**Extra supplemental material to**

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

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## 1. Methodology of PEMVECC

Practical aspects

The steering committee (SC) (MK (chair), DdL, PB, JB and PR) prepared and managed the PEMVECC initiative throughout the entire process (Figure 1). The SC was composed by the ESPNIC Respiratory section chairs and by the ESPNIC President and incoming or past-Presidents. The ESPNIC endorsed and approved the consensus conference. They defined the disease conditions to be discussed in PEMVECC. The following disease conditions were defined: a) normal lungs, b) obstructive / small airway disease, c) restrictive lung disease, d) mixed disease (i.e. obstructive and restrictive lung disease), e) congenital and chronic disease with acute deterioration, f) the cardiovascular patient, and g) lung hypoplasia syndromes (ESM Table 1). Ten European experts were identified by the SC on the basis of their international reputation as a researcher in the field of paediatric MV and presence of recent peer-reviewed publications in this field in the last 10 years. The SC also wanted to make sure that there was an even geographical distribution of experts coming from European countries. The above-mentioned topics were assigned to subgroups consisting of 3 experts, with one member of the SC acting as coordinator for each subgroup.

Review of the literature and drafting of the recommendations

A librarian of the University Medical Center Groningen performed an electronic literature search in PubMed and EMBASE between from inception and September 1st, 2015. A combination of medical subject heading terms and text words related mechanical ventilation and terms specific to each subgroup were used (see also electronic supplemental material). Identified publications were imported into a reference manager and duplicates removed. All experts of each subgroup screened all references for eligibility. Publications were eligible for the review if the following criteria were met: a) patients < 18 years of age on non-invasive support or mechanical ventilated for any reason, and b) studies were randomized and nonrandomized controlled trials, controlled before-and-after studies, cohort studies,

interrupted time series studies, historically controlled studies, cohort studies, cross-sectional studies, and uncontrolled longitudinal studies. Publications were excluded: if they had included children with any diseases exclusively linked to the perinatal period (eg. transient tachypnoea of the newborn, meconium aspiration syndrome or hyaline membrane disease); if they were case reports or case series with fewer than ten patients, review articles, commentary or editorial, and non-peer reviewed articles. After review of the literature, the experts drafted general and specific recommendations dictated by the disease conditions they were assigned to (short text) and to provide a context for these recommendations (long text). These recommendations were then submitted for voting.

For ventilator taxonomy, we used the proposal by Chatburn (Electronic Supplemental Material, Table 2) [1, 2].

Voting on the recommendations

The drafted recommendations were presented and discussed at a two-day meeting in Rome, Italy by all experts and members of the SC. The aim was not necessarily to reach a single and convergent opinion regarding all proposals, but to bring out the points of agreement, disagreement or equipoise with possible redrafting of individual recommendations. This final set of recommendations was subject to electronic voting in December 2015 using the RAND/UCLA appropriateness method scale [3]. Each expert and member of the SC rated all recommendations using a scoring system ranging from 1 (complete disagreement) to 9 (complete agreement) with each expert and member of the SC having an equal vote. After elimination of one lowest and one highest value, the median and confidence interval of the scores were calculated. A recommendation reached “strong agreement” if the median was between 7 – 9 and all experts rated the recommendation $\geq 7$. Recommendations were labelled “equipoise” if the median was between 7 – 9 but not all experts rated the recommendation $\geq 7$ or if the median was between 4 – 6, and “disagreement” if the median was between 1 – 3. All recommendations that did not reach

strong agreement in the first round were sent back to all experts and members for the SC for input on how it should be rephrased so that it could reach strong agreement. The SC redrafted these recommendations based on this input and subjected them to a second round of electronic voting (February 2016). The same approach was followed. Recommendations that did not reach strong agreement in the second round were classified as “weak agreement”. The percentage of agreement was calculated for these recommendations (i.e. the percentage of experts that rated the recommendation $\geq 7$) to quantify the level of disagreement. As it was expected a priori that there would be very little, if any, randomized controlled trials or systematic reviews, it was decided by the SC not to use the GRADE system but to keep the consensus guideline descriptive [4].

## 2. Disease definitions based on respiratory physiology

Healthy lungs

- Respiratory physiology: loss of respiratory drive, normal compliance, normal chest wall compliance, normal resistance
- Examples: patients who undergo elective ventilation for any reasons (e.g. surgery, procedural), emergency ventilation for depression of respiratory drive or acute neuromuscular disorder or semi – elective ventilation for underlying depression of respiratory drive or neuromuscular disorders

Obstructive respiratory disease

- Respiratory physiology: normal lung compliance, increased peripheral airway resistance leading to airflow limitation. Increased risk of dynamic hyperinflation potentially leading to intrinsic PEEP. Respiratory system compliance may be reduced at high lung volumes (overdistension)
- Examples: status asthmaticus, bronchopulmonary dysplasia, bronchiolitis obliterans, cystic fibrosis

Restrictive respiratory disease

- Respiratory physiology: reduced lung compliance and/or reduced chest wall compliance, normal airway resistance. inhomogeneous distribution of aeration, favouring the non-dependent lung. This leads to a reduced functional residual capacity (FRC) and increased physiological deadspace (Vd/Vt). The required pressure to open collapsed diseased lungs (and alveoli) and the pressure to maintain lung (or alveolar) volume is increased in acute restrictive lung disease. The closing pressure may be or is lower than the opening pressure. Recruitment and derecruitment are both time- and pressure dependent

- Examples: acute respiratory distress syndrome, pneumonia, pulmonary contusion, abdominal hypertension.

Mixed disease

- Respiratory physiology: reduced lung compliance and/or chest wall compliance. Respiratory system compliance can be reduced at low lung volumes or at high lung volumes (overdistension). Increased peripheral airway resistance resulting in airflow limitation. Increased risk for dynamic hyperinflation.
- Examples: status asthmaticus with both $CO_2$ retention and hypoxia due to acute lung injury, viral bronchiolitis / pneumonia, bronchopulmonary dysplasia with acute infection

Congenital and chronic restrictive disease

- Respiratory physiology: reduced compliance, reduced chest wall compliance, normal or increased resistance due to a congenital or chronic condition
- Examples: congenital diseases are linked to foetal and/or congenital conditions, such as congenital cystic adenomatous malformation, congenital lobar emphysema, chylothorax, congenital sequestration, congenital flail chest and other chest wall malformations, vascular lung malformations. Chronic restrictive include neuro-muscular diseases in severe phases, cerebral palsy, Jeune Syndrome, Jarcho-Levin Syndrome (spondylocostal dysostosis and spondylothoracic dysplasia), chest wall or spine abnormalities/deformities unrelated to the above described conditions

Lung hypoplasia syndromes including CDH

- Respiratory physiology: normal chest wall compliance, normal or reduced compliance and normal or increased resistance supposed to be related to lung hypoplasia
- Examples: congenital diaphragmatic hernia (various types), fibrotic post-ARDS lung hypoplasia, fibrotic post-radio or chemotherapy lung hypoplasia, Potter-like syndromes,

(lung hypoplasia associated to extreme prematurity, lung hypoplasia associated with multi-cystic kidney disease, lung hypoplasia associated to skeletal diseases (including Merckel-Grueber syndrome)), congenital unilateral lung hypoplasia/aplasia, congenital primitive fibrosis, certain massive pulmonary malformation treated by the section n°5 (e.g.: congenital pulmonary adenomatous malformation, giant sequestration, chylothorax) may also qualify if they cause a relative absence of functional lung tissue.

**3. Modes of respiratory support**

| Control variable | Breath sequence | Targeting scheme Primary, secondary breaths | Acronym | Examples |
|---|---|---|---|---|
| Volume | CMV | Set point | VC - CMVs | VC A/C |
| | IMV | Set point | VC – IMVs | VC SIMV |
| | | Set point (primary and secondary) | VC – IMVs,s, | VC SIMV + PS |
| Pressure | CMV | Set point | PC – CMVs | PC A/C |
| | | Adaptive | PC – CMVa | PRVC A/C |
| | IMV | Set point | PC-IMVs | PC SIMV |
| | | Set point (primary and secondary) | PC-IMVs,s | PC SIMV + PS |
| | | Adaptive | PC-IMVa | SIMV PRVC |
| | | Adaptive (primary), set point (secondary) | PC-IMVa,s | SIMV PRVC + PS |
| | | Adaptive (primary and secondary) | PC-IMVa,a | SIMV PRVC + VS |
| | CSV | Set point | PC – CSVs | PS |
| | | Adaptive | PC – CSVa | VS |

Adapted from [1, 2].

CMV continuous mandatory ventilation; IMV intermittent mandatory ventilation; CSV continuous spontaneous ventilation; VC – CMV volume controlled continuous mandatory ventilation**;** VC – IMV volume controlled intermittent mandatory ventilation; PC – CMV pressure controlled continuous mandatory ventilation**;** PC – IMV pressure controlled intermittent mandatory ventilation; PC – CSV pressure controlled spontaneous ventilation;

VC volume control; PC pressure control; A/C assist/control; SIMV synchronised intermittent mandatory ventilation; PS pressure support; VS volume support

Set point: the operator manually sets the targets; these are the same for all breaths.
Adaptive: the ventilator automatically determines the target pressure for each breath, the desired volume is set by the operator.

## 4. Full text of all recommendations

### A. General recommendations

1. The use of non-invasive ventilation should not delay endotracheal intubation and invasive ventilation if continued deterioration or failure to adequately improve. However, at present no specific cut-offs can be provided for any disease condition *(strong agreement)*
2. We recommend that in any triggered (non-invasive) positive pressure ventilation optimal patient ventilator synchrony should be targeted *(strong agreement)*
3. At present, there is insufficient data to provide a recommendation on the use of airway pressure release ventilation *(strong agreement)*
4. At present, there is insufficient data to provide a recommendation on high-frequency jet ventilation or high-frequency percussive ventilation *(strong agreement)*
5. We recommend against using liquid ventilation *(strong agreement)*
6. In the most severe cases, controlled mechanical ventilation (pressure or volume) should be preferred mandating the need for sedation and/or muscle relaxants. There is no agreement either mode to be preferential over other modes *(strong agreement)*
7. If the respiratory drive has been restored, pressure support ventilation may be considered for allowing the child to breath spontaneously. If this mode is used, the sensitivity of the flow cycling and rise time should be set to obtain a short inspiratory time *(strong agreement)*
8. We recommend that in the absence of data PEEP should always be set finding optimal balance between haemodynamics and oxygenation. In severe paediatric ARDS high levels of PEEP may be needed *(strong agreement)*
9. We recommend that extra-corporeal devices (ECMO or other devices) should be considered where available in reversible diseases if conventional and/or HFOV fails. If no ECMO is available, early consultation of an ECMO center is recommended because transporting patients who need ECMO can be hazardous *(strong agreement)*

10. At present, there is insufficient paediatric data to provide recommendations on the optimal interface for CPAP *(strong agreement)*
11. At present, there is insufficient paediatric data to provide recommendations on the optimal interface for non-invasive ventilation. However, we recommend that any interface with the least leakage needs to be used *(strong agreement)*
12. We recommend that, dependent on local experiences and materials, total-face mask, oral-nasal mask or helmet should be preferred for non - invasive ventilatory support *(93% agreement)*
13. Maintaining a clear airway is essential to mechanically ventilated children. There are insufficient data to support a recommendation on using an in-line suctioning system versus “open” suctioning. However, consideration should be given to the technique of suctioning with careful attention to minimize the potential for derecruitment *(strong agreement)*
14. The routine instillation of isotonic saline prior to endotracheal suctioning is not recommended. However, the instillation of isotonic saline prior to endotracheal suctioning may be indicated at times for lavage to remove thick tenacious secretions *(strong agreement)*
15. In the absence of evidence, based on adult data we recommend that all children should be maintained with the head of the bed elevated to 30-45 degrees, unless specific disease conditions may dictate otherwise *(strong agreement)*
16. At present, there is insufficient paediatric data to recommend chest physiotherapy as a standard of care in mechanically ventilated children *(strong agreement)*
17. We recommend airway humidification in ventilated patients. However, there is insufficient paediatric data to recommend on the approach to humidification (i.e. active or passive humidification) *(strong agreement)*
18. We recommended setting the inspiratory time and respiratory rate related respiratory system mechanics. Further adjustments may be needed to according to underlying disease and clinical evolution. Of importance, inspiratory time and rate are closely

correlated and cannot be judged independent from each other *(strong agreement)*

19. At present, there is insufficient paediatric outcome data to recommend on closed – loop ventilation in any mechanically ventilated patient *(strong agreement)*
20. We recommend that endotracheal high-volume low-pressure cuffed tubes can be used in all children. Meticulous attention to cuff pressure monitoring is indicated *(strong agreement)*
21. We recommend that all patients on respiratory support should preferably breath spontaneously, with the exception of the most severely ill patient requiring very high ventilator settings and intermittent neuromuscular blockade *(strong agreement)*
22. We recommend that caution is advised when using sedation and relaxation in paediatric patients with altered cardiac function of different origin *(strong agreement)*

