



Operational Definitions related to Pediatric Ventilator Liberation

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Abbreviation List

CPAP	Continuous positive airway pressure
ERT	Extubation readiness testing
ETT	Endotracheal tube
HFNC	High flow nasal cannula
MV	Mechanical ventilation
PICU	Pediatric intensive care unit
NIV	Non-invasive ventilation
NPV	Negative pressure ventilation
NRS	Non-invasive respiratory support
SBT	Spontaneous breathing trial
VFDs	Ventilator free days

Abstract: (295/300 words)**Background:**

Common, operational definitions are crucial to assess interventions and outcomes related to pediatric mechanical ventilation. These definitions can reduce unnecessary variability amongst research and quality improvement efforts, to ensure findings are generalizable and can be pooled to establish best practices.

Research Question:

Can we establish operational definitions for key elements related to pediatric ventilator liberation using a combination of detailed literature review and consensus-based approaches?

Study Design and Methods:

A panel of 26 international experts in pediatric ventilator liberation, two methodologists and two librarians conducted systematic reviews on eight topic areas related to pediatric ventilator liberation. Through a series of virtual meetings, we established draft definitions which were voted upon using an anonymous web-based process. Definitions were revised by incorporating extracted data gathered during the systematic review and discussed in another consensus meeting. A second round of voting was conducted to confirm the final definitions.

Results:

In eight topic areas identified by the experts, 16 preliminary definitions were established. Based on initial discussion and the first round of voting, modifications were suggested for 11 of the 16 definitions. There was significant variability in how these items were defined in the literature reviewed. The final round of voting achieved $\geq 80\%$ agreement for all 16 definitions in the following areas: what constitutes respiratory support (invasive mechanical ventilation and non-invasive respiratory support), liberation and failed attempts to liberate from invasive mechanical ventilation, liberation from respiratory support, duration of non-invasive respiratory support, total duration of invasive mechanical ventilation, spontaneous breathing trials, extubation readiness testing, 28-ventilator free days, and planned vs rescue use of post-extubation non-invasive respiratory support.

Interpretation:

We propose these consensus-based definitions for elements of pediatric ventilator liberation, informed by evidence, be used for future quality improvement initiatives and research studies to improve generalizability, and facilitate comparison.

Introduction:

Ventilator liberation is a daily practice in pediatric critical care, yet many aspects of pediatric ventilator liberation lack a clear evidence base.¹⁻⁶ There have been a multitude of studies published on aspects of pediatric ventilator liberation, but there is significant variability with regards to definitions of interventions and outcomes. This variability makes it difficult to synthesize the evidence to establish best practices. Furthermore, as the field moves towards multi-national and platform-based clinical trials with ventilated children, it is increasingly important for there to be a shared framework for definitions of terms related to ventilated children and ventilator liberation.

As part of a larger project to establish clinical practice guidelines for pediatric ventilator liberation,⁷ we assembled a multi-professional panel of international experts in pediatric ventilator liberation. This work included systematic reviews of the literature to identify the most common definitions for interventions and outcomes related to pediatric ventilator liberation. The goal was to establish operational definitions which could be used for future research and quality improvement projects.

Methods:

A panel of 26 international experts was convened in April 2020 based on their published work in pediatric ventilator liberation in the last 10 years. In addition to the panelists, two methodologists and two librarians were recruited to support the project. Between April 2020 and October 2021, the expert panel had three virtual meetings to establish the definitions (**Figure 1**).

Experts voted on the importance of establishing operational definitions for a list of topic areas related to pediatric ventilator liberation. Based on knowledge of the literature related to pediatric and adult ventilator liberation, the co-chairs of the pediatric ventilator liberation consensus conference drafted initial definitions for discussion and voting. The proposed definitions were presented during a virtual meeting for initial discussion with real-time modification of definitions as necessary.

Subsequently, all experts participated in anonymous online voting (Qualtrics, Provo, UT) with three options; (1) agree with definition as written (2) agree with fundamental concept of definition, but suggest following clarifications, or (3) disagree with fundamental concept of definition and would suggest the following instead. For options two and three the experts could type comments for consideration.

The co-chairs modified definitions based on this feedback and presented the voting results and modified definitions to experts in a subsequent virtual meeting.

Systematic Reviews:

In parallel, five systematic reviews were conducted as part of the parent project to answer eight PICO questions related to pediatric ventilator liberation. For all PICO questions, the population of interest focused on children ventilated for at least 24 hours. Key outcomes included the rates

of liberation from invasive and non-invasive mechanical ventilation, total duration of invasive mechanical ventilation, duration of non-invasive respiratory support, failure to liberate from invasive mechanical ventilation (including re-intubation rates), ventilator free days (VFDs), pediatric ICU (PICU) length of stay, hospital length of stay, effort/work of breathing and mortality. The questions are summarized in Table 1, and focused on methods to conduct spontaneous breathing trials, duration of spontaneous breathing trials, measures of respiratory muscle strength, post-extubation upper airway obstruction, noninvasive respiratory support after extubation, and sedation. Medline, Embase and CINAHL databases were searched based on a combination of medical subject headings terms and keywords. There were no language or date limitations (**Supplemental E-Tables 1-5**). Specific details about the inclusion and exclusion criteria and the methods for review have been previously published.⁷ For all articles which met inclusion and exclusion criteria for a given PICO question, experts extracted the definitions used in the individual studies related to proposed definition topic areas. Data extraction occurred in a REDCap database.

For each of the proposed definitions, the co-chairs (SA and RK) synthesized the extracted data from the published studies related to each definition and presented these summary findings to the expert panel for consideration during a virtual meeting. The data presented included the number of studies that explicitly defined the term of interest, and specifics about the definitions. Synthesis focused on common elements for each definition, as well as areas which differed (for example whether the study used a time frame for re-intubation such as 24, 48 or > 48 hours of planned extubation). Subsequently, final modifications were made to the definitions. A second round of anonymous online voting (Qualtrics, Provo, UT) was conducted, where experts were given only two options (agree/disagree) with the disagree option allowing inclusion of comments in a text box. An 80% agreement threshold was required to constitute agreement for a definition. Comments related to disagreement are synthesized into the rationale provided below for each definition.

Recommendations and Rationale:

There were eight topic areas identified by experts with 16 preliminary definitions established. Based on initial discussion and the first voting, modifications were suggested for 11 of the 16 definitions that did not reach the 80% agreement threshold: non-invasive ventilation, continuous positive airway pressure, high flow nasal cannula, conventional oxygen therapy, liberation from invasive mechanical ventilation, failed attempt to liberate from invasive mechanical ventilation, duration of non-invasive respiratory support, total duration of invasive mechanical ventilation, spontaneous breathing trial, extubation readiness testing, and 28-ventilator free days (**Supplemental E-Table 6**).

The systematic review yielded 49 articles for which definitions were extracted, although not all topics for definitions were addressed explicitly in the articles. In these circumstances, the panelists were informed that no studies were identified. The articles that were used to inform the definitions are cited in Table 2. During the final voting round the expert panel agreed on all

modified definitions (**Supplemental E-Table 7**). Final definitions are shown in **Table 2** and reported below.

Respiratory Support:

Respiratory support includes invasive mechanical ventilation (MV) and non-invasive respiratory support (NRS). NRS includes non-invasive ventilation (NIV), continuous positive airway pressure (CPAP), negative pressure ventilation (NPV), and high flow nasal cannula (HFNC) (**Figure 2**).

Definition 1. Invasive mechanical ventilation (MV): (100% agreement)

Positive pressure ventilation delivered via an artificial airway i.e. endotracheal tube (ETT), or tracheostomy tube into the trachea.

Background: Respiratory support modalities carry different risk/benefit profiles for patients and different values for critical care providers, caregivers, and policy makers. Invasive MV is often thought to have the highest risk profile due to known complications such as ventilator induced lung injury, ventilator associated events, airway trauma, exposure to opioids and sedatives, critical illness myopathy/neuropathy, cost, and long-term pediatric post intensive care syndrome.⁸⁻¹² Hence clear delineation of the course of invasive MV was felt to be crucial.

Summary of deliberations, studies, and implementation: The definition of invasive MV was relatively straightforward and consistent across reviewed studies.¹³⁻⁵⁸ In most circumstances, ventilators provide invasive MV through the endotracheal or tracheostomy tube, but in rare instances, hand-bag ventilation can be used, particularly in low resource settings. For this reason, the definition focuses on any positive pressure being delivered through a tube which passes into the trachea.

Definition 2. Non-invasive ventilation (NIV): (87% agreement)

Positive pressure with variable levels of pressure delivered without an artificial airway via any interface which aims to provide an occlusive fit (e.g. nasal mask, nasal pillows/prongs, full face mask or helmet). Examples include bi-level positive airway pressure (BiPAP), or nasal high frequency oscillation ventilation.

Definition 3. Continuous positive airway pressure (CPAP): (91% agreement)

Positive pressure with a single continuous distending pressure delivered without an artificial airway via any interface which aims to provide an occlusive fit (e.g. nasal mask, nasal pillows/prongs, full face mask or helmet).

Background: There are increasing varieties of interfaces and non-invasive modes which are used to deliver positive pressure. Interface fit, as well as the modality of support are crucial components to the benefits and risks of non-invasive modes. It is often difficult to generalize findings from individual studies related to NIV or CPAP without a clear description of the interface and systems used.⁵⁹ In addition, the therapeutic target of NIV may differ from CPAP, although these terms are often combined or used interchangeably in the literature.

Summary of deliberations, studies, and implementation: Ten (20.4%) of the 49 articles examined during the systematic review reported on the use of NIV or CPAP post-extubation.^{19,20,22,24,31,37,39,46,47,54} Post-extubation NIV and CPAP use was not clearly specified in four articles,^{20,22,24,37} while three articles combined NIV with CPAP,^{19,31,54} two reported NIV alone^{39,47} and one study reported CPAP alone.⁴⁶ The CPAP/NIV interface varied; four studies used full face or oro-nasal mask,^{19,39,47,54} two used nasal pillows/occlusive prongs,^{19,54} one used non-occlusive oral mask,⁴⁶ one used helmet,⁵⁴ two used oral mask,^{46,54} and five did not report the interface used.^{20,22,24,31,37}

In discussion with the panelists, the largest area for disagreement in defining CPAP or NIV was related to the occlusiveness of the interface. This affects the amount of pressure and oxygen delivered to the lungs. As an example, many studies of CPAP/NIV report using nasal cannula type interfaces, which most panel experts considered to deliver a different level of support than occlusive nasal interfaces (such as prongs or pillows), or oro-nasal interfaces.⁶⁰ These interfaces also have different risk profiles for pressure injury and patient comfort.⁶¹ Therefore, almost all panelists felt that occlusive fit was necessary to label a therapy CPAP or NIV. In addition, the panel felt it important to differentiate CPAP from NIV, because the addition of inspiratory pressure augmentation with NIV likely represents a different therapeutic target than positive end expiratory pressure alone with CPAP. These were also considered to have different risk benefit profiles, and potentially different levels of tolerance amongst patients. Future studies in pediatric ventilation liberation should report the specific interface used for CPAP/NIV and treat NIV and CPAP as different interventions.⁶²

Definition 4. Negative pressure ventilation (NPV): (96% agreement)

A type of respiratory support in which the surface of the thorax and/or abdomen is exposed to sub-atmospheric pressure (i.e. negative pressure).

Background: Negative Pressure Ventilation (NPV) is typically delivered through a cuirass-type device which can synchronize with patient effort to augment a reduction in pleural pressure to stimulate airflow delivery. While there are limited studies of NPV related to ventilator liberation in the PICU, devices are commercially available and have been used in some PICUs to provide respiratory support in addition to or in place of positive pressure ventilation.⁶³

Summary of deliberations, studies, and implementation: The definition of NPV was relatively straightforward, with minimal debate amongst the panelists. The panelists did feel that NPV constituted a form of respiratory support, and that NPV should be explicitly differentiated from other forms of respiratory support, in addition to reporting its concomitant use with other modes of respiratory support.

Definition 5. High flow nasal cannula (HFNC): (87% agreement)

Flow that is delivered through a heated humidified nasal cannula circuit and interface at a flow rate which is:

- a. ≥ 1 L/kg/min for patients up to 10 kg.
- b. ≥ 10 L/min for patients above 10 kg.

When the HFNC flow falls below the above rates, the patient is considered to be receiving conventional oxygen therapy (see below).

Definition 6. Conventional oxygen therapy: (96% agreement)

In the context of defining liberation from respiratory support, conventional oxygen therapy is not considered a respiratory support.

Conventional oxygen therapy is defined as the provision of more than 0.21 oxygen by any of the following devices applied to a spontaneously breathing patient regardless of presence of humidification:

- a. Face mask oxygen delivered via any type of non-occlusive mask
- b. Nasal cannula at flow rates less than HFNC rates (definition 5 above)
- c. Tracheostomy collar without positive pressure

Background: HFNC is increasingly used in PICU for various indications,^{64,65} but with significant controversy. Controversy even exists about the most appropriate terminology: High Flow Nasal Cannula (HFNC), Heated, Humidified High Flow Nasal Cannula (HHHFNC), or High Flow Nasal Oxygen (HFNO). Fundamentally, there is a need to differentiate HFNC from conventional oxygen therapy, CPAP and NIV, given different benefits, risks, and cost. There is inconsistency in the definition of HFNC, and whether this should be based on a minimum flow rate, the device or interface used, and whether there is a requirement for the gas to be heated and humidified. There is also inconsistency as to whether supplemental oxygen is required for HFNC, given HFNC is often used without supplemental oxygen for children who have high work of breathing.

