Recommendations for mechanical ventilation of critically ill children from the Paediatric Mechanical Ventilation Consensus Conference (PEMVECC)

KNEYBER, Martin C J, et al. & Respiratory Failure of the European Society for Paediatric and Neonatal Intensive Care

**Abstract**

Much of the common practice in paediatric mechanical ventilation is based on personal experiences and what paediatric critical care practitioners have adopted from adult and neonatal experience. This presents a barrier to planning and interpretation of clinical trials on the use of specific and targeted interventions. We aim to establish a European consensus guideline on mechanical ventilation of critically children.

**Reference**

KNEYBER, Martin C J, et al. & Respiratory Failure of the European Society for Paediatric and Neonatal Intensive Care. Recommendations for mechanical ventilation of critically ill children from the Paediatric Mechanical Ventilation Consensus Conference (PEMVECC). *Intensive Care Medicine*, 2017, vol. 43, no. 12, p. 1764-1780

DOI: 10.1007/s00134-017-4920-z
PMID: 28936698

Available at:
http://archive-ouverte.unige.ch/unige:108116

Disclaimer: layout of this document may differ from the published version.
Recommendations for mechanical ventilation of critically ill children from the Paediatric Mechanical Ventilation Consensus Conference (PEMVECC)

Martin C. J. Kneyber1,2*, Daniele de Luca3,4, Edoardo Calderini5, Pierre-Henri Jarreau6, Etienne Javouhey7,8, Jesus Lopez-Herce9,10, Jürg Hammer11, Duncan Macrae12, Dick G. Markhorst13, Alberto Medina14, Marti Pons-Odena15,16, Fabrizio Racca17, Gerhard Wolf18, Paolo Biban19, Joe Brierley20, Peter C. Rimensberger21 and on behalf of the section Respiratory Failure of the European Society for Paediatric and Neonatal Intensive Care

© 2017 The Author(s). This article is an open access publication

Abstract

Purpose: Much of the common practice in paediatric mechanical ventilation is based on personal experiences and what paediatric critical care practitioners have adopted from adult and neonatal experience. This presents a barrier to planning and interpretation of clinical trials on the use of specific and targeted interventions. We aim to establish a European consensus guideline on mechanical ventilation of critically children.

Methods: The European Society for Paediatric and Neonatal Intensive Care initiated a consensus conference of international European experts in paediatric mechanical ventilation to provide recommendations using the Research and Development/University of California, Los Angeles, appropriateness method. An electronic literature search in PubMed and EMBASE was performed using a combination of medical subject heading terms and text words related to mechanical ventilation and disease-specific terms.

Results: The Paediatric Mechanical Ventilation Consensus Conference (PEMVECC) consisted of a panel of 15 experts who developed and voted on 152 recommendations related to the following topics: (1) general recommendations, (2) monitoring, (3) targets of oxygenation and ventilation, (4) supportive measures, (5) weaning and extubation readiness, (6) normal lungs, (7) obstructive diseases, (8) restrictive diseases, (9) mixed diseases, (10) chronically ventilated

*Correspondence: m.c.j.kneyber@umcg.nl
1 Department of Paediatrics, Division of Paediatric Critical Care Medicine, Beatrix Children's Hospital Groningen, University Medical Center Groningen, The University of Groningen, PO. Box 30.001, 9700 RB Groningen, The Netherlands
Full author information is available at the end of the article

Take-home message: Much of the common practice in paediatric mechanical ventilation is based on personal experiences and what paediatric critical care practitioners have adopted from adult and neonatal experience. This presents a barrier to planning and interpretation of clinical trials on the use of specific and targeted interventions. The PEMVECC guidelines should help to harmonise the approach to paediatric mechanical ventilation and thereby propose a standard-of-care applicable in daily clinical practice and clinical research.
Introduction
Huge variability in size, lung maturity and the range of acute and chronic diagnoses have contributed to a lack of clinical evidence supporting the daily practice of paediatric mechanical ventilation (MV) (Fig. 1) [1, 2]. This prompted the Respiratory Failure Section of the European Society for Paediatric and Neonatal Intensive Care (ESPNIC) to convene the paediatric mechanical ventilation consensus conference (PEMVECC), aiming to harmonise the approach to paediatric MV and define a standard-of-care applicable in clinical practice and future collaborative clinical research. Specific aims were to provide recommendations regarding ventilation modalities, monitoring, targets of oxygenation and ventilation, supportive measures, and weaning and extubation readiness for patients with normal lungs, obstructive airway diseases, restrictive diseases, mixed diseases and chronically ventilated patients, cardiac patients and lung hypoplasia syndromes, and to provide directions for further research. From 138 recommendations drafted, 34 (32.7%) did not reach “strong agreement” and were redrafted (i.e. rewriting or rephrasing sometimes into two different recommendations), resulting in 52 recommendations for the second voting round. Of these, 142 (93.4%) reached “strong agreement”.  

Methods
The steering committee (M.K. (chair), D.d.L., J.B., P.B. and P.R.) defined disease conditions (see ESM) and identified ten European panel members who were internationally established paediatric MV investigators with recent peer-reviewed publications (last 10 years). An electronic literature search in PubMed and EMBASE (inception to September 1, 2015) was performed using a combination of medical subject heading terms, text words related to MV and disease-specific terms. All panel members screened the references for eligibility, defined by (1) age <18 years, (2) describing non-invasive or invasive respiratory support, and (3) type of design (i.e. any type of clinical study except for case-series and reports). Publications were excluded if they described diseases exclusively linked to the perinatal period. The proposal by Chatburn (ESM, Table 2) was used for ventilator taxonomy [3, 4]. Recommendations were drafted by all panel members, and subsequently discussed at a two-day meeting in Rome, Italy (September 2015). This resulted in a final set of recommendations, subjected to electronic voting (December 2015) using the Research and Development/University of California, Los Angeles (RAND/UCLA) appropriateness method scale [5]. Recommendations were scored from 1 (complete disagreement) to 9 (complete agreement). Median score (95% confidence interval) was calculated after eliminating one lowest and highest value. Recommendations were labelled “strong agreement” (median 7–9 and no score <7), “equipoise” (median 4–6) or “disagreement” (median 1–3). Recommendations without “strong agreement” were rephrased. Revised recommendations retaining “strong agreement” after the second electronic voting (February 2016) were

Conclusions: These recommendations should help to harmonise the approach to paediatric mechanical ventilation and can be proposed as a standard-of-care applicable in daily clinical practice and clinical research.

Keywords: Mechanical ventilation, Physiology, Paediatrics, Lung disease

Fig. 1 Graphical simplification of the gaps in knowledge regarding paediatric mechanical ventilation as a function of disease trajectory when the patient is getting worse or is getting better.

patients, (11) cardiac patients and (12) lung hypoplasia syndromes. There were 142 (93.4%) recommendations with “strong agreement”. The final iteration of the recommendations had none with equipoise or disagreement.

Conclusions: These recommendations should help to harmonise the approach to paediatric mechanical ventilation and can be proposed as a standard-of-care applicable in daily clinical practice and clinical research.

Keywords: Mechanical ventilation, Physiology, Paediatrics, Lung disease
labelled “weak agreement” and the percentage of agreement (number of individual scores ≥7 divided by 15) quantified the level of disagreement. As it was expected a priori that there would be very few RCTs or systematic reviews, it was decided by the steering committee to keep the consensus guideline descriptive and not use the GRADE system [6].

**Non-invasive support**

**High-flow nasal cannula (HFNC) and continuous positive airway pressure (CPAP)**

There is insufficient data to recommend on the use of HFNC in obstructive airway (strong agreement), restrictive (strong agreement) or mixed disease (strong agreement) or on the use CPAP in obstructive airway (strong agreement) or restrictive disease (93% agreement). CPAP may be considered if there are no contra-indications (strong agreement) as initial support in mixed disease (strong agreement) and mild-to-moderate cardiorespiratory failure (strong agreement). There is insufficient data to recommend on the optimal interface for CPAP (strong agreement).

Although HFNC or CPAP may reduce the work of breathing, there are no outcome data showing superiority of HFNC or CPAP over any other intervention [7–28].

**Non-invasive ventilation (NIV)**

NIV can be considered before resorting to intubation in obstructive airway (strong agreement), restrictive disease (93% agreement), mild-to-moderate PARDS (strong agreement) or cardiorespiratory failure (strong agreement). NIV should not delay endotracheal intubation, but no specific limits can be provided in any disease condition (strong agreement). There are no data to recommend on any method or timing of NIV (strong agreement). There are insufficient data to provide recommendations on the optimal interface for NIV. Any interface with the least leakage needs to be used (strong agreement). Dependent on local experiences and materials, full face mask, oral-nasal mask or helmet for NIV should be used (93% agreement).

Non-invasive ventilation (NIV) is increasingly being used in ARF [29–32], after cardiac surgery for congenital heart disease [33–36], status asthmaticus [37, 38], or neuromuscular patients with ARF [39–41]. Few uncontrolled studies suggested improved extubation success with NIV [42, 43]. Two RCTs comparing NIV versus oxygen supplementation on intubation prevention produced opposing results [43, 44]. In adult studies, NIV increased adverse outcomes in severe ARDS [45–52]. To avoid delayed intubation, success of NIV should be assessed already 1 h after initiation by observing heart and respiratory rate, SpO$_2$/FiO$_2$ ratio, pH, level of consciousness and presence of organ failure [44, 50, 53].

**Ventilator modes**

We cannot make recommendations on any mode of mechanical ventilation for children with normal lungs (strong agreement), obstructive airway (strong agreement), restrictive (strong agreement), mixed disease (strong agreement), chronically ventilated children (strong agreement), cardiac children (strong agreement) or children with lung hypoplasia (strong agreement). With restored respiratory drive, pressure support ventilation may be considered. If used, the sensitivity of the flow cycling and rise time should be set to obtain an appropriate inspiratory time (strong agreement). There are no outcome data to recommend on closed-loop ventilation (strong agreement).

There are no outcome data to recommend on any ventilatory or respiratory assist modes for children with or without lung pathology, cardiac children, or chronically ventilated children requiring escalation of support for acute exacerbations [2, 54–59]. Ventilator mode should be dictated by clinical experience and theoretical arguments, considering the pathophysiology of the disease [60, 61].