**B. Monitoring**

1. We recommend that $CO_2$ monitoring should be used in every child on conventional mechanical ventilation, preferably end-tidal $CO_2$. Attention must be paid the the added dead space when measuring end-tidal $CO_2$ *(strong agreement)*
2. We recommend that transcutaneous saturation ($SpO_2$) monitoring should be used in every ventilated child *(strong agreement)*
3. At present, we cannot recommend a specific lower or upper target for $SpO_2$ for any ventilated non-cardiac patient – by whatever means - with obstructive airway, restrictive disease or mixed disease *(strong agreement)*
4. We recommend adhering to the PALICC guidelines for patients who meet the pediatric ARDS criteria (i.e. $SpO_2$ generally 92 – 97% when PEEP is less than 10 $cmH_2O$ and 88 – 92% when the PEEP is 10 cmH2O or higher) *(strong agreement)*
5. We recommend that tidal volumes should be measured proximally (i.e. near the Y-piece of the patient circuit) in small children *(strong agreement)*
6. At present, there is insufficient paediatric data to recommend routine volumetric capnography. However, we suggest using volumetric capnography to measure and

assess changes in physiologic dead space in ventilated patients with lung disease *(Strong agreement)*

7. We recommend measuring intrinsic PEEP and plateau pressure during zero-flow conditions to obtain static compliance during mechanical ventilation in patients with or without lung disease *(93% agreement)*
8. We suggest that for patients with restrictive lung diseases measuring the trend in dynamic compliance may offer additional information about the disease course, although this needs to be judged in relation to ventilator settings *(87% agreement)*
9. We suggest that pulse oximetry is usually sufficient to assess oxygenation in ventilated patients with mild disease and patients on non-invasive ventilation *(strong agreement)*
10. We recommend using indwelling arterial lines in more severely ill patients on invasive ventilation, allowing $PaO_2$ measurements for an accurate assessment of oxygenation and measurements of pH and lactate *(strong agreement)*
11. We suggest that there is no strict indication for using indwelling arterial lines for the purpose of $pCO_2$ measurements *(93% agreement)*
12. We suggest that capillary $pCO_2$ is sufficient to assess gas exchange in ventilated patients with mild disease and patients on non-invasive ventilation *(strong agreement)*
13. We recommend that venous $pCO_2$ measurements are of limited use in providing reliable information about ventilatory gas exchange. They might be used for following evolution of disease *(strong agreement)*
14. In the absence of evidence, we suggest that transcutaneous $CO_2$ measurements may be considered in very young children and neonates; their value in older patients is unclear
15. At present, there is insufficient paediatric data to recommend the routine use of lung ultrasound as monitoring tool. In appropriately trained hands it can provide immediate bedside information about air leak, lung fluid status, pleural effusions and lung expansion *(strong agreement)*
16. We recommend monitoring central venous saturation ($SvO_2$ and/or arterial lactate

invasively mechanically ventilated patients with severe lung injury to assess the presence or absence of oxygen debt *(strong agreement)*

17. We recommend monitoring central venous saturation ($SvO_2$) in invasively and non-invasively mechanically ventilated cardiac patients as an indirect complementary marker for assessing cardiac output *(strong agreement)*
18. By observing the flow - time and/or flow - volume curve and/or measurement of total PEEP, it may be possible to set the appropriate expiratory time to allow the emptying of the lungs *(strong agreement)*

**C. Targets**

1. We recommend that $SpO_2$ > 95% at room air should be expected in patients with any normal lungs in the absence of extra-pulmonary manifestations *(strong agreement)*
2. At present, we cannot recommend a specific upper or lower target for $SpO_2$ for cardiac patients. In patients 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)*
3. We recommend achieving normal $CO_2$ levels in patients for elective ventilation in patients with normal lungs.
4. We recommend that for acute, non-pulmonary patients higher levels of $CO_2$ may be accepted unless specific disease conditions dictate otherwise. However, we cannot recommend on a specific pH limit. In the absence of evidence, we recommend to use permissive hypercapnia aiming for a pH > 7.20 *(strong agreement)*

**D. Supportive measures**

1. We recommend avoiding the routine use of hand-ventilation. If hand-ventilation is needed, pressure measurements or pressure pop – up valves should be used *(strong agreement)*
2. In the absence of evidence, we recommend that using cough-assist techniques should be considered for patients with neuromuscular disease who are on non-invasive ventilation modes *(strong agreement)*
3. We recommend reducing dead space apparatus as much as possible by using appropriate patient circuits and reduction of swivels *(strong agreement)*

**E. Weaning and extubation readiness**

1. At present, there is insufficient paediatric data to provide recommendations on the timing of initiation of weaning. In the absence of evidence, we recommend to start weaning as early as possible *(strong agreement)*
2. At present, there is insufficient paediatric data to provide recommendations on any specific weaning approach in ventilated children, irrespective of approach to ventilation (invasive, non-invasive) *(strong agreement)*
3. At present, there is insufficient paediatric data to recommend the routine use of non-invasive respiratory support after extubation. However, early application of non-invasive ventilation combined with cough-assist techniques should be considered in patients with neuromuscular diseases *(strong agreement)*
4. At present, there is insufficient paediatric data to provide recommendations on the routine use of any extubation readiness testing approach that is superior to clinical judgement in invasively ventilated children *(strong agreement)*
5. We recommend using corticosteroids in patients at increased risk for post-extubation stridor. However, the optimal dosage and timing is unclear *(strong agreement)*
6. At present, there is insufficient paediatric data to recommend the routine use of non-invasive respiratory support after extubation. However, early application of non-invasive

ventilation combined with cough-assist techniques should be considered in patients with neuromuscular diseases *(strong agreement)*

**F. Normal lungs**

1. At present, we cannot recommend on the optimal mode of ventilation (i.e. volume controlled versus pressure controlled) for patients with normal lungs *(strong agreement)*
2. At present, we cannot recommend a specific plateau pressure limit. In the absence of evidence, we recommend that delta pressure (i.e. the difference between end inspiratory and end expiratory pressure) levels should be expected to be less than 10 $cmH_2O$ for normal lungs *(strong agreement)*
3. We recommend using tidal volumes in the physiologic range (i.e. 5 - 8 mL/kg ideal bodyweight according to national growth charts) *(strong agreement)*
4. In the absence of evidence, we recommend using a certain level of PEEP in invasively mechanically ventilated children with healthy lungs to prevent alveolar collapse. However, we cannot provide any recommendation of how much PEEP should be used in these patients. Physiological data in children without lung injury suggests a range of 3 – 5 $cmH_2O$ *(strong agreement)*
5. At present, there is insufficient paediatric outcome data to recommend any lung recruitment manoeuvre in patients without lung injury *(strong agreement)*
6. At present, we cannot provide specific recommendations for the approach to ventilation mode or type of support for chronic neuromuscular patients and patients on chronic ventilation who have normal lungs. Also, we cannot provide any specific recommendations on any assisted mode of ventilation for chronic neuromuscular patients. However, preservation of spontaneous breathing should be aimed for these patients *(strong agreement)*

**G. Obstructive diseases**

1. There is insufficient paediatric outcome data to recommend on the routine use of high

flow nasal cannula in patients with obstructive airway disease *(strong agreement)*

2. There is insufficient paediatric outcome data to recommend on the routine use of CPAP and/or bi-level non-invasive ventilation in patients with obstructive airway disease. However, its use may be considered if there are no contra-indications (*strong agreement) i*
3. For invasive ventilation, there is insufficient paediatric data supporting which modalities of ventilation should be preferred: volume controlled ventilation (VC CMV), pressure controlled ventilation (PC CMVV) or pressure controlled with volume-targeted ventilation *(strong agreement)*
4. At present, there is no paediatric data to guide recommendations on the optimal tidal volume for patients with obstructive diseases. However, we recommend avoiding tidal volumes larger than 10 mL/kg ideal bodyweight in any circumstances *(strong agreement)*
5. At present, we cannot recommend a specific plateau pressure limit. In the absence of evidence, we propose to limit the plateau pressure to 30 $cmH_2O$ *(strong agreement)*
6. At present, there is no paediatric data to recommend on any acceptable distending airway pressure gradient (i.e. the difference between PIP and PEEP) *(strong agreement)*
7. At present, there is no paediatric data to recommend a specific level of external PEEP in sedated and/or paralysed patients who have sufficient expiratory times. However, assessing the level of intrinsic PEEP and plateau pressure may guide setting external PEEP in patients with air trapping who are mechanically ventilated and sedated *(strong agreement)*
8. At present, there is insufficient paediatric data to recommend on the use of high-frequency oscillatory ventilation for patients with obstructive disease *(strong agreement)*
9. In the most severe cases, controlled mechanical ventilation (pressure or volume) should be preferred mandating the need for sedation and/or muscle relaxants. There is no agreement either mode to be preferential over other modes *(strong agreement)*

10. By observing the flow - time and/or flow - volume curve and/or measurement of total PEEP, it may be possible to set the appropriate expiratory time to allow the emptying of the lungs *(strong agreement)*
11. At present, there is insufficient data to provide any recommendations on the use of heliox in patients with obstructive disease *(strong agreement)*
12. At present, there is insufficient data to provide any recommendations on the use of NAVA in patients with obstructive disease *(strong agreement)*
13. We recommend that high-frequency jet ventilation should not be used because of the risk of dynamic hyperinflation *(strong agreement)*

**H. Restrictive diseases**

1. There is insufficient paediatric outcome data to recommend on the routine use of high flow nasal cannula in patients with restrictive disease *(strong agreement)*
2. There is insufficient paediatric outcome data to recommend on the routine use of CPAP and/or bi-level non-invasive ventilation in patients with restrictive disease. However, its use may be considered if there are no contra-indications *(93% agreement)*
3. We suggest that in patients fulfilling mild-to-moderate ARDS criteria, non-invasive ventilation may be considered but this should not delay endotracheal intubation when indicated *(strong agreement)*
4. For invasive ventilation, there is insufficient paediatric data supporting which modalities of ventilation should be preferred: volume controlled ventilation (VC CMV), pressure controlled ventilation (PC CMV) or pressure controlled with volume-targeted ventilation. Therefore, we cannot recommend on the mode of ventilation for these patients *(strong agreement)*
5. At present, there is no paediatric data to recommend on any acceptable distending airway pressure gradient (i.e. the difference between PIP and PEEP) *(strong agreement)*
6. At present, there is no paediatric data to guide recommendations on the optimal tidal

volume for patients with acute restrictive lung disease. However, we recommend avoiding tidal volumes larger than 10 mL/kg ideal bodyweight in any circumstances *(strong agreement)*

7. In the absence of transpulmonary pressure measurements, we recommend an inspiratory plateau pressure limit of 28 cm water pressure *(87% agreement)*
8. In the absence of transpulmonary pressure measurements, we recommend an inspiratory plateau pressure limit of 29 – 32 cm water pressure as a rule of thumb for patients with increased chest wall elastance (i.e., reduced chest wall compliance) *(93% agreement)*
9. We recommend that high respiratory rate should be used to compensate for low tidal volume and maintain minute ventilation *(strong agreement)*
10. We recommend that in order to improve oxygenation, PEEP titration should be attempted. There is not a defined method to set the best PEEP. PEEP should always be set finding optimal balance between haemodynamics and oxygenation. In severe paediatric ARDS high levels of PEEP may be needed *(strong agreement)*
11. At present, there is insufficient paediatric outcome data to recommend any lung recruitment manoeuvre in patients with restrictive disease *(strong agreement)*
12. We recommend that HFOV may be considered in failing conventional ventilation, using an open lung strategy to obtain optimal lung volume *(strong agreement)*
13. We recommend adhering to the paediatric acute lung injury consensus collaborative (PALICC) recommendations on the use of nitric oxide, neuromuscular blockade, prone positioning, and surfactant use *(strong agreement)*

**I. Mixed disease**

1. There is insufficient paediatric outcome data to recommend on the routine use of high flow nasal cannula in patients with mixed disease *(strong agreement)*
2. We recommend that a non-invasive CPAP trial should be considered as a first approach if the clinical condition does not dictate otherwise *(strong agreement)*

