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Early View

Task force report

ERS Statement on pediatric long term noninvasive respiratory support

Brigitte Fauroux, François Abel, Alessandro Amaddeo, Elisabetta Bignamini, Elaine Chan, Linda Corel, Renato Cutrera, Refika Ersu, Sophie Installe, Sonia Khirani, Uros Krivec, Omendra Narayan, Joanna MacLean, Valeria Perez De Sa, Marti Pons-Odena, Florian Stehling, Rosario Trindade Ferreira, Stijn Verhulst

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ERS Statement on pediatric long term noninvasive respiratory support

Brigitte Fauroux[1,2], François Abel[3], Alessandro Amaddeo[4], Elisabetta Bignamini[5], Elaine Chan[3], Linda Corel[6], Renato Cutrera[7], Refika Ersu[8], Sophie Installe[9], Sonia Khirani[1,2,10], Uros Krivec[11], Omendra Narayan[12], Joanna MacLean[13], Valeria Perez De Sa[14], Marti Pons-Odena[15,16], Florian Stehling[17], Rosario Trindade Ferreira[18], Stijn Verhulst[9,19].

[1] AP-HP, Hôpital Necker, Pediatric noninvasive ventilation and sleep unit, F-75015 Paris, France
[2] Université de Paris, EA 7330 VIFASOM, F-75004 Paris, France
[3] Respiratory Department, Sleep & Long-term Ventilation Unit, Great Ormond Street Hospital for Children, London, UK
[4] Emergency department, Institute for Maternal and Child Health IRCCS Burlo Garofolo, Trieste, Italy.
[5] Pediatric Pulmonology Unit Regina Margherita Hospital AOU Città della Salute e della Scienza Turin Italy
[6] Pediatric ICU, Centre for Home Ventilation in Children, Erasmus university Hospital, Rotterdam, the Netherlands
[7] Pediatric Pulmonology Bambino Gesù Children's Hospital, IRCCS, Rome, Italy
[8] Division of Respiratory Medicine, Department of Pediatrics, Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa Canada
[9] Department of Pediatrics, Antwerp University Hospital, Edegem, Belgium.
[10] ASV Santé, Gennevilliers, F-92000 France
[11] Department of Paediatric Pulmonology, University Children's Hospital Ljubljana, University Medical Centre Ljubljana, Ljubljana, Slovenia
[12] Sleep and Long Term Ventilation unit, Royal Manchester Children's Hospital and University of Manchester, Manchester, UK
[13] Division of Respiratory Medicine, Department of Pediatrics, University of Alberta, 4-590 Edmonton Canada
[14] Department of Pediatric Anesthesia and Intensive Care, Children's Heart Center, Skåne University Hospital, Lund, Sweden
[15] Pediatric Home Ventilation Programme, University Hospital Sant Joan de Déu, Barcelona, Spain.
[16] Respiratory and Immune dysfunction research group, Institut de Recerca Sant Joan de Déu, Santa Rosa 39-57, 08950 Esplugues de Llobregat, Spain.
[17] Pediatric Pulmonology and Sleep Medicine, Cystic Fibrosis Center, Children´s Hospital, University of Duisburg-Essen, Essen, Germany
[18]Pediatric Respiratory Unit, Department of Paediatrics, Hospital de Santa Maria, Academic Medical Centre of Lisbon, Portugal
[19] Laboratory of Experimental Medicine and Pediatrics, University of Antwerp, Antwerp, Belgium.