There are insufficient data to recommend on high-frequency oscillatory ventilation (HFOV) in obstructive airway (strong agreement), restrictive (strong agreement), mixed disease (strong agreement), cardiac children (strong agreement), chronically ventilated children or children with a congenital disorder who suffer from an acute exacerbation (93% agreement). HFOV may be considered if conventional ventilation fails (strong agreement), using an open lung strategy to maintain optimal lung volume. Careful use of HFOV can be considered in cardiac children who developed severe respiratory failure. Particular caution is advised in children with passive pulmonary blood flow or right ventricular dysfunction (strong agreement).

A mortality benefit of HFOV in acute hypoxaemic respiratory failure (AHRF) has not been shown [62]. Recent retrospective cohort analyses seemed to confirm adult observations of even an increased mortality with HFOV, although major methodological issues have been raised regarding these studies [63–71]. HFOV can judiciously be performed in obstructive airway disease and cardiac children, including those with a Fontan circulation [72–78].

There are insufficient data to recommend on high-frequency jet or high-frequency percussive ventilation (strong agreement) or airway pressure release ventilation (strong agreement). HFJV should not be
used in obstructive airway disease because of the risk of dynamic hyperinflation (strong agreement).

There are no outcome data supporting high—frequency jet (HFJV) or high—frequency percussive ventilation (HFPV) for any disease condition outside the operating theatre when managing children with airway disorders [79–85].

We recommend considering extra-corporeal devices (ECMO or other devices) where available in reversible diseases if conventional and/or HFOV fails. If no ECMO is available, early consultation of an ECMO centre is recommended because transporting patients who need ECMO can be hazardous (strong agreement).

All aspects of ECMO in paediatric ARF are discussed in a Statement paper [86].

**Setting the ventilator**

**Triggering**

We recommend targeted patient ventilator synchrony in any triggered (non-invasive) positive pressure ventilation (strong agreement).

The effects of patient-ventilator asynchrony or interventions such as flow cycling on outcome are unclear [87–89]. However, better patient ventilator synchrony has been shown to improve patient comfort [89–92].

**Setting the I:E ratio/inspiratory time**

We recommend setting the inspiratory time and respiratory rate related to respiratory system mechanics and disease trajectory. Both are closely correlated and cannot be judged as independent from each other (strong agreement). In restrictive lung disease, we recommend a higher respiratory rate to compensate for low tidal volume and maintain minute ventilation (strong agreement).

There are no outcome data to guide the choice of inspiratory time or I:E ratio. However, the time constant (i.e. compliance times resistance) of the respiratory system (n) is an important parameter in this context. At the bedside, we suggest to avoid flow end-inspiratory or expiratory flow interruption, the latter to avoid air-trapping.

**Maintaining spontaneous breathing**

We recommend that all children on respiratory support preferably should breathe spontaneously, with the exception of the most severely ill child with obstructive airway (strong agreement), restrictive (strong agreement) or mixed disease (strong agreement) requiring very high ventilator settings and intermittent neuromuscular blockade (strong agreement). In these children, controlled mechanical ventilation (pressure or volume) should be preferred, mandating the need for continuous sedation and/or muscle relaxants (strong agreement). Caution is advised when using sedation and relaxation in the presence of cardiac dysfunction (strong agreement).

Although there are no data to recommend on maintaining spontaneous breathing, adult data suggest that maintaining spontaneous breathing during MV allows for a more homogeneous lung aeration and reduced risk of muscular atrophy and diaphragmatic dysfunction [93–97]. In adults, 48-h use of neuromuscular blocking agents (NMBA) in early severe ARDS significantly reduced 90-day crude mortality [98]. The only paediatric uncontrolled study on NMBA showed improved oxygenation [99]. No outcome data are available.

**Setting the pressures**

In the absence of transpulmonary pressure measurements, we recommend limiting the plateau pressure (Plat) ≤28 cmH₂O (87% agreement) or ≤29–32 cmH₂O if the chest wall elastance is increased in restrictive lung disease (93% agreement), mixed disease (strong agreement) and children with congenital/chronic disorders (strong agreement). We recommend limiting Pplat ≤30 cmH₂O in obstructive airway disease (strong agreement).

Observational studies in (severe) lung injury identified a direct relationship between peak inspiratory pressure (PIP) and mortality [100–103]. Measuring transpulmonary pressure (Ptp) instead of airway pressure (Paw) better defines lung strain in (severe) lung injury, especially in the presence of increased chest wall elastance [104, 105]. However, there are no studies identifying upper limits for PIP, Pplat or Ptp. For severe disease, we recommend adhering to the Pediatric Acute Lung Injury Consensus Conference (PALICC) recommendations [106].

We recommend delta pressure (i.e. the difference between end inspiratory and end expiratory pressure) <10 cmH₂O if there is no lung pathology (strong agreement). There are no data to recommend any acceptable delta pressure in restrictive (strong agreement), obstructive airway (strong agreement) or mixed disease (strong agreement). For children with reduced lung volumes, the driving pressure at zero-flow (Vt/Crs) may dictate the optimal tidal volume (Vt) (strong agreement).

Driving pressure (∆P = Vt/Crs) best stratified the risk for mortality in adults with ARDS [107]. These observations have not been replicated in children except for one study reporting an independent association between the airway pressure gradient (difference between PIP and PEEP) and mortality measured under dynamic flow conditions [103].

**Setting tidal volume**

There are no data to recommend optimal Vt in restrictive (strong agreement), obstructive airway (strong...
agreement), mixed disease (strong agreement), in cardiac children (strong agreement), children with congenital disorders or chronic ventilation (strong agreement). We recommend targeting physiologic Vt (strong agreement) and to avoid Vt > 10 mL/kg ideal bodyweight (strong agreement). In children with lung hypoplasia syndromes, optimal Vt may be smaller than physiologic because of the lower lung volumes (strong agreement).

So far, not a single value of Vt has been associated with mortality in children, irrespective of disease severity (i.e. ALI/ARDS vs. non-ALI/ARDS) [108, 109]. Interestingly, some observational studies reported better outcomes for children who were ventilated with Vt > 5–8 ml/kg and only one identified lower mortality associated with Vt ~8 mL/kg actual bodyweight compared with ~10 mL/kg [100, 101, 110–112].

Setting PEEP
We recommend PEEP to prevent alveolar collapse. However, we cannot recommend how much PEEP should be used. Physiological data in children without lung injury suggests 3–5 cmH2O (strong agreement). In severe disease, high PEEP may be needed (strong agreement). PEEP should always be set finding the optimal balance between haemodynamics and oxygenation. In order to improve oxygenation, PEEP titration should be attempted. There is no defined method to set best PEEP (strong agreement).

Moderate PEEP is sufficient when there is no lung pathology, but higher PEEP to restore EELV and improve respiratory system compliance (Crs) may be necessary in more severe disease and does not impair haemodynamics [1, 113–121]. There are no data comparing low versus high PEEP in (severe) lung injury. Also, it is unclear how to set PEEP and whether markers such as PaO2 or quasi-static Crs predict best PEEP [122].

In obstructive airway or mixed disease, there are no data to recommend the level of PEEP in sedated and/or paralysed children who have sufficient expiratory times. However, assessment of intrinsic PEEP and Pplat may guide setting external PEEP in children with air trapping who are mechanically ventilated and sedated (strong agreement). A balance needs to be found between alveolar recruitment and alveolar overdistension (strong agreement).

There are no data supporting external PEEP to attenuate gas-trapping by splitting the airways open or guiding the allowable amount of external PEEP to facilitate spontaneous breathing [123–126].

We recommend using high PEEP to stabilise airways in ventilated children with trachea- and/or bronchomalacia. Careful titration of PEEP is mandated to avoid cardiovascular compromise (strong agreement).

Observational data suggested reduced respiratory efforts with PEEP or CPAP in children with upper airway collapse. If used, it should be slowly titrated to avoid hemodynamic compromise [127, 128].

Lung recruitment
There are insufficient data to recommend any lung recruitment manoeuvre in children with (strong agreement) or without (strong agreement) lung injury or in cardiac children (strong agreement).

Recruitment manoeuvres (RM) may resolve atelectasis and improve gas exchange, but there are no data showing improved outcome [129–136]. There are no outcome data to recommend on the best RM (i.e. sustained inflation or PEEP titration) [115, 137–139]. There is no indication for routine RM after endotracheal suctioning [140].

Monitoring
Recommendations and long text on monitoring can be found in the ESM.

Targets for oxygenation and ventilation
Oxygenation
We cannot recommend a specific lower or upper limit for SpO2 for any ventilated non-cardiac child with obstructive airway, restrictive or mixed disease (strong agreement). SpO2 >95% at room air should be expected in children without lung injury and extra-pulmonary manifestations (strong agreement). We recommend adhering to the PALICC guidelines for PARDS (i.e. SpO2 92–97% when PEEP <10 cmH2O and 88–92% when PEEP ≥10 ) (strong agreement). We cannot recommend a specific upper or lower limit for SpO2 for cardiac children. In children with cardiorespiratory failure, oxygen therapy should be titrated, balancing pulmonary disease against the underlying cardiac disorder, as well as in some conditions (e.g., single ventricle physiology) balancing pulmonary versus systemic blood flow (strong agreement). Increasing FiO2 up to 1.0 in life-threatening acute pulmonary hypertension crisis may be required (strong agreement).

There are no studies identifying the optimal SpO2 range in the presence or absence of lung injury. In healthy children breathing room air, SpO2 >95% and PaO2 between 80 and 100 mmHg should be expected [141, 142]. In cardiac children, children with or at risk for lung injury or children with pulmonary hypertension, target SpO2 depends on the type and severity of lesions [143, 144]. PALICC proposed SpO2 between 92 and 97% when PEEP <10 cmH2O and 88–92% for PEEP ≥10 cmH2O in non-cardiac PARDS [106]. There are no data reporting the safety and necessity of liberal or restrictive oxygen
therapy, but as a rule of thumb the lowest FiO₂ should be targeted [145–147].

**Ventilation**

We recommend achieving normal CO₂ levels in children with normal lungs (strong agreement). For acute (non-)pulmonary children, higher levels of CO₂ may be accepted unless specific disease conditions dictate otherwise. However, we cannot recommend any specific pH limit. We recommend permissive hypercapnia targeting a pH > 7.20 (strong agreement). In children at risk for pulmonary hypertension, we recommend to maintain normal pH (strong agreement). We recommend using pH as non-pharmacologic tool to modify pulmonary vascular resistance for specific disease conditions (strong agreement).

There are no studies identifying optimal CO₂ in the presence or absence of lung injury. Normal CO₂ levels (i.e. 35–45 mmHg) should be expected in healthy children. Increasing ventilator settings in an attempt to normalise mild hypercapnia may be detrimental [148]. There are no outcome data on the effects of permissive hypercapnia or the lowest tolerable pH [149, 150]. Normal pH and PCO₂ should be targeted in severe traumatic brain injury and pulmonary hypertension.