3. In the absence of evidence, we recommend that the use of NIV can be considered before resorting to intubation, although there is no data on patient outcome *(strong agreement)*
4. At present, there is no paediatric data to recommend one method of non-invasive support over the other. Therefore, no specific recommendations when to use which mode of non-invasive support can be provided *(strong agreement)*
5. For invasive ventilation, there is insufficient paediatric data supporting which modalities of ventilation should be preferred: volume controlled ventilation (VC CMV), pressure controlled ventilation (PC CMV) or pressure controlled with volume-targeted ventilation. Therefore, we cannot recommend on the mode of ventilation for these patients *(strong agreement)*
6. At present, there is no paediatric data to guide recommendations on the optimal tidal volume. However, we recommend avoiding tidal volumes larger than 10 mL/kg ideal bodyweight in any circumstances *(strong agreement)*
7. We recommend adhering to the paediatric acute lung injury consensus collaborative (PALICC) recommendations on the use of nitric oxide, neuromuscular blockade, prone positioning, and surfactant use *(strong agreement)*
8. At present, there is no paediatric data to recommend a specific level of external PEEP in sedated and/or paralysed patients who have sufficient expiratory times. However, measuring the level of intrinsic PEEP and monitoring plateau pressure may guide setting external PEEP. A balance needs to be found between alveolar recruitment and alveolar over distension *(strong agreement)*
9. In the absence of transpulmonary pressure measurements, we recommend an inspiratory plateau pressure limit of 28 cm water pressure, allowing for slightly higher plateau pressures (29–32 cm water pressure) for patients with increased chest wall elastance (i.e., reduced chest wall compliance) *(strong agreement)*
10. At present, there is no paediatric data to recommend on any acceptable distending airway pressure gradient (i.e. the difference between PIP and PEEP) *(strong*

*agreement)*

11. At present, there is insufficient paediatric outcome data to recommend any lung recruitment manoeuvre in patients with mixed disease *(strong agreement)*
12. We recommend that HFOV may be considered in failing conventional ventilation, using an open lung strategy to obtain optimal lung volume *(strong agreement)*

**J. Chronically ventilated / congenital patient**

1. In severe or progressing underlying disease, we recommend considering whether invasive ventilation is beneficial for the particular child or not *(strong agreement)*
2. At present, we cannot provide specific recommendations for the approach to ventilation mode (i.e. non-invasive or invasive) or type of support for chronic neuromuscular patients and patients on chronic ventilation with acute deterioration. For these patients and for patients without long-term ventilation, the same recommendations as for patients with acute restrictive, acute obstructive or mixed disease are applicable *(strong agreement)*
3. At present, we cannot provide any specific recommendations on any assisted mode of ventilation for chronic neuromuscular patients and patients on chronic ventilation with acute deterioration. For these patients and for patients without long-term ventilation, the same recommendations as for patients with acute restrictive, acute obstructive or mixed disease are applicable *(strong agreement)*
4. In acute deterioration, for non-invasive and invasive ventilation, there is no paediatric data supporting which modalities of ventilation should be preferred: volume controlled ventilation (VC CMV), pressure controlled ventilation (PC CMV) or pressure controlled with volume targeted ventilation *(strong agreement)*
5. In acute deterioration, for non-invasive and invasive ventilation, there is no paediatric data supporting which modalities of ventilation should be preferred: volume controlled ventilation (VC CMV), pressure controlled ventilation (PC CMV) or pressure controlled with volume targeted ventilation *(strong agreement)*

6. At present, there is no paediatric data to guide recommendations on the optimal tidal volume. However, we recommend avoiding tidal volumes larger than 10 mL/kg ideal bodyweight in any circumstances *(strong agreement)*
7. In the absence of transpulmonary pressure measurements, we recommend an inspiratory plateau pressure limit of 28 cm water pressure, allowing for slightly higher plateau pressures (29–32 cm water pressure) for patients with increased chest wall elastance (i.e., reduced chest wall compliance) *(strong agreement)*
8. In the absence of evidence, based on adult data we recommend that for patients with reduced lung volumes, the driving pressure (Vt / Crs) target may dictate the optimal tidal volume *(strong agreement)*
9. In the absence of paediatric data, we recommend that early HFOV and/or extra-corporeal life support might be considered when conventional ventilation fails *(93% agreement)*
10. We recommend that high levels of PEEP may be used to stabilize airways in ventilated patients with trachea- and/or bronchomalacia. Careful titration of PEEP using is mandated to avoid cardiovascular compromise *(strong agreement)*
11. We recommend using double limb circuits for invasive ventilation *(strong agreement)*
12. We recommend preferentially using single limb circuit during NIV *(93% agreement)*

**K. Cardiac**

1. We recommend that CPAP or NIV can be used in patients with mild to moderate cardiorespiratory failure *(strong agreement)*
2. For invasive ventilation, there is insufficient paediatric data supporting which modalities of ventilation should be preferred: volume controlled ventilation (VC CMV), pressure controlled ventilation (PC CMV) or pressure controlled with volume-targeted ventilation *(strong agreement)*
3. We recommend that careful use of HFOV can be considered in cardiac patients who developed severe respiratory failure. Particular caution is advised in patients with

passive pulmonary blood flow or right ventricular dysfunction *(strong agreement)*

4. We recommend that positive pressure ventilation can be used to reduce work of breathing and decrease afterload in LV failure. In RV failure or passive blood flow it will reduce work of breathing but is likely to increase afterload *(strong agreement)*
5. At present, there is no paediatric data to guide recommendations on the optimal tidal volume for cardiac patients. However, we recommend avoiding tidal volumes larger than 10 mL/kg ideal bodyweight in any circumstances *(strong agreement)*
6. At present, we cannot recommend a specific level of PEEP in cardiac patients, irrespective of whether or not there is increased pulmonary blood flow. Based on physiology, we recommend using PEEP to maintain end-expiratory lung volume *(strong agreement)*
7. At present, there is insufficient paediatric outcome data to recommend any lung recruitment manoeuvre in cardiac patients. However, since these manoeuvres may be necessary in cardiac patients with severe pulmonary conditions, we suggest that the manoeuvres can be considered safe and feasible in cardiac patients *(strong agreement)*
8. We recommend that careful use of HFOV can be considered in cardiac patients who developed severe respiratory failure. Particular caution is advised in patients with passive pulmonary blood flow or right ventricular dysfunction *(strong agreement)*
9. We recommend that in cardiac patients with additional restrictive or obstructive lung disease the principles for that specific pathology will apply, but titration of ventilator settings should be done even more carefully *(strong agreement)*
10. We recommend that increasing $FiO_2$ up to 1,0 in life-threatening acute pulmonary hypertension crisis may be required *(strong agreement)*
11. In patients at risk for pulmonary hypertension, we recommend to maintain normal pH *(strong agreement)*
12. We recommend using pH as one non-pharmacologic tool to modify the pulmonary vascular resistance for specific disease conditions *(strong agreement)*

**L. Lung hypoplasia**

1. We recommend that recommendations proposed for patients with acute restrictive, obstructive or mixed disease are also applicable to patients with lung hypoplasia syndromes who suffer from acute deterioration *(strong agreement)*
2. At present, there is insufficient paediatric data to guide a recommendation on optimal tidal volume for these patients. Tidal volumes may be smaller than conventional because of lower residual lung volume in these patients *(strong agreement)*

## 5. Relevant papers published since voting

Targets for oxygenation and ventilation

In a pilot multicenter randomized clinical trial, Panwar *et al* assessed the feasibility of a conservative oxygenation strategy (target $SpO_2$ 88–92%) compared with a liberal oxygenation strategy (target $SpO_2$ >96%) during invasive mechanical ventilation in adult ICU patients [5]. No significant between-group differences in any measures of new organ dysfunction, or ICU or 90-day mortality were found. In another single-centre, open-label, randomized clinical trial, 434 ICU patients were randomly assigned to receive conservative oxygen therapy ($PaO_2$ between 70 and 100 mm Hg or $SpO_2$ between 94% and 98%) or conventional oxygen therapy ($PaO_2$ values up to 150 mm Hg or $SpO_2$ values between 97% and 100%) [6]. The aim was to assess whether a conservative protocol for oxygen supplementation could improve outcomes in patients admitted in ICU. Despite the study was stopped early due to difficulties in enrolment, mortality was significantly lower in the conservative oxygen therapy group (11.6% vs 44% respectively). Since no paediatric patients were included, this study will not affect our recommendations but underscore the need for paediatric investigations.

Non–invasive support

For high – flow nasal cannula (HFNC), some papers of interest were published since voting on the recommendations. Milesi and colleagues performed a randomised controlled trial in five paediatric intensive care units (PICU) to compare 7 $cmH_2O$ nCPAP with 2 L/kg/min high-flow oxygen therapy in infants < 6 months with moderate to severe acute viral bronchiolitis [7]. nCPAP was associated with a lower failure rate and non-inferiority of high-flow oxygen therapy could not be confirmed. This study suggests that nCPAP may be more efficient for initial respiratory support in this patient category. The effect on our recommendations would be that we would recommend against initial use of high-flow oxygen therapy in moderate-to-severe acute bronchiolitis and suggest that nCPAP is probably better than HFNC during the

initial phase of moderate to severe bronchiolitis. A single-center cohort study reported that the use of HFNC delayed non-invasive ventilation with inherent prolonged length of respiratory support and PICU stay in paediatric status asthmaticus, but this study has no effect on our recommendations [8]. From a systematic review and meta-analysis of adult data it was concluded that the use of high-flow oxygen therapy compared with usual care had no effect on mortality or intubation rates [9]. However, four recent RCTs in adults showed a clear benefit of HFNC over NIV in terms of patient outcome [10-13]. Since no paediatric patients were included in these studies, they will not affect our recommendations but underscore the need for paediatric investigations. A trial in adults reduced intubation rates and lower mortality in those who were managed with a helmet as opposed to a face mask, underscoring the need for paediatric explorations [14].

HFOV

Sud and co-workers updated their previous systematic review on high – frequency oscillatory ventilation (HFOV) in acute respiratory distress syndrome (ARDS), adding two published adult trials [15]. The findings of this systematic review were that HFOV did not reduce hospital and 30-day mortality due to ARDS, although the quality of evidence was very low. The effect of this systematic review on our recommendations are none, since there was no new paediatric data incorporated. Individual patient data meta-analysis of the OSCILLATE trial suggested that early HFOV may reduce mortality in those with severe ARDS, calling for proper patient stratification when using rescue therapies [16]. In fact, in the Gupta paper, early HFOV was associated with improved patient outcome [17].
Rowan and co-workers studied the current respiratory practice patterns in N = 222 paediatric haematopoietic stem cell recipients and noted that a more aggressive approach including endotracheal intubation and “early” HFOV was feasible and may offer an opportunity to improve outcomes [18].

Supportive measures

A recent systematic review in adults on head elevation concluded that a semi-recumbent position (≧ 30º) might reduce clinically suspected ventilator-associated pneumonia compared to a 0° to 10° supine position, although the available adult was seriously limited with a high risk of bias [19]. Since no paediatric patients were included, this study will not affect our recommendations but underscore the need for paediatric investigations.

Weaning and extubation

Faustino and co-workers performed a secondary analysis of data from the Randomized Evaluation of Sedation Titration for Respiratory Failure (RESTORE) clinical trial, showing that an extubation readiness test ($FiO_2$ 0.50, PEEP 5 $cmH_2O$ and pressure support) should be considered at least daily if the oxygenation index is less than or equal to 6 [20]. Once passed, there was a high likelihood of successful extubation. This study further adds to the need for ERTs in ventilated children.