Summary of deliberations, studies, and implementation: Six studies reported post-extubation HFNC.^{24,37,44,45,54,55} Three studies defined HFNC based on a flow of 1-1.99 L/kg/min,^{44,45,55} two did not specify a flow rate,^{24,37} while one study defined HFNC as 2 L/kg/min for children below 10 kg and specified minimum flow rates for different weight brackets.⁵⁴ Description of HFNC humidification and heating were only reported in two thirds of the included studies.^{44,45,54,55} The definition used to delineate the end of HFNC was not reported in the majority of studies,^{37,44,45,55} one study defined it as removal of HFNC interface regardless of flow rate.⁵⁴

There was extensive discussion amongst the expert panel with a general belief that the definition of HFNC should not be based on the interface or device type being used. Areas of disagreement focused mainly on the minimum flow rate for inclusion, particularly when considering how to define discontinuation of HFNC. While the minimal effective dose of HFNC remains somewhat controversial, existing physiologic studies were used to support inclusion in the definition of a minimal flow rate of 1L/kg/min for children less than 10 kg, based primarily on its effect on work of breathing. For children over 10 kg,^{66,67} a minimum flow rate of 10 L/min was considered pragmatic, to differentiate HFNC from conventional oxygen therapy. Moreover, since the intent of HFNC is often to reduce work of breathing, and not simply to deliver oxygen, experts did not feel oxygen supplementation was a necessary element in the definition. The use of heating and humidification was considered a crucial element of the potential therapeutic

benefit and patient tolerance of the therapy, hence the panel believed these should be contained in the definition.

There may be challenges to implementing this HFNC definition, as it will necessitate consideration of patient related factors (weight) to define the commencement and discontinuation of the therapy, rather than simply the interface being used. Weight is crucial for many elements of pediatric medicine, so it is likely widely available. The additional burden may relate to explicitly reporting the flow rate of HFNC. On balance, this additional burden was outweighed by the benefits of more clearly defining the time frame in which the patient is truly receiving what is believed to be HFNC therapy.

Definition 7. Liberation from Invasive MV: (96% agreement)

A patient is considered to be liberated from invasive MV when:

- a. **ETT:** An endotracheal tube is removed and is not re-inserted within 48 hours*.
- b. **Tracheostomy tube:** Positive pressure ventilation is no longer being delivered through a tracheostomy tube and is not re-initiated within 48 hours*. This includes application of controlled, assisted, supported or CPAP modes of positive pressure via a tracheostomy tube for any period during the day/night.

*Excluding use for temporary procedures

Definition 8. Failed attempt to liberate from Invasive MV (i.e extubation failure): (96% agreement)

- a. **ETT:** Re-intubation within 48 hours after extubation or a placement of a new tracheostomy with delivery of positive pressure ventilation for any period of the day*.
- b. **Tracheostomy tube:** Re-institution of positive pressure ventilation within 48 hours after attempt of liberation from invasive mechanical ventilation *. This includes application of controlled, assisted, supported or CPAP modes of positive pressure via a tracheostomy tube for any period during the day/night.

*Excluding use for temporary procedures

Background: Successful liberation from invasive MV is an important outcome reported in nearly all studies of ventilated children, yet there is significant inconsistency in the literature in terms of how it is defined. This inconsistency is complicated by increasing use of NIV after extubation,⁶⁸ which may prevent re-intubation for some, or simply prolong the time to re-intubation for others. It is unclear whether a patient who is re-intubated several days after extubation should be considered to have failed extubation, or whether the reason for re-intubation should be factored into the definition, as the need for re-intubation may relate to a new event such as development of a hospital acquired pneumonia.

Summary of deliberations, studies, and implementation: Most studies (36/49, 73.5%) used re-intubation as the definition for extubation failure,^{13-19,21-43,45-49,58} only two studies considered re-intubation and/or use of NIV post-extubation as extubation failure.^{20,44} The most common reported timeframe for extubation failure was 48-hours (44.7%), followed by 24-hours (28.9%) and 72-hours (7.9%) (**Figure 3**). None of the analyzed studies included patients with

tracheostomy with home mechanical ventilation, while one study included patients with tracheostomy without home mechanical ventilation who were receiving mechanical ventilation in the PICU.⁴⁸

The timeframe of liberation for invasive MV and extubation failure was a major discussion point amongst the panelists. Ultimately, the panel elected for a 48-hour timeframe to define extubation failure for several reasons. First, 48-hours is most commonly reported in the literature and is also consistent with adult ventilator liberation definitions.⁶⁹ Second, 24-hours was perceived as too short, given the increasing use of NRS after extubation, which may prolong the time to re-intubation. Third, extubation failures beyond 48 hours were thought to be less attributable to the primary ventilation course. Additional timeframes (i.e. 72-hours or 7-days) were considered to be beneficial as secondary outcomes for certain patient populations such as those with cardiac disease, chronic critical illness, neuromuscular disorders, and traumatic brain injury.

We added 'new tracheostomy with delivery of positive pressure ventilation' to the extubation failure definition for patients with an ETT, to explicitly characterize this as extubation failure. The panel felt that because invasive MV, NIV, and HFNC carry different benefit/risk profiles, failure to liberate from invasive MV and the time on invasive MV should be specifically differentiated from time on NIV and HFNC.

For patients with existing tracheostomy without home mechanical ventilation but who are receiving invasive MV in the PICU, the panel felt it important to clarify that all modes of positive pressure delivered through the tracheostomy constituted invasive mechanical ventilation. This was a point of discussion because the use of NIV was unlikely in these patients given they have an existing invasive airway. Patients with a tracheostomy and home ventilation are not commonly included in pediatric ventilator liberation research, but they are a growing population in the PICU. Future studies should specifically establish definitions related to pediatric ventilator liberation for this population.

Definition 9. Liberation from respiratory support: (100% agreement)

A patient is considered liberated from respiratory support when the patient is no longer receiving invasive MV or NRS and it is not re-initiated within 48 hours.

Definition 10. Duration of NRS: (100% agreement)

A measure of the total duration in which any of the NRS modes (definitions 2-5) are applied.

- If NRS is resumed >48 hours after an initial attempt to liberate from NRS, it is considered a new NRS course.
- If one of above NRS is re-initiated \leq 48 hours from an attempt to liberate from NRS, it is considered a failed liberation attempt, and the duration of NRS should include the time (\leq 48 hours) that the patient was not receiving one of these therapies.

Background: The last decade has seen increased use of NRS in the PICU. At times, reductions in length of invasive MV may be traded for increased use or duration of NRS.⁷⁰⁻⁷² These treatment

modalities may have differential impact and importance for families, patients, healthcare professionals, and policy makers.

Summary of deliberations, studies, and implementation: Definitions of NRS discontinuation were only explicitly reported in two studies and related to physical removal of the machine delivering NRS.^{24,46} Experts felt the concepts of NRS liberation should mimic the definition and time frame (i.e. 48 hours) of liberation from invasive MV. In addition, most patients are liberated from NRS within 48 hours of extubation.⁷³ The panel discussed the potential importance of identifying the subset of patients who receive prolonged NRS or those who go on to receive chronic NRS after PICU discharge. Furthermore, because tolerance and risk benefit profiles differ based on NRS modalities, it was felt that studies specifically focused on NRS after extubation should report the duration of different NRS modalities. Panel members did acknowledge that the additional resources required to gather these data may not always be available. Important areas for additional research were identified including patient, family member, policy maker, and clinician perspectives regarding trade-offs between the use of invasive MV vs NRS and prolonged NRS. Additional areas of research included methods to incorporate pre-existing use of NRS and nocturnal NRS in the definitions of NRS use and NRS duration, as well as appropriate benchmarks for optimal rate and duration of NRS use after extubation versus duration of invasive MV and extubation failure.

Definition 11. Total Duration of Invasive MV: (91% agreement)

Time from initiation of invasive MV until successful liberation from invasive MV or death.

- If invasive MV is resumed >48 hours after an initial attempt to liberate from invasive MV, it is considered a new ventilation course.
- If invasive MV is resumed ≤48 hours of an initial attempt to liberate from invasive MV, it is considered a failed liberation attempt, and the duration of invasive MV should include the time (≤ 48 hours) that the patient was not receiving invasive MV.

Background: Duration of invasive MV is one of the most important outcomes for pediatric ventilator liberation and it is used as a balancing measure to extubation failure. It is also an important metric for policy makers for considering resource allocation and utilization tracking. There is general consensus on how to define duration of invasive MV, although there remains some inconsistency in its measurement and reporting in randomized controlled trials.

Summary of deliberations, studies, and implementation: Almost all studies reported invasive MV duration. Only six of the analyzed studies reported the combination of invasive MV and NIV duration,^{15,17,18,20,35,38} while one study separately reported the duration of NRS from duration of invasive MV.¹⁹ Most studies (36/49, 73.5%) used initiation of invasive MV as the commencement anchoring point to calculate the duration of invasive MV, although two studies used randomization in the study as an anchoring point.^{38,45}

Panel experts selected the initiation of invasive MV as opposed to time of study randomization as the anchoring point to identify commencement of invasive MV for the calculation of total invasive MV duration because it captures the whole course of invasive MV and its associated

risks. Moreover, with effective randomization, duration of invasive MV pre-randomization should be similar. This definition can also be applied across study types (cohort, case control, randomized trials). There was also discussion about how to consider patients who die on invasive mechanical ventilation. The panel felt that length of invasive MV should be reported only in survivors, particularly when mortality rates are different between treatment groups. Use of composite outcomes such as ventilator free days (see below) may be more appropriate for studies with a significant number of patients who die while on invasive MV. Important areas for research included establishing benchmarks for invasive MV duration in subpopulations of children based on presenting illnesses, comorbidities, and severity of illness for use by PICU providers, researchers, and policy makers.

Definition 12. Spontaneous breathing trial (SBT): (91% agreement)

SBT is defined as a systematic method of reduction of invasive MV support to predetermined settings to assess the likelihood that a patient will be able to independently maintain adequate minute ventilation and gas exchange without excessive respiratory effort if liberated from invasive MV.

Definition 13. Extubation readiness testing (ERT): (96% agreement)

ERT is defined as a bundle of elements used to assess the patient's eligibility to be liberated from invasive MV. In addition to the SBT, this may include factors such as assessment of sedation level, adequacy of neurologic control of the airway (i.e. cough and gag), likelihood of post-extubation upper airway obstruction, assessment of respiratory muscle strength, magnitude of airway secretions, hemodynamic status and a plan for post-extubation respiratory support.

Background: SBT and ERT are often used interchangeably in the literature, although they represent different concepts, with an SBT often being a component of an ERT.

Summary of deliberations, studies, and implementation: Panelists built on the conceptual framework that the SBT is an element of the ERT. The SBT gauges whether the patient will be able to initiate spontaneous breaths and breathe independently without excessive respiratory effort after extubation. The SBT is an important element of the ERT bundle. However, there are other elements that need to be assessed to achieve successful extubation. The ERT bundle may additionally include elements such as sedation level, adequacy of neurologic control of the airway (i.e. cough and gag), likelihood of post-extubation upper airway obstruction, assessment of respiratory muscle strength, magnitude of airway secretions, hemodynamic status, and a plan for post-extubation respiratory support.

There was general agreement on the SBT and ERT definitions. The SBT definition was clarified by adding "reduction of ventilator support to pre-determined settings" to distinguish it from gradual reduction of ventilatory support. ERT elements were discussed to ensure inclusiveness of all important elements reported in the evidence, although panelists felt it was necessary to allow for inclusion of other elements which may be important based on local practice or

patient- specific risk factors. Panelists also acknowledged that the individual elements proposed for ERTs were not all mandatory to constitute an ERT.

Definition 14. 28-Ventilator free days (VFDs-28): (91% agreement)

- a. **For survivors:** equals 28 minus the sum of invasive MV days during the first 28 days after initiation of invasive MV.
- b. **For non-survivors:** VFDs-28 would be ZERO if death occurred within 28 days of initiation of invasive MV. If death occurs after 28 days, VFD-28 is calculated in the same way as for survivors.

Background: VFDs-28 are commonly reported in trials of mechanically ventilated patients as they capture a composite outcome of mortality and length of ventilation.⁷⁴ Because length of ventilation is influenced by the above definitions related to ventilator liberation, the panel felt it was important to specifically address VFDs in these definitions.

Summary of deliberations, studies, and implementation: The definition of VFDs-28 was not clearly reported in any of the studies included in our systematic review. The panel felt it important to stay consistent with existing definitions for VFDs-28, incorporating the definitions for duration of invasive MV reported above. The panel felt it may be relevant to use similar definitions for 28 NRS free days (28 NIV free days, 28 CPAP free days, and 28 HFNC free days), although the relevance of these outcomes was uncertain. Examples of VFDs-28 calculation is shown in **Supplemental E-Table 8**.

Definition 15. Planned NRS post-extubation use: (100% agreement)

The application of NRS (NIV, CPAP, NPV, or HFNC) which was planned to be initiated immediately after an attempt of liberation from invasive MV.

Definition 16. Rescue NRS post-extubation use: (100% agreement)

The application of NRS (NIV, CPAP, NPV, or HFNC) within 48 hours after an attempt of liberation from invasive MV which was NOT planned prior to the invasive MV liberation attempt.

Background: NRS is sometimes applied in a planned fashion (i.e. the practitioner intends to use it regardless of clinical status after extubation), while other times it is used when the patient is failing conventional therapies (rescue). The efficacy of using NRS post-extubation to prevent extubation failure in the pediatric population is still under investigation.^{68,75} It is still unclear if planned NRS use provides any advantage over rescue or delayed NRS use.

Summary of deliberations, studies, and implementation: Definitions of planned vs rescue NRS use post-extubation varied between studies.^{14,19,44,46,54} Intention to use NRS post-extubation defined planned NRS in three studies,^{44,46,54} while another study defined it as the initiation of NRS within 60 minutes of extubation.¹⁴ A focus of discussion amongst the panel was whether a specific time frame after extubation for initiation of NRS could be used to define planned versus rescue, given that it may be impossible to ascertain whether the therapy was planned simply by reviewing the medical record. For example, if NRS is started 30 minutes after extubation, this

could be in response to the patient failing conventional therapies, or as part of a predetermined treatment plan. As such, the panel felt the definition should not be based on time to initiate NRS, but rather clinician intent. Ascertainment of this may require some discussion with the care team. Using a specific data collection form to differentiate planned from rescue therapy or implementing documentation within the electronic health record would assist in making this data collection more feasible and accurate.

