglis in Lao PDR.⁶⁷ This figure appears in color at www.ajtmh.org.

started until a team is available to turn the patient back to supine.⁴¹ This team should be identified and always be readily available. Emergency endotracheal intubation equipment and materials must be close by and regularly checked for immediate use alongside relevant emergency drugs.

Finally, the group suggests awake proning should not be withheld in pregnant patients,^{42–47} but supplemental oxygen should be provided such that pulse oximetry remains $\geq 95\%$.⁴³ To prevent aortocaval compression in pregnant patients,⁴⁸ additional measures can be taken by organizing extra pillows and monitoring.

Reports from the subgroups: Recommendations for awake proning in LMICs. As awake proning does not require particular resources, it should be considered in hypoxemic patients with COVID-19 acute respiratory failure who do not respond to simple supplementary oxygen in settings where resources are limited. The group considers awake proning with any available method of respiratory support a safe intervention, also in LMICs. Awake proning may prevent the need for invasive ventilation which is important for settings with limited numbers of ventilators.^{14,32} In fact, at times, awake proning may be the only option to improve oxygenation in settings. Limitations regarding awake proning in LMICs

include a lack of human resources, training, and challenges with infrastructure and equipment.⁴⁹

The group recognizes the limitation of staffing in many LMICs and that a “proning team” may not always be feasible. The guidance by one trained healthcare professional, or two in an obese or a noncooperative patient, however, is seen as one minimal requirement to proceed with this intervention. It is always important that a patient can be turned back to supine with urgency to allow emergency procedures such as CPR. Training of staff becomes pivotal in limited-resource settings, as it is possible to spare time and resources when exact maneuvers are known by the team. Figures 1 and 2 provide additional training material.

Oxygen is listed as an essential medication by the WHO⁵⁰ but remains a very limited resource in many settings.^{51–53} Low-flow supplemental oxygen via nasal prongs, sponge-tipped catheters, or face masks are increasingly available and affordable, although one-quarter of hospitals surveyed in an LMIC study reported gaps in oxygen supply.⁵² Facemasks with reservoir allow increasing FiO_2 significantly and should be strongly considered (Figure 2). High-flow nasal oxygen and NIV are feasible in LMICs, but not widely available. They come at additional costs for the interfaces and devices. They also

come with technical challenges and practical concerns, as they depend on a reliable source of oxygen and electricity. Continuous positive airway pressure and HFNO apparatuses may rapidly use up oxygen supplies; indeed, HFNO consumes oxygen at more than four times the rate of low flow oxygen support, and typically, HFNO may consume the entire content of a large oxygen cylinder within 2–3 hours, rapidly depleting oxygen supply.

Close monitoring and clear escalation criteria are needed with awake proning, also in resource-limited settings. In LMICs, pulse oximeters are often not available, but recent initiatives have been set up to provide them on a larger scale.⁵⁴ Pulse oximetry together with monitoring of clinical and vital signs might help timely identification of those patients who need escalation of care.⁵⁵ In settings where blood gas analyzers are unavailable, SpO₂ relative to inspiratory oxygen concentration, or SpO₂/FiO₂ ratio, can be used for continuous monitoring, decision-making, and prognostication.^{56–58} The ROX index is likely to be useful because it requires simple input (SpO₂/FiO₂ and respiratory rate) and is easy to calculate at the bedside.⁵⁹

During the supine periods between awake proning, oral intake is to be encouraged to maintain normovolemia in resource-limited settings, as other resources for fluid intake are usually limited. The risk of aspiration, however, should be highlighted, especially in obese patients. The suggestion of using low-dose benzodiazepines or morphine to enhance awake proning should be conducted with care in environments with limited or absent patient monitoring.

DISCUSSION

A rapidly growing number of observational studies describe the use of awake proning in patients with COVID-19 acute respiratory failure in whom hypoxemia is refractory to simple supplementary oxygen. Awake proning improves oxygenation within minutes, and the effects are maintained for up to one hour after turning back to supine and disappear mostly after 6–12 hours. Awake proning is associated with few complications. Because no particular technological resources are required, it is particularly applicable in settings where resources are limited, or even absent. A set of pragmatic recommendations were formulated on awake proning in relation to indications and contraindications, oxygen supply, position, nutrition, monitoring, and risk management based on the available evidence and experiences of healthcare workers in LMICs.