**Table: relevant studies published since voting**

| Ref | Subject | Type of study | Main findings | Effect on recommendations |
|---|---|---|---|---|
| *Non–invasive support* | | | | |
| [7] | HFNC | RCT | nCPAP was associated with a lower failure rate; no non-inferiority of high-flow oxygen therapy | Recommend against initial use of high-flow oxygen therapy in moderate-to-severe acute bronchiolitis and suggest that nCPAP is probably better than HFNC during the initial phase of moderate to severe bronchiolitis |
| [8] | HFNC | Retrospective observational study | Use of HFNC delayed use of NIV and increased morbidity in severe asthma | None; no randomised controlled trial |
| [9] | HFNC | Systematic review | High-flow oxygen therapy compared with usual care had no effect on mortality or intubation rates | None; only adult data |
| [10] | HFNC | RCT | High-flow oxygen therapy was not associated with increased reintubation rates | None; only adult data |
| [11] | HFNC | RCT | High-flow nasal cannula oxygen compared with conventional oxygen therapy reduced the risk of reintubation within 72 hours | None; only adult data |

| | | | | |
|---|---|---|---|---|
| [12] | HFNC | RCT | High-flow oxygen therapy was not associated with increased reintubation rates | None; only adult data |
| [13] | HFNC | RCT | High-flow oxygen therapy was associated with lower 90-day mortality | None; only adult data |
| [14] | NIV | RCT | NIV through helmet was associated with lower intubation rates compared with face mask | None; only adult data |
| *Ventilator mode* | | | | |
| [15] | HFOV | Systematic review | HFOV does not reduce hospital and 30-day mortality due to ARDS | None; no new paediatric data added |
| [16] | HFOV | Individual patient data meta-analysis | HFOV may reduce mortality in severe ARDS | None; no paediatric data |
| *Supportive measures* | | | | |
| [18] | Patient selection | Retrospective study | A more aggressive approach to children after haematopoietic stem cell transplantation was safe and feasible | None; observational cohort. Food for thought |
| [19] | Positioning | Systematic review | Head elevation ≥ 30º may reduce risk of VAP | None; only adult data in systematic review |

| | | | | |
|---|---|---|---|---|
| *Weaning* | | | | |
| [20] | Extubation readiness testing | Post-hoc analysis of randomised controlled trial | Consider daily extubation readiness testing if oxygenation index < 6 | Perform daily extubation readiness testing |
| *Targets of oxygenationan and ventilation* | | | | |
| [21] | $SpO_2/FiO_2$ | Retrospective study | $SpO_2/FiO_2$ may also be suitable when the $SpO_2$ > 97% | $SpO_2/FiO_2$ reflects $PaO_2/FiO_2$ irrespective of $SpO_2$ range. However, study is retrospective. |

## 6. Monitoring

Monitoring of ventilation

**Indwelling arterial lines are not mandated for $PCO_2$ measurements *(93% agreement)*. Capillary $PCO_2$ is sufficient to assess gas exchange in mild disease and during NIV (*strong agreement*). Venous $PCO_2$ measurements provide limited information but could be used as a trend to assess the disease trajectory *(strong agreement)*. We suggest considering transcutaneous $CO_2$ measurements in very young children and neonates; their value in older patients is unclear (*strong agreement)***

Capillary $PCO_2$ adequately reflects arterial $PCO_2$ in the absence of (severe) hypotension or poor peripheral perfusion, thereby not mandating indwelling arterial lines [22-24]. Alternatively, central but not peripheral venous $PCO_2$ can be monitored albeit that it poorly correlates with $PaCO_2$ [22, 25-27]. Transcutaneous $CO_2$ ($TcCO_2$) monitoring may be applicable in infants and older children [28-33].

**Capnography, preferably end-tidal $CO_2$ (ET- $CO_2$), should be used during conventional MV. Added dead space when measuring ET- $CO_2$ should be minimal, especially in small children *(strong agreement)*. There is insufficient data to recommend routine volumetric capnography. However, we suggest using volumetric capnography to assess changes in physiologic dead space in ventilated children with restrictive lung disease (*strong agreement*)**

Monitoring end-tidal $CO_2$ (ET-$CO_2$) allowing for rapid assessment of respiration, haemodynamics and artificial airway patency is considered standard-of-care despite the lack of outcome data [34-38]. ET-$CO_2$ can also be used to calculate end-tidal alveolar dead space fraction (AVDSF) [39-42]. There is no data showing improved outcomes with capnography-guided therapy, although high dead space is associated with disease severity [39, 43].

Monitoring of oxygenation

**We recommend transcutaneous saturation ($tcSpO_2$) monitoring (i.e. pulse oximetry) in every ventilated child *(strong agreement)*. Pulse oximetry is usually sufficient to assess oxygenation in mild disease and during NIV (*strong agreement*). We recommend using indwelling arterial lines in more severely ill children on invasive ventilation to measure $PaO_2$ accurate assessment of oxygenation *(strong agreement)*. We recommend monitoring central venous saturation ($SvO_2$) and/or arterial lactate in invasively mechanically ventilated children with severe lung injury to assess oxygen debt *(strong agreement)* and as an indirect assessment of cardiac output *(strong agreement)***

Pulse oximetry allowing for non-invasive, continuous, fast and easy assessment of oxygenation and peripheral perfusion (unless $tcSpO_2 \leq 80\%$ or haemoglobin anomalies are present) is to be considered standard-of-care monitoring despite the lack of outcome data [34, 35, 44-46]. $PO_2$ can only be measured reliably in arterial blood, hence metrics of oxygenation ($PaO_2/FiO_2$ or oxygenation index) mandate indwelling arterial lines [22, 23, 47]. Alternative metrics include $SpO_2/FiO_2$ ratio and oxygen saturation index when $SpO_2 \leq 97\%$ [47-51]. Mixed central venous saturation ($SvO_2$) and arterial lactate may better reflect tissue oxygen need, but there is no data identifying their usefulness in ARF [52, 53].

Monitoring of tidal volume

**We recommend proximal Vt measurements (i.e. near the Y-piece of the patient circuit) in small children *(strong agreement)*.**

Delivered Vt may be underestimated in small children (< 10 kg) when no proximal flow sensors are used [54]. Compensating for circuit volume does not overcome this, suggesting using a proximal flow sensor [54-56]. However, there is no outcome data to recommend on the necessity of highly precise Vt measurements.

Monitoring of lung mechanics

**We recommend measuring PEEPi and Pplat during zero-flow conditions to obtain quasi-static Crs during mechanical ventilation in children with or without lung disease *(93% agreement)*. By observing the flow - time scalar and/or flow - volume loop and/or measurement of total PEEP, it may be possible to set the appropriate expiratory time to allow emptying of the lungs *(strong agreement)*. For children with restrictive lung disease, measuring the trend in dynamic compliance in relation to ventilator settings may offer additional information about the course of disease *(87% agreement)***

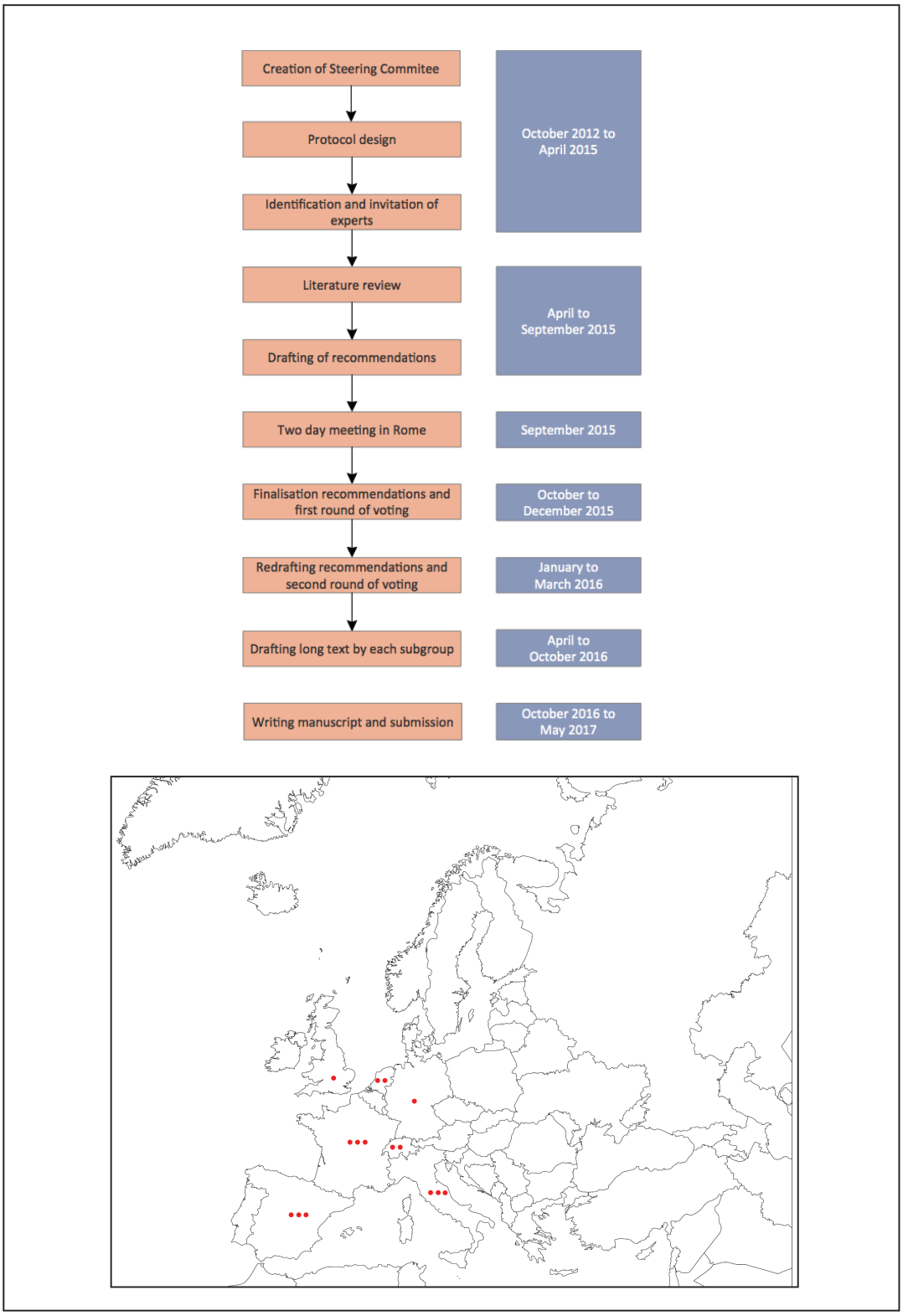
Monitoring PIP at zero inspiratory flow or Pplat giving a better reflection of alveolar pressure, mean airway (mPaw) and PEEP is mandated [57]. There is no outcome data on the usefulness of monitoring Ptp, Crs or PEEPi. Despite the absence of outcome data, ventilators should at least display pressure – time and flow – time scalars [58, 59]. The flow – time scalar provides information on the set inspiratory time, the presence of inspiratory or expiratory flow limitation, detection of dynamic hyperinflation and patient-ventilator interaction [60]. Noisy expiratory flow patterns suggest the presence of tracheal secretions [61].

Lung ultrasound

**There is insufficient data to recommend the routine use of lung ultrasound as monitoring tool. In appropriately trained hands it can provide immediate bedside information about air leak, lung fluid status, pleural effusions and lung expansion *(strong agreement)***

Use of lung ultrasound in critically ill children could be considered to detect lung abnormalities including pleural effusion, pneumothorax or consolidation [62-64].

## 7. Pediatric Mechanical Ventilation Consensus Conference (PEMVECC): workflow and origin of panel members



**8. Bibliography PEMVECC**


1. Santschi M, Jouvet, P, Leclerc, F, Gauvin, F, Newth, CJ, Carroll, 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-Khatib, M, Mireles-Cabodevila, 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, McDonell, J, Vader, JP, Kahan, JP (2001) The RAND/UCLA Appropriateness Method User's Manual. RAND, Santa Monica, CA, USA.
6. Atkins D, Best, D, Briss, PA, Eccles, M, Falck-Ytter, Y, Flottorp, S, Guyatt, GH, Harbour, RT, Haugh, MC, Henry, D, Hill, S, Jaeschke, R, Leng, G, Liberati, A, Magrini, N, Mason, J, Middleton, P, Mrukowicz, J, O'Connell, D, Oxman, AD, Phillips, B, Schunemann, HJ, Edejer, T, Varonen, H, Vist, GE, Williams, JW, Jr., Zaza, S, Group, GW (2004) Grading quality of evidence and strength of recommendations. BMJ 328: 1490
7. Schwabbauer N, Berg, B, Blumenstock, G, Haap, M, Hetzel, J, Riessen, R (2014) Nasal high-flow oxygen therapy in patients with hypoxic respiratory failure: effect on functional and subjective respiratory parameters compared to conventional oxygen therapy and non-invasive ventilation (NIV). BMC Anesthesiol 14: 66

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 in infants with bronchiolitis. Pediatr Crit Care Med 15: e214-219
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-Cooke, 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, Combes, 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, Pietroni, 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, Sturm, 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. McKiernan 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, Molina Cambra, 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, Alverson, 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. Schibler 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. Wing R, James, C, Maranda, LS, Armsby, 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 then invasive mechanical ventilation. Acta Paediatr 103: 81-85
23. Cambonie G, Milesi, C, Jaber, S, Amsallem, F, Barbotte, 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, Fontela, 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, Chevret, 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, Combes, C, Rideau Batista Novais, A, 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, Combes, 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 IP, McBride, AK, Smith, R, Fernandes, RM (2015) 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. Pancera CF, Hayashi, M, Fregnani, JH, Negri, EM, Deheinzelin, D, de Camargo, B (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, Nahum, E (2009) Bi-level 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, Arnolde, V, Gossett, JM, Prodhan, P, Venkataraman, S, Roth, SJ (2013) Efficacy and predictors of success of noninvasive ventilation for prevention of extubation failure in critically ill children with heart disease. Pediatric cardiology 34: 964-977
34. Kovacikova L, Skrak, P, Dobos, D, Zahorec, M (2014) Noninvasive positive pressure ventilation in critically ill children with cardiac disease. Pediatric cardiology 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 Lafever S, Toledo, B, Leiva, M, Padron, 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, Dai, ZK, Chen, IC, 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 49: 589-596