Potential gaps with these proposed definitions:

These proposed definitions are intended to represent the spectrum of respiratory support for pediatric ventilator liberation. However, there are some gaps. First, given the changing landscape of respiratory support devices, the panel was unclear how to best characterize CPAP/NIV delivered with non-occlusive interfaces. The panel felt strongly that these types of interfaces (i.e. nasal cannula) did not provide the same level of support as CPAP/NIV delivered with occlusive interfaces, and should be treated separately. At the same time, they are likely distinct from HFNC and conventional oxygen therapy. At this point, the panel did not suggest a clear definition or label for this group of patients, and encourages future studies capture data related to the occlusive fit of CPAP/NIV interfaces to inform future definitions.

Second, there was not clear consensus about how to characterize respiratory support for children who are receiving HFNC or “conventional oxygen” with 0.21 FiO₂. The panel felt that when heating and humidification was used with flow rates exceeding 1L/kg or 10L, that these patients met the definitions for HFNC. It remains unclear how to categorize these patients when flow rates fall below HFNC flow rates, but 0.21 FiO₂ is used. Technically, these patients don’t meet our proposed definitions for conventional oxygen therapy, and likely represent a different group.

Third, we did not address use of extracorporeal therapies (i.e. extracorporeal membrane oxygenation, and extracorporeal carbon dioxide removal) which may provide respiratory support. It is certainly possible that some patients could meet our definitions for liberation from respiratory support but are still receiving extracorporeal therapies. This is likely to constitute a small proportion of patients in most studies of pediatric ventilator liberation, but investigators should specifically address these scenarios in studies where there are likely to be a significant number of patients on extracorporeal support.

Limitations:

In addition to the potential gaps identified above, there are important limitations of this work. First, the expert panel was chosen based on the criterion of having published on pediatric ventilator liberation in the last 10 years. While this has advantages of experts with experience in this domain, it may lead to under-representation of experts from resource limited settings, or more junior investigators. To overcome this limitation, we attempted to focus on including more junior investigators, as well as multi-professional international representatives. Second, there is a risk in consensus-based approaches that people feel obligated to agree with definitions. We attempted to reduce the impact of this by using anonymous online voting. Third, while we conducted systematic reviews to identify relevant evidence, we analyzed only

articles included in the systematic reviews related to the parent project focused on developing pediatric ventilator liberation guidelines.⁷ We did not conduct a separate search to specifically identify all the pediatric respiratory evidence related to these modalities. Finally, we chose topic areas which we felt were most relevant to standardize in studies of pediatric ventilator liberation but acknowledge that there are likely many more topic areas which would benefit from this type of approach.

Conclusion:

Although we have made substantial progress in research related to pediatric ventilator liberation, there continue to be many unanswered questions. It is imperative that definitions for important elements in pediatric ventilator liberation are standardized to facilitate pooling of data across studies and help generalize findings from research into clinical practice. We propose that these pediatric ventilator liberation operational definitions be used in future quality improvement and research studies. Future work is needed to study the feasibility of implementing these definitions in different ICU settings and populations and identify areas in need of refinement.

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Figures legends

Figure 1: Conceptual Framework of Pediatric Ventilator Liberation Operational Definitions

CPAP: continuous positive airway pressure; ERT: extubation readiness testing; HFNC: high flow nasal cannula; MV: mechanical ventilation; NIV: non-invasive ventilation; NPV: negative pressure ventilation; NRS: Non-invasive respiratory support; SBT: spontaneous breathing trial; VFDs: Ventilator free days

Figure 2: Respiratory Support Types

Figure 3: Reported Extubation Failure Timeframe (n=38)

Journal Pre-proof

Table 1: List of Pediatric Ventilator Liberation Guidelines PICO Questions

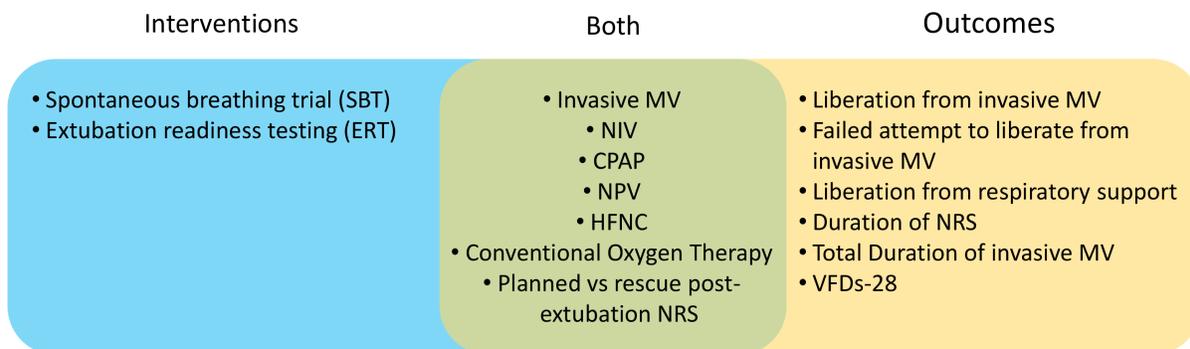
PICO	Question
1.	Spontaneous breathing trial (SBT) method In acutely hospitalized children receiving conventional mechanical ventilation for more than 24 hours who are undergoing a SBT as part of extubation readiness assessments, should inspiratory pressure augmentation (i.e. pressure support [PS] or automatic tube compensation) be used?
2.	SBT duration In acutely hospitalized children receiving conventional mechanical ventilation for more than 24 hours who are undergoing a spontaneous breathing trial to assess for extubation readiness, should the SBT be conducted for 30 minutes or 60-120 minutes?
3.	Utility of measuring respiratory muscle strength/function In acutely hospitalized children receiving conventional mechanical ventilation for more than 24 hours should a measure of respiratory muscle strength during airway occlusion (i.e. the negative inspiratory force [NIF] or maximal inspiratory pressure during airway occlusion [PiMax]) be included in determining extubation readiness?
4.	Utility of using air leak test to predict upper airway obstruction In acutely hospitalized children receiving conventional mechanical ventilation for more than 24 hours should an endotracheal tube air leak test be measured prior to extubation to predict post-extubation upper airway obstruction?
5.	Utility of using corticosteroids to prevent upper airway obstruction In acutely hospitalized children receiving conventional mechanical ventilation for more than 24 hours should systemic corticosteroids be administered prior to extubation to prevent post-extubation upper airway obstruction?
6.	Post-extubation non-invasive respiratory support vs conventional oxygen therapy In acutely hospitalized children receiving conventional mechanical ventilation for more than 24 hours should planned non-invasive respiratory support (high flow nasal cannula [HFNC], continuous positive airway pressure [CPAP], or non-invasive ventilation [NIV]) be used post-extubation?
7.	Post-extubation NIV/CPAP vs HFNC In acutely hospitalized children being extubated to planned non-invasive respiratory support (NIV, CPAP or HFNC), would NIV/CPAP be superior to HFNC?
8.	Sedation management In acutely hospitalized children receiving conventional mechanical ventilation for more than 24 hours, should a goal-directed sedation protocol be used compared to non-protocolized sedation management to guide sedation management during mechanical ventilation and endotracheal extubation?

Table 2: Pediatric Ventilator Liberation Operational Definitions

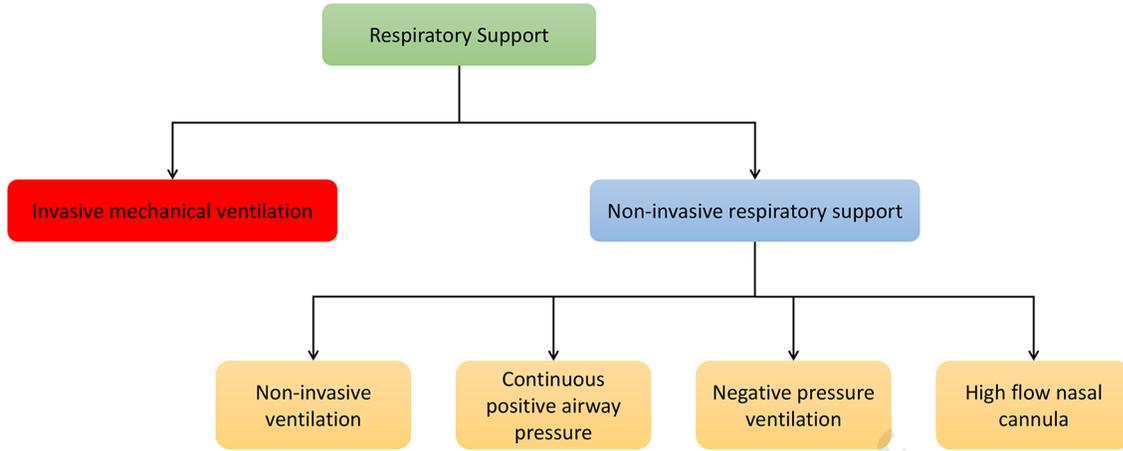
Topic	Definition
A.	<p>Respiratory Support: respiratory support includes invasive mechanical ventilation and non-invasive respiratory support</p> <p>1. Invasive mechanical ventilation (MV):¹³⁻⁵⁸ Positive pressure ventilation delivered via an artificial airway i.e endotracheal tube (ETT), or tracheostomy tube into the trachea.</p> <p>Non-invasive respiratory support (NRS):</p> <p>2. Non-invasive ventilation (NIV):^{19,20,22,24,31,37,39,46,47,54} Positive pressure with variable levels of pressure delivered without an artificial airway via any interface which aims to provide an occlusive fit (e.g. nasal mask, nasal pillows/prongs, full face mask or helmet). Examples include bi-level positive airway pressure (BiPAP), or nasal high frequency oscillation ventilation.</p> <p>3. Continuous positive airway pressure (CPAP): Positive pressure with a single continuous distending pressure delivered without an artificial airway via any interface which aims to provide an occlusive fit (e.g. nasal mask, nasal pillows/prongs, full face mask or helmet).</p> <p>4. Negative pressure ventilation (NPV): A type of respiratory support in which the surface of the thorax and/or abdomen is exposed to sub-atmospheric pressure (i.e. negative pressure).</p> <p>5. High flow nasal cannula (HFNC):^{24,37,44,45,54,55} Flow that is delivered through a heated humidified nasal cannula circuit and interface at a flow rate which is:</p> <ul style="list-style-type: none"> • ≥ 1 L/kg/min for patients up to 10 kg • ≥ 10 L/min for patients above 10 kg <p>When the HFNC flow falls below the above rates, the patient is considered to be receiving conventional oxygen therapy (see below).</p> <p>6. Conventional oxygen therapy: In the context of defining liberation from respiratory support, conventional oxygen therapy is not considered a respiratory support.</p> <p>Conventional oxygen therapy is defined as the provision of more than 0.21 oxygen by any of the following devices applied to a spontaneously breathing patient regardless of presence of humidification:</p> <ol style="list-style-type: none"> a. Face mask oxygen delivered via any type of non-occlusive mask b. Nasal cannula at flow rates less than HFNC rates (definition 5 above) c. Tracheostomy collar without positive pressure

B.	<p>7. Liberation from Invasive MV: ^{13-49,58} A patient is considered to be liberated from invasive MV when:</p> <ol style="list-style-type: none"> ETT: An endotracheal tube is removed and is not re-inserted within 48 hours*. Tracheostomy tube: Positive pressure ventilation is no longer being delivered through a tracheostomy tube and is not re-initiated within 48 hours*. This includes application of controlled, assisted, supported or CPAP modes of positive pressure via a tracheostomy tube for any period during the day/night. <p>*Excluding use for temporary procedures</p> <p>8. Failed attempt to liberate from Invasive MV (i.e extubation failure):</p> <ol style="list-style-type: none"> ETT: Re-intubation within 48 hours after extubation or a placement of a new tracheostomy with delivery of positive pressure ventilation for any period of the day*. Tracheostomy tube: Re-institution of positive pressure ventilation within 48 hours after attempt of liberation from invasive mechanical ventilation *. This includes application of controlled, assisted, supported or CPAP modes of positive pressure via a tracheostomy tube for any period during the day/night. <p>*Excluding use for temporary procedures</p>
C.	<p>9. Liberation from respiratory support: ^{24,46} A patient is considered liberated from respiratory support when the patient is no longer receiving invasive MV or NRS and it is not re-initiated within 48 hours.</p>
D.	<p>10. Duration of NRS: ^{15,17,18,20,24,35,38,46} A measure of the total duration in which any of the NRS modes (definitions 2-5) are applied.</p> <ul style="list-style-type: none"> If NRS is resumed >48 hours after an initial attempt to liberate from NRS, it is considered a new NRS course. If one of the above NRS modes is re-initiated ≤48 hours from an attempt to liberate from NRS, it is considered a failed liberation attempt, and the duration of NRS should include the time (≤48 hours) that the patient was not receiving one of these therapies.
E.	<p>11. Total Duration of Invasive MV: ¹³⁻⁵⁷ Time from initiation of invasive MV until successful liberation from invasive MV or death.</p> <ul style="list-style-type: none"> If invasive MV is resumed >48 hours after an initial attempt to liberate from invasive MV, it is considered a new ventilation course. If invasive MV is resumed ≤48 hours of an initial attempt to liberate from invasive MV, it is considered a failed liberation attempt, and the duration of invasive MV should include the time (≤ 48 hours) that the patient was not receiving invasive MV.