It is important to notice that so far there is no randomized trial evidence for the effect of awake proning in patients with COVID-19 acute respiratory failure. Current evidence comes from few studies, mostly case reports and single-center observations. None of these originated in LMICs. The available results, however, suggest that awake proning could be effective adjunctive therapy that is also safe and tolerable. The suggestion that it may prevent the need for invasive ventilation or increased need of oxygen makes this intervention worth a try, certainly in settings where there is a shortage of ventilators or where ventilators are absent^{20,22} or health care is unaffordable for patients.

One strength of this guidance on awake proning is the cooperation of a set of healthcare workers from resource-limited settings in high-income countries and from resource-limited settings in LMICs. There was a large expertise in proning, and a deep understanding of the challenges in

intensive care units in LMICs. Also, the group consisted of various types of healthcare workers, including (ICU) doctors, (ICU) nurses, and physiotherapists.

This work also has limitations. We emphasize that this is not a systematic review, but rather a clinical appraisal of the available literature and personal clinical experiences of healthcare workers in various settings around the world. We cannot exclude selection and information bias.

CONCLUSION

Awake proning is an attractive and safe adjunctive treatment for hypoxemia refractory to supplemental oxygen in patients with COVID-19 acute respiratory failure, especially in settings where there is shortage or absolute lack of ventilators. Here, this could be the only option to improve oxygenation. It may even prevent the need for invasive ventilation; although randomized trial evidence remains lacking, randomized clinical trials are urgently needed.

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SUBGROUP CHAIRS AND MEMBERS

Group 1: Evidence for benefit of awake proning

Chairs: Willemke Stilma and Marcus J. Schultz; members (in alphabetic order): Andrew Bentley, Hendrik de Bruin, Gregg Chesney, Domenico L. Grieco, Giovanni Landoni, Diego de Mendoza, Luis Morales-Quinteros, Gianluca Paternoster, Oriol Roca, Chiara Sartini, Vittorio Scaravilli, Chaisit Sivakorn, Peter E. Spronk, Jaques Sztajn-bok, and Youssef Trigui.

Group 2: Practical application of awake proning

Chairs: Frederique Paulus and Lieuwe D. Bos; members (in alphabetic order): Eva Åkerman, Thomas J.C. Bosman, Laura A. Buiteman-Kruizinga, Gregg Chesney, Cindy Chu, Paul Dark, Harm J.H. Gijssbers, Weihua Lu, Lisa M.N. Maduro, Bairbre McNicholas, Eloi Prud'homme, and Margaretha C.E. van der Woude.

Group 3: Specific recommendations for use of awake proning in LMICs

Chairs: Luigi Pisani and Marcus J. Schultz; members (in alphabetic order): Eva Åkerman, Antonio Artigas, Andrew Bentley, Tobias Brummaier, Francesco Carcò, Cindy Chu, Arjen M. Dondorp, Mary Ellen Gilder, Rebecca Inglis, John G. Laffey, Rose McGready, François Nosten, Gianluca Paternoster, Alfred Papali, Jean-Damien Ricard, Oriol Roca, Chaisith Sivakorn, Peter E. Spronk, and Kathleen M. Vollman.

Authors' addresses: Willemke Stilma and Frederique Paulus, Department of Intensive Care, Amsterdam University Medical Centers, Location 'AMC', Amsterdam, The Netherlands, and Faculty of Health, Center of Expertise Urban Vitality, Amsterdam University of