**Weaning and extubation readiness testing**

There are insufficient data to recommend on the timing of initiation (strong agreement) and approach to weaning (strong agreement) and the routine use of any extubation readiness testing that is superior to clinical judgement (strong agreement).

Assessing daily weaning readiness may reduce duration of ventilation [150–152]. There are no data supporting superiority of any approach such as protocolised weaning, closed-loop protocols, nurse-led weaning, or the usefulness of predictors for weaning success [123, 151, 153–172].

There are no data to recommend how to perform and evaluate extubation readiness testing (ERT), although some studies suggest that using a minimum pressure support overestimates extubation success [173–175].

There are insufficient data to recommend the routine use of non-invasive respiratory support after extubation for any patient category. However, early application of NIV combined with cough-assist techniques should be considered in neuromuscular diseases to prevent extubation failure (strong agreement).

There is only one small pilot study suggesting that the use of NIV may prevent reintubation in children at high-risk for extubation failure [42]. Although appealing, post-extubation NIV in combination with cough-assist techniques has not been confirmed to prevent extubation failure in neuromuscular patients yet [176–179].

**Supportive measures**

**Humidification, suctioning, positioning and chest physiotherapy**

We recommend airway humidification in ventilated children, but there are insufficient data to recommend any type of humidification (strong agreement).

There are no data showing superiority or inferiority of either active or passive humidification [180–182]. However, there is great variability amongst commercially available HMEs regarding humidification efficacy, dead space volumes and imposed work of breathing [183].

There are insufficient data to recommend on the approach to endotracheal suctioning (strong agreement), but the likelihood of derecruitment during suctioning needs to be minimised (strong agreement). The routine instillation of isotonic saline prior to endotracheal suctioning is not recommended (strong agreement).

There is no scientific basis for routine endotracheal suctioning or the approach to suctioning (open vs. closed) albeit that open suctioning may lead to more derecruitment or the instillation of isotonic saline prior to suctioning [140, 184–188].

There are insufficient data to recommend chest physiotherapy as a standard of care (strong agreement). Use of cough-assist techniques should be considered for patients with neuromuscular disease on NIV to prevent failure (strong agreement).

Chest physiotherapy for airway clearance and sputum evacuation cannot be considered standard of care [189, 190]. It is unclear whether cough-assist techniques add any value to patients with neuromuscular disease who require NIV, but their use should be considered to prevent endotracheal intubation [176, 178, 191–195].

We recommend that all children should be maintained with the head of the bed elevated to 30–45°, unless specific disease conditions dictate otherwise (strong agreement).

**Endotracheal tube and patient circuit**

Endotracheal high-volume low-pressure cuffed tubes can be used in all children. Meticulous attention to cuff pressure monitoring is indicated (strong agreement).

Cuffed ETTs can be safely used without increased risk for post-extubation stridor when the cuff pressure is
maintained ≤20 cmH2O [196, 197]. Cuff pressure monitoring has to be routinely performed using cuff-specific devices [198].

Dead space apparatus should be reduced as much as possible by using appropriate patient circuits and reduction of swivels (strong agreement).

Any component that is added after the Y piece increases dead space and may have clinical relevance [199].

Double-limb circuits should be used for invasive ventilation (strong agreement), and preferentially a single-limb circuit for NIV (93% agreement). Single-limb circuits are very sensitive to leaks [200]. Therefore, single-limb home ventilators are not suitable for invasive ventilation in the PICU [201].

Miscellaneous
We recommend avoiding routine use of hand-ventilation. If needed, pressure measurements and pressure pop-off valves should be used (strong agreement).

Manual ventilation should be avoided to prevent the delivery of inappropriate high airway pressure and/or volume [202].

Specific patient populations
Lung hypoplasia
Recommendations for children with acute restrictive, obstructive or mixed disease should also be applied to children with lung hypoplasia syndromes who suffer from acute deterioration (strong agreement).

Chronically ventilated/congenital patient
In severe or progressive underlying disease, we recommend considering whether or not invasive ventilation is beneficial for the particular child (strong agreement). For chronic neuromuscular children and other children on chronic ventilation with acute deterioration, the same recommendations as for children with normal lungs, acute restrictive, acute obstructive or mixed disease are applicable (strong agreement). Preservation of spontaneous breathing should be aimed for in these children (strong agreement).

Invasive ventilation may be life-saving, but the risk/benefit ratio should be carefully evaluated in each ventilator-dependent child who suffers from acute exacerbations or in children with life-limiting congenital disorders [203–208]. In the absence of data, we suggest that the recommendations for children with acute restrictive, obstructive or mixed disease are also applicable in this patient category.

Cardiac children
Positive pressure ventilation may reduce work of breathing and afterload in LV failure, but it may increase afterload in RV failure (strong agreement). In cardiac children with or without lung disease, the principles for any specific pathology will apply, but titration of ventilator settings should be carried out more carefully (strong agreement). We cannot recommend on a specific level of PEEP in cardiac children with or without lung disease, irrespective of whether or not there is increased pulmonary blood flow, but sufficient PEEP should be used to maintain end-expiratory lung volume (strong agreement).

Many of the assumptions on cardiopulmonary interactions in children are mainly based on adult data [209–212]. For cardiac children, assisted rather than controlled ventilation may be preferable [57, 59]. However, in patients with passive pulmonary blood flow, spontaneous breathing on CPAP 3–5 cmH2O reduced FRC and increased PVRI, whereas MV with PEEP 3–5 cmH2O did not [213]. Neither CPAP nor PEEP ≤15 cmH2O impaired venous return or cardiac output after cardiac surgery [214–217]. This means that, for cardiac children, the same principles for MV apply as for non-cardiac children [211, 218].

Reflecting on the consensus conference
Our consensus conference has clearly but also painfully emphasised that there is very little, if any, scientific evidence supporting our current approach to paediatric mechanical ventilation (Fig. 1; Tables 1, 2). Given this absence of evidence, our recommendations reflect a consensus on a specific topic that we agreed upon. To date, most of what we do is either based on personal experiences or how it works in adults. In fact, when it comes to paediatric MV “each paediatric critical care practitioner is a maven and savant and knows the only correct way to ventilate a child” (by Christopher Newth). This lack of scientific background should challenge everybody involved in paediatric mechanical ventilation to embark on local or global initiatives to fill this huge gap of knowledge. We are in desperate need of well-designed studies and must constantly remind us that “Anecdotes” are not plural for “Evidence” [219–221]. This European paediatric mechanical ventilation consensus conference is a first step towards a better and substantiated use of this life-saving technique in critically ill children (Figs. 2, 3, 4).
Table 1  Overview of published literature related to all aspects of paediatric mechanical ventilation for the disease conditions discussed in the consensus conference

| Subject                          | Available data | Applicability to specific disease conditions                      |
|----------------------------------|----------------|-------------------------------------------------------------------|
|                                  | RCT            | Observational                                                   |
| Non-invasive support             |                |                                                                  |
| Use of HFNC                      | None           | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions                             |
| Use of CPAP                      | None           | Yes                                                              |
|                                  |                | All disease conditions                                           |
| Non-invasive ventilation         | Yes (n = 2)    | Yes                                                              |
|                                  |                | All disease conditions                                           |
| Ventilator modes                 |                |                                                                  |
| Conventional modes               | None           | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions                             |
| HFOV                             | Yes (n = 2)    | Yes                                                              |
|                                  |                | All disease conditions                                           |
| HFJV, HFPV                       | No             | Yes                                                              |
|                                  |                | All disease conditions                                           |
| Liquid ventilation               | No             | No                                                               |
|                                  |                | All disease conditions                                           |
| ECMO                             | No             | Yes                                                              |
|                                  |                | All disease conditions                                           |
| Setting the ventilator           |                |                                                                  |
| Patient-ventilator synchrony     | No             | Yes                                                              |
|                                  |                | All disease conditions                                           |
| I:E ratio/inspiratory time       | No             | No                                                               |
|                                  |                | All disease conditions                                           |
| Maintaining spontaneous breathing| No             | No                                                               |
|                                  |                | Healthy lungs, all disease conditions                             |
| Plateau pressure                 | No             | No                                                               |
|                                  |                | Healthy lungs, all disease conditions                             |
| Delta pressure/driving pressure  | No             | No                                                               |
|                                  |                | Healthy lungs, all disease conditions                             |
| Tidal volume                     | No             | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions                             |
| PEEP                             | No             | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions, upper airway disorders     |
| Lung recruitment                 | No             | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions                             |
| Monitoring                       |                |                                                                  |
| Ventilation                      | No             | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions                             |
| Oxygenation                      | No             | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions                             |
| Tidal volume                     | No             | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions                             |
| Lung mechanics                   | No             | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions                             |
| Lung ultrasound                  | No             | Yes                                                              |
|                                  |                | All disease conditions                                           |
| Targets for oxygenation and ventilation |        |                                                                  |
| Oxygenation                      | No             | No                                                               |
|                                  |                | Healthy lungs, all disease conditions                             |
| Ventilation                      | No             | No                                                               |
|                                  |                | Healthy lungs, all disease conditions                             |
| Weaning and extubation readiness testing |        |                                                                  |
| Weaning                          | Yes (n = 2)    | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions                             |
| NIV after extubation             | No             | Yes                                                              |
|                                  |                | All disease conditions                                           |
| Use of corticosteroids           | Yes            | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions                             |
| Supportive measures              |                |                                                                  |
| Humidification                   | No             | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions                             |
| Endotracheal suctioning          | No             | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions                             |
| Chest physiotherapy              | No             | Yes                                                              |
|                                  |                | All disease conditions                                           |
| Bed head elevation               | No             | No                                                               |
|                                  |                | Healthy lungs, all disease conditions                             |
| ETT and patient circuit          | No             | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions                             |
| Reducing dead space apparatus    | No             | Yes                                                              |
|                                  |                | Healthy lungs, all disease conditions                             |
| Heliox                           | No             | Yes                                                              |
|                                  |                | Obstructive airway disease                                       |
| Use of manual ventilation        | No             | No                                                               |
|                                  |                | Healthy lungs, all disease conditions                             |
Table 2 Potential clinical implications of the recommendations from the paediatric mechanical ventilation consensus conference (PEMVECC)