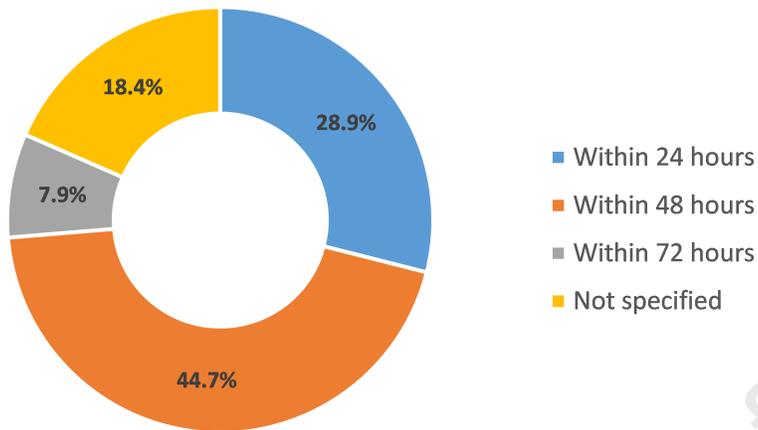
F.	<p>12. Spontaneous breathing trial (SBT): is defined as a systematic method of reduction of invasive MV support to predetermined settings to assess the likelihood that a patient will be able to independently maintain adequate minute ventilation and gas exchange without excessive respiratory effort if liberated from invasive MV.</p> <p>13. Extubation readiness testing (ERT): is defined as a bundle of elements used to assess the patient's eligibility to be liberated from invasive MV. In addition to the SBT, this may include factors such as assessment of sedation level, adequacy of neurologic control of the airway (i.e. cough and gag), likelihood of post-extubation upper airway obstruction, assessment of respiratory muscle strength, magnitude of airway secretions, hemodynamic status and a plan for post-extubation respiratory support.</p>
G.	<p>14. 28-Ventilator free days (VFDs-28):</p> <ul style="list-style-type: none"> a. For survivors: equals 28 minus the sum of invasive MV days during the first 28 days after initiation of invasive MV. b. For non-survivors: VFDs-28 would be ZERO if death occurred within 28 days of initiation of invasive MV. If death occurs after 28 days, VFD-28 is calculated in the same way as for survivors.
H.	<p>Planned vs rescue post-extubation NRS use: ^{14,19,44,46,54}</p> <p>15. Planned: application of NRS (NIV, CPAP, NPV, or HFNC) which was planned to be initiated immediately after an attempt of liberation from invasive MV.</p> <p>16. Rescue: application of NRS (NIV, CPAP, NPV, or HFNC) within 48 hours after an attempt of liberation from invasive MV which was NOT planned prior to the invasive MV liberation attempt.</p>



Journal Pre-proof



Journal Pre-proof



Journal Pre-proof

Conflict of Interest and Role of Funding Source Statements:

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Supplemental Material for Pediatric Ventilator Liberation Consensus Conference: Operational Definitions

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Supplemental E-Table 1: Search strategies for SBT method and duration

I. MEDLINE (Ovid)

PICO 1: Spontaneous breathing trial (SBT) method question

In acutely hospitalized children receiving conventional mechanical ventilation for more than 24 hours who are undergoing a SBT as part of extubation readiness assessments, should inspiratory pressure augmentation (i.e. PS or automatic tube compensation) be used?

P Pediatric patients receiving conventional mechanical ventilation >24 hours undergoing a spontaneous breathing trial

I Spontaneous breathing trial using any level of inspiratory pressure augmentation (pressure support or automatic tube compensation)

C Spontaneous breathing trial done without any level of inspiratory pressure augmentation (i.e. continuous positive airway pressure or T-tube)

O Liberation from non-invasive respiratory support rate, liberation from invasive mechanical ventilation rate, total duration of invasive mechanical ventilation, duration of non-invasive respiratory support, failure rate to liberate from invasive mechanical ventilation (including re-intubation rates), ventilator free days (VFDs), pediatric ICU (PICU) length of stay, hospital length of stay, effort/work of breathing, mortality

PICO 2: SBT duration question

In acutely hospitalized children receiving conventional mechanical ventilation for more than 24 hours who are undergoing a spontaneous breathing trial to assess for extubation readiness, should the SBT be conducted for 30 minutes or 60-120 minutes?

P Pediatric patients receiving conventional mechanical ventilation >24 hours undergoing a spontaneous breathing trial

I Spontaneous breathing trial conducted for 30 minutes

C Spontaneous breathing trial conducted for 60-120 minutes

O Liberation from non-invasive respiratory support rate, liberation from invasive mechanical ventilation rate, total duration of invasive mechanical ventilation, duration of non-invasive respiratory support, failure rate to liberate from invasive mechanical ventilation (including re-intubation rates), VFDs, PICU length of stay, hospital length of stay, mortality

Databases selected: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R)

Line	Query
1	(Adaptive adj2 Support Ventilat*).mp.
2	Airway Extubation/
3	Airway extubat*.mp.

4	Artificial Respirati*.mp.
5	((intubation or extubation*) adj3 (airway or tracheal or intratracheal or endotracheal)).mp.
6	exp Intermittent Positive-Pressure Breathing/
7	Intermittent Positive-Pressure Breathing.mp.
8	exp Intermittent Positive-Pressure Ventilation/
9	Intermittent Positive-Pressure Ventilat*.mp.
10	Intubation, Intratracheal/
11	Mechanical Ventilat*.mp.
12	Neurally Adjusted Ventilatory Assist*.mp.
13	open lung ventilat*.mp.
14	Peep.mp.
15	Positive End Expiratory Pressure*.mp.
16	exp Positive-Pressure Respiration/
17	Positive-Pressure Ventilat*.mp.
18	pressure controlled ventilat*.mp.
19	Proportional Assist Ventilat*.mp.
20	Reintubat*.mp.
21	Respiration, Artificial/
22	Respirator Weaning*.mp.
23	Ventilator*.mp.
24	(Ventilat* adj3 Liberation*).mp.
25	exp Ventilators, Mechanical/
26	exp Ventilator Weaning/
27	Ventilator* Weaning*.mp.
28	Ventilation Weaning*.mp.
29	Adolescent/
30	Adolescen*.mp.
31	Teen*.mp.
32	Youth*.mp.
33	exp Child/
34	Child*.mp.
35	Infant/
36	Infant, Newborn/
37	Infant*.mp.
38	Infanc*.mp.
39	Newborn*.mp.
40	Neonat*.mp.
41	Pediatrics/
42	P?ediatric*.mp.
43	Hospitals, Pediatric/
44	Intensive Care Units, Pediatric/
45	PICU*.mp.
46	(Kid or kids).mp.
47	Toddler*.mp.
48	Continuous Positive Airway Pressure/
49	Continuous Positive Airway Pressure*.mp.

50	CPAP.mp.
51	Spontaneous breathing.mp.
52	SBT.mp.
53	Automatic tube compensation*.mp.
54	T-piece*.mp.
55	T-tube*.mp.
56	(ventilat* adj3 liberation).mp.
57	Pressure support*.mp.
58	(extubation* adj2 (readiness or failure* or outcome*)).mp.
59	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28
60	29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47
61	48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58
62	59 and 60 and 61

II. Embase (Elsevier)

Line	Query
#1	'continuous positive airway pressure'/de
#2	'continuous positive airway pressure*'
#3	cpap
#4	'spontaneous breathing trial'/exp
#5	'spontaneous breathing'/exp
#6	'spontaneous breathing'
#7	sbt
#8	extubation* NEAR/2 (readiness OR failure* OR outcome*)
#9	'automatic tube compensation'/exp
#10	'automatic tube compensation'
#11	't piece'/exp
#12	't piece*' OR 't tube*'
#13	ventilat* NEAR/3 liberation
#14	'pressure support ventilation'/exp
#15	'pressure support ventilator'/exp
#16	'pressure support*'
#17	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16
#18	adaptive NEAR/2 support NEXT/1 ventilat*
#19	'extubation'/de
#20	'airway extubat*'
#21	(intubation* OR extubation*) NEAR/3 (airway OR tracheal OR intratracheal OR endotracheal)
#22	'intermittent mandatory ventilation'/exp
#23	'intermittent positive-pressure breathing'
#24	'intermittent positive pressure ventilation'/exp
#25	'intermittent positive-pressure ventilat*'
#26	'endotracheal intubation'/exp
#27	'invasive ventilation'/exp

#28	'inverse ratio ventilation'/de
#29	'mechanical ventilat*'
#30	'neurally adjusted ventilatory assist*'
#31	'noninvasive positive pressure ventilation'/exp
#32	'open lung ventilat*'
#33	peep
#34	'positive end expiratory pressure ventilation'/exp
#35	'positive end expiratory pressure*'
#36	'positive pressure ventilation'/de
#37	'positive-pressure ventilat*'
#38	'pressure controlled ventilation'/de
#39	'pressure controlled ventilat*'
#40	'pressure support ventilation'/de
#41	'proportional assist ventilat*'
#42	'protective ventilation'/exp
#43	reintubat*
#44	'artificial ventilation'/de
#45	'respirator weaning*'
#46	'tracheal extubation'/de
#47	'ventilator'/de
#48	ventilator*
#49	ventilat* NEAR/3 liberation*
#50	'mechanical ventilator'/de
#51	'ventilator weaning'/de
#52	'ventilator* weaning*'
#53	'ventilation weaning*'
#54	'volume controlled ventilation'/exp
#55	'artificial respirati*'
#56	#18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55
#57	'adolescent'/exp
#58	'adolescence'/de
#59	adolescen*
#60	teen*
#61	youth*
#62	'child'/exp
#63	child*
#64	'infant'/exp
#65	'infancy'/exp
#66	'newborn'/exp
#67	infant*
#68	infanc*
#69	newborn*
#70	neonat*

#71	'pediatrics'/de
#72	p\$ediatric*
#73	'pediatric intensive care unit'/de
#74	picu*
#75	kid OR kids
#76	'toddler'/exp
#77	toddler*
#78	#57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77
#79	#17 AND #56 AND #78

III. CINAHL Complete (EBSCO)

Line	Query
S1	(MH "Continuous Positive Airway Pressure")
S2	continuous positive airway pressure*
S3	CPAP
S4	Spontaneous breathing
S5	SBT
S6	Extubation* N2 (readiness OR failure* OR outcome*)
S7	Automatic tube compensation
S8	(MH "T-Piece")
S9	T-piece* or t-tube*
S10	Ventilat* N3 liberation
S11	(MH "Pressure Support Ventilation")
S12	Pressure support*
S13	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12
S14	Ventilation Weaning*
S15	ventilator* weaning*
S16	(MH "Ventilator Weaning")
S17	(MH "Ventilators, Mechanical")
S18	ventilat* N3 liberation*
S19	ventilator*
S20	'respirator weaning*'
S21	(MH "Respiration, Artificial")
S22	reintubat*
S24	(MH "Pressure Support Ventilation")
S25	pressure controlled ventilat*
S26	positive-pressure ventilat*
S27	(MH "Positive Pressure Ventilation")
S28	Positive End Expiratory Pressure*
S29	(MH "Positive End- Expiratory Pressure")
S30	peep
S31	open lung ventilat*
S32	neurally adjusted ventilatory assist*
S33	mechanical ventilat*
S34	(MH "Mandatory Minute Volume Ventilation")

S35	(MH "Inverse Ratio Ventilation")
S36	(MH "Intubation, Intratracheal")
S37	Intermittent Positive- Pressure Ventilat*
S38	(MH "Intermittent Positive Pressure Ventilation")
S39	Intermittent Positive-Pressure Breathing
S40	(MH "Intermittent Positive Pressure Breathing")
S41	(intubation* OR extubation*) N3 (airway OR tracheal OR intratracheal OR endotracheal)
S42	artificial respirati*
S43	airway extubat*
S44	(MH "Extubation")
S45	adaptive N2 support ventilat*
S46	Toddler*
S47	Kid OR kids
S48	PICU*
S49	(MH "Intensive Care Units, Pediatric")
S50	P#ediatric*
S51	(MH "Pediatrics")
S52	Neonat*
S53	Newborn*
S54	Infanc*
S55	Infant*
S56	(MH "Infant, Newborn")
S57	(MH "Infant") OR (MH "Infant, Hospitalized") OR (MH "Infant, High Risk")
S58	Child*
S59	(MH "Child") OR (MH "Child, Hospitalized") OR (MH "Child, Medically Fragile") OR (MH "Child, Preschool")
S60	Youth*
S61	Teen*
S62	Adolescen*
S63	(MH "Adolescence+")
S64	S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45
S65	S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63
S66	S13 AND S64 AND S65

Supplemental E-Table 2: Search strategies for measures of respiratory muscle strength/function

PICO3: Measures of respiratory muscle strength/function question

In acutely hospitalized children receiving conventional mechanical ventilation for more than 24 hours should a measure of respiratory muscle strength during airway occlusion (i.e. the negative inspiratory force [NIF] or maximal inspiratory pressure during airway occlusion [PiMax]) be included in determining extubation readiness?

P Acutely hospitalized children receiving conventional mechanical ventilation for at least 24 hours, and deemed ready for an extubation readiness trial

I A measure of respiratory muscle strength (NIF or PiMax) as part of extubation readiness assessment

C No assessment of respiratory muscle strength prior to extubation

O Liberation from non-invasive respiratory support rate, liberation from invasive mechanical ventilation rate, total duration of invasive mechanical ventilation, duration of non-invasive respiratory support, failure rate to liberate from invasive mechanical ventilation (including re-intubation rates), VFDs, PICU length of stay, hospital length of stay, mortality

I. MEDLINE (Ovid)

Databases selected: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R)

Line	Query
1	(diaphragm* adj3 electrical adj3 activit*).mp.
2	(diaphragm* adj3 EMG).mp.
3	(diaphragm* adj (function* or strength*)).mp.
4	diaphragm* paralys#s.mp.
5	eadi.mp.
6	EDI.mp.
7	Electromyogram*.mp.
8	Electromyography/
9	electromyograph*.mp.
10	EMGdi.mp.
11	?esophageal pressure*.mp.
12	?esophagus pressure*.mp.
13	(Expiratory muscle* adj (function* or strength*)).mp.
14	Extubation readiness test*.mp.
15	(Inspiratory muscle adj (function* or strength*)).mp.
16	Maximal airway pressure*.mp.
17	Maximal breathing capacit*.mp.
18	(maximal adj2 inspiratory adj (force* or pressure*)).mp.
19	Maximal Respiratory Pressures/
20	Maximal Respiratory Pressure*.mp.
21	negative inspiratory force*.mp.
22	Pdimax.mp.
23	Peak cough* flow*.mp.