41. Demaret P, Mulder, A, Loeckx, I, 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 (2010) Non invasive ventilation after extubation in paediatric patients: a preliminary study. BMC Pediatr 10: 29

43. Fioretto JR, Ribeiro, CF, Carpi, MF, Bonatto, RC, Moraes, MA, Fioretto, 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, Emilfork, M, Lapadula, M, Alcantara, A, Fernandez, C, Lozano, J, Contreras, M, Conto, L, Arevalo, C, Gayan, A, Hernandez, F, Pedraza, M, Feddersen, M, Bejares, M, Morales, M, Mallea, F, Glasinovic, 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. Essouri S, Chevret, L, Durand, P, Haas, V, Fauroux, B, Devictor, D (2006) Noninvasive positive pressure ventilation: five years of experience in a pediatric intensive care unit. PediatrCrit 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 JI, 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, Genovese, O, 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. Crulli B, Loron, G, Nishisaki, A, Harrington, K, Essouri, S, Emeriaud, G (2016) Safety of paediatric tracheal intubation after non-invasive ventilation failure. Pediatric pulmonology 51: 165-172
53. Bernet V, Hug, MI, Frey, B (2005) Predictive factors for the success of noninvasive mask ventilation in infants and children with acute respiratory failure. Pediatr Crit Care Med 6: 660-664
54. Habashi NM (2005) Other approaches to open-lung ventilation: airway pressure release ventilation. Crit Care Med 33: S228-240
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: e147-156
56. Yehya N, Topjian, AA, Lin, R, Berg, RA, 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, Kopelman, BI, Gurgueira, GL, Bonassa, J (2000) [Airway pressure release in postoperative cardiac surgery in pediatric patients]. Rev Assoc Med Bras (1992) 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, Kazzi, 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. JAMA pediatrics

64. Bateman ST, Borasino, S, Asaro, LA, Cheifetz, 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) It is too early to declare early or late rescue high-frequency oscillatory ventilation dead. JAMA pediatrics 168: 861

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

67. Essouri S, Emeriaud, G, Jouvet, P (2014) It is too early to declare early or late rescue high-frequency oscillatory ventilation dead. JAMA pediatrics 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: c2327

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. Kornecki A, Shekerdemian, LS, Adatia, I, Bohn, D (2002) High-frequency oscillation 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 ELIM, van Vught, AJ (2000) Status asthmaticus treated by high-frequency oscillatory ventilation. Pediatr Pulmonol 30 350-353

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: 1459-1461

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: II127-132

81. Meliones JN, Bove, EL, Dekeon, MK, Custer, JR, Moler, FW, Callow, LR, Wilton, NC, Rosen, DB (1991) High-frequency jet ventilation improves cardiac function after the Fontan procedure. Circulation 84: III364-368

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: 314 e311-317

83. Cortiella J, Mlcak, R, Herndon, D (1999) High frequency percussive ventilation in pediatric patients with inhalation injury. The Journal of burn care & rehabilitation 20: 232-235

84. Yehya N, Dominick, CL, Connelly, JT, Davis, DH, Minneci, PC, Deans, KJ, McCloskey, JJ, Kilbaugh, TJ (2014) High-frequency percussive ventilation and bronchoscopy during extracorporeal life support in children. ASAIO journal 60: 424-428

85. Carman B, Cahill, T, Warden, G, McCall, J (2002) A prospective, randomized comparison of the Volume Diffusive Respirator vs conventional ventilation for ventilation of burned children. 2001 ABA paper. The Journal of burn care & rehabilitation 23: 444-448

86. MacLaren G, Dodge-Khatami, A, Dalton, HJ, Writing, C, MacLaren, G, Dodge-Khatami, A, Dalton, HJ, Adachi, I, Almodovar, M, Annich, G, Bartlett, R, Bronicki, R, Brown, K, Butt, W, Cooper, D, Demuth, M, D'Udekem, Y, Fraser, C, Guerguerian, AM, Heard, M, Horton, S, Ichord, R, Jaquiss, R, Laussen, P, Lequier, L, Lou, S, Marino, B, McMullan, M, Ogino, M, Peek, G, Pretre, R, Rodefeld, M, Schmidt, A, Schwartz, S, Shekerdemian, L, Shime, N, Sivarajan, B, Stiller, B, Thiagarajan, R (2013) Joint

statement on mechanical circulatory support in children: a consensus review from the Pediatric Cardiac Intensive Care Society and Extracorporeal Life Support Organization. Pediatr Crit Care Med 14: S1-2

87. Blokpoel RG, Burgerhof, JG, Markhorst, DG, Kneyber, MC (2016) Patient-Ventilator Asynchrony During Assisted Ventilation in Children. Pediatr Crit Care Med 17: e204-211

88. Vignaux L, Grazioli, S, Piquilloud, L, Bochaton, N, Karam, O, Jaecklin, T, Levy-Jamet, Y, Tourneux, P, Jolliet, P, Rimensberger, PC (2013) Optimizing patient-ventilator synchrony during invasive ventilator assist in children and infants remains a difficult task*. Pediatr Crit Care Med 14: e316-325

89. Vignaux L, Grazioli, S, Piquilloud, L, Bochaton, N, Karam, O, Levy-Jamet, Y, Jaecklin, T, Tourneux, P, Jolliet, P, Rimensberger, PC (2013) Patient-ventilator asynchrony during noninvasive pressure support ventilation and neurally adjusted ventilatory assist in infants and children. Pediatr Crit Care Med 14: e357-364

90. de la Oliva P, Schuffelmann, C, Gomez-Zamora, A, Villar, J, Kacmarek, RM (2012) Asynchrony, neural drive, ventilatory variability and COMFORT: NAVA versus pressure support in pediatric patients. A non-randomized cross-over trial. Intensive Care Med 38: 838-846

91. Piastra M, De Luca, D, Costa, R, Pizza, A, De Sanctis, R, Marzano, L, Biasucci, D, Visconti, F, Conti, G (2014) Neurally adjusted ventilatory assist vs pressure support ventilation in infants recovering from severe acute respiratory distress syndrome: nested study. J Crit Care 29: 312 e311-315

92. Kallio M, Peltoniemi, O, Anttila, E, Pokka, T, Kontiokari, T (2015) Neurally adjusted ventilatory assist (NAVA) in pediatric intensive care-A randomized controlled trial. Pediatr Pulmonol 50 : 55-62

93. Froese AB, Bryan, AC (1974) Effects of anesthesia and paralysis on diaphragmatic mechanics in man. Anesthesiology 41: 242-255

94. Putensen C, Hering, R, Muders, T, Wrigge, H (2005) Assisted breathing is better in acute respiratory failure. CurrOpinCrit Care 11: 63-68

95. Putensen C, Muders, T, Varelmann, D, Wrigge, H (2006) The impact of spontaneous breathing during mechanical ventilation. Curr Opin Crit Care 12: 13-18

96. Petrof BJ, Hussain, SN (2016) Ventilator-induced diaphragmatic dysfunction: what have we learned? Curr Opin Crit Care 22: 67-72

97. Emeriaud G, Larouche, A, Ducharme-Crevier, L, Massicotte, E, Flechelles, O, Pellerin-Leblanc, AA, Morneau, S, Beck, J, Jouvet, P (2014) Evolution of inspiratory diaphragm activity in children over the course of the PICU stay. Intensive Care Med 40: 1718-1726

98. Papazian L, Forel, JM, Gacouin, A, Penot-Ragon, C, Perrin, G, Loundou, A, Jaber, S, Arnal, JM, Perez, D, Seghboyan, JM, Constantin, JM, Courant, P, Lefrant, 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

99. Wilsterman ME, de Jager, P, Blokpoel, R, Frerichs, 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

100. Erickson 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

101. Khemani RG, Conti, D, Alonzo, TA, Bart, RD, III, Newth, CJ (2009) Effect of tidal volume in children with acute hypoxemic respiratory failure. Intensive Care Med 35 : 1428-1437

102. Flori HR, Glidden, DV, Rutherford, GW, Matthay, MA (2005) Pediatric acute lung injury: prospective evaluation of risk factors associated with mortality. Am J Respir Crit Care Med 171: 995-1001

103. 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: e194-200
104. Chiumello D, Carlesso, E, Cadringher, P, Caironi, P, Valenza, F, Polli, F, Tallarini, F, Cozzi, P, Cressoni, M, Colombo, A, Marini, JJ, 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, Chidini, G, Calderini, E, Colombo, A, Crimella, F, Brioni, M (2016) Respiratory mechanics and lung stress/strain in children with acute respiratory distress syndrome. Ann Intensive care 6: 11
106. Rimensberger PC, Cheifetz, IM, Pediatric Acute Lung Injury Consensus Conference, G (2015) Ventilatory support in children with pediatric acute respiratory distress syndrome: proceedings from the Pediatric Acute Lung Injury Consensus Conference. Pediatr Crit Care Med 16: S51-60
107. Amato MB, Meade, MO, Slutsky, AS, Brochard, L, Costa, EL, Schoenfeld, DA, Stewart, TE, Briel, M, Talmor, D, Mercat, A, Richard, JC, Carvalho, CR, Brower, RG (2015) Driving pressure and survival in the acute respiratory distress syndrome. N Engl J Med 372: 747-755
108. de Jager P, Burgerhof, JG, van Heerde, M, Albers, MJ, Markhorst, DG, Kneyber, MC (2014) Tidal volume and mortality in mechanically ventilated children: a systematic review and meta-analysis of observational studies*. Crit Care Med 42: 2461-2472
109. Kneyber MC, Rimensberger, PC (2012) The need for and feasibility of a pediatric ventilation trial: reflections on a survey among pediatric intensivists*. Pediatr Crit Care Med 13: 632-638
110. Yu WL, Lu, ZJ, Wang, Y, Shi, LP, Kuang, FW, Qian, SY, Zeng, QY, Xie, MH, Zhang, GY, Zhuang, DY, Fan, XM, Sun, B, Collaborative Study Group of Pediatric

Respiratory, F (2009) The epidemiology of acute respiratory distress syndrome in pediatric intensive care units in China. Intensive Care Med 35: 136-143

111. Zhu YF, Xu, F, Lu, XL, Wang, Y, Chen, JL, Chao, JX, Zhou, XW, Zhang, JH, Huang, YZ, Yu, WL, Xie, MH, Yan, CY, Lu, ZJ, Sun, B, Chinese Collaborative Study Group for Pediatric Hypoxemic Respiratory, F (2012) Mortality and morbidity of acute hypoxemic respiratory failure and acute respiratory distress syndrome in infants and young children. Chinese medical journal 125: 2265-2271
112. Albuali WH, Singh, RN, Fraser, DD, Seabrook, JA, Kavanagh, BP, Parshuram, CS, Komecki, A (2007) Have changes in ventilation practice improved outcome in children with acute lung injury? Pediatr Crit Care Med 8: 324-330
113. Pulitano S, Mancino, A, Pietrini, D, Piastra, M, De Rosa, S, Tosi, F, De Luca, D, Conti, G (2013) Effects of positive end expiratory pressure (PEEP) on intracranial and cerebral perfusion pressure in pediatric neurosurgical patients. J Neurosurg Anesthesiol 25: 330-334
114. von Ungern-Sternberg BS, Regli, A, Schibler, A, Hammer, J, Frei, FJ, Erb, TO (2007) The impact of positive end-expiratory pressure on functional residual capacity and ventilation homogeneity impairment in anesthetized children exposed to high levels of inspired oxygen. Anesth Analg 104: 1364-1368
115. Tusman G, Bohm, SH, Tempra, A, Melkun, F, Garcia, E, Turchetto, E, Mulder, PG, Lachmann, B (2003) Effects of recruitment maneuver on atelectasis in anesthetized children. Anesthesiology 98: 14-22
116. Russell RI, Greenough, A, Giffin, F (1993) The effect of variations in positive end expiratory pressure on gas exchange in ventilated children with liver disease. Eur J Pediatr 152: 742-744
117. Giffin F, Greenough, A (1994) Effect of positive end expiratory pressure and mean airway pressure on respiratory compliance and gas exchange in children with liver disease. Eur J Pediatr 153: 28-33

