Contents lists available at ScienceDirect



African Journal of Emergency Medicine

journal homepage: www.elsevier.com/locate/afjem

REVIEW ARTICLE

Review of supplemental oxygen and respiratory support for paediatric emergency care in sub-Saharan Africa



Andreas Hansmann^{a,*}, Brenda May Morrow^b, Hans-Joerg Lang^c

^a Universitätsklinikum Bonn, Zentrum für Kinderheilkunde and, Queen Elizabeth Central Hospital Blantyre, Department of Paediatrics, Germany

^b University of Cape Town, Department of Paediatrics and Child Health, South Africa

^c Médecins sans Frontières, Switzerland

ABSTRACT

Introduction: In African countries, respiratory infections and severe sepsis are common causes of respiratory failure and mortality in children under five years of age. Mortality and morbidity in these children could be reduced with adequate respiratory support in the emergency care setting. The purpose of this review is to describe management priorities in the emergency care of critically ill children presenting with respiratory problems. Basic and advanced respiratory support measures are described for implementation according to available resources, work load and skill-levels.

Methods: We did a focused search of respiratory support for critically ill children in resource-limited settings over the past ten years, using the search tools PubMed and Google Scholar, the latest WHO guidelines, international 'Advanced Paediatric Life Support' guidelines and paediatric critical care textbooks.

Results: The implementation of triage and rapid recognition of respiratory distress and hypoxia with pulse oximetry is important to correctly identify critically ill children with increased risk of mortality in all health facilities in resource constrained settings. Basic, effective airway management and respiratory support are essential elements of emergency care. Correct provision of supplemental oxygen is safe and its application alone can significantly improve the outcome of critically ill children. Non-invasive ventilatory support is cost-effective and feasible, with the potential to improve emergency care packages for children with respiratory failure and other organ dysfunctions. Non-invasive ventilation is particularly important in severely under-resourced regions unable to provide intubation and invasive mechanical ventilation support. Malnutrition and HIV-infection are important co-morbid conditions, associated with increased mortality in children with respiratory dysfunction. *Discussion:* A multi-disciplinary approach is required to optimise emergency care for critically ill children in low-resource settings. In this context, it is important to consider aspects of training of staff, technical support and pragmatic research.

African relevance

- The burden of disease from respiratory failure is high in critically ill children.
- This article reviews respiratory support options feasible in African emergency centres.
- Pulse oximetry and a reliable oxygen supply are a priority in the care for critically ill children.
- Continuous positive airway pressure (CPAP) is a simple non-invasive ventilation option feasible in many low-resource settings.

Introduction

In 2013, 6.3 million children died before the age of five years. Approximately 50% of these deaths occurred in sub-Saharan Africa (SSA), where severe pneumonia remains a leading cause of child mortality [1].

A review from Malawi reported a considerable decline in paediatric hospital mortality from pneumonia between 2000 and 2012. However, mortality remained high in critical sub-groups including those with very severe pneumonia, suspected *Pneumocystis jirovecii* pneumonia and malnutrition [2].

Respiratory failure is also a common feature of critically ill children

Peer review under responsibility of African Federation for Emergency Medicine. * Corresponding author.

E-mail address: andreashansmann@yahoo.de (A. Hansmann).

https://doi.org/10.1016/j.afjem.2017.10.001

Available online 14 November 2017

2211-419X/ 2017 African Federation for Emergency Medicine. Publishing services provided by Elsevier. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/BY-NC-ND/4.0/).

with severe sepsis. Kissoon et al. suggest that the global burden of severe sepsis as a cause of death and disability is under-estimated [3]. Severe infections such as pneumonia, bacteraemia and malaria can coexist and can lead to a complex systemic inflammatory response [4]. Without rapid, efficient management, significant organ dysfunction, including respiratory failure, can occur [3]. Respiratory support is as essential in the management of these critically ill children as in respiratory disease [5,6].

Improvement of living conditions, preventative public health measures (e.g. vaccinations, malaria control programs) and communitybased care can have a major impact on child health in low resource settings. However, strengthening of paediatric emergency care in peripheral health facilities and paediatric hospital departments also has the potential to significantly contribute to improvements of child survival [7]. Improvement of oxygen systems and respiratory support plays an important role in this context. A review of first level referral health facilities in twelve African countries showed that a large percentage of these facilities were not adequately equipped to provide basic supplemental oxygen [8].

A World Health Organisation (WHO) expert committee recently reviewed aspects of oxygen administration and peripheral oxygen saturation (SpO2) targets for paediatric emergency care [9]. This review did not include non-invasive or invasive respiratory support.

In well-resourced settings, non-invasive ventilation (NIV) is used routinely in neonatal care and together with application of surfactant has significantly reduced the need for mechanical ventilation, especially in pre-term newborns [10]. Adapted forms of NIV such as bubble continuous positive airway pressure (bCPAP) were introduced successfully in several low- and middle-income countries (LMICs) [11].

This review will focus on respiratory care in critically ill children beyond the neonatal age. We outline the importance of oxygen supply and non-invasive respiratory support as integral to paediatric emergency care. Priorities in the care of critically ill children are described and suggestions for when to consider mechanical ventilation in the emergency centre are provided.

Methods

A comprehensive literature search was conducted, using electronic search engines and databases (PubMed, Google Scholar) as well as references in review articles, focusing on articles published within the past ten years. No limitations in terms of scientific methodology were implemented. The following guidelines were reviewed:

- Emergency Triage Assessment and Treatment/ETAT [12]
- Updated guidelines for ETAT 2016 [9]
- Oxygen Therapy for Children 2016 [1]
- Pocket Book of Hospital Care for Children 2013; Technical Specifications for Oxygen Concentrators 2015 [14,15]
- International Advanced Paediatric Life Support manuals e.g. APLS, EPALS/PALS [16,17]
- Critical care training manuals (Paediatric BASIC [18]
- The latest editions of paediatric critical care and anaesthetic textbooks [5]

The following main topics were included in the review:

- Causes of child mortality; respiratory illnesses in the context of single and multi-organ-dysfunction.
- Paediatric emergency care; basic to advanced respiratory support modalities.
- Supportive care in paediatric respiratory illness including airway support, monitoring, fluids and nutrition.

The selection of evidence and clinical recommendations were discussed among authors and peers with experience in paediatric emergency and critical care in low- and middle-income countries, to be appropriate to this context. The authors were guided by the recommendations for resource tiered reviews [19].

Oxygen and respiratory support

Critically ill children are at risk of tissue hypoxia due to increased oxygen demand, impaired oxygen delivery or a combination of both. Inadequate oxygen delivery to tissues can lead to cell death and multiorgan failure (MOF). Hypoxaemia, the reduced percentage of oxygensaturated haemoglobin in blood, contributes to tissue hypoxia and is associated with increased mortality and severity of disease in patients with pneumonia [20].