24	(Phrenic nerve adj3 stimulat*).mp.
25	Pimax.mp.
26	(Respiratory muscle* adj (function* or strength*)).mp.
27	Tension Time Index.mp.
28	transdiaphragmatic pressure*.mp.
29	(twitch adj4 pressure*).mp.
30	Ventilat* muscle*.mp.
31	Diaphragm/
32	diaphragm*.mp.
33	Ultrasonography/
34	ultrasonograph*.mp.
35	ultrasound*.mp.
36	31 or 32
37	33 or 34 or 35
38	36 and 37
39	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 38
40	Adolescent/
41	Adolescen*.mp.
42	Teen*.mp.
43	Youth*.mp.
44	exp Child/
45	Child*.mp.
46	Infant/
47	Infant, Newborn/
48	Infant*.mp.
49	Infanc*.mp.
50	Newborn*.mp.
51	Neonat*.mp.
52	Pediatrics/
53	P?ediatric*.mp.
54	Hospitals, Pediatric/
55	Intensive Care Units, Pediatric/
56	PICU*.mp.
57	(Kid or kids).mp.
58	Toddler*.mp.
59	40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58
60	(Adaptive adj2 Support Ventilat*).mp.
61	Airway Extubation/
62	Airway extubat*.mp.
63	Artificial Respirati*.mp.
64	((intubation or extubation*) adj3 (airway or tracheal or intratracheal or endotracheal)).mp.
65	exp Intermittent Positive-Pressure Breathing/
66	Intermittent Positive-Pressure Breathing.mp.
67	exp Intermittent Positive-Pressure Ventilation/

68	Intermittent Positive-Pressure Ventilat*.mp.
69	Intubation, Intratracheal/
70	Mechanical Ventilat*.mp.
71	Neurally Adjusted Ventilatory Assist*.mp.
72	open lung ventilat*.mp.
73	Peep.mp.
74	Positive End Expiratory Pressure*.mp.
75	exp Positive-Pressure Respiration/
76	Positive-Pressure Ventilat*.mp.
77	pressure controlled ventilat*.mp.
78	Proportional Assist Ventilat*.mp.
79	Reintubat*.mp.
80	Respiration, Artificial/
81	Respirator Weaning*.mp.
82	Ventilator*.mp.
83	(Ventilat* adj3 Liberation*).mp.
84	exp Ventilators, Mechanical/
85	exp Ventilator Weaning/
86	Ventilator* Weaning*.mp.
87	Ventilation Weaning*.mp.
88	60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87
89	39 and 59 and 88

II. Embase (Elsevier)

Line	Query
#1	diaphragm* NEAR/3 electrical NEAR/3 activit*
#2	diaphragm* NEAR/3 emg
#3	diaphragm* NEAR/2 (function* OR strength*)
#4	'diaphragm* paralys?s'
#5	eadi
#6	edi
#7	'electromyogram'/de
#8	electromyogram*
#9	'electromyography'/exp
#10	electromyograph*
#11	emgdi
#12	'\$esophageal pressure*'
#13	'esophagus pressure'/exp
#14	'\$esophagus pressure*'
#15	'expiratory muscle*' NEAR/2 (function* OR strength*)
#16	'extubation readiness test*'
#17	'inspiratory muscle*' NEAR/2 (function* OR strength*)
#18	maximal NEXT/3 airway NEXT/3 pressure*
#19	'maximal breathing capacit*'

#20	'maximal expiratory pressure'/de
#21	'maximal expiratory pressure*'
#22	'maximal inspiratory pressure'/de
#23	maximal NEAR/3 inspiratory NEAR/2 (force* OR pressure*)
#24	'maximal respiratory pressure'/de
#25	'maximal respiratory pressure*'
#26	'negative inspiratory force*'
#27	pdimax
#28	'peak cough flow'/de
#29	'peak cough* flow*'
#30	'phrenic nerve' NEAR/3 stimulat*
#31	pimax
#32	'respiratory muscle*' NEAR/2 (function* OR strength*)
#33	'tension time index'
#34	'transdiaphragmatic pressure*'
#35	twitch NEAR/4 pressure*
#36	'ventilat* muscle*'
#37	'diaphragm'/de
#38	diaphragm*
#39	'ultrasound'/de
#40	ultrasonograph*
#41	ultrasound*
#42	#37 OR #38
#43	#39 OR #40 OR #41
#44	#42 AND #43
#45	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #44
#46	'adolescent'/exp
#47	'adolescence'/de
#48	adolescen*
#49	teen*
#50	youth*
#51	'child'/exp
#52	child*
#53	'infant'/exp
#54	'infancy'/exp
#55	'newborn'/exp
#56	infant*
#57	infanc*
#58	newborn*
#59	neonat*
#60	'pediatrics'/de
#61	p\$ediatric*

#62	'pediatric intensive care unit'/de
#63	picu*
#64	kid OR kids
#65	'toddler'/exp
#66	toddler*
#67	#46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66
#68	adaptive NEAR/2 support NEXT/1 ventilat*
#69	'extubation'/de
#70	'airway extubat*'
#71	(intubation* OR extubation*) NEAR/3 (airway OR tracheal OR intratracheal OR endotracheal)
#72	'intermittent mandatory ventilation'/exp
#73	'intermittent positive-pressure breathing'
#74	'intermittent positive pressure ventilation'/exp
#75	'intermittent positive-pressure ventilat*'
#76	'endotracheal intubation'/exp
#77	'invasive ventilation'/exp
#78	'inverse ratio ventilation'/de
#79	'mechanical ventilat*'
#80	'neurally adjusted ventilatory assist*'
#81	'noninvasive positive pressure ventilation'/exp
#82	'open lung ventilat*'
#83	peep
#84	'positive end expiratory pressure ventilation'/exp
#85	'positive end expiratory pressure*'
#86	'positive pressure ventilation'/de
#87	'positive-pressure ventilat*'
#88	'pressure controlled ventilation'/de
#89	'pressure controlled ventilat*'
#90	'pressure support ventilation'/de
#91	'proportional assist ventilat*'
#92	'protective ventilation'/exp
#93	reintubat*
#94	'artificial ventilation'/de
#95	'respirator weaning*'
#96	'tracheal extubation'/de
#97	'ventilator'/de
#98	ventilator*
#99	ventilat* NEAR/3 liberation*
#100	'mechanical ventilator'/de
#101	'ventilator weaning'/de
#102	'ventilator* weaning*'
#103	'ventilation weaning*'
#104	'volume controlled ventilation'/exp

#105	'artificial respirati*'
#106	#68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93 OR #94 OR #95 OR #96 OR #97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105
#107	#45 AND #67 AND #106

III. CINAHL Complete (EBSCO)

Line	Query
S1	diaphragm* N3 electrical N3 activit*
S2	diaphragm* N3 emg
S3	diaphragm* N2 (function* OR strength*)
S4	'diaphragm* paralys?s'
S5	eadl
S6	edi
S7	electromyogram*
S8	(MH "Electromyography")
S9	electromyograph*
S10	emgdi
S11	'#esophageal pressure*'
S12	'#esophagus pressure*'
S13	'expiratory muscle*' N2 (function* OR strength*)
S14	'extubation readiness test*'
S15	'inspiratory muscle*' N2 (function* OR strength*)
S16	maximal N3 airway N3 pressure*
S17	'maximal breathing capacit*'
S18	'maximal expiratory pressure*'
S19	maximal N3 inspiratory N2 (force* OR pressure*)
S20	'maximal respiratory pressure*'
S21	'negative inspiratory force*'
S22	pdimax
S23	'peak cough* flow*'
S24	phrenic nerve stimulat*
S25	pimax
S26	'respiratory muscle*' N2 (function* OR strength*)
S27	'tension time index'
S28	'transdiaphragmatic pressure*'
S29	twitch N4 pressure*
S30	'ventilat* muscle*'
S31	(MH "Diaphragm")
S32	diaphragm*
S33	(MH "Ultrasonography")
S34	ultrasonograph*
S35	ultrasound*
S36	S31 OR S32
S37	S33 OR S34 OR S35

S38	S36 AND S37
S39	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S38
S40	Toddler*
S41	Kid OR kids
S42	PICU*
S43	(MH "Intensive Care Units, Pediatric")
S44	P#ediatric*
S45	(MH "Pediatrics")
S46	Neonat*
S47	Newborn*
S48	Infanc*
S49	Infant*
S50	(MH "Infant, Newborn")
S51	(MH "Infant") OR (MH "Infant, Hospitalized") OR (MH "Infant, High Risk")
S52	Child*
S53	(MH "Child") OR (MH "Child, Hospitalized") OR (MH "Child, Medically Fragile") OR (MH "Child, Preschool")
S54	Youth*
S55	Teen*
S56	Adolescen*
S57	(MH "Adolescence+")
S58	Ventilation Weaning*
S59	ventilator* weaning*
S60	(MH "Ventilator Weaning")
S61	(MH "Ventilators, Mechanical")
S62	ventilat* N3 liberation*
S63	ventilator*
S64	'respirator weaning*'
S65	(MH "Respiration, Artificial")
S66	reintubat*
S67	proportional assist ventilat*
S68	(MH "Pressure Support Ventilation")
S69	pressure controlled ventilat*
S70	positive-pressure ventilat*
S71	(MH "Positive Pressure Ventilation")
S72	Positive End Expiratory Pressure*
S73	(MH "Positive End-Expiratory Pressure")
S74	peep
S75	open lung ventilat*
S76	neurally adjusted ventilatory assist*
S77	mechanical ventilat*
S78	(MH "Mandatory Minute Volume Ventilation")
S79	(MH "Inverse Ratio Ventilation")
S80	(MH "Intubation, Intratracheal")

S81	Intermittent Positive-Pressure Ventilat*
S82	(MH "Intermittent Positive Pressure Ventilation")
S83	Intermittent Positive-Pressure Breathing
S84	(MH "Intermittent Positive Pressure Breathing")
S85	(intubation* OR extubation*) N3 (airway OR tracheal OR intratracheal OR endotracheal)
S86	artificial respirati*
S87	airway extubat*
S88	(MH "Extubation")
S89	adaptive N2 support ventilat*
S90	S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69 OR S70 OR S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83 OR S84 OR S85 OR S86 OR S87 OR S88 OR S89
S91	S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53 OR S54 OR S55 OR S56 OR S57
S92	S39 AND S90 AND S91

Supplemental E-Table 3: Search strategies for air leak test and corticosteroids

PICO 4: Air leak test question

In acutely hospitalized children receiving conventional mechanical ventilation for more than 24 hours should an endotracheal tube air leak test be measured prior to extubation to predict post-extubation upper airway obstruction?

P Pediatric patients receiving conventional mechanical ventilation more than 24 hours

I Measurement of endotracheal tube air leak test as part of extubation readiness assessment

C No endotracheal tube air leak test prior to extubation

O Liberation from non-invasive respiratory support rate, liberation from invasive mechanical ventilation rate, total duration of invasive mechanical ventilation, duration of non-invasive respiratory support, failure rate to liberate from invasive mechanical ventilation (including re-intubation rates), VFDs, PICU length of stay, hospital length of stay, post-extubation upper airway obstruction (UAO), new tracheostomy rate, mortality

PICO 5: Corticosteroids question

In acutely hospitalized children receiving conventional mechanical ventilation for more than 24 hours should systemic corticosteroids be administered prior to extubation to prevent post-extubation upper airway obstruction?

P Pediatric patients receiving conventional mechanical ventilation more than 24 hours

I Use of systemic corticosteroids prior to extubation to prevent post-extubation upper airway obstruction

C No use of systemic corticosteroids prior to extubation to prevent post-extubation upper airway obstruction

O Liberation from non-invasive respiratory support rate, liberation from invasive mechanical ventilation rate, total duration of invasive mechanical ventilation, duration of non-invasive respiratory support, failure rate to liberate from invasive mechanical ventilation (including re-intubation rates), VFDs, PICU length of stay, hospital length of stay, post-extubation upper airway obstruction, new tracheostomy rate, GI bleeding, hyperglycemia, mortality.

I. MEDLINE (Ovid)

Databases selected: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R)

Line	Query
1	Adolescent/
2	Adolescen*.mp.
3	Teen*.mp.
4	Youth*.mp.

5	exp Child/
6	Child*.mp.
7	Infant/
8	Infant, Newborn/
9	Infant*.mp.
10	Infanc*.mp.
11	Newborn*.mp.
12	Neonat*.mp.
13	Pediatrics/
14	P?ediatric*.mp.
15	Hospitals, Pediatric/
16	Intensive Care Units, Pediatric/
17	PICU*.mp.
18	(Kid or kids).mp.
19	Toddler*.mp.
20	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19
21	(Adaptive adj2 Support Ventilat*).mp.
22	Airway Extubation/
23	Airway extubat*.mp.
24	Artificial Respirati*.mp.
25	((intubation or extubation*) adj3 (airway or tracheal or intratracheal or endotracheal)).mp.
26	exp Intermittent Positive-Pressure Breathing/
27	Intermittent Positive-Pressure Breathing.mp.
28	exp Intermittent Positive-Pressure Ventilation/
29	Intermittent Positive-Pressure Ventilat*.mp.
30	Intubation, Intratracheal/
31	Mechanical Ventilat*.mp.
32	Neurally Adjusted Ventilatory Assist*.mp.
33	open lung ventilat*.mp.
34	Peep.mp.
35	Positive End Expiratory Pressure*.mp.
36	exp Positive-Pressure Respiration/
37	Positive-Pressure Ventilat*.mp.
38	pressure controlled ventilat*.mp.
39	Proportional Assist Ventilat*.mp.
40	Reintubat*.mp.
41	Respiration, Artificial/
42	Respirator Weaning*.mp.
43	Ventilator*.mp.
44	(Ventilat* adj3 Liberation*).mp.
45	exp Ventilators, Mechanical/
46	exp Ventilator Weaning/
47	Ventilator* Weaning*.mp.
48	Ventilation Weaning*.mp.