118. Ingaramo OA, Ngo, T, Khemani, RG, Newth, CJ (2014) Impact of positive end-expiratory pressure on cardiac index measured by ultrasound cardiac output monitor*. Pediatr Crit Care Med 15: 15-20
119. Khemani RG, Markovitz, BP, Curley, MA (2009) Characteristics of children intubated and mechanically ventilated in 16 PICUs. Chest 136: 765-771
120. Paulson TE, Spear, RM, Silva, PD, Peterson, BM (1996) High-frequency pressure-control ventilation with high positive end-expiratory pressure in children with acute respiratory distress syndrome. J Pediatr 129: 566-573
121. Sivan Y, Deakers, TW, Newth, CJ (1991) Effect of positive end-expiratory pressure on respiratory compliance in children with acute respiratory failure. Pediatr Pulmonol 11: 103-107
122. White MK, Galli, SA, Chatburn, RL, Blumer, JL (1988) Optimal positive end-expiratory pressure therapy in infants and children with acute respiratory failure. Pediatr Res 24: 217-221
123. Graham AS, Chandrashekharaiah, G, Citak, A, Wetzel, RC, Newth, CJ (2007) Positive end-expiratory pressure and pressure support in peripheral airways obstruction : work of breathing in intubated children. Intensive Care Med 33: 120-127
124. Parrilla FJ, Moran, I, Roche-Campo, F, Mancebo, J (2014) Ventilatory strategies in obstructive lung disease. Seminars in respiratory and critical care medicine 35: 431-440
125. Caramez MP, Borges, JB, Tucci, MR, Okamoto, VN, Carvalho, CR, Kacmarek, RM, Malhotra, A, Velasco, IT, Amato, MB (2005) Paradoxical responses to positive end-expiratory pressure in patients with airway obstruction during controlled ventilation. Crit Care Med 33: 1519-1528
126. Stather DR, Stewart, TE (2005) Clinical review: Mechanical ventilation in severe asthma. Crit Care 9: 581-587

127. Davis S, Jones, M, Kisling, J, Angelicchio, C, Tepper, RS (1998) Effect of continuous positive airway pressure on forced expiratory flows in infants with tracheomalacia. Am J Respir Crit Care Med 158: 148-152
128. Essouri S, Nicot, F, Clement, A, Garabedian, EN, Roger, G, Lofaso, F, Fauroux, B (2005) Noninvasive positive pressure ventilation in infants with upper airway obstruction: comparison of continuous and bilevel positive pressure. Intensive Care Med 31: 574-580
129. Halbertsma FJ, Vaneker, M, van der Hoeven, JG (2007) Use of recruitment maneuvers during mechanical ventilation in pediatric and neonatal intensive care units in the Netherlands. Intensive Care Med 33: 1673-1674
130. Halbertsma FJ, van der Hoeven, JG (2005) Lung recruitment during mechanical positive pressure ventilation in the PICU: what can be learned from the literature? Anaesthesia 60: 779-790
131. Cruces P, Donoso, A, Valenzuela, J, Diaz, F (2013) Respiratory and hemodynamic effects of a stepwise lung recruitment maneuver in pediatric ARDS: a feasibility study. Pediatr Pulmonol 48: 1135-1143
132. Scohy TV, Bikker, IG, Hofland, J, de Jong, PL, Bogers, AJ, Gommers, D (2009) Alveolar recruitment strategy and PEEP improve oxygenation, dynamic compliance of respiratory system and end-expiratory lung volume in pediatric patients undergoing cardiac surgery for congenital heart disease. Paediatr Anaesth 19: 1207-1212
133. Boriosi JP, Sapru, A, Hanson, JH, Asselin, J, Gildengorin, G, Newman, V, Sabato, K, Flori, HR (2011) Efficacy and safety of lung recruitment in pediatric patients with acute lung injury. Pediatr Crit Care Med 12: 431-436
134. Kheir JN, Walsh, BK, Smallwood, CD, Rettig, JS, Thompson, JE, Gomez-Laberge, C, Wolf, GK, Arnold, JH (2013) Comparison of 2 lung recruitment strategies in children with acute lung injury. Respir Care 58: 1280-1290

135. Wolf GK, Gomez-Laberge, C, Kheir, JN, Zurakowski, D, Walsh, BK, Adler, A, Arnold, JH (2012) Reversal of dependent lung collapse predicts response to lung recruitment in children with early acute lung injury. Pediatr Crit Care Med 13: 509-515
136. Boriosi JP, Cohen, RA, Summers, E, Sapru, A, Hanson, JH, Gildengorin, G, Newman, V, Flori, HR (2012) Lung aeration changes after lung recruitment in children with acute lung injury: a feasibility study. Pediatr Pulmonol 47: 771-779
137. Kaditis AG, Motoyama, EK, Zin, W, Maekawa, N, Nishio, I, Imai, T, Milic-Emili, J (2008) The effect of lung expansion and positive end-expiratory pressure on respiratory mechanics in anesthetized children. Anesth Analg 106: 775-785
138. Duff JP, Rosychuk, RJ, Joffe, AR (2007) The safety and efficacy of sustained inflations as a lung recruitment maneuver in pediatric intensive care unit patients. Intensive Care Med 33: 1778-1786
139. Nacoti M, Spagnolli, E, Bonanomi, E, Barbanti, C, Cereda, M, Fumagalli, R (2012) Sigh improves gas exchange and respiratory mechanics in children undergoing pressure support after major surgery. Minerva Anesthesiol 78: 920-929
140. Morrow B, Futter, M, Argent, A (2007) A recruitment manoeuvre performed after endotracheal suction does not increase dynamic compliance in ventilated paediatric patients: a randomised controlled trial. The Australian journal of physiotherapy 53: 163-169
141. Gregory GA (1994) Pediatric anesthesia. Churchill Livingstone, New York
142. Mau MK, Yamasato, KS, Yamamoto, LG (2005) Normal oxygen saturation values in pediatric patients. Hawaii Med J 64: 42, 44-45
143. Vengsarkar AS, Swan, HJ (1964) Variations in Oxygen Saturation of Arterial Blood in Infants and Children with Congenital Heart Disease. Am J Cardiol 14: 622-627
144. Abman SH, Hansmann, G, Archer, SL, Ivy, DD, Adatia, I, Chung, WK, Hanna, BD, Rosenzweig, EB, Raj, JU, Cornfield, D, Stenmark, KR, Steinhorn, R, Thebaud, B, Fineman, JR, Kuehne, T, Feinstein, JA, Friedberg, MK, Earing, M, Barst, RJ, Keller, RL, Kinsella, JP, Mullen, M, Deterding, R, Kulik, T, Mallory, G, Humpl, T, Wessel, DL,

American Heart Association Council on Cardiopulmonary, CCP, Resuscitation, Council on Clinical, C, Council on Cardiovascular Disease in the, Y, Council on Cardiovascular, R, Intervention, Council on Cardiovascular, S, Anesthesia, the American Thoracic, S (2015) Pediatric Pulmonary Hypertension: Guidelines From the American Heart Association and American Thoracic Society. Circulation 132: 2037-2099

145. Jenkinson SG (1993) Oxygen toxicity. New Horiz 1: 504-511
146. Pannu SR (2016) Too Much Oxygen: Hyperoxia and Oxygen Management in Mechanically Ventilated Patients. Sem Respir Crit Care Med 37: 16-22
147. Abdelsalam M, Cheifetz, IM (2010) Goal-directed therapy for severely hypoxic patients with acute respiratory distress syndrome: permissive hypoxemia. Respir Care 55: 1483-1490
148. Neto AS, Simonis, FD, Barbas, CS, Biehl, M, Determann, RM, Elmer, J, Friedman, G, Gajic, O, Goldstein, JN, Linko, R, Pinheiro de Oliveira, R, Sundar, S, Talmor, D, Wolthuis, EK, Gama de Abreu, M, Pelosi, P, Schultz, MJ, Investigators, PRVN (2015) Lung-Protective Ventilation With Low Tidal Volumes and the Occurrence of Pulmonary Complications in Patients Without Acute Respiratory Distress Syndrome: A Systematic Review and Individual Patient Data Analysis. Crit Care Med 43: 2155-2163
149. Laffey JG, O'Croinin, D, McLoughlin, P, Kavanagh, BP (2004) Permissive hypercapnia--role in protective lung ventilatory strategies. Intensive Care Med 30: 347-356
150. Goldstein B, Shannon, DC, Todres, ID (1990) Supercarbia in children: clinical course and outcome. Crit Care Med 18: 166-168
151. Curley MA, Fackler, JC (1998) Weaning from mechanical ventilation: patterns in young children recovering from acute hypoxemic 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, Anand, KJ, Carcillo, JA, Nicholson, CE (2009) Weaning and extubation readiness in pediatric patients. Pediatr Crit Care Med 10: 1-11
153. Foronda FK, Troster, EJ, Farias, JA, Barbas, CS, Ferraro, AA, Faria, LS, Bousso, 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, Wypij, D, Venkataraman, ST, Hanson, JH, Gedeit, RG, Meert, KL, Luckett, PM, Forbes, P, Lilley, M, Thompson, J, Cheifetz, IM, Hibberd, P, Wetzel, R, 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: 2561-2568
155. Schultz 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 PA, 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 (2015) Automated versus non-automated weaning for reducing the duration of mechanical

ventilation for critically ill adults and children: a cochrane systematic review and meta-analysis. Crit Care 19: 48

160. Jouvet P, Farges, C, Hatzakis, G, Monir, A, Lesage, F, Dupic, L, Brochard, L, Hubert, P (2007) Weaning children from mechanical ventilation with a computer-driven system (closed-loop protocol): a pilot study. Pediatr Crit Care Med 8: 425-432
161. Rushforth K (2005) A randomised controlled trial of weaning from mechanical ventilation in paediatric intensive care (PIC). Methodological and practical issues. Intensive Crit Care Nurs 21: 76-86
162. Suominen PK, Tuominen, NA, Salminen, JT, Korpela, RE, Klockars, JG, Taivainen, TR, Meretoja, OA (2007) The air-leak test is not a good predictor of postextubation adverse events in children undergoing cardiac surgery. J Ccardiothorac Vasc Anesthesia 21: 197-202
163. Takeuchi M, Imanaka, H, Miyano, H, Kumon, K, Nishimura, M (2000) Effect of patient-triggered ventilation on respiratory workload in infants after cardiac surgery. Anesthesiology 93: 1238-1244; discussion 1235A
164. Wolf GK, Walsh, BK, Green, ML, Arnold, JH (2011) Electrical activity of the diaphragm during extubation readiness testing in critically ill children. Pediatr Crit Care Med 12: e220-224
165. Withington DE, Davis, GM, Vallinis, P, Del Sonno, P, Bevan, JC (1998) Respiratory function in children during recovery from neuromuscular blockade. Paediatr Anaesth 8: 41-47
166. Harikumar G, Egberongbe, Y, Nadel, S, Wheatley, E, Moxham, J, Greenough, A, Rafferty, GF (2009) Tension-time index as a predictor of extubation outcome in ventilated children. Am J Respir Crit Care Med 180: 982-988
167. Mohr AM, Rutherford, EJ, Cairns, BA, Boysen, PG (2001) The role of dead space ventilation in predicting outcome of successful weaning from mechanical ventilation. J Trauma 51: 843-848

168. Noizet O, Leclerc, F, Sadik, A, Grandbastien, B, Riou, Y, Dorkenoo, A, Fourier, C, Cremer, R, Leteurtre, S (2005) Does taking endurance into account improve the prediction of weaning outcome in mechanically ventilated children? Crit Care 9: R798-807

169. Farias JA, Alia, I, Esteban, A, Golubicki, AN, Olazarri, FA (1998) Weaning from mechanical ventilation in pediatric intensive care patients. Intensive Care Med 24: 1070-1075

170. Gaies M, Tabbutt, S, Schwartz, SM, Bird, GL, Alten, JA, Shekerdemian, LS, Klugman, D, Thiagarajan, RR, Gaynor, JW, Jacobs, JP, Nicolson, SC, Donohue, JE, Yu, S, Pasquali, SK, Cooper, DS (2015) Clinical Epidemiology of Extubation Failure in the Pediatric Cardiac ICU: A Report From the Pediatric Cardiac Critical Care Consortium. Pediatr Crit Care Med 16: 837-845

171. Willis BC, Graham, AS, Yoon, E, Wetzel, RC, Newth, CJ (2005) Pressure-rate products and phase angles in children on minimal support ventilation and after extubation. Intensive Care Med 31: 1700-1705

172. Wratney AT, Benjamin, DK, Jr., Slonim, AD, He, J, Hamel, DS, Cheifetz, IM (2008) The endotracheal tube air leak test does not predict extubation outcome in critically ill pediatric patients. Pediatr Crit Care Med 9: 490-496

173. Randolph AG, Forbes, PW, Gedeit, RG, Arnold, JH, Wetzel, RC, Luckett, PM, O'Neil, ME, Venkataraman, ST, Meert, KL, Cheifetz, 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