| Non-invasive support                          |  |
|----------------------------------------------|---|
| High-flow nasal cannula                      | No recommendation |
| Continuous positive airway pressure          | Consider in mixed disease  
Consider in mild-to-moderate cardiorespiratory failure  
No recommendation on optimal interface |
| Non-invasive ventilation                     | Consider in mild-to-moderate disease, but not severe disease  
Consider in mild-to-moderate cardiorespiratory failure  
Should not delay intubation  
No recommendation on optimal interface |

| Invasive ventilation                         |  |
|----------------------------------------------|---|
| Mode                                         | No recommendation |
| High-frequency oscillatory ventilation        | Consider when conventional ventilation fails  
May be used in cardiac patients |
| High-frequency jet/percussive ventilation    | No recommendation  
Do not use high-frequency jet ventilation in obstructive airway disease |
| Liquid ventilation                           | Do not use |
| Extra-corporeal life support                 | Consider in reversible disease if conventional ventilation and/or HFOV fails |
| Triggering                                   | Target patient-ventilator synchrony |
| Inspiratory time/I:E ratio                  | Set inspiratory time by respiratory system mechanics and underlying disease (use time constant and observe flow-time scalar)  
Use higher rates in restrictive disease |
| Maintaining spontaneous breathing            | No recommendation |
| Plateau pressure                             | Keep \( \leq 28 \) or \( \leq 29–32 \) cmH\(_2\)O with increased chest wall elastance, \( \leq 30 \) cmH\(_2\)O in obstructive airway disease |
| Delta pressure                               | Keep \( \leq 10 \) cmH\(_2\)O for healthy lungs, unknown for any disease condition |
| Tidal volume                                 | Keep \( \leq 10 \) mL/kg ideal bodyweight, maybe lower in lung hypoplasia syndromes |
| PEEP                                         | 5–8 cmH\(_2\)O, higher PEEP necessary dictated by underlying disease severity (also in cardiac patients)  
Use PEEP titration, consider lung recruitment (also in cardiac patients)  
Add PEEP in obstructive airway disease when there is air-trapping and to facilitate triggering  
Use PEEP to stent upper airways in case of malacia |

| Monitoring                                   |  |
|----------------------------------------------|---|
| Ventilation                                  | Measure PCO\(_2\) in arterial or capillary blood samples  
Consider transcutaneous CO\(_2\) monitoring  
Measure end-tidal CO\(_2\) in all ventilated children |
| Oxygenation                                  | Measure SpO\(_2\) in all ventilated children  
Measure arterial PO\(_2\) in moderate-to-severe disease  
Measure pH, lactate and central venous saturation in moderate-to-severe disease  
Measure central venous saturation as marker for cardiac output |
| Tidal volume                                 | Measure near Y-piece of patient circuit in children <10 kg |
| Lung mechanics                               | Measure peak inspiratory pressure and/or plateau pressure, mean airway pressure, positive end-expiratory pressure. Consider measuring transpulmonary pressure, (dynamic) compliance, intrinsic PEEP  
Monitor pressure–time and flow-time scalar |
| Lung ultrasound                              | Consider in appropriately trained hands |

| Targets                                      |  |
|----------------------------------------------|---|
| Oxygenation                                  | SpO\(_2\) \(\geq 95\)\% when breathing room air for healthy lungs  
No threshold for any disease condition or cardiac patients, but keep SpO\(_2\) \(< 97\)\%  
For PARDS: SpO\(_2\) 92–97\% when PEEP < 10 cmH\(_2\)O and 88–92\% when PEEP \(\geq 10\) cmH\(_2\)O |
| Ventilation                                  | PCO\(_2\) 35–45 mmHg for healthy lungs  
Higher PCO\(_2\) accepted for acute (non-)pulmonary patients unless specific diseases dictate otherwise  
Target pH > 7.20  
Target normal pH for patients with pulmonary hypertension |

Weaning and extubation readiness

|----------------------------------------------|---|
|----------------------------------------------|---|
| Weaning                                      | Start weaning as soon as possible  
Perform daily extubation readiness testing |
| Non-invasive ventilation after extubation    | Consider non-invasive ventilation in neuromuscular patients |
| Corticosteroids                              | Use in patients at increased risk for post-extubation stridor |
### Table 2 continued

| Supportive measures          | Use humidification |
|------------------------------|--------------------|
| Endotracheal suctioning      | Do not perform routinely, only on indication. No routine instillation of isotonic saline prior to suctioning |
| Chest physiotherapy          | Do not use routinely |
|                              | Consider using cough-assist devices in neuromuscular patients |
| Positioning                  | Maintain head of bed elevated 30-45° |
| Endotracheal tube and patient circuit | Use cuffed endotracheal tube, keep cuff pressure $\leq 20$ cmH$_2$O |
|                              | Minimise dead space by added components |
|                              | Use double-limb circuits for invasive ventilation |
|                              | Do not use home ventilators during the acute phase in the intensive care unit |

### Miscellaneous

| Hand-ventilation | Avoid hand ventilation unless specific conditions dictate otherwise |

---

**Fig. 2**  Graphical simplification of the recommendations on “ventilator mode”, “setting the ventilator” and “supportive measures” in the context of healthy lungs, obstructive airway, restrictive and mixed disease. It is also applicable for cardiac patients, patients with congenital of chronic disease and patients with lung hypoplasia syndromes. The colour gradient denotes increasing applicability of a specific consideration with increasing disease severity. Absence of the colour gradient indicates that there is no relationship with disease severity. The question mark associated with specific interventions highlights the uncertainties because of the lack of paediatric data. HFNC high flow nasal cannula, CPAP continuous positive airway pressure, NIV non-invasive ventilation, PIP peak inspiratory pressure, Pplat plateau pressure, Vt tidal volume, PEEP positive end-expiratory pressure, HFOV high-frequency oscillatory ventilation, ECLS extracorporeal life support, NMB neuromuscular blockade.
**Fig. 3** Graphical simplification of the recommendations on “monitoring” in the context of healthy lungs, obstructive airway, restrictive and mixed disease. It is also applicable for cardiac patients, patients with congenital of chronic disease and patients with lung hypoplasia syndromes. The *colour gradient* denotes increasing applicability of a specific consideration with increasing disease severity. *Absence of the colour gradient* indicates that there is no relationship with disease severity. The *question mark* associated with specific interventions highlights the uncertainties because of the lack of paediatric data. *PIP* peak inspiratory pressure, *Pplat* plateau pressure, *Vt* tidal volume, *PEEP* positive end-expiratory pressure, *mPaw* mean airway pressure, *SvO₂* venous oxygen saturation

**Fig. 4** Graphical simplification of the recommendations on “targets of oxygenation and ventilation” in the context of healthy lungs, obstructive airway, restrictive and mixed disease. It is also applicable for cardiac patients, patients with congenital of chronic disease and patients with lung hypoplasia syndromes. The *colour gradient* denotes increasing applicability of a specific consideration with increasing disease severity. *Absence of the colour gradient* indicates that there is no relationship with disease severity. The *question mark* associated with specific interventions highlights the uncertainties because of the lack of paediatric data. PALICC pediatric acute lung injury consensus conference

---

**Electronic supplementary material**

The online version of this article (doi:10.1007/s00134-017-4920-z) contains supplementary material, which is available to authorized users.

**Author details**

1 Department of Paediatrics, Division of Paediatric Critical Care Medicine, Bea­trix Children's Hospital Groningen, University Medical Center Groningen, The University of Groningen, P.O. Box 30.001, 9700 RB Groningen, The Netherlands.

2 Critical Care, Anaesthesiology, Peri-operative and Emergency Medicine (CAPE), the University of Groningen, Groningen, The Netherlands. 3 Division of Pediatrics and Neonatal Critical Care, A.Belecere' Medical Center, South Paris University Hospitals, APHP and South Paris-Saclay University, Paris, France. 4 Institute of Anaesthesiology and Critical Care, Catholic University of the Sacred Heart, Rome, Italy. 5 Department of Anaesthesia, Intensive Care and Emer­gency, Fondazione IRCCS Ca'Granda, Ospedale Maggiore Policlinico, Milan, Italy. 6 Service de Médecine et Réanimation néonatales de Port-Royal, Hôpital Cochin, Hôpitaux Universitaires Paris Centre and Paris Descartes University, Paris, France. 7 Pediatric Intensive Care Unit, Hôpital Femme Mère Enfant, Hôp­i­ces Civils de Lyon, Lyon, France. 8 University Lyon 1, University of Lyon, Lyon, France. 9 Pediatric Intensive Care Department, Gregorio Marañón General University Hospital, School of Medicine, Complutense University of Madrid, Madrid, Spain. 10 Gregorio Marañón Health Research Institute, Mother–Child Health and Development Network (Red SAMIDI) of Carlos III Health Institute, Madrid, Spain. 11 Division of Respiratory and Critical Care Medicine, University Children's Hospital Basel, University of Basel, Basel, Switzerland. 12 Royal Brompton and Harefield NHS Trust, London, UK. 13 Department of Paediatrics, Division of Paediatric Critical Care Medicine, VU University Medical Center, Amsterdam, The Netherlands. 14 Paediatric Intensive Care Unit, Hospital Universitario Central de Asturias, Oviedo, Spain. 15 Paediatric Intensive Care and Intermediate Care Department, Sant Joan de Déu University Hospital, Universitat de Barcelona, Esplugues de Llobregat, Spain. 16 Critical Care Research Group, Institut de Recerca Sant Joan de Déu, Santa Rosa 39-57, 08950 Esplugues de Llobregat, Spain. 17 Department of Anaesthesiology and Intensive Care, Division of Paediatric Intensive Care Unit, Alessandria General Hospital, Alessandria, Italy. 18 Department of Pediatrics,Children's Hospital Traunstein, Ludwig Maximili­ans University Munich, Munich, Germany. 19 Department of Paediatrics, Division of Paediatric Emergency and Critical Care, Verona University Hospital, Verona, Italy. 20 Departments of Critical Care and Paediatric Bioethics, Great Ormond St Hospital for Children NHS Trust, London, UK. 21 Service of Neo­natology and Pediatric Intensive Care, Department of Paediatrics, University Hospital of Geneva, Geneva, Switzerland.

**Acknowledgements**

This project has received funding and technical support by the European Society for Paediatric and Neonatal Intensive Care (ESPNIC) and by the Department of Anaesthesiology and Critical Care, Catholic University of the Sacred Heart, University Hospital “A.Gemelli” (Rome, Italy). We like to express our sincerest gratitude to Professor Massimo Antonelli and Professor Giorgio Coniti for facilitating the 2-day PEMVECC meeting at the Catholic University of the Sacred Heart, University Hospital “A.Gemelli”, Rome, Italy. We also like to thank Mrs. Sjoouke van der Werf from the library of the University Medical Center Groningen for performing the literature search.