49	21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48
50	Dexamethasone/
51	Dexamethasone*.mp.
52	Adrenal Cortex Hormones/
53	((adrenal or adreno or adrenocortical or corticoadrenal) adj2 (steroid* or hormone*)).mp.
54	adrenocorticosteroid*.mp.
55	Corticoid*.mp.
56	Corticosteroid*.mp.
57	Cortico steroid*.mp.
58	Cortical steroid*.mp.
59	Glucocorticoids/
60	Glucocorticoid*.mp.
61	Hydrocortisone/
62	Hydrocortisone*.mp.
63	Cortisone/
64	Cortisone*.mp.
65	Prednisolone/
66	prednisolone*.mp.
67	Predonine*.mp.
68	Methylprednisolone/
69	Methylprednisolone*.mp.
70	Prednisone/
71	Prednison*.mp.
72	Anti-Inflammatory Agents/
73	Anti inflammator*.mp.
74	Antiinflamator*.mp.
75	Antiinflammation*.mp.
76	Anti inflammation*.mp.
77	50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76
78	airleak test*.mp.
79	leak test*.mp.
80	(leak adj5 extubation*).mp.
81	(leak adj3 endotracheal).mp.
82	tube leak*.mp.
83	cuff leak*.mp.
84	cuffleak*.mp.
85	leak pressure*.mp.
86	stridor*.mp.
87	inspiratory flow limitation*.mp.
88	(puls* adj2 paradox*).mp.
89	laryngeal ultrasound*.mp.
90	larynx ?edema*.mp.
91	laryngeal ?edema*.mp.
92	Racpinephrine/

93	Racepinefrine*.mp.
94	Racepinephrine*.mp.
95	racinephrine*.mp.
96	(racemic adj2 (epinephrine* or adrenaline*)).mp.
97	Racadrenalin*.mp.
98	vaponephrin*.mp.
99	Vaponefrin*.mp.
100	Micronefrin*.mp.
101	Micronephrine*.mp.
102	Mikronephrin*.mp.
103	78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102
104	77 or 103
105	20 and 49 and 104

II. Embase (Elsevier)

Line	Query
#1	'adolescent'/exp
#2	'adolescence'/de
#3	adolescenc*
#4	teen*
#5	youth*
#6	'child'/exp
#7	child*
#8	'infant'/exp
#9	'infancy'/exp
#10	'newborn'/exp
#11	infant*
#12	infanc*
#13	newborn*
#14	neonat*
#15	'pediatrics'/de
#16	p\$ediatric*
#17	'pediatric intensive care unit'/de
#18	picu*
#19	kid OR kids
#20	'toddler'/exp
#21	toddler*
#22	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21
#23	adaptive NEAR/2 support NEXT/1 ventilat*
#24	'extubation'/de
#25	'airway extubat*'
#26	(intubation* OR extubation*) NEAR/3 (airway OR tracheal OR intratracheal OR endotracheal)
#27	'intermittent mandatory ventilation'/exp
#28	'intermittent positive-pressure breathing'

#29	'intermittent positive pressure ventilation'/exp
#30	'intermittent positive-pressure ventilat*'
#31	'endotracheal intubation'/exp
#32	'invasive ventilation'/exp
#33	'inverse ratio ventilation'/de
#34	'mechanical ventilat*'
#35	'neurally adjusted ventilatory assist*'
#36	'noninvasive positive pressure ventilation'/exp
#37	'open lung ventilat*'
#38	peep
#39	'positive end expiratory pressure ventilation'/exp
#40	'positive end expiratory pressure*'
#41	'positive pressure ventilation'/de
#42	'positive-pressure ventilat*'
#43	'pressure controlled ventilation'/de
#44	'pressure controlled ventilat*'
#45	'pressure support ventilation'/de
#46	'proportional assist ventilat*'
#47	'protective ventilation'/exp
#48	reintubat*
#49	'artificial ventilation'/de
#50	'respirator weaning*'
#51	'tracheal extubation'/de
#52	'ventilator'/de
#53	ventilator*
#54	ventilat* NEAR/3 liberation*
#55	'mechanical ventilator'/de
#56	'ventilator weaning'/de
#57	'ventilator* weaning*'
#58	'ventilation weaning*'
#59	'volume controlled ventilation'/exp
#60	'artificial respirati*'
#61	#23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60
#62	'air leak'/exp
#63	'air leak test'/exp
#64	'airleak test*'
#65	'leak test*'
#66	leak NEAR/5 extubation*
#67	leak NEAR/3 endotracheal
#68	'tube leak*'
#69	'cuff leak test'/exp
#70	'cuff leak*' OR cuffleak*
#71	'leak pressure*'

#72	'stridor'/exp
#73	stridor*
#74	'inspiratory flow limitation*'
#75	'paradoxical pulse'/exp
#76	paradox* NEAR/2 puls*
#77	'laryngeal ultrasound*'
#78	'larynx edema'/exp
#79	'larynx Şedema*'
#80	'laryngeal Şedema*'
#81	'racepinefrine'/exp
#82	racepinefrine*
#83	racepinephrine*
#84	racinephrine*
#85	racemic NEAR/2 (epinephrine* OR adrenaline*)
#86	racadrenalin*
#87	vaponephrin*
#88	vaponefrin*
#89	micronefrin*
#90	micronephrine*
#91	mikronephrin*
#92	#62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91
#93	'dexamethasone'/de
#94	dexamethasone*
#95	(adrenal OR adreno OR adrenocortical OR corticoadrenal) NEAR/2 (steroid* OR hormone*)
#96	adrenocorticosteroid*
#97	corticoid*
#98	'corticosteroid'/de
#99	corticosteroid*
#100	'cortico steroid*'
#101	'cortical steroid*'
#102	'glucocorticoid'/de
#103	glucocorticoid*
#104	'hydrocortisone'/exp
#105	hydrocortisone*
#106	'cortisone'/exp
#107	cortisone*
#108	'prednisolone'/de
#109	prednisolone*
#110	predonine*
#111	'methylprednisolone'/exp
#112	methylprednisolone*
#113	'prednisone'/exp
#114	prednison*
#115	'antiinflammatory agent'/de

#116	'anti inflammator*'
#117	antiinflamator*
#118	antiinflammation*
#119	'anti inflammation*'
#120	#93 OR #94 OR #95 OR #96 OR #97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105 OR #106 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118 OR #119
#121	#92 OR #120
#122	#22 AND #61 AND #121

III. CINAHL Complete (EBSCO)

Line	Query
S1	"airleak test*"
S2	"leak test*"
S3	leak N5 extubation*
S4	leak N3 endotracheal
S5	"tube leak*"
S6	"cuff leak*"
S7	Cuffleak*
S8	"leak pressure*"
S9	stridor*
S10	"inspiratory flow limitation*"
S11	paradox* N2 puls*
S12	"laryngeal ultrasound*"
S13	"larynx #edema*"
S14	(MH "Laryngeal Edema")
S15	"laryngeal #edema*"
S16	racepinefrine*
S17	racepinephrine*
S18	racinephrine*
S19	racemic N2 (epinephrine* OR adrenaline*)
S20	Racadrenalin*
S21	vaponephrin*
S22	vaponefrin*
S23	micronefrin*
S24	micronephrine*
S25	mikronephrin*
S26	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25
S27	"Anti inflammation*"
S28	Antiinflammation*
S29	Antiinflamator*
S30	"Anti inflammator*"
S31	(MH "Antiinflammatory Agents")
S32	Prednison*
S33	(MH "Prednisone")

S34	Methylprednisolone*
S35	Predonine*
S36	prednisolone*
S37	(MH "Prednisolone+")
S38	Cortisone*
S39	Hydrocortisone*
S40	Glucocorticoid*
S41	(MH "Glucocorticoids+")
S42	"Cortical steroid*"
S43	"Cortico steroid*"
S44	Corticosteroid*
S45	Corticoid*
S46	adrenocorticosteroid*
S47	(adrenal OR adreno OR adrenocortical OR corticoadrenal) N2 (steroid* OR hormone*)
S48	(MH "Adrenal Cortex Hormones")
S49	Dexamethasone*
S50	(MH "Dexamethasone")
S51	S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50
S52	Toddler*
S53	Kid OR kids
S54	PICU*
S55	(MH "Intensive Care Units, Pediatric")
S56	P#ediatric*
S57	(MH "Pediatrics")
S58	Neonat*
S59	Newborn*
S60	Infanc*
S61	Infant*
S62	(MH "Infant, Newborn")
S63	(MH "Infant") OR (MH "Infant, Hospitalized") OR (MH "Infant, High Risk")
S64	Child*
S65	(MH "Child") OR (MH "Child, Hospitalized") OR (MH "Child, Medically Fragile") OR (MH "Child, Preschool")
S66	Youth*
S67	Teen*
S68	Adolescen*
S69	(MH "Adolescence+")
S70	S52 OR S53 OR S54 OR S55 OR S56 OR S57 OR S58 OR S59 OR S60 OR S61 OR S62 OR S63 OR S64 OR S65 OR S66 OR S67 OR S68 OR S69
S71	Ventilation Weaning*
S72	ventilator* weaning*
S73	(MH "Ventilator Weaning")
S74	(MH "Ventilators, Mechanical")
S75	ventilat* N3 liberation*
S76	ventilator*

S77	'respirator weaning*'
S78	(MH "Respiration, Artificial")
S79	reintubat*
S80	proportional assist ventilat*
S81	(MH "Pressure Support Ventilation")
S82	pressure controlled ventilat*
S83	positive-pressure ventilat*
S84	(MH "Positive Pressure Ventilation")
S85	Positive End Expiratory Pressure*
S86	(MH "Positive End- Expiratory Pressure")
S87	peep
S88	open lung ventilat*
S89	neurally adjusted ventilatory assist*
S90	mechanical ventilat*
S91	(MH "Mandatory Minute Volume Ventilation")
S92	(MH "Inverse Ratio Ventilation")
S93	(MH "Intubation, Intratracheal")
S94	Intermittent Positive- Pressure Ventilat*
S95	(MH "Intermittent Positive Pressure Ventilation")
S96	Intermittent Positive- Pressure Breathing
S97	(MH "Intermittent Positive Pressure Breathing")
S98	(intubation* OR extubation*) N3 (airway OR tracheal OR intratracheal OR endotracheal)
S99	artificial respirati*
S100	airway extubat*
S101	(MH "Extubation")
S102	adaptive N2 support ventilat*
S103	S71 OR S72 OR S73 OR S74 OR S75 OR S76 OR S77 OR S78 OR S79 OR S80 OR S81 OR S82 OR S83 OR S84 OR S85 OR S86 OR S87 OR S88 OR S89 OR S90 OR S91 OR S92 OR S93 OR S94 OR S95 OR S96 OR S97 OR S98 OR S99 OR S100 OR S101 OR S102
S104	S26 OR S51
S105	S70 AND S103 AND S104

Supplemental E-Table 4: Search strategies for non-invasive respiratory support

PICO 6: Non-invasive respiratory support vs conventional oxygen therapy question

In acutely hospitalized children receiving conventional mechanical ventilation for more than 24 hours should planned non-invasive respiratory support (high flow nasal cannula [HFNC], CPAP, or non-invasive ventilation [NIV]) be used post-extubation?

P Pediatric patients receiving conventional mechanical ventilation >24 hours

I Planned use of non-invasive respiratory support (NIV, CPAP or HFNC) post-extubation

C Unplanned or no use of non-invasive respiratory support

O Liberation from non-invasive respiratory support rate, liberation from invasive mechanical ventilation rate, total duration of invasive mechanical ventilation, duration of non-invasive respiratory support, failure rate to liberate from invasive mechanical ventilation (including re-intubation rates), VFDs, PICU length of stay, hospital length of stay, pressure injuries to the face, mortality

PICO 7: NIV/CPAP vs HFNC question

In acutely hospitalized children being extubated to planned non-invasive respiratory support (NIV, CPAP or HFNC), would NIV/CPAP be superior to HFNC?

P Pediatric patients receiving conventional mechanical ventilation >24 hours who are planned to be extubated to non-invasive respiratory support

I Planned use of NIV/CPAP post-extubation

C Planned use of HFNC post-extubation

O Liberation from non-invasive respiratory support rate, liberation from invasive mechanical ventilation rate, total duration of invasive mechanical ventilation, duration of non-invasive respiratory support, failure rate to liberate from invasive mechanical ventilation (including re-intubation rates), VFDs, PICU length of stay, hospital length of stay, cross-over to other treatment, pressure injuries to the face, modality.