Respiratory failure and hypoxaemia occur frequently with lung pathologies (e.g. pneumonia, bronchiolitis, tuberculosis, asthma) but are also associated with other organ-dysfunctions often seen in African emergency centres including coma, convulsions and shock, which can be caused by conditions like meningitis, bacterial sepsis, malaria and common neonatal pathologies. Critically ill children with HIV infection and malnutrition have an increased mortality risk.

Oxygen treatment

Hypoxaemia is related to increased mortality and severity of disease in children with pneumonia. In a meta-analysis of twelve studies, the presence of hypoxaemia increased the risk of dying by more than fivefold [2]. Yet oxygen, the standard treatment for hypoxaemia and included in the WHO List of Essential Medicines, is often lacking in many African district hospitals [8]. The introduction of routine SpO2 measurements on admission and the provision of oxygen to hypoxic children with pneumonia resulted in a 35% reduction in mortality in Papua New Guinea [21]. However there is insufficient evidence to suggest that oxygen delivery to normoxaemic patients with pneumonia prevents the later development of hypoxaemia [22].

Table 1	
SpO2 oxygen	targets.

SpO2 target level	Patient category
≥90%	Children with respiratory distress only (e.g. with bronchiolitis, pneumonia)
≥94%	Children with potentially reduced oxygen delivery capacity and vulnerable to moderate hypoxia include those with ETAT emergency signs* from conditions like severe sepsis, anaemia,
	cardiac failure, etc.
	* Obstructed or absent breathing
	* Severe respiratory distress
	* Central cyanosis
	* Signs of shock, defined as cold extremities with capillary refill time > 3 s and weak and fast pulse
	* Coma (or seriously reduced level of consciousness)
	* Seizures
	* Signs of severe dehydration in a child with diarrhoea
	Patients with severe anaemia and evidence of oxygen tissue deficit
	will require blood transfusion to increase oxygen carrying
	capacity. When the emergency condition has resolved, aim for SpO2 $\geq 90\%$
Oxygen supplem	entation should be given continuously until the child maintains SpO2

reliably above these levels without support

SpO2, peripheral capillary oxygen saturation; ETAT, Emergency Triage Assessment and Treatment.

Detecting hypoxaemia

Clinical assessment of respiratory dysfunction remains an indispensable tool to identify critically ill children. The most useful clinical signs of severe disease and hypoxaemia are cyanosis, nasal flaring, severe recessions/lower chest wall in-drawing, inability to feed, grunting, head nodding, fast breathing in children and slow respiratory rate in infants [23,24]. Pulse oximetry classifies 20–30% more children correctly as hypoxaemic than clinical signs alone [25]. Pulse oximetry also assists in assessing the efficacy of oxygen treatment and can contribute to more rational use of supplemental oxygen. Blood gas analysis is rarely available, expensive and invasive [9].

Oxygen delivery systems

In LMICs, most hospitals use oxygen cylinders and oxygen concentrators as sources of oxygen. Oxygen concentrators filter nitrogen from ambient air and provide > 85% oxygen at flows of 5–10 litres/ min. Flow-splitters are commercially available to distribute the oxygen to up to five children. There is a larger up-front cost involved in purchasing an oxygen concentrator (upwards of USD300) but it can run continuously for several years, often with minimal maintenance, and is

Table 2

Nasal prongs and nasal/nasopharyngeal catheter.

the most cost-effective method where electricity supply is reliable [26]. Where power failures occur, battery packs, uninterrupted power supply systems or oxygen cylinders can act as back-ups. Oxygen cylinders can be used where electricity is not available or scarce. However, they are bulky, heavy, costly to keep filling and require well-organised logistics. In well-resourced hospitals, piped wall oxygen may be available. For details about oxygen delivery systems see WHO Technical Specifications for Oxygen Concentrators WHO 2016 [15]. Howie et al. have proposed an algorithm for deciding the most cost effective main oxygen supply for health facilities in low resources settings [26].

Patient interface

The methods used to deliver oxygen should be safe, simple, effective and inexpensive. The preferred and safest method of oxygen delivery to infants and children is via nasal prongs. Where nasal prongs are not available, nasal or nasopharyngeal catheters can be used as alternatives (Table 2 and pictures D and E in Fig. 1) [27]. Face masks (picture D in Fig. 1) and head boxes (picture E in Fig. 1) are no longer recommended for oxygen delivery. Some of the disadvantages are discussed in Fig. 1 (Fig. 2, Table 3).

Condition	Nasal prongs	Nasal/nasopharyngeal catheter
Application, see Fig. 1	- Correctly sized (neonate to adult)	– 5–8 French gauges
	 Applied into both nostrils 	 Fixed with tape to side of nostril
	 Concave side downwards Fixed with tape to both sides of the nostrils 	 Length of nasal catheter: distance equal to that from the side of the nostril to the inner margin of the eyebrow
		- Length of nasopharyngeal catheter: from the side of the nostril to the front of the ear
Standard flow-rate	– Infants: 1–2 L/min	– Infants: 1–2 L/min
	– Children: 1–4 L/min	– Children: 1–4 L/min
	Flow-rates above 4 L/min require humidification and	heating.
Advantages	- Well tolerated	 Nasal catheter: Does not require humidification
C C	– Safest option	 Nasopharyngeal catheter: Develops PEEP at higher flow rates and increases FiO2 and SpO2 compared to Nasal Prongs or Catheter
Disadvantages	 More expensive than nasal/nasopharyngeal catheters 	 Both can lead to obstruction of upper airways more frequently than nasal prongs Nasopharyngeal catheter: Requires humidification as nasal turbines are bypassed When dislodged can lead to gagging, vomiting, gastric distension

Discussion of the preferred patient interfaces for low-flow oxygen delivery. For a full discussion of patient interfaces see: 'WHO Oxygen Therapy for Children' 2016, pp 22–28 [13]. PEEP, positive end-expiratory pressure; FiO2, fraction of inspired oxygen.

a) Nasal Prongs

b) Nasal Catheter

c) Nasopharyngeal Catheter







Fig. 1. Different oxygen delivery systems. *Note*: Modified from B Frey, F Shann [28]. ⁵Face mask and head box are no longer recommended as they require a high flow of oxygen, carry the risk of rebreathing and obstruct access to the face for oral feeding and suctioning, reducing oxygen delivery during these interventions.





e) Head Box*

S12

Non-Invasive ventilation/respiratory support

When disease progression leads to worsening ventilation/perfusion mismatch and intra-pulmonary shunts, the simple administration of supplemental oxygen becomes less effective [29]. In such cases, escalation of respiratory support, initially using non-invasive methods, may be indicated (see treatment algorithm, Fig. 3).