**Compliance with ethical standards**

**Conflicts of interest**

The authors declare the following conflicts of interest: M.K. received research funding from Stichting Beatrice Kinderziekenhuis, Fonds NutsOha, ZonMW, UMC Groningen, TerMeulen Fonds/Royal Dutch Academy of Sciences and VU university medical center and serves as a consultant for and has received lecture fees from Vyaire. His institution received research technical support from Vyaire and Applied Biosignals. P.B. received honoraria from Abbvie, a travel grant from Maquet and served on an advisory board for Masimo. F.R. received consultancy fees from Vitalaire and Philips Respironics. P.R. received travel support from, Maquet, Acutronic, Nymcomed, Philips, to run international teaching courses on mechanical ventilation. His institution received funding from Maquet, SLE, Stephan (unrestricted funding for clinical research) and from the European Union’s Framework Programme for Research and Innovation Horizon2020 (CRADL). Grant no. 668259. M.P. received honoraria from Air-liqueide Healthcare and served as speaker for Fisher & Paykel and ResMed. His institution received disposable materials.
from Philips, ResMed and Fisher & Paykel. D.d.L. has received travel grants from Acutronic, consultancy fees from Vyaire and Acutronic and research technical support from Vyaire and Acutronic. P-H.J. received consultancy fees from Air Liquide Medical System (finished in 2013). Abbvie as member of the French Board of Neonatologists, and punctual fees from CHIESI France for oral presentations. G.W., D.M., A.M., J.H., E.J., E.C., J.B. and J.L.H. have no conflicts of interest.

Open Access This article is distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (http://creativecommons.org/licenses/by-nc/4.0/), which permits any noncommercial use, distribution, and reproduction in any medium, provided you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made.

Received: 24 May 2017 Accepted: 22 August 2017
Published online: 22 September 2017

References

1. Santtchi M, Jouret P, Leclerc F, Gauvin F, Nethwell CJ, Carrol CL, Flori H, Tasker RC, Rimensberger PC, Randolph AG, Investigators P, Pediatric Acute Lung I, Sepsis Investigators N, European Society of P, Neonatal Intensive C (2010) Acute lung injury in children: therapeutic practice and feasibility of international clinical trials. Pediatr Crit Care Med 11:681–689

2. Duyndam A, Ista E, Houmes RJ, van Driel B, Reiss I, Tibboel D (2011) Invasive ventilation modes in children: a systematic review and meta-analysis. Crit Care 15:R24

3. Chatburn RL, El-Khattab M, Mireles-Cabodevilla E (2014) A taxonomy for mechanical ventilation: 10 fundamental maxims. Respir Care 59:1747–1763

4. Chatburn RL (2007) Classification of ventilator modes: update and proposal for implementation. Respir Care 52:301–323

5. Fitch K, Bernstein SJ, Aguilar MD, Burnand B, LaCalle JR, Lazaro P van het Loo M, McDonnell J, Vander JP, Kahan JP (2001) The RAND/UCLA appropriateness method user’s manual. RAND, Santa Monica

6. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, Guyatt GH, Helfand M, Lewin S, Rennie D, Rivara F, Forster G, Schunemann HJ, Edejer TT, Varonen H, Vist GE, Williams JB Jr, Oxman AD, Vist GE, Liberati A, Altman DG, Grimes DA, Schulz KF (2004) Grading quality of evidence and strength of recommendations. BMJ 328:1490

7. Schwabauer N, Berg B, Blumenstock G, Haap M, Hetzel J, Riessen R (2010) Acute lung injury in children: therapeutic practice and feasibility of international clinical trials. Pediatr Crit Care Med 11:681–689

8. Pham TM, O’Malley L, Mayfield S, Martin S, Schibler A (2015) The effect of high flow nasal cannula therapy on the work of breathing in infants with bronchiolitis. Pediatr Pulmonol 50:713–720

9. Hough JL, Pham TM, Schibler A (2014) Physiologic effect of high-flow nasal cannula therapy in infants with bronchiolitis. Pediatr Crit Care Med 15:e214–e219

10. Mayfield S, Bogossian F, O’Malley L, Schibler A (2014) High-flow nasal cannula oxygen therapy for infants with bronchiolitis: pilot study. J Paediatr Child Health 50:373–378

11. Mayfield S, Jauncey-Cookie J, Hough JL, Schibler A, Gibbons K, Bogossian F (2014) High-flow nasal cannula therapy for respiratory support in children. Cochrane Database Syst Rev: CD009850

12. Milesi C, Baleine J, Matecki S, Durand S, Combos C, Novais AR, Cambonie G (2013) Is treatment with a high flow nasal cannula effective in acute viral bronchiolitis? A physiologic study. Intensive Care Med 39:1088–1094

13. Rubin S, Ghuman A, Deakers T, Khemani R, Ross P, Newth CJ (2014) Effort of breathing in children receiving high-flow nasal cannula. Pediatr Crit Care Med 15:1–6

14. Chisti MJ, Salam MA, Smith JH, Ahmed T, Petroni MA, Shahunja KM, Shahid AS, Faruque AS, Ashraf H, Bardhan PK, Sharifuzzaman, Graham SM, Duke T (2015) Bubble continuous positive airway pressure for children with severe pneumonia and hypoxaemia in Bangladesh: an open, randomised controlled trial. Lancet 386:1057–1065

15. Kelly GS, Simon HK, Sturms JJ (2013) High-flow nasal cannula use in children with respiratory distress in the emergency department: predicting the need for subsequent intubation. Pediatr Emerg Care 29:888–892

16. Kneyber MC (2013) Question 1: Is there a role for high-flow nasal cannula oxygen therapy to prevent endotracheal intubation in children with viral bronchiolitis? Arch Dis Child 98:1018–1020

17. McKernan C, Chua LC, Visintainer PF, Allen H (2010) High-flow nasal cannulae therapy in infants with bronchiolitis. J Pediatr 156:634–638

18. Modesto IAV, Khemani RG, Medina A, Del Villar Guerra P, MolinaCambra A (2017) Bayes to the rescue: continuous positive airway pressure has less mortality than high-flow oxygen. Pediatr Crit Care Med 18:e92–e99

19. Riese J, Fierce J, Riese A, Alversion BK (2015) Effect of a hospital-wide high-flow nasal cannula protocol on clinical outcomes and resource utilization of bronchiolitis patients admitted to the PICU. Hosp Pediatr 5:613–618

20. Schibli A, Pham TM, Dunster KR, Foster K, Barlow A, Gibbons K, Hough JL (2011) Reduced intubation rates for infants after introduction of high-flow nasal prong oxygen delivery. Intensive Care Med 37:847–852

21. Wells R, James C, Maraseda LS, Armbys CC (2012) Use of high-flow nasal cannula support in the emergency department reduces the need for intubation in pediatric acute respiratory insufficiency. Pediatr Emerg Care 28:1117–1123

22. Borckink I, Essouri S, Laurent M, Albers MJ, Burgerhof JG, Tissieres P, Kneyber MC (2014) Infants with severe respiratory syncytial virus needed less ventilator time with nasal continuous airways pressure than invasive mechanical ventilation. Acta Paediatr 103:81–85

23. Cambonie G, Milesi C, Jaber S, Alsamilem F, Barbette E, Picaud JC, Matecki S (2008) Nasal continuous positive airway pressure decreases respiratory muscles overload in young infants with severe acute viral bronchiolitis. Intensive Care Med 34:1865–1872

24. Donlan M, Fontella PS, Puligandla PS (2011) Use of continuous positive airway pressure (CPAP) in acute viral bronchiolitis: a systematic review. Pediatr Pulmonol 46:736–746

25. Essouri S, Durand P, Chevet L, Balu L, Devictor D, Fauroux B, Tissieres P (2011) Optimal level of nasal continuous positive airway pressure in severe viral bronchiolitis. Intensive Care Med 37:2002–2007

26. Milesi C, Baleine J, Matecki S, Durand S, Combos C, Novais AR, Combonie G (2013) Is treatment with a high flow nasal cannula effective in acute viral bronchiolitis? A Physiologic study. Intensive Care Med 39:1088–1094

27. Milesi C, Matecki S, Jaber S, Mura T, Jacquot A, Pidoux O, Chautemps N, Novais AR, Combos C, Picaud JC, Cambonie G (2013) 6 cmH2O continuous positive airway pressure versus conventional oxygen therapy in severe viral bronchiolitis: a randomized trial. Pediatr Pulmonol 48:45–51

28. Sinha JP, McBride AK, Smith R, Fernandes RM (2013) CPAP and high-flow nasal cannula oxygen in bronchiolitis. Chest 148:810–823

29. Fortenberry JD, Del Toro J, Jefferson LS, Evey L, Haase D (1995) Management of pediatric acute hypoxemic respiratory insufficiency with bilevel positive pressure (BiPAP) nasal mask ventilation. Chest 108:1059–1064

30. Pancreza CF, Hayashi M, Fregnani JH, Negi EM, Deheinzelen D, de Camargo BG (2008) Noninvasive ventilation in immunocompromised pediatric patients: eight years of experience in a pediatric oncology intensive care unit. J Pediatr Hematol Oncol 30:533–538

31. Schiller O, Schonfeld T, Yaniv I, Stein J, Kadmon G, Nahan E (2009) Biphasic positive airway pressure ventilation in pediatric oncology patients with acute respiratory failure. J Intensive Care Med 24:383–388

32. Piastra M, De Luca D, Pietrini D, Pulitano S, D’Arrigo S, Mancino A, Conti G (2009) Noninvasive pressure-support ventilation in immunocompromised children with ARDS: a feasibility study. Intensive Care Med 35:1420–1427

33. Gupta P, Kuperstock JE, Hashmi S, Arnoldo V, Gossett JM, Prodhon P, Venkatakrishnan S, Roth SJ (2013) Efficacy and predictors of success of noninvasive ventilation for prevention of extubation failure in critically ill children with heart disease. Pediatr Cardiol 34:964–977
34. Kovacikova L, Skrak P, Dobos D, Zahorec M (2014) Noninvasive positive pressure ventilation in critically ill children with cardiac disease. Pediatr Cardiol 35:676–683