174. Tobin MJ (2012) Extubation and the myth of "minimal ventilator settings". Am J Respir Crit Care Med 185: 349-350

175. 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

176. Khemani RG, Hotz, J, Morzov, R, Flink, RC, Kamerkar, 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
177. Vianello A, Arcaro, G, Braccioni, F, Gallan, F, Marchi, MR, Chizio, S, Zampieri, D, Pegoraro, E, Salvador, V (2011) Prevention of extubation failure in high-risk patients with neuromuscular disease. J Crit Care 26: 517-524
178. Bach JR, Goncalves, MR, Hamdani, I, Winck, JC (2010) Extubation of patients with neuromuscular weakness: a new management paradigm. Chest 137: 1033-1039
179. Hull J, Aniapravan, 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: i1-40
180. Racca F, Mongini, T, Wolfler, A, Vianello, A, Cutrera, R, Del Sorbo, L, Capello, EC, Gregoretti, C, Massa, R, De Luca, D, Conti, G, Tegazzin, V, Toscano, A, Ranieri, VM (2013) Recommendations for anesthesia and perioperative management of patients with neuromuscular disorders. Minerva Anestesiol 79: 419-433
181. Bissonnette B, Sessler, DI, LaFlamme, P (1989) Passive and active inspired gas humidification in infants and children. Anesthesiology 71: 350-354
182. Bissonnette B, Sessler, DI (1989) Passive or active inspired gas humidification increases thermal steady-state temperatures in anesthetized infants. Anesth Analg 69: 783-787
183. 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
184. Lellouche 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, A-H (2009) Humidification performance of 48 passive airway humidifiers: comparison with manufacturer data. Chest 135: 276-286

185. Morrow B, Futter, M, Argent, A (2006) Effect of endotracheal suction on lung dynamics in mechanically-ventilated paediatric patients. The Australian journal of physiotherapy 52: 121-126
186. Avena MJ, de Carvalho, WB, Beppu, OS (2003) [Evaluation of oxygenation, ventilation and respiratory mechanics before and after endotracheal suction in mechanically ventilated children]. Rev Assoc Med Bras 49: 156-161
187. Choong K, Chatrkaw, P, Frndova, H, Cox, PN (2003) Comparison of loss in lung volume with open versus in-line catheter endotracheal suctioning. Pediatr Crit Care Med 4: 69-73
188. Copnell B, Fergusson, D (1995) Endotracheal suctioning: time-worn ritual or timely intervention? Am J Crit Care 4: 100-105
189. Gilbert M (1999) Assessing the need for endotracheal suction. Paediatric nursing 11: 14-17
190. Krause MF, Hoehn, T (2000) Chest physiotherapy in mechanically ventilated children: a review. Crit Care Med 28: 1648-1651
191. Hawkins E, 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. American journal of physical medicine & rehabilitation / Association of Academic Physiatrists 84: 83-88; discussion 89-91
193. Miske LJ, Hickey, EM, Kolb, SM, Weiner, DJ, Panitch, HB (2004) Use of the mechanical in-exsufflator in pediatric patients with neuromuscular disease and impaired cough. Chest 125: 1406-1412

194. Fauroux B, Guillemot, N, Aubertin, G, Nathan, N, Labit, A, Clement, A, Lofaso, F (2008) Physiologic benefits of mechanical insufflation-exsufflation in children with neuromuscular diseases. Chest 133: 161-168
195. 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
196. 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
197. 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
198. Weiss M, Dullenkopf, A, Fischer, JE, Keller, C, Gerber, AC, European Paediatric 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
199. Rabello L, Conceicao, C, Ebecken, K, Lisboa, T, Bozza, FA, Soares, M, Povoa, P, Salluh, JI (2015) Management of severe community-acquired pneumonia in Brazil: a secondary analysis of an international survey. Rev Bras Ter Intensiva 27: 57-63
200. Pearsall MF, Feldman, JM (2014) When does apparatus dead space matter for the pediatric patient? Anesth Analg 118: 776-780
201. Lujan M, Sogo, A, Grimau, C, Pomares, X, Blanch, L, Monso, E (2015) Influence of dynamic leaks in volume-targeted pressure support noninvasive ventilation: a bench study. Respir Care 60: 191-200
202. Fauroux 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

203. Hussey SG, Ryan, CA, Murphy, BP (2004) Comparison of three manual ventilation devices using an intubated mannequin. Arch Dis Child Fetal Neonatal Ed 89: F490-493
204. Boussaid G, Lofaso, F, Santos, DB, Vaugier, I, Pottier, S, Prigent, H, Bahrami, S, Orlikowski, 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
205. Rul B, Carnevale, F, Estournet, B, Rudler, M, Herve, C (2012) Tracheotomy and children with spinal muscular atrophy type 1: ethical considerations in the French context. Nurs Ethics 19: 408-418
206. Benson RC, Hardy, KA, Gildengorin, G, Hsia, D (2012) International survey of physician recommendation for tracheostomy for Spinal Muscular Atrophy Type I. Pediatr Pulmonol 47: 606-611
207. Simonds AK (2007) Respiratory support for the severely handicapped child with neuromuscular disease: ethics and practicality. Sem Respir Crit Care Med 28: 342-354
208. Bush A (2006) Spinal muscular atrophy with respiratory disease (SMARD): an ethical dilemma. Intensive Care Med 32: 1691-1693
209. 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
210. Rimensberger PC, Heulitt, MJ, Meliones, J, Pons, M, Bronicki, RA (2011) Mechanical ventilation in the pediatric cardiac intensive care unit: the essentials. World journal for pediatric & congenital heart surgery 2: 609-619
211. Bronicki RA, Penny, DJ, Anas, NG, Fuhrman, B (2016) Cardiopulmonary Interactions. Pediatr Crit Care Med 17: S182-193
212. Shekerdemian L, Bohn, D (1999) Cardiovascular effects of mechanical ventilation. Arch Dis Child 80: 475-480

213. Bronicki RA, Herrera, M, Mink, RB, Domico, M, Tucker, D, Chang, AC, N.G., A (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
214. Jenkins J, Lynn, A, Edmonds, J, Barker, G (1985) Effects of mechanical ventilation on cardiopulmonary function in children after open-heart surgery. Crit Care Med 13: 77-80
215. Gregory GA, Edmunds, LH, Jr., Kitterman, 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
216. Colgan FJ, Stewart, S (1979) PEEP and CPAP following open-heart surgery in infants and children. Anesthesiology 50: 336-341
217. Kardos A, Vereczkey, G, Szentirmai, C (2005) Haemodynamic changes during positive-pressure ventilation in children. Acta Anaesthesiol Scand 49: 649-653
218. Levett JM, Culpepper, WS, Lin, CY, Arcilla, RA, Replogle, RL (1983) Cardiovascular responses to PEEP and CPAP following repair of complicated congenital heart defects. Ann Thorac Surg 36: 411-416
219. Alexi-Meskhisvili VV, Falkowski, GE, Nikoljuk, AP, Popov, SA (1985) Hemodynamic changes during mechanical ventilation in infants and small children after open heart surgery. The Thoracic and cardiovascular surgeon 33: 215-217
220. Vincent JL (2010) We should abandon randomized controlled trials in the intensive care unit. Crit Care Med 38: S534-S538
221. Khemani RG, Newth, CJ (2010) The design of future pediatric mechanical ventilation trials for acute lung injury. Am J Respir Crit Care Med 182: 1465-1474
222. Conti G, Piastra, M (2016) Mechanical ventilation for children. Curr Opin Crit Care 22: 60-66

## 9. References


1. Chatburn RL, El-Khatib, M, Mireles-Cabodevila, E (2014) A taxonomy for mechanical ventilation: 10 fundamental maxims. Respir Care 59: 1747-1763
2. Chatburn RL (2007) Classification of ventilator modes: update and proposal for implementation. Respir Care 52: 301-323
3. Fitch K, Bernstein, SJ, Aguilar, MD, Burnand, B, LaCalle, JR, Lazaro, P, van het Loo, M, McDonell, J, Vader, JP, Kahan, JP (2001) The RAND/UCLA Appropriateness Method User's Manual. RAND, Santa Monica, CA, USA.
4. Atkins D, Best, D, Briss, PA, Eccles, M, Falck-Ytter, Y, Flottorp, S, Guyatt, GH, Harbour, RT, Haugh, MC, Henry, D, Hill, S, Jaeschke, R, Leng, G, Liberati, A, Magrini, N, Mason, J, Middleton, P, Mrukowicz, J, O'Connell, D, Oxman, AD, Phillips, B, Schunemann, HJ, Edejer, T, Varonen, H, Vist, GE, Williams, JW, Jr., Zaza, S, Group, GW (2004) Grading quality of evidence and strength of recommendations. BMJ 328: 1490
5. Panwar R, Hardie, M, Bellomo, R, Barrot, L, Eastwood, GM, Young, PJ, Capellier, G, Harrigan, PW, Bailey, M, Investigators, CS, Group, ACT (2016) Conservative versus Liberal Oxygenation Targets for Mechanically Ventilated Patients. A Pilot Multicenter Randomized Controlled Trial. Am J Respir Crit Care Med 193: 43-51
6. Girardis M, Busani, S, Damiani, E, Donati, A, Rinaldi, L, Marudi, A, Morelli, A, Antonelli, M, Singer, M (2016) Effect of Conservative vs Conventional Oxygen Therapy on Mortality Among Patients in an Intensive Care Unit: The Oxygen-ICU Randomized Clinical Trial. JAMA 316: 1583-1589
7. Milesi C, Essouri, S, Pouyau, R, Liet, JM, Afanetti, M, Portefaix, A, Baleine, J, Durand, S, Combes, C, Douillard, A, Cambonie, G, Groupe Francophone de Reanimation et d'Urgences, P (2017) High flow nasal cannula (HFNC) versus nasal continuous positive airway pressure (nCPAP) for the initial respiratory management of acute viral bronchiolitis in young infants: a multicenter randomized controlled trial (TRAMONTANE study). Intensive Care Med 43: 209-216

8. Pilar J, Modesto, IAV, Lopez-Fernandez, YM, Lopez-Macias, O, Garcia-Urabayen, D, Amores-Hernandez, I (2017) High-flow nasal cannula therapy versus non-invasive ventilation in children with severe acute asthma exacerbation: An observational cohort study. Med Intensiva: in press
9. Monro-Somerville T, Sim, M, Ruddy, J, Vilas, M, Gillies, MA (2017) The Effect of High-Flow Nasal Cannula Oxygen Therapy on Mortality and Intubation Rate in Acute Respiratory Failure: A Systematic Review and Meta-Analysis. Crit Care Med 45: e449-e456
10. Hernandez G, Vaquero, C, Colinas, L, Cuena, R, Gonzalez, P, Canabal, A, Sanchez, S, Rodriguez, ML, Villasclaras, A, Fernandez, R (2016) Effect of Postextubation High-Flow Nasal Cannula vs Noninvasive Ventilation on Reintubation and Postextubation Respiratory Failure in High-Risk Patients: A Randomized Clinical Trial. JAMA 316: 1565-1574
11. Hernandez G, Vaquero, C, Gonzalez, P, Subira, C, Frutos-Vivar, F, Rialp, G, Laborda, C, Colinas, L, Cuena, R, Fernandez, R (2016) Effect of Postextubation High-Flow Nasal Cannula vs Conventional Oxygen Therapy on Reintubation in Low-Risk Patients: A Randomized Clinical Trial. JAMA 315: 1354-1361
12. Stephan F, Barrucand, B, Petit, P, Rezaiguia-Delclaux, S, Medard, A, Delannoy, B, Cosserant, B, Flicoteaux, G, Imbert, A, Pilorge, C, Berard, L, Bi, POPSG (2015) High-Flow Nasal Oxygen vs Noninvasive Positive Airway Pressure in Hypoxemic Patients After Cardiothoracic Surgery: A Randomized Clinical Trial. JAMA 313: 2331-2339
13. Frat JP, Thille, AW, Mercat, A, Girault, C, Ragot, S, Perbet, S, Prat, G, Boulain, T, Morawiec, E, Cottereau, A, Devaquet, J, Nseir, S, Razazi, K, Mira, JP, Argaud, L, Chakarian, JC, Ricard, JD, Wittebole, X, Chevalier, S, Herbland, A, Fartoukh, M, Constantin, JM, Tonnelier, JM, Pierrot, M, Mathonnet, A, Beduneau, G, Deletage-Metreau, C, Richard, JC, Brochard, L, Robert, R, Group, FS, Network, R (2015) High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. N Engl J Med 372: 2185-2196