We use the term non-invasive ventilation (NIV) for all modalities, which provide respiratory support without the use of endotracheal intubation. NIV includes: continuous positive airway pressure (CPAP), bubble CPAP (bCPAP), heated humidified high-flow nasal cannula therapy (HFNC) and all modes of non-invasive bi-level positive airway pressure (BIPAP) [30]. In well-resourced settings NIV is routinely used for children with signs of severe pneumonia/bronchiolitis in order to provide respiratory support and prevent the need for intubation and mechanical ventilation, or as a 'step-down' method of ventilatory support after extubation (see Fig. 4) [5]. NIV is not an option for children with inadequate "respiratory drive" (e.g. coma, convulsions) (see treatment algorithm, Fig. 3).

In order to successfully introduce NIV on a paediatric unit, good quality triage, basic emergency and critical care measures should be in place. Children with very severe symptoms, severe hypoxia, multi organ failure (MOF) or children not responding to a trial of NIV ideally need a 'secure airway' (intubation) and mechanical ventilation [5].

NIV options

Different forms of NIV are summarised in a recent review [30]. CPAP, applied throughout the respiratory cycle, is commonly used in children with respiratory failure (single organ failure), where it may recruit collapsed airspaces and prevent airway closure [30,31]. Bubble CPAP is a cost-effective and efficient form of CPAP also used on paediatric intensive care units in high resource settings. Improvised bCPAP can be set up by using minimal resources [32].

Several studies from sub-Saharan Africa have shown that bCPAP for the treatment of children with respiratory failure is feasible in busy, low- resourced paediatric units [33,34]. A recent randomised control trial conducted in Bangladesh demonstrated that children with severe respiratory infections managed with bCPAP had significantly better outcomes than children receiving conventional low flow oxygen therapy (Chisti et al., 2015) [35]. Humidified high flow air/oxygen delivered via nasal cannula (HFNC), has similar indications as CPAP, and could be very useful in low-resource settings [30,36].

To evaluate the roles of CPAP and HFNC in the management of children (< 16 years) with respiratory failure in more detail a study is currently being conducted in three hospitals in London, UK (FIRST_ABC - https://clinicaltrials.gov/ct2/show/NCT02612415).

Fig. 2. Bubble continuous positive airway pressure. *Note:* Example of a bubble continuous positive airway pressure set-up as outlined in the WHO document: "Oxygen therapy for children" [13]. There are also bCPAP set-ups available which use modified oxygen concentrators with an air and oxygen outlet. bCPAP, Bubble continuous positive airway pressure.

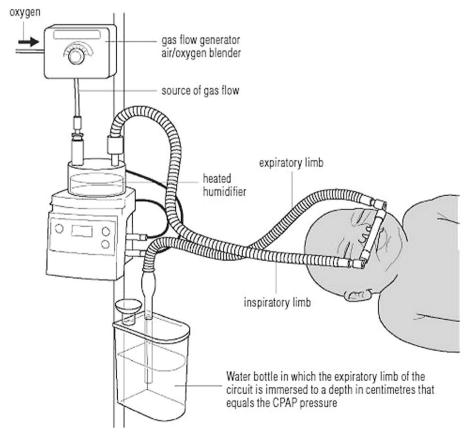


Table 3

Different Non-Invasive Ventilation Modalities.

NIV modality	Function, technical issues, logistics and costs	Clinical considerations and potential side effects	
CPAP by ventilators or specific CPAP-devices ('flow drivers')	An initial pressure of 6–8 cmH2O is recommended for children with severe pneumonia [37] Effects of CPAP:	All forms of NIV are reported to have a low rate of complications [30] Essouri et al. reported a reduced risk of	
	 Recruitment of collapsed airways and 	ventilation-associated complications when using CPAP as primary respiratory support in children	
	prevention of further airway collapse	with severe bronchiolitis [38]. However, patients	
	 Improvement of ventilation/perfusion 	and equipment need to be observed carefully in	
	 mismatch and improved gas exchange Improved compliance and reduced work of breathing and therefore reduced oxygen consumption 	order to prevent complications e.g. facial skin lesions, pneumothoraces See Table 1 for SpO2 target levels	
	 Increased intra-thoracic pressure can reduce 		
	afterload with a positive effect on cardiac output [29]		
	Venous return should only be minimally affected at		
	pressures of 6-8 cmH2O		
Bubble CPAP: An efficient and	See CPAP	Potential complications – see above	
cost-effective form of CPAP	The air/oxygen flow required for the generation of	The pressure measured at the level of the child's	
	bCPAP can be generated by modified oxygen concentrators	upper airway oscillates around a set pressure	
	A flow of 6–10LPM is usually required for children	[39]. This might have additional benefits on respiratory function but needs further evaluation	
	≤ 10 kg. Higher flows are needed for children > 10 kg	respiratory function but needs further evaluation	
	The CPAP pressure is generated and regulated by		
	the length of the distal part of the 'expiratory limb'		
	of the air/oxygen-tubing submerged under the		
	water level in a water bottle. Constant bubbles		
	indicate adequate positive airway distending		
ligh flow of humidified and	pressure is generated Suggested flow requirements for efficient HFNC:	Side effects: See above	
warmed air/oxygen flow by	≤ 10 kg: 2,0 LPM/kg for any kg > 10 kg add:0,5	Size of the nasal prongs: The nasal prong	
nasal cannula - HFNC	LPM/kg [40]	diameter should be no more than half that of the	
	HFNC provides:	nostril	
	• CPAP effect (see above).		
	 "Splinting" of the upper airway. 		
	 Flushing of the upper airway, (a significant 		
	part of the patient's ventilatory dead space).		
	This effect facilitates CO2 clearance and		
	oxygenation All these mechanisms can reduce WOB, improve		
	ventilation/perfusion – mismatch & gas exchange		
	[41,42]		
3i-level positive airway	BIPAP has the same effect as CPAP but offers	Comparable to side effects described for CPAP	
pressure - BlPAP	additional support for inspiratory alveolar	modes [30]	
	ventilation. CO2 clearance can be further improved and WOB is reduced. Synchronised BIPAP set-ups crist [00]		
exist [29] Logistic consideration and Most medical devices requiring air/oxygen flow need reliable electricity systems wit		electricity systems with adequate back-up	
"biomedical training"	For all devices, well-organised maintenance, repair-logistics and supply of consumables needs to be established Standard operation procedures need to be in place for:		
	Maintenance and cleaning of devices		
	• Infection control measures, cleaning, sterilisation of required material		
	Training programs for local medical technicians should be established		
Costs implications Humidification	bCPAP and HFNC devices are relatively cost-effective. Machines used for BIPAP are more expensive		
	To protect the patency of airways, and mucosal function of upper and lower airways the relatively high air/oxygen flows used to provide NIV needs to be humidified and warmed [42]. Regular care of airways is an essential detail of respiratory support		
	to provide NIV needs to be humidified and warmed [43]. Regular care of airways is an essential detail of respiratory support, which can determine success or failure of NIV (see under nursing care). Infection control measures need to be in place in order		
	to reduce the risk of nosocomial infections		
Training and required skill	Clinical teams who established basic, good quality emergency	and critical care can be trained to use simple forms of NIV lik	
levels	bCPAP and HFNC on HDU wards. Regular senior support and supervision is needed		

The table describes some modalities of NIV, including some aspects of function and side effects. NIV modalities like neuronally-adjusted ventilator assist (NAVA), non-invasive high frequency oscillation and negative pressure approaches are not discussed in this review.