Applied Science, Amsterdam, The Netherlands, E-mail: w.stilma@amsterdamumc.nl and f.paulus@amsterdamumc.nl. Eva Åkerman, Division of Nursing, Department of Neurobiology, Care Sciences and Society, Karolinska Institute, Stockholm, Sweden, and Function of Perioperative Medicine and Intensive Care, Department of Intensive Care, Karolinska University Hospital, Stockholm, Sweden, E-mail: eva.akerman@gmail.com. Antonio Artigas, Department of Intensive Care, Hospital de Sabadell, CIBER Enfermedades Respiratorias, Sabadell, Barcelona, Spain, and Autonomous University of Barcelona, Sabadell, Barcelona, Spain, E-mail: aartigas@tauli.cat. Andrew Bentley, Acute Intensive Care Unit, Manchester University NHS Foundation, Manchester, United Kingdom, and Faculty of Biology, Medicine and Health, Manchester Academic Health Science Centre, University of Manchester, Manchester, United Kingdom, E-mail: andrew.bentley@manchester.ac.uk. Lieuwe D. Bos, Thomas J. C. Bosman, and Hendrik de Bruin, Department of Intensive Care, Amsterdam University Medical Centers, Location 'AMC', Amsterdam, The Netherlands, E-mails: l.d.bos@amsterdamumc.nl, t.j.bosman@amsterdamumc.nl, and h.debruin2@amsterdamumc.nl. Tobias Brummaier, Cindy Chu, Rose McGready, Francois Nosten, Shoklo Malaria Research Unit, Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Mae Sot, Thailand, and Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom, E-mails: tobias.brummaier@gmx.at, cindy@tropmedres.ac, rose@shoklo-unit.com, and francois@tropmedres.ac. Laura A. Buiteman-Kruizinga, Department of Intensive Care, Amsterdam University Medical Centers, Location 'AMC', Amsterdam, The Netherlands, and Department of Intensive Care, Reinier de Graaf Hospital, Delft, The Netherlands, E-mail: l.kruizinga@rdgg.nl. Francesco Carcò, Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute, Milan, Italy, E-mail: carco.fn@gmail.com. Gregg Chesney, Division of Emergency Medicine-Critical Care, Department of Emergency Medicine, NYU Grossman School of Medicine, New York, NY, E-mail: gregg.chesney@nyulangone.org. Paul Dark, Critical Care Medicine, NIHR Manchester Biomedical Research Centre, University of Manchester, Manchester, United Kingdom, Division of Infection, Immunity and Respiratory Medicine, NIHR Manchester Biomedical Research Centre, University of Manchester, Manchester, United Kingdom, and Humanitarian and Conflict Response Institute, University of Manchester, Manchester, United Kingdom, E-mail: paul.m.dark@manchester.ac.uk. Arjen M. Dondorp, Faculty of Tropical Medicine, Mahidol-Oxford Tropical Medicine Research Unit (MORU), Mahidol University, Bangkok, Thailand, E-mail: arjen@tropmedres.ac. Harm J. H. Gijssbers and Lisa M. N. Maduro, Department of Rehabilitation Medicine, Amsterdam University Medical Centers, Location 'AMC', Amsterdam, The Netherlands, E-mails: h.j.gijssbers@amsterdamumc.nl and l.m.maduro@amsterdamumc.nl. Mary Ellen Gilder, Department of Family Medicine, Faculty of Medicine, Chiang Mai University, Chiang Mai, Thailand, E-mail: mellietyros@gmail.com. Domenico L. Grieco, Department of Emergency, Intensive Care Medicine and Anesthesia, Fondazione Policlinico Universitario A. Gemelli IRCCS, Rome, Italy, and Department of Anesthesiology and Intensive Care Medicine, Catholic University of the Sacred Heart, Rome, Italy, E-mail: dlgrico@outlook.it. Rebecca Inglis, Lao-Oxford-Mahosot Hospital-Wellcome Trust Research Unit (LOMWRU), Mahosot Hospital, University of Oxford, Vientiane, Lao People's Democratic Republic, E-mail: rebecca.i@tropmedres.ac. John G. Laffey, Department of Anaesthesia and Intensive Care, MedicineGalway University Hospitals, Galway, Ireland, and School of Medicine, Disciplines of Anaesthesia and Intensive Care Medicine, National University of Ireland, Galway, Ireland, E-mail: john.laffey@nuigalway.ie. Giovanni Landoni, Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute, Milan, Italy, and School of Medicine, Vita Salute San Raffaele University, Milan, Italy, E-mail: landoni.giovanni@hsr.it. Weihua Lu, Department of Critical Care Medicine, Yijishan Hospital of Wannan Medical College, Wuhu, China, E-mail: lwh683@126.com. Bairbre McNicholas, Department of Anaesthesia and Intensive Care, MedicineGalway University Hospitals, Galway, Ireland, E-mail: bairbre.nimhaille@hse.ie. Diego de Mendoza, Intensive Care Department, Hospital Universitari Sagrat Cor. Grupo Quironsalud, Barcelona, Spain, Emergency Department, Hospital Universitari Sagrat Cor. Grupo Quironsalud, Barcelona, Spain, and Ciber Enfermedades Respiratorias (CIBERES), Instituto de Salud Carlos III, Madrid, Spain, E-mail: diego.mendoza@