14. Patel BK, Wolfe, KS, A.S., P, Hall, JB, Kress, JP (2016) Effect of Noninvasive Ventilation Delivered by Helmet vs Face Mask on the Rate of Endotracheal Intubation in Patients With Acute Respiratory Distress Syndrome: A Randomized Clinical Trial. JAMA 315: 2435-2441
15. Sud S, Sud, M, Friedrich, JO, Wunsch, H, Meade, MO, Ferguson, ND, Adhikari, NK (2016) High-frequency oscillatory ventilation versus conventional ventilation for acute respiratory distress syndrome. Cochrane Database Syst Rev 4: CD004085
16. Meade MO, Young, D, Hanna, S, Zhou, Q, Bachman, TE, Bollen, C, Slutsky, AS, Lamb, SE, Adhikari, NK, Mentzelopoulos, SD, Cook, DJ, Sud, S, Brower, RG, Thompson, BT, Shah, S, Stenzler, A, Guyatt, G, Ferguson, ND (2017) Severity of Hypoxemia and Effect of High Frequency Oscillatory Ventilation in ARDS. Am J Respir Crit Care Med: in press
17. 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. JAMA pediatrics. JAMA Pediatr 168:243-249
18. Rowan CM, Gertz, SJ, McArthur, J, Fitzgerald, JC, Nitu, ME, Loomis, A, Hsing, DD, Duncan, CN, Mahadeo, KM, Smith, LS, Moffet, J, Hall, MW, Pinos, EL, Cheifetz, IM, Tamburro, RF, Investigators of the Pediatric Acute Lung, I, Sepsis, N (2016) Invasive Mechanical Ventilation and Mortality in Pediatric Hematopoietic Stem Cell Transplantation: A Multicenter Study. Pediatr Crit Care Med 17: 294-302
19. Wang L, Li, X, Yang, Z, Tang, X, Yuan, Q, Deng, L, Sun, X (2016) Semi-recumbent position versus supine position for the prevention of ventilator-associated pneumonia in adults requiring mechanical ventilation. Cochrane Database Syst Rev: CD009946
20. Faustino EV, Gedeit, R, Schwarz, AJ, Asaro, LA, Wypij, D, Curley, MA, Randomized Evaluation of Sedation Titration for Respiratory Failure Study, I (2017) Accuracy of an Extubation Readiness Test in Predicting Successful Extubation in Children With Acute Respiratory Failure From Lower Respiratory Tract Disease. Crit Care Med 45: 94-102

21. Ray S, Rogers, L, Pagel, C, Raman, S, Peters, MJ, Ramnarayan, P (2017) PaO2/FIO2 Ratio Derived From the SpO2/FIO2 Ratio to Improve Mortality Prediction Using the Pediatric Index of Mortality-3 Score in Transported Intensive Care Admissions. Pediatr Crit Care Med 18: e131-e136
22. Yildizdas D, Yapicioglu, H, Yilmaz, HL, Sertdemir, Y (2004) Correlation of simultaneously obtained capillary, venous, and arterial blood gases of patients in a paediatric intensive care unit. Arch Dis Child 89: 176-180
23. Harrison AM, Lynch, JM, Dean, JM, Witte, MK (1997) Comparison of simultaneously obtained arterial and capillary blood gases in pediatric intensive care unit patients. Crit Care Med 25: 1904-1908
24. Escalante-Kanashiro R, Tantalean-Da-Fieno, J (2000) Capillary blood gases in a pediatric intensive care unit. Crit Care Med 28: 224-226
25. Bilan N, Behbahan, AG, Khosroshahi, AJ (2008) Validity of venous blood gas analysis for diagnosis of acid-base imbalance in children admitted to pediatric intensive care unit. World J Pediatr 4: 114-117
26. Kirubakaran C, Gnananayagam, JE, Sundaravalli, EK (2003) Comparison of blood gas values in arterial and venous blood. Indian journal of pediatrics 70: 781-785
27. Fernandez EG, Green, TP, Sweeney, M (2004) Low inferior vena caval catheters for hemodynamic and pulmonary function monitoring in pediatric critical care patients. Pediatr Crit Care Med 5: 14-18
28. Bruschettini M, Romantsik, O, Zappettini, S, Ramenghi, LA, Calevo, MG (2016) Transcutaneous carbon dioxide monitoring for the prevention of neonatal morbidity and mortality. Cochrane Database Syst Rev 2: CD011494
29. Tobias JD (2009) Transcutaneous carbon dioxide monitoring in infants and children. Paediatr Anaesth 19: 434-444
30. Berkenbosch JW, Tobias, JD (2002) Transcutaneous carbon dioxide monitoring during high-frequency oscillatory ventilation in infants and children. Crit Care Med 30: 1024-1027

31. Tobias JD, Wilson, WR, Jr., Meyer, DJ (1999) Transcutaneous monitoring of carbon dioxide tension after cardiothoracic surgery in infants and children. Anesth Analg 88: 531-534
32. Tobias JD, Meyer, DJ (1997) Noninvasive monitoring of carbon dioxide during respiratory failure in toddlers and infants: end-tidal versus transcutaneous carbon dioxide. Anesth Analg 85: 55-58
33. Monaco F, Nickerson, BG, McQuitty, JC (1982) Continuous transcutaneous oxygen and carbon dioxide monitoring in the pediatric ICU. Crit Care Med 10: 765-766
34. Sivarajan VB, Bohn, D (2011) Monitoring of standard hemodynamic parameters: heart rate, systemic blood pressure, atrial pressure, pulse oximetry, and end-tidal CO2. Pediatr Crit Care Med 12: S2-S11
35. do Amaral JL, Ferreira, AC, de Carvalho, WB (1993) Respiratory monitoring: pulse oximetry and capnography in children during anesthesia and intensive care. Rev Paul Med 111: 320-334
36. Lum L, Saville, A, Venkataraman, ST (1998) Accuracy of physiologic deadspace measurement in intubated pediatric patients using a metabolic monitor: comparison with the Douglas bag method. Crit Care Med 26: 760-764
37. Bhende MS, LaCovey, DC (2001) End-tidal carbon dioxide monitoring in the prehospital setting. Prehosp Emerg Care 5: 208-213
38. Tobias JD, Lynch, A, Garrett, J (1996) Alterations of end-tidal carbon dioxide during the intrahospital transport of children. Pediatr Emerg Care 12: 249-251
39. Bhalla AK, Belani, S, Leung, D, Newth, CJ, Khemani, RG (2015) Higher Dead Space Is Associated With Increased Mortality in Critically Ill Children. Crit Care Med 43: 2439-2445
40. Bhalla AK, Rubin, S, Newth, CJ, Ross, P, Morzov, R, Soto-Campos, G, Khemani, R (2015) Monitoring Dead Space in Mechanically Ventilated Children: Volumetric Capnography Versus Time-Based Capnography. Respir Care 60: 1548-1555

41. Ghuman AK, Newth, CJ, Khemani, RG (2012) The association between the end tidal alveolar dead space fraction and mortality in pediatric acute hypoxemic respiratory failure. Pediatr Crit Care Med 13: 11-15
42. Hubble CL, Gentile, MA, Tripp, DS, Craig, DM, Meliones, JN, Cheifetz, IM (2000) Deadspace to tidal volume ratio predicts successful extubation in infants and children. Crit Care Med 28: 2034-2040
43. Almeida-Junior AA, da Silva, MT, Almeida, CC, Ribeiro, JD (2007) Relationship between physiologic deadspace/tidal volume ratio and gas exchange in infants with acute bronchiolitis on invasive mechanical ventilation. Pediatr Crit Care Med 8: 372-377
44. Cote CJ, Goldstein, EA, Cote, MA, Hoaglin, DC, Ryan, JF (1988) A single-blind study of pulse oximetry in children. Anesthesiology 68: 184-188
45. Fanconi S, Doherty, P, Edmonds, JF, Barker, GA, Bohn, DJ (1985) Pulse oximetry in pediatric intensive care: comparison with measured saturations and transcutaneous oxygen tension. J Pediatr 107: 362-366
46. Sinha IP, Mayell, SJ, Halfhide, C (2014) Pulse oximetry in children. Archives of disease in childhood Education and practice edition 99: 117-118
47. Khemani RG, Rubin, S, Belani, S, Leung, D, Erickson, S, Smith, LS, Zimmerman, JJ, Newth, CJ (2015) Pulse oximetry vs. PaO2 metrics in mechanically ventilated children: Berlin definition of ARDS and mortality risk. Intensive Care Med 41: 94-102
48. Khemani RG, Patel, NR, Bart, RD, 3rd, Newth, CJ (2009) Comparison of the pulse oximetric saturation/fraction of inspired oxygen ratio and the PaO2/fraction of inspired oxygen ratio in children. Chest 135: 662-668
49. Lobete C, Medina, A, Rey, C, Mayordomo-Colunga, J, Concha, A, Menendez, S (2013) Correlation of oxygen saturation as measured by pulse oximetry/fraction of inspired oxygen ratio with Pao2/fraction of inspired oxygen ratio in a heterogeneous sample of critically ill children. J Crit Care 28: 538 e531-537

50. Khemani RG, Thomas, NJ, Venkatachalam, V, Scimeme, JP, Berutti, T, Schneider, JB, Ross, PA, Willson, DF, Hall, MW, Newth, CJ, Pediatric Acute Lung, I, Sepsis Network, I (2012) Comparison of SpO2 to PaO2 based markers of lung disease severity for children with acute lung injury. Crit Care Med 40: 1309-1316
51. Thomas NJ, Shaffer, ML, Willson, DF, Shih, MC, Curley, MA (2010) Defining acute lung disease in children with the oxygenation saturation index. Pediatr Crit Care Med 11: 12-17
52. Huang YC (2005) Monitoring oxygen delivery in the critically ill. Chest 128: 554S-560S
53. Levy MM (2005) Pathophysiology of oxygen delivery in respiratory failure. Chest 128: 547S-553S
54. Cannon ML, Cornell, J, Tripp-Hamel, DS, Gentile, MA, Hubble, CL, Meliones, JN, Cheifetz, IM (2000) Tidal volumes for ventilated infants should be determined with a pneumotachometer placed at the endotracheal tube. Am J Respir Crit Care Med 162: 2109-2112
55. Castle RA, Dunne, CJ, Mok, Q, Wade, AM, Stocks, J (2002) Accuracy of displayed values of tidal volume in the pediatric intensive care unit. Crit Care Med 30: 2566-2574
56. Heulitt MJ, Thurman, TL, Holt, SJ, Jo, CH, Simpson, P (2009) Reliability of displayed tidal volume in infants and children during dual-controlled ventilation. Pediatr Crit Care Med 10: 661-667
57. Peterson-Carmichael S, Seddon, PC, Cheifetz, IM, Frerichs, I, Hall, GL, Hammer, J, Hantos, Z, van Kaam, AH, McEvoy, CT, Newth, CJ, Pillow, JJ, Rafferty, GF, Rosenfeld, M, Stocks, J, Ranganathan, SC, Infant, AEWGo, Young Children Pulmonary Function, T (2016) An Official American Thoracic Society/European Respiratory Society Workshop Report: Evaluation of Respiratory Mechanics and Function in the Pediatric and Neonatal Intensive Care Units. Ann Am Thorac Soc 13: S1-11

58. Fisher JB, Mammel, MC, Coleman, JM, Bing, DR, Boros, SJ (1988) Identifying lung overdistention during mechanical ventilation by using volume-pressure loops. Pediatr Pulmonol 5: 10-14

59. Grasso S, Stripoli, T, De Michele, M, Bruno, F, Moschetta, M, Angelelli, G, Munno, I, Ruggiero, V, Anaclerio, R, Cafarelli, A, Driessen, B, Fiore, T (2007) ARDSnet ventilatory protocol and alveolar hyperinflation: role of positive end-expiratory pressure. Am J Respir Crit Care Med 176: 761-767

60. Blokpoel RG, Burgerhof, JG, Markhorst, DG, Kneyber, MC (2016) Patient-Ventilator Asynchrony During Assisted Ventilation in Children. Pediatr Crit Care Med 17: e204-211

61. Leclerc F, Riou, Y, Martinot, A, Deschildre, A, Neve, V, Hue, V, Fourier, C (1996) Use of the flow-volume loop to detect secretions in ventilated children. Intensive Care Med 22: 88

62. Lichtenstein DA (2014) Lung ultrasound in the critically ill. Annals of intensive care 4: 1

63. Riu B, Ruiz, J, Mari, A, Silva, S (2013) [Chest ultrasonography in pediatric critical care practice]. Annales francaises d'anesthesie et de reanimation 32: e219-223

64. Volpicelli G, Elbarbary, M, Blaivas, M, Lichtenstein, DA, Mathis, G, Kirkpatrick, AW, Melniker, L, Gargani, L, Noble, VE, Via, G, Dean, A, J.W., T, Soldati, G, Copetti, R, Bouhemad, B, Reissig, A, Agricola, E, Rouby, JJ, Arbelot, C, Liteplo, A, Sargsyan, A, Silva, FG, Hoppmann, R, Breitkreutz, R, Seibel, A, Neri, L, Storti, E, Petrovic, T (2012) International Liaison Committee on Lung Ultrasound (ILC-LUS) for International Consensus Conference on Lung Ultrasound (ICC-LUS): International evidence-based recommendations for point-of-care lung ultrasound. Intensive Care Med 38: 577-591