NIV, non-invasive ventilation; NAVA, neuronally adjusted ventilator assist; bCPAP, bubble continuous positive airway pressure; HFNC, high flow nasal cannula; WOB, work of breathing; BIPAP, bilevel positive airway pressure; HDU, high-dependency unit.

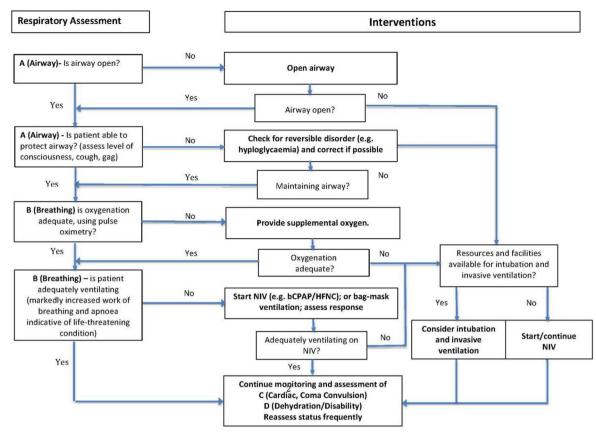


Fig. 3. Treatment algorithm for respiratory support in the emergency centre where options for NIV and mechanical ventilation exist. NIV, non-invasive ventilation; bCPAP, bubble continuous positive airway pressure; HFNC, high-flow nasal cannula.

NIV in the management of critically ill children with multi-organ dysfunction

Acute respiratory distress syndrome (ARDS) is life-threatening organ-dysfunction in severe sepsis [3]. Fluid resuscitation and administration of blood products administered to improve cardiovascular function as well as to correct anaemia and coagulation disorders can be associated with worsening respiratory function [29].

In high-resource settings proactive respiratory support is part of standard care in the management of children with multi-organ

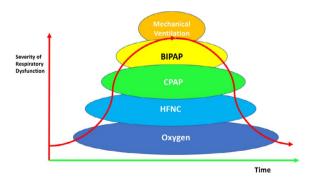


Fig. 4. Severity of respiratory dysfunction and modes of respiratory support. *Note*: Reproduced with thanks to Dr. Ramnarajan, PICU, St. Mary's Hospital, London, UK. Suggestion for the use of supplemental oxygen, different forms of NIV and mechanical ventilation, depending on the severity of respiratory severity/general clinical condition and response to management. The possibility to "escalate" levels of critical care depends on available resources and work-load. If facilities for mechanical ventilation are available, it is important not to delay intubation if the child is in a very critical state and/or NIV is clearly not successful. Further research is required in order to evaluate the role of different NIV-modalities in the management of different causes of respiratory failure and other aspects of NIV-use. NIV, non-invasive ventilation; BIPAP, bi-level positive airway pressure; CPAP, continuous positive airway pressure; HFNC, high-flow nasal cannula. dysfunction [6]. In this context, the role of NIV in less severe ARDS requires further evaluation [44]. This strategy could be transferred to low-resource settings, where NIV has the potential to improve respiratory emergency and in-hospital care for a large number of critically ill children.

A randomised controlled trial is in progress in Malawi comparing the use of bCPAP and low-flow oxygen in children with respiratory failure with and without further organ-dysfunctions. Children with HIV and malnutrition are included in this study (IMPACT; https:// clinicaltrials.gov/ct2/show/NCT02484183).

Indication for intubation and ventilation

Mortality is high in African children with respiratory failure. When emergency care with provision of oxygen and NIV fails to stabilise a child in the resuscitation room, intubation and mechanical ventilation may be the last resort to ensure survival. These efforts to save a child's life need to be balanced against the realities of intubation and ventilation in the under-resourced settings of many hospitals. Available publications from intensive care units in sub-Saharan Africa report that children are usually ventilated on adult intensive care units (ICUs) to which they are often admitted at a late stage of their disease process with high mortality risks. Many units also face significant challenges in terms of resources and infrastructure [45–47]. In a paediatric intensive care unit in Johannesburg mortality risk was reported to be increased in those children with the following conditions: bacterial sepsis, lower respiratory tract infection, HIV infection and HIV exposure [48]. There are reports that intubation and ventilation could put children at increased risk in resource poor settings and basic airway management and respiratory support should be continued where this is not feasible [49].

Intubation

Intubation and ventilation carries a significant risk and requires an experienced team and good teamwork. Logistics and good communication between emergency centres and intensive care units needs to be well established in order to manage these critically ill children safely. With the availability of NIV the emergency centre clinician has additional options to optimise respiratory care of sick children and potentially avoid intubation.

A robust triaging system should be in place and known across all departments to facilitate rational decisions in stressful situations. These arrangements should help to identify which patients are most likely to benefit from mechanical ventilation in the local context, and ensure equal access and effective use of resources [50]. These guidelines need regular updating in view of treatment outcomes in the respective institution.

The most experienced clinician available should be present for safe intubation of a child. S/he will require trained assistance and a range of paediatric-sized equipment. In order to be best prepared under individual circumstances, a checklist of requirements, difficult airway algorithms and a dedicated intubation box containing all equipment needed is invaluable (see APLS manuals). The process of intubation often has a significant haemodynamic effect on the child. The reduced pulmonary reserve in children leads to a rapid onset hypoxia and there is a potential for a vagal response during intubation. Negative inotropic effects of sedative drugs and the suppression of the endogenous response can all lead to arterial hypotension, bradycardia and rapid cardiac arrest in the critically ill child. This can be prevented with adequate fluid loading, commencement of positive inotropic drugs before intubation and carefully selecting and titrating the drugs used for intubation. Ketamine could be a good choice in these situations.

Ventilation

It is a challenge to organise safe ventilation for children in resource limited environments, where unreliable electricity and oxygen supply,

Table 4

Considerations for intubation and ventilation.

understaffed wards, inadequate or un-serviced equipment, lack of diagnostic support and a bare minimum of drugs and consumables often prevail [51]. The introduction of mechanical ventilation for children should not be seen as a priority, unless efficient emergency care as well as non-invasive respiratory support are reliably established. Physicians caring for ventilated children must be trained in ventilation management so they can adjust the ventilation mode and settings to the condition of the child and understand when to escalate support and when to begin weaning ventilation as the patient shows deterioration or improvement of pulmonary compliance.