quironsalud.es. Luis Morales-Quinteros, Intensive Care Department, Hospital Universitari Sagrat Cor. Grupo Quironsalud, Barcelona, Spain, and Institut d' Investigació i Innovació Parc Taulí I3PT, Universidad Autónoma de Barcelona, Barcelona, Spain, E-mail: luchomq2077@gmail.com. Alfred Papali, Division of Pulmonary and Critical Medicine, Atrium Health, Charlotte, NC, and School of Medicine, University of Maryland, Baltimore, MD, E-mail: alfred.papali@atriumhealth.org. Gianluca Paternoster, Department of Cardiovascular Anaesthesia and ICU, San Carlo Hospital, Potenza, Italy, E-mail: paternostergianluca@gmail.com. Luigi Pisani, Department of Intensive Care, Amsterdam University Medical Centers, Location 'AMC', Amsterdam, The Netherlands, Faculty of Tropical Medicine, Mahidol-Oxford Tropical Medicine Research Unit (MORU), Mahidol University, Bangkok, Thailand, and Section of Operational Research, Doctors with Africa CUAMM, Padova, Italy, E-mail: luigipisani@gmail.com. Eloi Prud'homme, Intensive Care Unit, D tresse Respiratoire Infections S v res, Assistance Publique H pitaux de Marseille, Marseille, France, E-mail: eloiprudhomme@gmail.com. Jean-Damien Ricard, DMU ESPRIT-Enseignements et Soins de Proximit , Recherche, Innovation et Territoires, Universit  de Paris, Paris, France, Infection, Antimicrobiens, Mod lisation, Evolution (IAME), Universit  de Paris, Paris, France, and Service de M decine Intensive R animation, H pital Louis Mourier, Assistance Publique – H pitaux de Paris, Colombes, France, E-mail: jean-damien.ricard@aphp.fr. Oriol Roca, Servei de Medicina Intensiva, Hospital Vall d'Hebron, Barcelona, Spain, E-mail: oroca@vhebron.net. Chiara Sartini, Department of Anesthesia and Intensive Care, IRCCS San Raffaele Scientific Institute, Milan, Italy, E-mail: doc.chiara.sartini@gmail.com. Vittorio Scaravilli, Department of Anesthesia, Critical Care and Emergency, Fondazione IRCCS Ca' Granda - Ospedale Maggiore Policlinico, Milan, Italy, E-mail: vittorio.scaravilli@gmail.com. Marcus J. Schultz, Department of Intensive Care, Amsterdam University Medical Centers, Location 'AMC', Amsterdam, The Netherlands, Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Oxford, United Kingdom, and Faculty of Tropical Medicine, Mahidol-Oxford Tropical Medicine Research Unit (MORU), Mahidol University, Bangkok, Thailand, E-mail: marcus.j.schultz@gmail.com. Chaisith Sivakorn, Department of Clinical Tropical Medicine, Mahidol University, Bangkok, Thailand, E-mail: chaisith.siv@mahidol.edu. Peter E. Spronk, Expertise Center for Intensive Care Rehabilitation Apeldoorn, Gelre Hospitals Apeldoorn, Apeldoorn, The Netherlands, E-mail: p.spronk@gelre.nl. Jaques Sztajn bok, Intensive Care Unit, Instituto de Infectologia Emilio Ribas, S o Paulo, Brazil, E-mail: jaques.sztajn bok@hc.fm.usp.br. Youssef Trigui, Service des Maladies Respiratoires, Centre Hospitalier D'Aix-en-Provence, Aix-en-Provence, France, E-mail: youssef.trigui@gmail.com. Kathleen M. Vollman, Clinical Nurse Specialist/Critical Care Consultant, Advancing Nursing LLC, Northville, MI, E-mail: kvollman@comcast.net. Margaretha C. E. van der Woude, Intensive Care Unit, Zuyderland Medisch Centrum, Location 'Heerlen', Heerlen, The Netherlands, E-mail: m.vanderwoude@zuyderland.nl.

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