35. Chin K, Takahashi K, Ohmori K, Toru I, Matsumoto H, Niimi A, Doi H, Ikeda T, Nakahata T, Komeda M, Mishima M (2007) Noninvasive ventilation for pediatric patients under 1 year of age after cardiac surgery. J Thorac Cardiovasc Surg 134:260–261

36. Fernandez Lafeyer S, Toledo B, Leiva M, Padrón M, Balseiro M, Carrillo A, Lopez-Herce J (2016) Non-invasive mechanical ventilation after heart surgery in children. BMC Pulm Med 16:167

37. Thill PJ, McGuire JK, Baden HP, Green TP, Checchia PA (2004) Noninvasive positive-pressure ventilation in children with lower airway obstruction. Pediatr Crit Care Med. 5:337–342

38. Basnet S, Mander G, Andoh J, Klaska H, Verhulst S, Koirala J (2012) Safety, efficacy, and tolerability of early initiation of noninvasive positive pressure ventilation in pediatric patients admitted with status asthmaticus: a pilot study. Pediatr Crit Care Med 13:393–398

39. Piastra M, Antonelli M, Caresta E, Chiaretti A, Polidori G, Conti G (2006) Noninvasive ventilation in childhood acute neuromuscular respiratory failure: a pilot study. Respiration 73:791–798

40. Chen TH, Hsu JH, Wu JR, Liang WC, Yang SN, Jong YJ (2014) Combined noninvasive ventilation and mechanical in-exsufflator in the treatment of pediatric acute neuromuscular respiratory failure. Pediatr Pulmonol 50:459–466

41. Demaret P, Mulder A, Loeckx T, Trippaerts M, Lebrun F (2015) Non-invasive ventilation is useful in paediatric intensive care units if children are appropriately selected and carefully monitored. Acta Paediatr 104:861–871

42. Mayordomo-Colunga J, Medina A, Rey C, Concha A, Menendez S, Los Arcos M, Garcia I (2013) Non-invasive ventilation after extubation in paediatric patients: a preliminary study. BMC Pediatr 13:209

43. Fioletto JR, Ribeiro CF, Carpi MF, Bonatto RC, Moraes MA, Fioletto EB, Fagundes DJ (2015) Comparison between noninvasive mechanical ventilation and standard oxygen therapy in children up to 3 years old with respiratory failure after extubation: a pilot prospective randomized clinical study. Pediatr Crit Care Med 16:124–130

44. Yanez LJ, Yunge M, Emflork M, Lapadula M, Alcantara A, Fernandez C, Lozano J, Contreras M, Conuto L, Arevaco C, Gayan A, Hernandez F, Pedraza M, Feddersen M, Bejares M, Morales M, Mallea F, Glassinovic M, Cavada G (2008) A prospective, randomized, controlled trial of noninvasive ventilation in pediatric acute respiratory failure. Pediatr Crit Care Med 9:484–489

45. Calderini E, Chidini G, Pelosi P (2010) What are the current indications for noninvasive ventilation in children? Curr Opin Anaesthesiol 23:368–374

46. Essouni S, Chevet L, Durand P, Haai V, Fauroux B, Devictor D (2006) Noninvasive positive pressure ventilation: five years of experience in a pediatric intensive care unit. Pediatr Crit Care Med 7:329–334

47. James CS, Hallewell CP, James DP, Wade A, Mok QQ (2011) Predicting the success of non-invasive ventilation in preventing intubation and re-intubation in the paediatric intensive care unit. Intensive Care Med 37:1994–2001

48. Mayordomo-Colunga J, Medina A, Rey C, Diaz JJ, Concha A, Los Arcos M, Menendez S (2009) Predictive factors of non invasive ventilation failure in critically ill children: a prospective epidemiological study. Intensive Care Med 35:527–536

49. Munoz-Bonet JL, Flor-Macian EM, Brines J, Rosello-Millet PM, Cruz Llopis M, Lopez-Prats JL, Castillo S (2010) Predictive factors for the outcome of noninvasive ventilation in pediatric acute respiratory failure. Pediatr Crit Care Med 11:675–680

50. Piastra M, De Luca D, Marzano L, Stival E, Genovesi E, Pietrini D, Conti G (2011) The number of failing organs predicts non-invasive ventilation failure in children with ALI/ARDS. Intensive Care Med 37:1510–1516

51. Antonelli M, Conti G, Esquinas A, Montini L, Maggiore SM, Bello G, Rocco M, Maviglia R, Pennisi MA, Gonzalez-Diaz G, Meduri GU (2007) A multiple-center survey on the use in clinical practice of noninvasive ventilation as a first-line intervention for acute respiratory distress syndrome. Crit Care Med 35:18–25

52. Crull B, Lorrain G, Nishikawa A, Harrington K, Essouni S, Emeriaud G (2016) Safety of paediatric tracheal intubation after non-invasive ventilation failure. Pediatr Pulmonol 51:165–172

53. Bernet V, Hug MI, Frey B (2005) Predictive factors for the success of non-invasive mask ventilation in infants and children with acute respiratory failure. Pediatr Crit Care Med 6:660–664

54. Habashi NW (2005) Other approaches to open-lung ventilation: airway pressure release ventilation. Crit Care Med 33:5228–5240

55. Yehya N, Topjian AA, Thomas NJ, Friess SH (2014) Improved oxygenation 24 hours after transition to airway pressure release ventilation or high-frequency oscillatory ventilation accurately discriminates survival in immunocompromised pediatric patients with acute respiratory distress syndrome. Pediatr Crit Care Med 15:e147–e156

56. Yehya N, Topjian AA, Lin R, Breg PA, Thomas NJ, Friess SH (2014) High frequency oscillation and airway pressure release ventilation in pediatric respiratory failure. Pediatr Pulmonol 49:707–715

57. Walsh MA, Merat M, La Rotta G, Joshi P, Joshi V, Tran T, Jarvis S, Caldarone CA, Van Arsdell GS, Redington AN, Kavanagh BP (2011) Airway pressure release ventilation improves pulmonary blood flow in infants after cardiac surgery. Crit Care Med 39:2599–2604

58. Krishnan J, Morrison W (2007) Airway pressure release ventilation: a pediatric case series. Pediatr Pulmonol 42:83–88

59. de Carvalho WB, Koppelman BI, Gurgueira GL, Bonassa J (2000) Airway pressure release ventilation in postoperative cardiac surgery in pediatric patients. Rev Assoc Med Bras 46:166–173

60. Medina A, Modesto-Alapont V, Lobete C, Vidal-Mico S, Alvarez-Caro F, Pons- Odena M, Mayordomo-Colunga J, Ibiza-Palacios E, (2014) Is pressure-regulated volume control mode appropriate for severely obstructed patients? J Crit Care 29:1041–1045

61. Brenner B, Corbridge T, Kazi A (2009) Intubation and mechanical ventilation of the asthmatic patient in respiratory failure. Proc Am Thorac Soc 6:371–379

62. Arnold JH, Hanson JH, Toro-Figuero LO, Gutierrez J, Berens RJ, Anglin DL (1994) Prospective, randomized comparison of high-frequency oscillatory ventilation and conventional mechanical ventilation in pediatric respiratory failure. Crit Care Med 22:1530–1539

63. Gupta P, Green JW, Tang X, Gall CM, Gossett JM, Rice TB, Kacmarek RM, Wetzel RC (2014) Comparison of high-frequency oscillatory ventilation and conventional mechanical ventilation in pediatric respiratory failure. Pediatr Crit Care Med 15:499–504

64. Bateman ST, Borasino S, Asaro LA, Cheffetz IM, Diane S, Wypij D, Curley MA, Investigators RS (2016) Early high-frequency oscillatory ventilation in pediatric acute respiratory failure: a propensity score analysis. Am J Respir Crit Care Med 193:495–503

65. Kneyber MC, van Heerde M, Markhorst DG (2014) Is it too early to declare early or late rescue high-frequency oscillatory ventilation dead. JAMA Pediatr 168:861

66. Rimensberger PC, Bachman TE (2014) Is it too early to declare early or late rescue high-frequency oscillatory ventilation dead. JAMA Pediatr 168:862–863

67. Essouni S, Emeriaud G, Jouvet P (2014) Is it too early to declare early or late rescue high-frequency oscillatory ventilation dead. JAMA Pediatr 168:861–862

68. Ferguson ND, Cook DJ, Guyatt GH, Mehta S, Hand L, Austin P, Zhou Q, Matte A, Walter SD, Lamontagne F, Granton JT, Arabi YM, Arroliga AC, Stewart TE, Slutsky AS, Meade MO, Investigators OT, Canadian Critical Care Trials G (2013) High-frequency oscillation in early acute respiratory distress syndrome. N Engl J Med 368:795–805

69. Kneyber MC, van Heerde M, Markhorst DG (2012) Reflections on pediatric high-frequency oscillatory ventilation from a physiologic perspective. Respir Care 57:1496–1504

70. Sud S, Sud M, Friedrich JO, Meade MO, Ferguson ND, Wunsch H, Adhikari NK (2010) High frequency oscillation in patients with acute lung injury and acute respiratory distress syndrome (ARDS): systematic review and meta-analysis. BMJ 340:c3237.