One major challenge is the training and retention of a pool of dedicated nursing staff able to handle the demanding routine care of an intubated and sedated child, and to respond immediately to airway and breathing emergencies that may arise with intubated children (e.g. dislodged or blocked endotracheal tube, secretion obstruction, pneumothorax, and ventilator malfunction). Patient selection needs to ensure that patients with a high probability of long term survival and good neurological outcome are intubated. These indications will depend on available resources, local standards of care and experience but generally would include acutely ill children with respiratory failure, who are expected to recover in a short period of time (See Table 4).

Ventilators

To safely ventilate a child with a ventilator, it needs to be certified for the respective weight category of the child. The ventilator needs to be fully operational, pass a pre-use test and be fitted with a paediatricsize ventilation circuit. Staff must be familiar with the specific ventilators in use and ventilator settings need to be documented. Many ventilators lack satisfactory sensitivity to trigger inspiration and monitor tidal volumes. Inspiratory gas should be heated and humidified and infection control measures in place to prevent ventilator associated pneumonias. Regular calibration and servicing of the ventilators is mandatory, but is often challenging in resource poor settings (Table 5).

Diagnosis	Comments
Upper airway obstruction e.g. burns, anaphylaxis, foreign body, vocal cord pathology	Early intubation might be life-saving. Underlying condition will guide decision to intubate. Difficult airway algorithms need to be considered
Unable to maintain upper airway e.g.: Coma (GCS \leq 8), status epilepticus, side effect of drugs	These are conditions with possibly good outcome. A thorough history and regular clinical exam will help guide the decision as the severity of the underlying condition will predict outcome
Trauma	Intubation might facilitate surgical care if realistic chance of good outcome and potentially reduce secondary neurological injury in traumatic brain injury. Severity of trauma will need to guide decision to intubate
Peri-operative care	Peri-operative stabilisation can improve the outcome of patients with surgical conditions. Good communication between critical care and surgical teams is needed
Lower respiratory tract infection unresponsive to NIV	Mortality is considerable in these patients and will depend on local care and on co-morbidities
Pneumothoraces and pleural fluid.	Outcomes depends on underlying conditions. Prompt drainage can rapidly improve the clinical condition and intubation can often be prevented
Asthma	Optimising nebulisation, drug treatment and NIV are usually successful. Mechanical ventilation of children with bronchospasm needs to be carefully adapted by skilled clinicians
Specific medical conditions e.g.: Guillain-Barré Syndrome	Long term ventilation is expected and a tracheostomy should be performed early on. Consider early transfer to a hospital with ventilation facilities
Patients with MOF e.g. sepsis, encephalopathy, shock, acute renal failure, liver failure, disseminated intra- vascular coagulation	Patients with MOF have a significant mortality risk. Prognosis needs to be reviewed in light of additional organ dysfunctions. Limitation of critical care and palliative care might be more appropriate for these children and their families
Underlying co-morbidities e.g.: severe malnutrition, late stage HIV, congenital heart diseases, cardiomyopathy, congenital disorders, chronic renal or liver failure, severe neurological disability, malignancies	

Some considerations for intubation and ventilation of critically ill children in low resource settings. This list is not exhaustive and indications will differ greatly according to local resources, experience and burden of disease. The prognosis of children needs to be considered before intubation and their progress regularly re-evaluated. NIV, non-invasive ventilation; MOF, multi-organ failure.

Table 5

Summary of ancillary interventions associated with the management of children requiring respiratory support.