I. MEDLINE (Ovid)

Databases selected: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R)

Line	Query
1	Continuous Positive Airway Pressure/
2	Continuous Positive Airway Pressure*.mp.
3	CPAP.mp.
4	1 or 2 or 3
5	exp Sleep Apnea Syndromes/
6	sleep apnea*.mp.
7	5 or 6
8	4 not 7

9	(extubation* adj2 (readiness or failure* or outcome*)).mp.
10	((face or nasal) adj mask ventilat*).mp.
11	helmet ventilat*.mp.
12	((High-flow or highflow) adj3 nasal cannula*).mp.
13	((high-flow or highflow or humidified) adj3 oxygen*).mp.
14	(negative pressure adj2 ventilator*).mp.
15	NIV.mp.
16	Noninvasive Ventilation/
17	Noninvasive Ventilation*.mp.
18	Non invasive Ventilation*.mp.
19	Oxygen Inhalation Therapy/
20	Oxygen inhalat* therap*.mp.
21	8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20
22	Adolescent/
23	Adolescen*.mp.
24	Teen*.mp.
25	Youth*.mp.
26	exp Child/
27	Child*.mp.
28	Infant/
29	Infant, Newborn/
30	Infant*.mp.
31	Infanc*.mp.
32	Newborn*.mp.
33	Neonat*.mp.
34	Pediatrics/
35	P?ediatric*.mp.
36	Hospitals, Pediatric/
37	Intensive Care Units, Pediatric/
38	PICU*.mp.
39	(Kid or kids).mp.
40	Toddler*.mp.
41	22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40
42	(Adaptive adj2 Support Ventilat*).mp.
43	Airway Extubation/
44	Airway extubat*.mp.
45	Artificial Respirati*.mp.
46	((intubation or extubation*) adj3 (airway or tracheal or intratracheal or endotracheal)).mp.
47	exp Intermittent Positive-Pressure Breathing/
48	Intermittent Positive-Pressure Breathing.mp.
49	exp Intermittent Positive-Pressure Ventilation/
50	Intermittent Positive-Pressure Ventilat*.mp.
51	Intubation, Intratracheal/
52	Mechanical Ventilat*.mp.

53	Neurally Adjusted Ventilatory Assist*.mp.
54	open lung ventilat*.mp.
55	Peep.mp.
56	Positive End Expiratory Pressure*.mp.
57	exp Positive-Pressure Respiration/
58	Positive-Pressure Ventilat*.mp.
59	pressure controlled ventilat*.mp.
60	Proportional Assist Ventilat*.mp.
61	Reintubat*.mp.
62	Respiration, Artificial/
63	Respirator Weaning*.mp.
64	Ventilator*.mp.
65	(Ventilat* adj3 Liberation*).mp.
66	exp Ventilators, Mechanical/
67	exp Ventilator Weaning/
68	Ventilator* Weaning*.mp.
69	Ventilation Weaning*.mp.
70	42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69
71	21 and 41 and 70

II. Embase (Elsevier)

Line	Query
#1	'continuous positive airway pressure'/de
#2	'continuous positive airway pressure*'
#3	cpap
#4	extubation* NEAR/2 (readiness OR failure* OR outcome*)
#5	(face OR nasal) NEXT/1 'mask ventilat*'
#6	'heated humidifier'/de
#7	'helmet ventilat*'
#8	('high flow' OR highflow OR humidified) NEAR/3 'nasal cannula*'
#9	'high flow oxygen therapy'/de
#10	('high flow' OR highflow OR humidified) NEAR/3 oxygen*
#11	'negative pressure' NEAR/2 ventilat*
#12	niv
#13	'noninvasive ventilation'/de
#14	'noninvasive ventilat*'
#15	'non-invasive ventilat*'
#16	'oxygen inhalat* therap*'
#17	'sleep disordered breathing'/exp
#18	'sleep apnea*'
#19	#1 OR #2 OR #3
#20	#17 OR #18
#21	#19 NOT #20

#22	#4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #21
#23	'adolescent'/exp
#24	'adolescence'/de
#25	adolescen*
#26	teen*
#27	youth*
#28	'child'/exp
#29	child*
#30	'infant'/exp
#31	'infancy'/exp
#32	'newborn'/exp
#33	infant*
#34	infanc*
#35	newborn*
#36	neonat*
#37	'pediatrics'/de
#38	p\$ediatric*
#39	'pediatric intensive care unit'/de
#40	picu*
#41	kid OR kids
#42	'toddler'/exp
#43	toddler*
#44	#23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38 OR #39 OR #40 OR #41 OR #42 OR #43
#45	adaptive NEAR/2 support NEXT/1 ventilat*
#46	'extubation'/de
#47	'airway extubat*'
#48	(intubation* OR extubation*) NEAR/3 (airway OR tracheal OR intratracheal OR endotracheal)
#49	'intermittent mandatory ventilation'/exp
#50	'intermittent positive-pressure breathing'
#51	'intermittent positive pressure ventilation'/exp
#52	'intermittent positive-pressure ventilat*'
#53	'endotracheal intubation'/exp
#54	'invasive ventilation'/exp
#55	'inverse ratio ventilation'/de
#56	'mechanical ventilat*'
#57	'neurally adjusted ventilatory assist*'
#58	'noninvasive positive pressure ventilation'/exp
#59	'open lung ventilat*'
#60	peep
#61	'positive end expiratory pressure ventilation'/exp
#62	'positive end expiratory pressure*'
#63	'positive pressure ventilation'/de

#64	'positive-pressure ventilat*'
#65	'pressure controlled ventilation'/de
#66	'pressure controlled ventilat*'
#67	'pressure support ventilation'/de
#68	'proportional assist ventilat*'
#69	'protective ventilation'/exp
#70	reintubat*
#71	'artificial ventilation'/de
#72	'respirator weaning*'
#73	'tracheal extubation'/de
#74	'ventilator'/de
#75	ventilator*
#76	ventilat* NEAR/3 liberation*
#77	'mechanical ventilator'/de
#78	'ventilator weaning'/de
#79	'ventilator* weaning*'
#80	'ventilation weaning*'
#81	'volume controlled ventilation'/exp
#82	'artificial respirati*'
#83	#45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60 OR #61 OR #62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82
#84	#22 AND #44 AND #83

III. CINAHL Complete (EBSCO)

Line	Query
S1	(MH "Continuous Positive Airway Pressure")
S2	"continuous positive airway pressure*"
S3	CPAP
S4	(MH "Sleep Apnea Syndromes+")
S5	"sleep apnea*"
S6	S1 OR S2 OR S3
S7	S4 OR S5
S8	S6 NOT S7
S9	Extubation* N2 (readiness OR failure* OR outcome*)
S10	(face OR nasal) N1 "mask ventilat*"
S11	"helmet ventilat*"
S12	("high flow" OR highflow OR humidified) N3 "nasal cannula*"
S13	("high flow" OR highflow OR humidified) N3 oxygen*
S14	"negative pressure" N2 ventilat*
S15	niv
S16	"noninvasive ventilat*"
S17	"non invasive ventilat*"
S18	"oxygen inhalat* therap*"

S19	(MH "Ventilation, Negative Pressure")
S20	S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19
S21	Toddler*
S22	Kid OR kids
S23	PICU*
S24	(MH "Intensive Care Units, Pediatric")
S25	P#ediatric*
S26	(MH "Pediatrics")
S27	Neonat*
S28	Newborn*
S29	Infanc*
S30	Infant*
S31	(MH "Infant, Newborn")
S32	(MH "Infant") OR (MH "Infant, Hospitalized") OR (MH "Infant, High Risk")
S33	Child*
S34	(MH "Child") OR (MH "Child, Hospitalized") OR (MH "Child, Medically Fragile") OR (MH "Child, Preschool")
S35	Youth*
S36	Teen*
S37	Adolescen*
S38	(MH "Adolescence+")
S39	Ventilation Weaning*
S40	ventilator* weaning*
S41	(MH "Ventilator Weaning")
S42	(MH "Ventilators, Mechanical")
S43	ventilat* N3 liberation*
S44	ventilator*
S45	'respirator weaning*'
S46	(MH "Respiration, Artificial")
S47	reintubat*
S48	proportional assist ventilat*
S49	(MH "Pressure Support Ventilation")
S50	pressure controlled ventilat*
S51	positive-pressure ventilat*
S52	(MH "Positive Pressure Ventilation")
S53	Positive End Expiratory Pressure*
S54	(MH "Positive End-Expiratory Pressure")
S55	peep
S56	open lung ventilat*
S57	neurally adjusted ventilatory assist*
S58	mechanical ventilat*
S59	(MH "Mandatory Minute Volume Ventilation")
S60	(MH "Inverse Ratio Ventilation")
S61	(MH "Intubation, Intratracheal")
S62	Intermittent Positive-Pressure Ventilat*
S63	(MH "Intermittent Positive Pressure Ventilation")

S64	Intermittent Positive-Pressure Breathing
S65	(MH "Intermittent Positive Pressure Breathing")
S66	(intubation* OR extubation*) N3 (airway OR tracheal OR intratracheal OR endotracheal)
S67	artificial respirati*
S68	airway extubat*
S69	(MH "Extubation")
S70	adapptive N2 support ventilat*
S71	S38 OR S37 OR S36 OR S35 OR S34 OR S33 OR S32 OR S31 OR S30 OR S29 OR S28 OR S27 OR S26 OR S25 OR S24 OR S23 OR S22 OR S21
S72	S70 OR S69 OR S68 OR S67 OR S66 OR S65 OR S64 OR S63 OR S62 OR S61 OR S60 OR S59 OR S58 OR S57 OR S56 OR S55 OR S54 OR S53 OR S52 OR S51 OR S50 OR S49 OR S48 OR S47 OR S46 OR S45 OR S44 OR S43 OR S42 OR S41 OR S40 OR S39
S73	S20 AND S71 AND S72

Supplemental E-Table 5: Search strategies for sedation management

PICO 8: Sedation management question

In acutely hospitalized children receiving conventional mechanical ventilation for more than 24 hours, should a goal-directed sedation protocol be used compared to non-protocolized sedation management to guide sedation management during mechanical ventilation and endotracheal extubation?

P Pediatric patients receiving conventional mechanical ventilation > 24 hours

I Goal-directed sedation protocol during mechanical ventilation and endotracheal extubation

C Non-protocolized sedation management

O Liberation from non-invasive respiratory support rate, liberation from invasive mechanical ventilation rate, total duration of invasive mechanical ventilation, duration of non-invasive respiratory support, failure rate to liberate from invasive mechanical ventilation (including re-intubation rates), VFDs, PICU length of stay, hospital length of stay, Incidence of delirium, incidence of withdrawal, mortality.

I. MEDLINE (Ovid)

Databases selected: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process, In-Data-Review & Other Non-Indexed Citations, Daily and Versions(R)

Line	Query
1	(Adaptive adj2 Support Ventilat*).mp.
2	Airway Extubation/
3	Airway extubat*.mp.
4	Artificial Respirati*.mp.
5	((intubation or extubation*) adj3 (airway or tracheal or intratracheal or endotracheal or early)).mp.
6	exp Intermittent Positive-Pressure Breathing/
7	Intermittent Positive-Pressure Breathing.mp.
8	exp Intermittent Positive-Pressure Ventilation/
9	Intermittent Positive-Pressure Ventilat*.mp.
10	Intubation, Intratracheal/
11	Mechanical* Ventilat*.mp.
12	Neurally Adjusted Ventilatory Assist*.mp.
13	open lung ventilat*.mp.
14	Peep.mp.
15	Positive End Expiratory Pressure*.mp.
16	exp Positive-Pressure Respiration/
17	Positive-Pressure Ventilat*.mp.
18	pressure controlled ventilat*.mp.
19	Proportional Assist Ventilat*.mp.
20	Reintubat*.mp.
21	Respiration, Artificial/
22	Respirator Weaning*.mp.
23	Ventilator*.mp.

24	(Ventilat* adj3 Liberation*).mp.
25	exp Ventilators, Mechanical/
26	exp Ventilator Weaning/
27	Ventilator* Weaning*.mp.
28	Ventilation Weaning*.mp.
29	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28
30	Adolescent/
31	Adolescen*.mp.
32	Teen*.mp.
33	Youth*.mp.
34	exp Child/
35	Child*.mp.
36	Infant/
37	Infant, Newborn/
38	Infant*.mp.
39	Infanc*.mp.
40	Newborn*.mp.
41	Neonat*.mp.
42	Pediatrics/
43	P?ediatric*.mp.
44	Hospitals, Pediatric/
45	Intensive Care Units, Pediatric/
46	PICU*.mp.
47	(Kid or kids).mp.
48	Toddler*.mp.
49	30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48
50	Agitation*.ti,ab.
51	Deep Sedation/
52	((pain or agitat* or arousal or withdrawal) adj2 (measurement* or assessment*)).ti,ab.
53	(pain adj2 (scale* or test* or score* or questionnaire* or evaluation*)).ti,ab.
54	Pain Measurement/
55	Numeric rating scale*.ti,ab.
56	Sedation*.ti,ab.
57	Wake-up test*.ti,ab.
58	Pain/
59	Breakthrough Pain/
60	Pain, Procedural/
61	(pain* adj (breakthrough or procedural)).mp.
62	Analgesics/
63	Analgesic*.ti,ab.
64	Clonidine/
65	Clonidine*.ti,ab.