71. Young D, Lamb SE, Shah S, Mackenzie I, Tunnicliffe W, Lall R, Rowan K, Cuthbertson BH, Group OS (2013) High-frequency oscillation for acute respiratory distress syndrome. N Engl J Med 368:806–813

72. Bojan M, Gioanni S, Mauriat P, Pouard P (2011) High-frequency oscillatory ventilation and short-term outcome in neonates and infants undergoing cardiac surgery: a propensity score analysis. Crit Care 15:R259
73. Li S, Wang X, Li S, Yan J (2013) High-frequency oscillatory ventilation for cardiac surgery children with severe acute respiratory distress syndrome. Pediatr Cardiol 34:1382–1388
74. Kocis KC, Meliones JN, Dekeon MK, Callow LB, Lupinetti FM, Bove EL (2000) Status asthmaticus treated by high-frequency oscillatory ventilation in children after Fontan operation. Pediatr Crit Care Med 3:144–147
75. Duval EL, Leroy PL, Gemke RJ, van Vught AJ (1999) High-frequency oscillatory ventilation in RSV bronchiolitis patients. Respir Med 93:435–440
76. Duval EL, Markhorst DG, Gemke RJ, van Vught AJ (2000) High-frequency oscillatory ventilation in pediatric patients. Neth J Med 56:177–185
77. Duval EL, van Vught AJ (2000) Status asthmaticus treated by high-frequency oscillatory ventilation. Pediatr Pulmonol 30:330–333
78. Kneyber MC, Plotz FB, Sibarani-Ponsen RD, Markhorst DG (2005) High-frequency oscillatory ventilation (HFOV) facilitates CO₂ elimination in small airway disease: the open airway concept. Respir Med 99:1459–1463
79. Davis DA, Russo PA, Greenspan JS, Speziali G, Spitzer A (1994) High-frequency jet versus conventional ventilation in infants undergoing Blalock-Taussig shunts. Ann Thorac Surg 57:846–849
80. Kocis KC, Meliones JN, Dekeon MK, Callow LB, Lupinetti FM, Bove EL (1992) High-frequency jet ventilation for respiratory failure after congenital heart surgery. Circulation 86(12):II32–II36
81. Meliones JN, Bow EL, Dekeon MK, Custer JR, Moler FW, Callow L, Wilton NC, Rosen DB (1991) High-frequency jet ventilation improves cardiac function after the Fontan procedure. Circulation 84(8):III64–III68
82. Rizkalla NA, Dominick CL, Fitzgerald JC, Thomas NJ, Yehya N (2014) High-frequency percussive ventilation improves oxygenation and ventilation in pediatric patients with acute respiratory failure. J Crit Care 29(3):e311–e317
83. Cortella J, Milac R, Herndon D (1999) High-frequency ventilation in pediatric patients with inhalation injury. J Burn Care Rehabil 20:232–235
84. Yehya N, Dominick CL, Connelly JT, Davis DH, Minneci PC, Deans KJ, Lober W, Moler FW, Callow L, Wilton NC, Rosen DB (1991) High-frequency jet ventilation improves cardiac function after the Fontan procedure. Circulation 84(8):III64–III68
85. Papazian L, Forlenza A, Ducharme-Crevier L, Massicotte E, Penot-Ragon C, Perrin G, Loundou A, Jaber S, Arnal JM, Perez D, Seghobian JM, Constantijn JM, Courant P, Lefranct JY, Guerin C, Prat G, Morange S, Roch A (2010) Neuromuscular blockers in early acute respiratory distress syndrome. N Engl J Med 363:1107–1116
86. Wilsterman ME, de Jager P, Blokpoel R, Freiachs I, Dijkstra SK, Albers MJ, Burgerhof JG, Markhorst DG, Kneyber MC (2016) Short-term effects of neuromuscular blockade on global and regional lung mechanics, oxygenation and ventilation in pediatric acute hypoxemic respiratory failure. Ann Intensive Care 6:103
87. Eriksson S, Schibler A, Numa A, Nuthall G, Yung M, Pascoe E, Wilkins B (2007) Acute lung injury in pediatric intensive care in Australia and New Zealand: a prospective, multicenter, observational study. Pediatr Crit Care Med 8:317–323
88. Kocis KC, Meliones JN, Dekeon MK, Callow LB, Lupinetti FM, Bove EL (1992) High-frequency jet ventilation for respiratory failure after congenital heart surgery. Circulation 86(12):II32–II36
89. Yehya N, Dominick CL, Connelly JT, Davis DH, Minneci PC, Deans KJ, Lober W, Moler FW, Callow L, Wilton NC, Rosen DB (1991) High-frequency jet ventilation improves cardiac function after the Fontan procedure. Circulation 84(8):III64–III68
90. Rizkalla NA, Dominick CL, Fitzgerald JC, Thomas NJ, Yehya N (2014) High-frequency percussive ventilation improves oxygenation and ventilation in pediatric patients with acute respiratory failure. J Crit Care 29(3):e311–e317
91. Cortella J, Milac R, Herndon D (1999) High-frequency ventilation in pediatric patients with inhalation injury. J Burn Care Rehabil 20:232–235
92. Papazian L, Forlenza A, Ducharme-Crevier L, Massicotte E, Penot-Ragon C, Perrin G, Loundou A, Jaber S, Arnal JM, Perez D, Seghobian JM, Constantijn JM, Courant P, Lefranct JY, Guerin C, Prat G, Morange S, Roch A (2010) Neuromuscular blockers in early acute respiratory distress syndrome. N Engl J Med 363:1107–1116
93. Wilsterman ME, de Jager P, Blokpoel R, Freiachs I, Dijkstra SK, Albers MJ, Burgerhof JG, Markhorst DG, Kneyber MC (2016) Short-term effects of neuromuscular blockade on global and regional lung mechanics, oxygenation and ventilation in pediatric acute hypoxemic respiratory failure. Ann Intensive Care 6:103
94. Eriksson S, Schibler A, Numa A, Nuthall G, Yung M, Pascoe E, Wilkins B (2007) Acute lung injury in pediatric intensive care in Australia and New Zealand: a prospective, multicenter, observational study. Pediatr Crit Care Med 8:317–323
95. Kocis KC, Meliones JN, Dekeon MK, Callow LB, Lupinetti FM, Bove EL (1992) High-frequency jet ventilation for respiratory failure after congenital heart surgery. Circulation 86(12):II32–II36
96. Yehya N, Dominick CL, Connelly JT, Davis DH, Minneci PC, Deans KJ, Lober W, Moler FW, Callow L, Wilton NC, Rosen DB (1991) High-frequency jet ventilation improves cardiac function after the Fontan procedure. Circulation 84(8):III64–III68
97. Wilsterman ME, de Jager P, Blokpoel R, Freiachs I, Dijkstra SK, Albers MJ, Burgerhof JG, Markhorst DG, Kneyber MC (2016) Short-term effects of neuromuscular blockade on global and regional lung mechanics, oxygenation and ventilation in pediatric acute hypoxemic respiratory failure. Ann Intensive Care 6:103
98. Eriksson S, Schibler A, Numa A, Nuthall G, Yung M, Pascoe E, Wilkins B (2007) Acute lung injury in pediatric intensive care in Australia and New Zealand: a prospective, multicenter, observational study. Pediatr Crit Care Med 8:317–323
99. Kocis KC, Meliones JN, Dekeon MK, Callow LB, Lupinetti FM, Bove EL (1992) High-frequency jet ventilation for respiratory failure after congenital heart surgery. Circulation 86(12):II32–II36
100. Yehya N, Dominick CL, Connelly JT, Davis DH, Minneci PC, Deans KJ, Lober W, Moler FW, Callow L, Wilton NC, Rosen DB (1991) High-frequency jet ventilation improves cardiac function after the Fontan procedure. Circulation 84(8):III64–III68
101. Wilsterman ME, de Jager P, Blokpoel R, Freiachs I, Dijkstra SK, Albers MJ, Burgerhof JG, Markhorst DG, Kneyber MC (2016) Short-term effects of neuromuscular blockade on global and regional lung mechanics, oxygenation and ventilation in pediatric acute hypoxemic respiratory failure. Ann Intensive Care 6:103
102. Panico FF, Troster EJ, Oliveira CS, Faria A, Lucena M, Joao PR, Saad ED, Foronda FA, Delgado AF, de Carvalho WB (2015) Risk factors for mortality and outcomes in pediatric acute lung injury/acute respiratory distress syndrome. Pediatr Crit Care Med 16:e194–e200
103. Chiumello D, Carlesso E, Cadringher P, Caironi P, Valenza F, Polli F, Tallarini F, Cozzi P, Cressoni M, Colombo A, Marinini J,Gattinoni L (2008) Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome. Am J Respir Crit Care Med 178:346–355
104. Chiumello D, Carlesso E, Cadringher P, Caironi P, Valenza F, Polli F, Tallarini F, Cozzi P, Cressoni M, Colombo A, Marinini J,Gattinoni L (2008) Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome. Am J Respir Crit Care Med 178:346–355
105. Chiumello D, Carlesso E, Cadringher P, Caironi P, Valenza F, Polli F, Tallarini F, Cozzi P, Cressoni M, Colombo A, Marinini J,Gattinoni L (2008) Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome. Am J Respir Crit Care Med 178:346–355
106. Panico FF, Troster EJ, Oliveira CS, Faria A, Lucena M, Joao PR, Saad ED, Foronda FA, Delgado AF, de Carvalho WB (2015) Risk factors for mortality and outcomes in pediatric acute lung injury/acute respiratory distress syndrome. Pediatr Crit Care Med 16:e194–e200
107. Chiumello D, Carlesso E, Cadringher P, Caironi P, Valenza F, Polli F, Tallarini F, Cozzi P, Cressoni M, Colombo A, Marinini J,Gattinoni L (2008) Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome. Am J Respir Crit Care Med 178:346–355
108. Chiumello D, Carlesso E, Cadringher P, Caironi P, Valenza F, Polli F, Tallarini F, Cozzi P, Cressoni M, Colombo A, Marinini J,Gattinoni L (2008) Lung stress and strain during mechanical ventilation for acute respiratory distress syndrome. Am J Respir Crit Care Med 178:346–355
151. Curley MA, Fackler JC (1998) Weaning from mechanical ventilation: patterns in young children recovering from acute hypoxic respiratory failure. Am J Crit Care 7:335–345
152. Newth CJ, Venkataraman S, Willson DF, Meert KL, Harrison R, Dean JM, Pollack M, Zimmerman J, Aranda KD, Carillo JA, Nicholson CE (2009) Weaning and extubation readiness in pediatric patients. Pediatr Crit Care Med 10:1–11
153. Foronda FK, Troster EI, Farias JA, Barbas CS, Ferraro AA, Faria LS, Bousoo A, Panico FF, Delgado AF (2011) The impact of daily evaluation and spontaneous breathing test on the duration of pediatric mechanical ventilation: a randomized controlled trial. Crit Care Med 39:2526–2533
154. Randolph AG, Forbes PW, Gedeit RG, Arnold JH, Wetzel RL, Cox PN, Arnold JH, Pediatric Acute Lung I, Sepsis Investigators N (2002) Effect of mechanical ventilator weaning protocols on respiratory outcomes in infants and children: a randomized controlled trial. JAMA 288:2561–2566
155. Schulz TR, Lin RJ, Watzman HM, Durning SM, Hales R, Woodson A, Francis B, Tyler L, Napoli L, Godinez RI (2001) Weaning children from mechanical ventilation: a prospective randomized trial of protocol-directed versus physician-directed weaning. Respir Care 46:772–782
156. Blackwood B, Murray M, Chisakuta A, Cardwell CR, O’Halloran P (2013) Protocolized versus non-protocolized weaning for reducing the duration of invasive mechanical ventilation in critically ill paediatric patients. Cochrane Database Syst Rev. CD009082
157. Jouvet P, Eddington A, Payen V, Bordessoule A, Emeriaud G, Gasco RL, Wysocki M (2012) A pilot prospective study on closed loop controlled ventilation and oxygenation in ventilated children during the weaning phase. Crit Care 16:R85
158. Jouvet P, Payen V, Gauvin F, Emeriaud G, Lacroix J (2013) Weaning children from mechanical ventilation with a computer-driven protocol: a pilot trial. Intensive Care Med 39:919–925
159. Rose L, Schultz MJ, Cardwell CR, Jouvet P, McAuley DF, Blackwood B, Pollack M, Zimmerman J, Anand KJ, Carcillo JA, Nicholson CE (2009) The endotracheal tube air leak test does not predict extubation outcome in critically ill pediatric patients. Pediatr Crit Care Med 10:1–11
160. Randolf AG, Forbes PW, Gedeit RG, Arnold JH, Wetzel RL, O’Neil ME, Venkataraman ST, Meet KL, Chifetz IM, Cox PN, Hanson JH, Pediatric Acute Lung I, Sepsis Investigators N (2005) Cumulative fluid intake minus output is not associated with ventilator weaning duration or extubation outcomes in children. Pediatr Crit Care Med 6:642–647
161. Tobin MJ (2012) Extubation and the myth of “minimal ventilator settings”. Am J Respir Crit Care Med 185:349–350
162. Manczur T, Greenough A, Nicholson GP, Rafferty GF (2000) Resistance of pediatric and neonatal endotracheal tubes: influence of flow rate, size, and shape. Crit Care Med 28:1595–1598
163. Khemani RG, Hotz J, Moroz K, Fink RC, Kamarer A, LaFortune M, Rafferty GF, Ross PA, Newth CJ (2016) Pediatric extubation readiness tests should not use pressure support. Intensive Care Med 42:1214–1222
164. Vianello A, Arcaro G, Braccioni G, Gallan F, Marchi MR, Chizio S, Zampieri D, Pogoraro E, Salvador V (2011) Prevention of extubation failure in high-risk patients with neuromuscular disease. J Crit Care 26:517–524
165. Bach JR, Goncalves MR, Hamdani I, Winck JC (2013) Extubation of patients with neuromuscular weakness: a new management paradigm. Chest 137:1033–1039
166. Hull J, Aniaparvan R, Chan E, Chatwin M, Forton J, Gallagher J, Gibson N, Gordon J, Hughes I, McCulloch R, Russell RR, Simonds A (2012) British Thoracic Society guideline for respiratory management of children with neuromuscular weakness. Thorax 67(Suppl 1):11–40
167. Racca F, Mongini T, Wolffer A, Vianello A, Cutrera R, Del Sorbo L, Capello EC, Gregoretti C, Massa R, de Luca D, Conti G, Tegazzini V, Tomasino A, Ranieri VM (2013) Recommendations for anesthesia and perioperative management of patients with neuromuscular disorders. Minerva Anestesiol 79:419–433
168. Bissonnette B, Sessler DI, LaFlamme PM (1989) Passive and active inspired gas humidification in infants and children. Anesthesiology 71:350–354
169. Bissonnette B, Sessler DI (1989) Passive or active inspired gas humidification increases thermal steady-state temperatures in anesthetized infants. Anesth Analg 69:783–787
170. Kelly M, Gillies D, Todd DA, Lockwood C (2010) Heated humidification versus heat and moisture exchangers for ventilated adults and children. Cochrane Database Syst Rev. CD004711
171. Leclerc F, Taille S, Lefrancois F, Deye N, Maggiore SM, Jouvet P, Ricard JD, Fumagalli B, Brochard L, Groupe de travail sur les Respirateurs de l’ECS, Gregoretti C, Massa R, de Luca D, Conti G, Tegazzini V, Tomasino A, Ranieri VM (2013) Recommendations for anesthesia and perioperative management of patients with neuromuscular disorders. Minerva Anestesiol 79:419–433
172. Chlopkowski B, Sessler DI, LaFlamme PM (1989) Passive and active inspired gas humidification in infants and children. Anesthesiology 71:350–354
173. Choong K, Chatrkaw P, Frndova H, Cox PN (2003) Comparison of loss in lung dynamics in mechanically-ventilated paediatric patients. Aust J Physiother 52:121–126
174. Hawkins P, Jones A (2015) What is the role of the physiotherapist in paediatric intensive care units? A systematic review of the evidence for
respiratory and rehabilitation interventions for mechanically ventilated patients. Physiotherapy 101:303–309.