Interventions	Details
Airway management	Ensure airway patency and prevent obstruction by pulmonary secretions, with or without an artificial airway. Routine endotracheal suctioning, in the presence of an endotracheal tube, should never be undertaken owing to potentially severe complications [53]. When indicated, observe safe and effective suction technique, including the provision of hyperoxia prior to an during the suctioning procedure. Limit the diameter of the suction catheter, the applied suction pressure, the duration of suctionin, and the depth of insertion [53]. Nasopharyngeal or oropharyngeal suction may be necessary in children requiring NIV or oxyger support, to maintain patency of upper airways. In such cases, the depth of suction catheter insertion should be limited to avoid mucosal trauma, by measuring the distance from the nostril to tragus of the ear. Where mechanical/foot pump suction devices ar not available, manual "Penguin" or "Bulb" suction devices may be used to clear the upper airways. If nasal prongs are used, check for secretion emptions in the two, and during the order to earway actioning of the upper airways. If nasal prongs are used, check for secretion emption is the two, and clear these products are order to advect and a during the more action of the prove of deplaced to allow effective suctioning of the upper airways. If nasal prongs are used, check for secretion emption is the two and clear the prove of deplaced to allow effective suctioning of the upper airways. If nasal prongs are used, check for secretion emption is the two prove depression.
NIV Interface	crusting in the tubes, and clear these in order to ensure optimal gas delivery NIV interfaces should consider patient comfort, fit, access to the airways and efficacy; as well as culture and cosmetic acceptability communication (particularly for older children) and feeding. Adapted nasal prongs, nasopharyngeal tubes, nasal masks or mask covering mouth and nose are commonly used [54]. Regular checks and exchanges of the interface should be implemented to ensure
Nebulisation	optimal fit and effective respiratory support and to prevent pressure ulcers and skin breakdown [54] Nebulisation is not routine but is required in certain situations (e.g. short-acting bronchodilators and inhaled steroids). If inhale medication is required, some ventilators have effective in-line nebulisation systems, in other cases the child may have to be brieff disconnected from the NIV support and the drug given with supplementary oxygen. In cases where children are dependent on NIV and an in-line nebulisation system is unavailable or ineffective, inhaled medication can be given using a metered dose inhaler and are accurately using the NIV interfere. In the medication can be given using a metered dose inhaler and are accurated by the medication can be given using a metered dose inhaler and are accurated by the medication can be given using a metered dose inhaler and are accurated by the medication of the NIV interfere.
Positioning	spacer with mask, after briefly removing the NIV interface, but maintaining oxygen delivery if needed Appropriate positioning, and regular changes in position may optimise ventilation and ventilation/perfusion matching (thereby improving oxygenation), and prevent pressure-related skin ulcers and postural deformities, amongst other benefits. Elevation of th head of the bed, in adults, has been shown to reduce the development of ventilator associated pneumonia [55]. Whilst there is no clear evidence supporting this practice in children, it makes physiological sense to elevate the bed-head by 30 degrees to preven macro- and micro-aspiration and to optimise functional residual capacity (FRC) [56]. In small children FRC is very close to closing capacity, therefore optimising FRC by lowering the diaphragm is essential to prevent atelectasis In hypoxic children with acute respiratory distress syndrome (ARDS), prone positioning has been associated with improved oxygenation although no improved clinical outcome has been shown in children [57]. However, prone turning is safe in ventilated children, and is recommended as a "rescue manoeuvre" in severe hypoxaemia [57]. Care should be taken to avoid tube and devic dislodgements
Mobilisation and rehabilitation	Critical illness, sedation and related immobility are associated with a number of complications, including muscle disuse atrophy with resulting physical, neurocognitive and emotional consequences [58,59]. Despite a paucity of objective evidence, mobility- based rehabilitation is recommended for critically ill children, as soon as they are physiologically stable enough to tolerate this intervention
Naso/orogastric tubes and enteral nutrition	The child's premorbid nutritional state, in addition to the nutrition provided during the illness may impact on clinical outcomes Energy and protein deficiencies, in particular, are associated with increased risk of infection, poor wound healing and prolonge dependency on respiratory support [60]. Early enteral nutrition can improve outcomes, and is preferred over parenteral nutritio where there are no clear contraindications (e.g. high risk of aspiration or intolerance) [61]. Recurrent feeding interruptions shoul be avoided as far as possible to optimise nutrition [62] It is recommended that all children with very severe respiratory distress should initially receive an orogastric or nasogastric tub (OGT/NGT) in order to aspirate and drain gastric contents. The NGT/OGT should be well fixed and its position should be marked Once the child stabilises, NGT feeds and then oral feeds can be introduced gradually and IV fluids reduced accordingly. Guideline for safe feeding practices should be used
IV fluids	Recommendations for fluid resuscitation have been published recently [9]. Maintenance fluid requirements of critically ill childre are very variable and require regular re-evaluation. Increased levels of anti-diuretic hormone secretion can lead to fluid overload s that maintenance fluid is frequently restricted to two thirds of the commonly used '4–2-1-rule'. Isotonic electrolyte solutions containing glucose are preferred to reduce the risk of electrolyte imbalance and hypoglycaemia [63]
Psychological and emotional support	Assessment of delirium is recommended where possible. Tools such as the Cornell Assessment of Paediatric Delirium Scale are use in children requiring respiratory support [64]. Ensuring sedation is kept to an effective minimum helped prevent a range of morbidities, including delirium [65]. Non-pharmacological methods of preventing delirium are as yet unproven, but providing favourite toys or other items from home may help to prevent adverse psycho-emotional effects A parent or caregiver presence at the child's bedside is likely to be in the child's best interests, and the family should be integrall
Manual chest physiotherapy	involved in care decisions and interventions [66,67] There is little high-level evidence supporting the use of manual chest physiotherapy (percussions, vibrations and thoracic "squeezing" techniques, amongst others) for clearing pulmonary secretions in children with respiratory compromise, and this intervention is associated with a number of potentially severe complications. Manual chest physiotherapy is therefore not recommended for routine use but considered when obstructive pulmonary secretions affect lung mechanics or gaseous exchange and/or to prevent long-term pulmonary complications and where there are no contraindications. A clear indication for chest physiotherapy is the presence of leber or lung colleare acued by intrinsic obstruction by automary secretions [69].
Monitoring	physiotherapy is the presence of lobar or lung collapse caused by intrinsic obstruction by pulmonary secretions [68]. Children with respiratory distress in the emergency centre require close observation and monitoring of airway patency, respirator effort, vital signs, level of consciousness, capillary refill time, hydration status and oxygen saturation (SpO2). As point of care testing, blood glucose, Hb/Hct and a malaria test (where indicated) are priorities Children who improve (reduced respiratory effort) with stable SpO2 readings can be transferred on O2 therapy and possibly NIV t a 'high dependency unit'. The carer is taught to observe and assist his/her child and when to call for help. Monitoring tools such a 'Paediatric Early Warning Scores (PEWS)' or 'Critical Care Pathways (CCPs)' may help identify children, who are deteriorating. I clinically stable children, who maintain SpO2 > 90% on oxygen, a daily trial of room air respiration should be done [14] <i>Ventilated children</i> Ventilated children Ventilated children meed patient-to-nursing ratios ideally not exceeding 2:1. A nurse supervisor and a designated clinician need t be available at all times. Vitals signs should be documented frequently. Continuous monitoring of SpO2 and pulse is a minimur requirement, whilst ECG-monitoring, capnography (end-tidal or trans-cutaneous CO2 measurement) or blood-gas-monitoring wit electrolytes are desirable. Where CO2 monitoring is not possible precise monitoring of tidal volumes becomes more important t optimise ventilation

NIV, non-invasive ventilation; FRC, functional residual capacity; ARDS, acute respiratory distress syndrome; OGT/NGT, orogastric or nasogastric tube; Sp02, oxygen saturation.

Support

Apart from oxygen a reliable electric supply with back-up generators and battery-packs is indispensable. Diagnostic imaging with Xray facilities and point-of-care ultrasound can confirm correct placing of an endotracheal tube, can rapidly exclude a pneumothorax and pleural fluid and will greatly enhance diagnostic capabilities of cardiac and intra-thoracic pathology [52].

Other nursing and holistic care considerations for children requiring respiratory support

Comprehensive nursing and ancillary care considerations for children receiving respiratory support are essential, and important components thereof are summarised in the table below. Ideally, these interventions would be applied by a team of individual health care workers including nurses, physiotherapists, dieticians, occupational therapists, speech and language therapists, and psychologists (amongst others). However, where access to the full range of ancillary professionals is limited, it is important for all members of the healthcare team to consider the provision of holistic, safe and effective care to children requiring respiratory support.

Summary

Respiratory infections and other conditions associated with respiratory dysfunction are a leading cause of death among children in sub-Saharan Africa. Public health interventions like vaccinations play a major role in preventing these conditions.

Nevertheless, basic, good quality emergency care in hospitals plays an important role in improving the outcome of critically ill children. Rapid triage and early recognition of children with respiratory distress and hypoxia using pulse oximetry needs to be followed by immediate efficient airway management and respiratory support. Subsequent effective in-hospital treatment and monitoring with good holistic care will reduce inpatient mortality further.

The implementation of non-invasive ventilation like bCPAP and HFNC at the district hospital level has the potential to optimise the respiratory care of a large number of critically ill children. Mechanical ventilation is challenging and can only be offered in some hospitals with adequate resources and trained clinical teams.

Training and research programs can contribute to improvements of early diagnosis and efficient management of children with respiratory distress and hypoxaemia. The role of different modalities of NIV in the management of critically ill children needs further evaluation in the African context. More efforts are needed to support oxygen supply in health facilities and to design durable, affordable and easy-to-use respiratory support devices.