66	Ketamine/
67	Ketamine*.ti,ab.
68	Narcotics/
69	Narcotic*.ti,ab.
70	Morphine/
71	Morphine*.ti,ab.
72	Hydromorphone/
73	Hydromorphone*.ti,ab.
74	Sufentanil/
75	Sufentanil*.ti,ab.
76	Analgesics, Opioid/
77	Opioid*.ti,ab.
78	Opiate*.ti,ab.
79	Fentanyl/
80	Fentanyl*.ti,ab.
81	Remifentanil/
82	Remifentanil*.ti,ab.
83	"Hypnotics and Sedatives"/
84	Hypnotic*.ti,ab.
85	Sedative*.ti,ab.
86	Chloral Hydrate/
87	Chloral Hydrate*.ti,ab.
88	Dexmedetomidine/
89	Dexmedetomidine*.ti,ab.
90	Diazepam/
91	Diazepam*.ti,ab.
92	Lorazepam/
93	Lorazepam*.ti,ab.
94	Medetomidine/
95	Medetomidine*.ti,ab.
96	Midazolam/
97	Midazolam*.ti,ab.
98	Pentobarbital/
99	Pentobarbital*.ti,ab.
100	Propofol/
101	Propofol*.ti,ab.
102	Benzodiazepines/
103	Benzodiazepine*.ti,ab.
104	50 or 51 or 52 or 53 or 54 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103
105	29 and 49 and 104

II. Embase (Elsevier)

Line	Query
#1	adaptive NEAR/2 support NEXT/1 ventilat*
#2	'extubation'/de
#3	'airway extubat*'
#4	(intubation* OR extubation*) NEAR/3 (airway OR tracheal OR intratracheal OR endotracheal OR early)
#5	'intermittent mandatory ventilation'/exp
#6	'intermittent positive-pressure breathing'
#7	'intermittent positive pressure ventilation'/exp
#8	'intermittent positive-pressure ventilat*'
#9	'endotracheal intubation'/exp
#10	'invasive ventilation'/exp
#11	'inverse ratio ventilation'/de
#12	'mechanical* ventilat*'
#13	'neurally adjusted ventilatory assist*'
#14	'noninvasive positive pressure ventilation'/exp
#15	'open lung ventilat*'
#16	peep
#17	'positive end expiratory pressure ventilation'/exp
#18	'positive end expiratory pressure*'
#19	'positive pressure ventilation'/de
#20	'positive-pressure ventilat*'
#21	'pressure controlled ventilation'/de
#22	'pressure controlled ventilat*'
#23	'pressure support ventilation'/de
#24	'proportional assist ventilat*'
#25	'protective ventilation'/exp
#26	reintubat*
#27	'artificial ventilation'/de
#28	'respirator weaning*'
#29	'tracheal extubation'/de
#30	'ventilator'/de
#31	ventilator*
#32	ventilat* NEAR/3 liberation*
#33	'mechanical ventilator'/de
#34	'ventilator weaning'/de
#35	'ventilator* weaning*'
#36	'ventilation weaning*'
#37	'volume controlled ventilation'/exp
#38	'artificial respirati*'
#39	#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7 OR #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28 OR #29 OR #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36 OR #37 OR #38
#40	'adolescent'/exp/mj
#41	'adolescence'/mj
#42	adolescen*:ti,ab

#43	teen*:ti,ab
#44	youth*:ti,ab
#45	'child'/exp/mj
#46	child*:ti,ab
#47	'infant'/exp/mj
#48	'infancy'/exp/mj
#49	'newborn'/exp/mj
#50	infant*:ti,ab
#51	infanc*:ti,ab
#52	newborn*:ti,ab
#53	neonat*:ti,ab
#54	'pediatrics'/mj
#55	p\$ediatric*:ti,ab
#56	'pediatric intensive care unit'/mj
#57	picu*:ti,ab
#58	kid:ti,ab OR kids:ti,ab
#59	'toddler'/exp/mj
#60	toddler*:ti,ab
#61	#40 OR #41 OR #42 OR #43 OR #44 OR #45 OR #46 OR #47 OR #48 OR #49 OR #50 OR #51 OR #52 OR #53 OR #54 OR #55 OR #56 OR #57 OR #58 OR #59 OR #60
#62	'agitation'/mj
#63	'agitation assessment'/exp/mj
#64	agitation*:ti,ab
#65	'sedation'/mj
#66	'deep sedation'/mj
#67	((pain OR agitat* OR arousal OR withdrawal) NEAR/2 (measurement* OR assessment*)):ti,ab
#68	(pain NEAR/2 (scale* OR test* OR score* OR questionnaire* OR evaluation*)):ti,ab
#69	'pain measurement'/mj OR 'numeric rating scale'/mj
#70	sedation*:ti,ab
#71	'wake up test'/mj
#72	'wake-up test*':ti,ab
#73	'pain'/mj
#74	'breakthrough pain'/mj
#75	'procedural pain'/mj
#76	(pain* NEAR/1 (breakthrough OR procedural)):ti,ab
#77	'analgesic agent'/mj
#78	analgesic*:ti,ab
#79	'clonidine'/mj
#80	clonidine*:ti,ab
#81	'ketamine'/mj
#82	ketamine*:ti,ab
#83	'narcotic agent'/mj
#84	narcotic*:ti,ab
#85	'morphine'/mj
#86	morphine*:ti,ab
#87	'hydromorphone'/mj

#88	hydromorphone*:ti,ab
#89	'sufentanil'/mj
#90	sufentanil*:ti,ab
#91	'opiate'/mj
#92	opioid*:ti,ab
#93	opiate*:ti,ab
#94	'fentanyl'/mj
#95	fentanyl*:ti,ab
#96	'remifentanil'/mj
#97	remifentanil*:ti,ab
#98	'hypnotic sedative agent'/mj
#99	'hypnotic agent'/mj
#100	'sedative agent'/mj
#101	hypnotic*:ti,ab
#102	sedative*:ti,ab
#103	'chloral hydrate'/mj
#104	'chloral hydrate*':ti,ab
#105	'dexmedetomidine'/mj
#106	dexmedetomidine*:ti,ab
#107	'diazepam'/mj
#108	diazepam*:ti,ab
#109	'lorazepam'/mj
#110	lorazepam*:ti,ab
#111	'medetomidine'/mj
#112	medetomidine*:ti,ab
#113	'midazolam'/mj
#114	midazolam*:ti,ab
#115	'pentobarbital'/mj
#116	pentobarbital*:ti,ab
#117	'propofol'/mj
#118	propofol*:ti,ab
#119	'benzodiazepine'/mj
#120	benzodiazepine*:ti,ab
#121	#62 OR #63 OR #64 OR #65 OR #66 OR #67 OR #68 OR #69 OR #70 OR #71 OR #72 OR #73 OR #74 OR #75 OR #76 OR #77 OR #78 OR #79 OR #80 OR #81 OR #82 OR #83 OR #84 OR #85 OR #86 OR #87 OR #88 OR #89 OR #90 OR #91 OR #92 OR #93 OR #94 OR #95 OR #96 OR #97 OR #98 OR #99 OR #100 OR #101 OR #102 OR #103 OR #104 OR #105 OR #106 OR #107 OR #108 OR #109 OR #110 OR #111 OR #112 OR #113 OR #114 OR #115 OR #116 OR #117 OR #118 OR #119 OR #120
#122	#39 AND #61 AND #121
#123	#122 AND [21-4-2021]/sd NOT [5-10-2021]/sd

III. CINAHL Complete (EBSCO)

Line	Query
S1	(MH "Agitation")
S2	Agitation*

S3	(MH "Sedation")
S4	((pain or agitat* or arousal or withdrawal) N2 (measurement* or assessment*))
S5	(pain N2 (scale* or test* or score* or questionnaire* or evaluation*))
S6	(MH "Pain Measurement") OR "numeric rating scale*"
S7	Sedation*
S8	"wake up test**"
S9	(MH "Pain")
S10	(MH "Breakthrough Pain")
S11	(MH "Pain, Procedural")
S12	Pain* N1 (breakthrough OR procedural)
S13	(MH "Analgesics")
S14	Analgesic*
S15	(MH "Clonidine")
S16	Clonidine*
S17	(MH "Ketamine")
S18	Ketamine*
S19	(MH "Analgesics, Nonnarcotic")
S20	Narcotic*
S21	(MH "Morphine")
S22	Morphine*
S23	Hydromorphone*
S24	(MH "Sufentanil")
S25	Sufentanil*
S26	(MH "Analgesics, Opioid")
S27	Opioid*
S28	Opiate*
S29	(MH "Fentanyl")
S30	Fentanyl*
S31	(MH "Remifentanil")
S32	Remifentanil*
S33	(MH "Hypnotics and Sedatives")
S34	(MH "Sedatives, Barbiturate")
S35	(MH "Sedatives, Nonbarbiturate")
S36	Hypnotic*
S37	Sedative*
S38	(MH "Chloral Hydrate")
S39	"chloral hydrate**"
S40	Dexmedetomidine*
S41	(MH "Diazepam")
S42	Diazepam*
S43	(MH "Lorazepam")
S44	Lorazepam*
S45	Medetomidine*
S46	(MH "Midazolam")
S47	Midazolam*
S48	(MH "Pentobarbital")
S49	Pentobarbital*

S50	(MH "Propofol")
S51	Propofol*
S52	(MH "Antianxiety Agents, Benzodiazepine")
S53	Benzodiazepine*
S54	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14 OR S15 OR S16 OR S17 OR S18 OR S19 OR S20 OR S21 OR S22 OR S23 OR S24 OR S25 OR S26 OR S27 OR S28 OR S29 OR S30 OR S31 OR S32 OR S33 OR S34 OR S35 OR S36 OR S37 OR S38 OR S39 OR S40 OR S41 OR S42 OR S43 OR S44 OR S45 OR S46 OR S47 OR S48 OR S49 OR S50 OR S51 OR S52 OR S53
S55	Toddler*
S56	Kid OR kids
S57	PICU*
S58	(MH "Intensive Care Units, Pediatric")
S59	P#ediatric*
S60	(MH "Pediatrics")
S61	Neonat*
S62	Newborn*
S63	Infanc*
S64	Infant*
S65	(MH "Infant, Newborn")
S66	(MH "Infant") OR (MH "Infant, Hospitalized") OR (MH "Infant, High Risk")
S67	Child*
S68	(MH "Child") OR (MH "Child, Hospitalized") OR (MH "Child, Medically Fragile") OR (MH "Child, Preschool")
S69	Youth*
S70	Teen*
S71	Adolescen*
S72	(MH "Adolescence+")
S73	S72 OR S71 OR S70 OR S69 OR S68 OR S67 OR S66 OR S65 OR S64 OR S63 OR S62 OR S61 OR S60 OR S59 OR S58 OR S57 OR S56 OR S55
S74	Ventilation Weaning*
S75	ventilator* weaning*
S76	(MH "Ventilator Weaning")
S77	(MH "Ventilators, Mechanical")
S78	ventilat* N3 liberation*
S79	ventilator*
S80	'respirator weaning*'
S81	(MH "Respiration, Artificial")
S82	reintubat*
S83	proportional assist ventilat*
S84	(MH "Pressure Support Ventilation")
S85	pressure controlled ventilat*
S86	positive-pressure ventilat*
S87	(MH "Positive Pressure Ventilation")
S88	Positive End Expiratory Pressure*
S89	(MH "Positive End-Expiratory Pressure")
S90	peep

S91	open lung ventilat*
S92	neurally adjusted ventilatory assist*
S93	mechanical* ventilat*
S94	(MH "Mandatory Minute Volume Ventilation")
S95	(MH "Inverse Ratio Ventilation")
S96	(MH "Intubation, Intratracheal")
S97	Intermittent Positive-Pressure Ventilat*
S98	(MH "Intermittent Positive Pressure Ventilation")
S99	intermittent positive pressure breathing
S100	(MH "Intermittent Positive Pressure Breathing")
S101	(intubation* OR extubation*) N3 (airway OR tracheal OR intratracheal OR endotracheal OR early)
S102	artificial respirati*
S103	airway extubat*
S104	(MH "Extubation")
S105	adaptive N2 support ventilat*
S106	S105 OR S104 OR S103 OR S102 OR S101 OR S100 OR S99 OR S98 OR S97 OR S96 OR S95 OR S94 OR S93 OR S92 OR S91 OR S90 OR S89 OR S88 OR S87 OR S86 OR S85 OR S84 OR S83 OR S82 OR S81 OR S80 OR S79 OR S78 OR S77 OR S76 OR S75 OR S74
S107	S54 AND S73 AND S106

Supplemental E-Table 6: First Voting Results (N=23)

Definition	% Agree	% Agree with concept with modification	% Disagree
1. Invasive mechanical ventilation (MV)	83%	17%	0%
2. & 3. Non-invasive ventilation (NIV)*	61%	35%	4%
4. Negative pressure ventilation (NPV)	87%	13%	0%
5. High flow nasal oxygen (HFNC)	70%	17%	13%
6. Conventional oxygen therapy	74%	26%	0%
7. Liberation from invasive MV	70%	30%	0%
8. Failed attempt to liberate from invasive MV	61%	39%	0%
9. Liberation from respiratory support	83%	13%	4%
10. Duration of non-invasive respiratory support	78%	13%	9%
11. Total duration of invasive MV	78%	9%	13%
12. & 13. Spontaneous breathing trial (SBT) vs Extubation readiness testing (ERT)	78%	17%	4%
14. 28-ventilator free days (VFDs)	78%	17%	4%
15. & 16. Planned vs rescue use of post-extubation non-invasive respiratory support	83%	17%	0%

*Continuous positive airway pressure (CPAP) definition was separated from NIV definition after the first voting

Supplemental E-Table 7: Final Voting Results (N=23)

Definition	% Agree	% Disagree
1. Invasive mechanical ventilation (MV)	100%	0
2. Non-invasive ventilation (NIV)	87%	13%
3. Continuous positive airway pressure (CPAP)	91%	9%
4. Negative pressure ventilation (NPV)	96%	4%
5. High flow nasal oxygen (HFNC)	87%	13%
6. Conventional oxygen therapy	96%	4%
7. Liberation from invasive MV	96%	4%
8. Failed attempt to liberate from invasive MV	96%	4%
9. Liberation from respiratory support	100%	0
10. Duration of non-invasive respiratory support	100%	0
11. Total duration of invasive MV	91%	9%
12. Spontaneous breathing trial (SBT)	91%	9%
13. Extubation readiness testing (ERT)	96%	4%
14. 28-ventilator free days (VFDs)	91%	9%
15. & 16. Planned vs rescue use of post-extubation non-invasive respiratory support	100%	0

Supplemental E-Table 8: Examples of 28-Ventilator Free Days (VFDs-28) Calculation

#	Scenario	VFDs-28
1.	Patient intubated upon admission, extubated on day 7 and survived.	21
2.	Patient intubated upon admission, never extubated, and died on day 7.	Zero
3.	Patient intubated upon admission, extubated on day 7 without re-intubation, and died on day 27.	Zero
4.	Patient intubated upon admission, extubated on day 7, re-intubated on day 29 and died on day 30.	21