192. Vianello A, Corrado A, Arcaro G, Gallan F, Ori C, Minuzzo M, Bevilacqua M (2005) Mechanical insufflation–exsufflation improves outcomes for neuromuscular disease patients with respiratory tract infections. Am J Phys Med Rehabil 84:83–88 (discussion 89–91).

193. Miske L, Hickey EM, Kollo SM, Werner DJ, Panitch HB (2004) Use of the mechanical in-exsufflator in pediatric patients with neuromuscular disease and impaired cough. Chest 125:1406–1412.

194. Faureux B, Guillemot N, Aubertin G, Nathan N, Labit A, Clement A, Chatwin M, Ross E, Hart N, Nickol AH, Polkey MI, Simonds AK (2003) Cough augmentation with mechanical insufflation/exsufflation in patients with neuromuscular weakness. Eur Respir J 21:502–508.

195. Racca F, Del Sorbo L, Mongini T, Vianello A, Ranieri VM (2010) Respiratory management of acute respiratory failure in neuromuscular diseases. Minerva Anestesiol 76:51–62.

196. Newth CJ, Rachman B, Patel N, Hammer J (2004) The use of cuffed versus uncuffed endotracheal tubes in pediatric intensive care. J Pediatr 144:333–337.

197. Weiss M, Dullenkopf A, Fischer JE, Keller C, Gerber AC, European Pediatric Endotracheal Intubation Study G (2009) Prospective randomized controlled multi-centre trial of cuffed or uncuffed endotracheal tubes in small children. Br J Anaesth 103:867–873.

198. Rabello L, Conceição C, Ebecken K, Lisboa T, Bozza FA, Soares M, Povoa P, Saliba J (2015) Management of severe community-acquired pneumonia in Brazil: a secondary analysis of an international survey. Rev Bras Ter Intensiva 27:57–63.

199. Boussaid G, Lofaso F, Santos DB, Vaugier I, Pottier S, Prigent H, Bahrami B (2008) Performance of ventilators for noninvasive positive-pressure ventilation in children. Eur Respir J 31:1300–1307.

200. Faureux B, Leroux K, Desmarais G, Isabey D, Clement A, Lofaso F, Louis B (2008) Performance of ventilators for noninvasive positive-pressure ventilation in children. Eur Respir J 31:1300–1307.

201. Hussein SG, Ryan CA, Murphy BP (2004) Comparison of three manual ventilation devices using an intubated mannequin. Arch Dis Child Fetal Neonatal Ed 89:F490–F493.

202. Boussaid G, Lofaso F, Santos DB, Vaugier I, Potier S, Prigent H, Bahrami S, Ohikowski D (2016) Impact of invasive ventilation on survival when non-invasive ventilation is ineffective in patients with Duchenne muscular dystrophy: a prospective cohort. Respir Med 115:26–32.

203. Rul B, Carnevale F, Estournet B, Ruder M, Herve C (2012) Tracheostomy and children with spinal muscular atrophy type I: ethical considerations in the French context. Nurs Ethics 19:408–418.

204. Benson RC, Hardy KA, Gildengorin G, Hsaia D (2012) International survey of physician recommendation for tracheostomy for spinal muscular atrophy type I. Pediatr Pulmonol 47:606–611.

205. Simonds AK (2007) Respiratory support for the severely handicapped child with neuromuscular disease: ethics and practicality. Sem Respir Crit Care Med 28:342–354.

206. Bush A (2006) Spinal muscular atrophy with respiratory disease (SMARD): an ethical dilemma. Intensive Care Med 32:1691–1693.

207. Yamaguchi M, Suzuki M (2013) Independent living with Duchenne muscular dystrophy and home mechanical ventilation in areas of Japan with insufficient national welfare services. Int J Qual Stud Health Well-being 8:20914.

208. Rimminsberger PC, Heullitt MJ, Meliones J, Pons M, Bronicki RA (2011) Mechanical ventilation in the pediatric cardiac intensive care unit: the essentials. World J Pediatr Congenit Heart Surg 2:609–619.

209. Bronicki RA, Penny DJ, Anas NG, Fuhrman B (2016) Cardiopulmonary Interactions. Pediatr Crit Care Med 17:S182–S193.

210. Shekerdemian L, Bohn D (1999) Cardiovascular effects of mechanical ventilation. Arch Dis Child 80:475–480.

211. Bronicki RA, Herrera M, Mink RB, Domico M, Tucker D, Chang AC, Anas NG (2010) Hemodynamics and cerebral oxygenation following repair of tetralogy of Fallot: the effects of converting from positive pressure ventilation to spontaneous breathing. Congen Heart Dis 5:416–421.

212. Jenkins J, Lynn A, Emdons J, Barker G (1985) Effects of mechanical ventilation on cardiopulmonary function in children after open-heart surgery. Crit Care Med 13:77–80.

213. Gregory GA, Emdons LH Jr, Kittlerman JA, Phibbs RH, Tooley WH (1975) Continuous positive airway pressure and pulmonary and circulatory function after cardiac surgery in infants less than three months of age. Anesthesiology 43:426–431.

214. Colgan FJ, Stewart S (1979) PEEP and CPAP following open-heart surgery in infants and children. Anesthesiology 50:336–341.

215. Kardos A, Vereczkey G, Szentirmai C (2005) Haemodynamic changes during positive-pressure ventilation in children. Acta Anaesthesiol Scand 49:649–653.

216. Levett JM, Pulpepper WS, Lin CY, Arcilla RA, Reploge RL (1983) Cardiovascular responses to PEEP and CPAP following repair of complicated congenital heart defects. Ann Thorac Surg 36:411–416.

217. Alexi-Meskishvili W, Falkowicz GE, Nikolajuk AP, Popen SA (1985) Hemodynamic changes during mechanical ventilation in infants and small children after open heart surgery. Thorac Cardiovasc Surg 33:215–217.

218. Vincent JL (2010) We should abandon randomized controlled trials in the intensive care unit. Crit Care Med 38:5334–5338.

219. Khemani RG, Newth CJ (2010) The design of future pediatric mechanical ventilation trials for acute lung injury. Ann J Respir Crit Care Med 182:1465–1474.

220. Conti G, Piastra M (2016) Mechanical ventilation for children. Curr Opin Crit Care 22:60–66.