Acknowledgments

The authors would like to thank Prof. Elizabeth Molyneux for reviewing the manuscript.

Conflict of interest

The authors have no conflict of interest to declare.

Authors' contributions

BM, HJL and AH participated in the conception, drafting and revising of the manuscript and approved the final submitted version.

References

in 2000-13, with projections to inform post-2015 priorities: an updated systematic analysis. Lancet 2015;385(9966):430-40.

- [2] Lazzerini M, Seward N, Lufesi N, et al. Mortality and its risk factors in Malawian children admitted to hospital with clinical pneumonia, 2001–12: a retrospective observational study. Lancet Glob Health 2016;4(1):e57–68.
- [3] Kissoon N, Uyeki TM. Sepsis and the global burden of disease in children. JAMA Pediatr 2016;170(2):107–8.
- [4] Takem EN, Roca A, Cunnington A. The association between malaria and non-typhoid Salmonella bacteraemia in children in sub-Saharan Africa: a literature review. Malar J 2014;13:400.
- Barry P, Morris K, Tariq A. Oxford specialist handbook: paediatric intensive care. Oxford University Press 2010. http://dx.doi.org/10.1093/med/9780199233274. 001.1.
- [6] Brierley J, Carcillo JA, Choong K, et al. Clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock: 2007 update from the American College of Critical Care Medicine. Crit Care Med 2009;37(2):666–88.
- [7] Molyneux EM. Paediatric emergency care in resource-constrained health services is usually neglected: time for change. Ann Trop Paediatr 2010;30(3):165–76.
- [8] Belle J, Cohen H, Shindo N, et al. Influenza preparedness in low-resource settings: a look at oxygen delivery in 12 African countries. J Infect Dev Ctries 2010;4(7):419-24.
- [9] Guideline: Updates on Paediatric Emergency Triage, Assessment and Treatment: Care of Critically-Ill Children. (2016). Guideline: Updates on Paediatric Emergency Triage, Assessment and Treatment: Care of Critically-Ill Children. World Health Organization. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/27010047.
- [10] Göpel W, Kribs A, Ziegler A, et al. Avoidance of mechanical ventilation by surfactant treatment of spontaneously breathing preterm infants (AMV): an open-label, randomised, controlled trial. Lancet 2011;378(9803):1627–34.
- [11] Martin S, Duke T, Davis P. Efficacy and safety of bubble CPAP in neonatal care in low and middle income countries: a systematic review. Arch Dis Child Fetal Neonatal Ed 2014;99(6):F495–504.
- [12] WHO. Emergency Triage Assessment and Treatment (ETAT) course, WHO, 2016.
- [13] WHO. Oxygen therapy for children: a manual for health workers, WHO, 2016.
- [14] WHO. Pocket book of hospital care for children : guidelines for the management of common childhood illnesses. Guidelines for the management of common illnesses, 2013.
- [15] WHO, WHO technical specifications for oxygen concentrators, WHO, 2016.[16] Samuels M, Wieteska S, editors. Advanced paediatric life support. Chichester, UK:
- John Wiley & Sons Ltd; 2016. doi: 10.1002/9781119241225. [17] EPALS - European Paediatric Advanced Life Support course. (n.d.). Retrieved
- January 7, 2017, from https://www.resus.org.uk/information-on-courses/ european-paediatric-advanced-life-support/.
- [18] Paediatric BASIC. (n.d.). Retrieved January 11, 2017, from http://www.aic.cuhk. edu.hk/web8/BASIC paeds.htm.
- [19] Van Hoving DJ, Chipps J, Jacquet G. Resource tiered reviews a provisional reporting checklist. Afr J Emerg Med 2014;4(3):99–101.
- [20] Duke T, Mgone J, Frank D. Hypoxaemia in children with severe pneumonia in Papua New Guinea. Int J Tuberc Lung Dis 2001;5(6):511–9.
- [21] Duke T, Wandi F, Jonathan M, et al. Improved oxygen systems for childhood pneumonia: a multihospital effectiveness study in Papua New Guinea. Lancet 2008;372(9646):1328–33.
- [22] Singhi SC, Baranwal AK, Guruprasad, et al. Potential risk of hypoxaemia in patients with severe pneumonia but no hypoxaemia on initial assessment: a prospective pilot trial. Paediatr Int Child Health 2012;32(1):22–6.
- [23] Duke T, Blaschke AJ, Sialis S. Hypoxaemia in acute respiratory and non-respiratory illnesses in neonates and children in a developing country. Arch Dis Child 2002;86(2):108–12.
- [24] Chisti MJ, Duke T, Robertson CF, et al. Clinical predictors and outcome of hypoxaemia among under-five diarrhoeal children with or without pneumonia in an urban hospital, Dhaka, Bangladesh. Trop Med Int Health 2012;17(1):106–11.
- [25] Zhang L, Mendoza-Sassi R, Santos JC, et al. Accuracy of symptoms and signs in predicting hypoxaemia among young children with acute respiratory infection: a meta-analysis. Int J Tuberc Lung Dis 2011;15(3):317–25.
- [26] Howie SR, Hill S, Ebonyi A, et al. Meeting oxygen needs in Africa: an options analysis from the Gambia. Bull World Health Organ 2009;87(10):763–71.
- [27] 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. In: Rojas-Reyes MX, editor. Cochrane database of systematic reviews. Chichester, UK: John Wiley & Sons Ltd; 2014. doi: 10.1002/14651858.CD005975.pub3.
- [28] Frey B, Shann F. Oxygen administration in infants. Arch Dis Child Fetal Neonatal Ed 2003;88(2):F84–8.
- [29] Hughes M, Black R. Oxford specialist handbook: advanced respiratory critical care. Oxford University Press 2011. http://dx.doi.org/10.1093/med/9780199569281. 001.0001.
- [30] Argent AC, Biban P. What's new on NIV in the PICU: does everyone in respiratory failure require endotracheal intubation? Intensive Care Med 2014;40(6):880–4.
- [31] Essouri S, Chevret L, Durand P, et al. Noninvasive positive pressure ventilation: five years of experience in a pediatric intensive care unit. Pediatr Crit Care Med 2006;7(4):329–34.
- [32] Duke T. CPAP: a guide for clinicians in developing countries. Paediatr Int Child Health 2014;34(1):3–11.
- [33] Walk J, Dinga P, Banda C, et al. Non-invasive ventilation with bubble CPAP is feasible and improves respiratory physiology in hospitalised Malawian children with acute respiratory failure. Paediatr Int Child Health 2016;36(1):28–33.
- [34] Machen HE, Mwanza ZV, Brown JK, et al. Outcomes of patients with respiratory distress treated with bubble CPAP on a pediatric ward in Malawi. J Trop Pediatr

A. Hansmann et al.

2015;61(6):421-7.

- [35] Chisti MJ, Salam MA, Smith JH, et al. Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: an open, randomised controlled trial. Lancet 2015;386(9998):1057–65.
- [36] Milési C, Boubal M, Jacquot A, et al. High-flow nasal cannula: recommendations for daily practice in pediatrics. Ann Intensive Care 2014;4:29.
- [37] Essouri S, Durand P, Chevret L, et al. Optimal level of nasal continuous positive airway pressure in severe viral bronchiolitis. Intensive Care Med 2011;37(12):2002–7.
- [38] Essouri S, Laurent M, Chevret L, et al. Improved clinical and economic outcomes in severe bronchiolitis with pre-emptive nCPAP ventilatory strategy. Intensive Care Med 2014;40(1):84–91.
- [39] Brown J, Machen H, Kawaza K, et al. A high-value, low-cost bubble continuous positive airway pressure system for low-resource settings: technical assessment and initial case reports. PLoS ONE 2013;8(1):e53622.
- [40] Padmanabhan R. FIRST-line Support for Assistance in Breathing in Children (FIRST-ABC) Feasibility Study ClinicalTrials.gov. Retrieved from https://clinicaltrials.gov/ct2/show/record/NCT02612415, 2016.
- [41] Milési C, Baleine J, Matecki S, et al. Is treatment with a high flow nasal cannula effective in acute viral bronchiolitis? A physiologic study. Intensive Care Med 2013;39(6):1088–94.
- [42] Frizzola M, Miller TL, Rodriguez ME, et al. High-flow nasal cannula: impact on oxygenation and ventilation in an acute lung injury model. Pediatr Pulmonol 2011;46(1):67–74.
- [43] Esquinas Rodriguez AM, Scala R, Soroksky A, et al. Clinical review: humidifiers during non-invasive ventilation-key topics and practical implications. Crit Care 2012;16(1):203.
- [44] Essouri S, Carroll C. Pediatric acute lung injury consensus conference group. Noninvasive support and ventilation for pediatric acute respiratory distress syndrome. Pediatr Crit Care Med 2015;16(5 Suppl 1):S102–10.
- [45] Dünser MW, Towey RM, Amito J, et al. Intensive care medicine in rural sub-Saharan Africa. Anaesthesia 2017;72(2):181–9.
- [46] Kwizera A, Dünser M, Nakibuuka J. National intensive care unit bed capacity and ICU patient characteristics in a low income country. BMC Res Notes 2012;5:475.
- [47] Sawe HR, Mfinanga JA, Lidenge SJ, et al. Disease patterns and clinical outcomes of patients admitted in intensive care units of tertiary referral hospitals of Tanzania. BMC Int Health Hum Rights 2014;14:26.
- [48] Ballot DE, Davies VA, Cooper PA, et al. Retrospective cross-sectional review of survival rates in critically ill children admitted to a combined paediatric/neonatal intensive care unit in Johannesburg, South Africa, 2013–2015. BMJ Open 2016;6(6):e010850.
- [49] Earle Jr M, Martinez Natera O, Zaslavsky A, et al. Outcome of pediatric intensive care at six centers in Mexico and Ecuador. Crit Care Med 1997;25(9):1462–7.
- [50] Argent AC, Ahrens J, Morrow BM, et al. Pediatric intensive care in South Africa: an account of making optimum use of limited resources at the Red Cross War Memorial Children's Hospital. Pediatr Crit Care Med 2014;15(1):7–14.
- [51] Baker T, Lugazia E, Eriksen J, et al. Emergency and critical care services in Tanzania: a survey of ten hospitals. BMC Health Serv Res 2013;13:140.

- [52] Frankel HL, Kirkpatrick AW, Elbarbary M, 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.
- [53] Morrow BM, Argent AC. A comprehensive review of pediatric endotracheal suctioning: effects, indications, and clinical practice. Pediatr Crit Care Med 2008;9(5):465–77.
- [54] Newnam KM, McGrath JM, Salyer J, et al. A comparative effectiveness study of continuous positive airway pressure-related skin breakdown when using different nasal interfaces in the extremely low birth weight neonate. Appl Nurs Res 2015;28(1):36–41.
- [55] Drakulovic MB, Torres A, Bauer TT, et al. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. Lancet 1999;354(9193):1851–8.
- [56] Morrow BM, Argent AC, Jeena PM, et al. Guideline for the diagnosis, prevention and treatment of paediatric ventilator-associated pneumonia. S Afr Med J 2009;99:255–67.
- [57] Curley MA, Hibberd PL, Fineman LD, et al. Effect of prone positioning on clinical outcomes in children with acute lung injury: a randomized controlled trial. JAMA 2005;294(2):229–37.
- [58] Knoester H, Bronner MB, Bos AP. Surviving pediatric intensive care: physical outcome after 3 months. Intensive Care Med 2008;34(6):1076–82.
- [59] Knoester H, Bronner MB, Bos AP, et al. Quality of life in children three and nine months after discharge from a paediatric intensive care unit: a prospective cohort study. Health Qual Life Outcomes 2008;6:21.
- [60] Hulst JM, van Goudoever JB, Zimmermann LJ, et al. The effect of cumulative energy and protein deficiency on anthropometric parameters in a pediatric ICU population. Clin Nutr 2004;23(6):1381–9.
- [61] Mehta NM, Compher C. A.S.P.E.N. Board of Directors. A.S.P.E.N. Clinical guidelines: nutrition support of the critically Ill child. JPEN J Parenter Enteral Nutr 2009;33(3):260–76.
- [62] Zebuhr C, Sinha A, Skillman H, et al. Active rehabilitation in a pediatric extracorporeal membrane oxygenation patient. PM R 2014;6(5):456–60.
- [63] McNab S, Duke T, South M, et al. 140 mmol/L of sodium versus 77 mmol/L of sodium in maintenance intravenous fluid therapy for children in hospital (PIMS): a randomised controlled double-blind trial. Lancet 2015;385(9974):1190–7.
- [64] Traube C, Silver G, Kearney J, et al. Cornell assessment of pediatric delirium: a valid, rapid, observational tool for screening delirium in the PICU. Crit Care Med 2014;42(3):656–63.
- [65] Motta E, Luglio M, Delgado AF, et al. Importance of the use of protocols for the management of analgesia and sedation in pediatric intensive care unit. Rev Assoc Med Bras (1992) 2016;62(6):602–9.
- [66] Colville GA. Psychological aspects of care of the critically Ill child. J Pediatr Intensive Care 2015;4:182–7.
- [67] Meert KL, Clark J, Eggly S. Family-centered care in the pediatric intensive care unit. Pediatr Clin North Am 2013;60(3):761–72.
- [68] Morrow B. Chest physiotherapy in the pediatric intensive care unit. J Pediatr Intensive Care 2015;4(4):174–81.