Address correspondence to:
Brigitte Fauroux, AP-HP, Hôpital Necker, Pediatric noninvasive ventilation and sleep unit, 149 rue de Sèvres, Paris, F-75015 France. [brigitte.fauroux@nck.aphp.fr], Tel: +33.1.71.19.60.92; Fax: +33.1.71.19.57.70

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Abstract

Long term noninvasive respiratory support, comprising continuous positive airway pressure (CPAP) and noninvasive ventilation (NIV), in children is expanding worldwide, with increasing complexities of children being considered for this type of ventilator support and expanding indications such as palliative care. There have been improvements in equipment and interfaces. Despite growing experience, there are still gaps in a significant number of areas: there is a lack of validated criteria for CPAP/NIV initiation, optimal follow-up and monitoring; weaning and long term benefits have not been evaluated. Therapeutic education of the caregivers and the patient is of paramount importance, as well as continuous support and assistance, in order to achieve optimal adherence. The preservation or improvement of the quality of life of the patient and caregivers should be a concern for all children treated with long term CPAP/NIV. As NIV is a highly specialised treatment, patients are usually managed by an experienced pediatric multidisciplinary team. This Statement written by experts in the field of pediatric long term CPAP/NIV aims to emphasize on the most recent scientific input and should open up to new perspectives and research areas.

Keywords

Noninvasive ventilation; home care; quality of life; therapeutic education; child; sleep-disordered breathing.

Introduction

Long-term noninvasive respiratory support consists of delivering a ventilatory assistance through a noninvasive interface, as opposed to invasive ventilation via an endotracheal tube or a tracheostomy. Noninvasive respiratory support comprises 1) continuous positive airway pressure (CPAP) which is based on the delivery of a constant positive pressure in the airways aiming to maintain airway patency and, 2) noninvasive ventilation (NIV) *per se* (or bilevel positive airway pressure, BPAP) which aims to assist the breathing of the patient by delivering a supplemental higher positive pressure during each inspiration [1]. CPAP is mainly indicated in case of obstruction of the upper airways where the restoration of airway patency throughout the entire breathing cycle is sufficient to normalize breathing. NIV is indicated for disorders that cause disequilibrium in the respiratory balance. This balance comprises the load imposed on the respiratory system by airway obstruction and/or gas exchange impairment due to lung disease, the capacity of the respiratory muscles to initiate and sustain breathing, and adequate/functional central breathing control. In healthy subjects, the respiratory load, i.e. the effort to generate a breath, is low, the capacity of the respiratory muscles is normal, and the central drive appropriately commands the respiratory muscles. In disorders characterized by an increase in respiratory load, or by weakness of the respiratory muscles, the central drive increases its demands on the respiratory muscles. However, when the demand outstrips the capacity to respond, alveolar hypoventilation, defined by hypercapnia ± hypoxemia, occurs. Hypoventilation may also be observed in case of an abnormal central drive. The aim of NIV will be to “unload” the respiratory muscles by relieving airway obstruction and/or facilitating lung recruitment in case of an increase in respiratory load, to “assist” or “take over” the respiratory muscles in the case of respiratory muscle weakness, and to “take over” the command of the respiratory

muscles in the case of central drive dysfunction [1]. The experience with long term CPAP/NIV is growing and the number of children treated at home with CPAP/NIV is increasing around the world, due to a better screening of patients and expanding experience [2]. Accordingly, this ERS Task Force reviewed the literature on long-term CPAP/NIV in children and summarized the most recent clinical experience and scientific developments in order to describe the best care strategies and identify areas for future research and progress.

Methods

The ERS Scientific Committee approved the development of a Statement on "Pediatric Long-Term Noninvasive Respiratory Support" by a Task Force (TF-2019-01) in 2019. Experts from several European countries and from countries outside Europe who were active within the ERS participated in the Task Force. All members signed forms disclosing conflicts of interest annually. The Task Force sought to answer a series of questions, formed by consensus of all members during multiple online exchanges and one online meeting, with answers based on summarizing the relevant literature and expert opinion of participating authors. A systematic search of the literature was completed by the two chairs of the Task Force (BF and SV) to answer the formulated questions. The MEDLINE, Embase, Wiley Cochrane, CINAHL and Child Development & Adolescent Health databases were searched for the period between January 2016 and September 2019. This search strategy was intended to capture articles published since the last update of the systematic search used for an extensive review by Castro-Codesal et al. on pediatric (0 – 18 years) long term noninvasive respiratory support, which included references from 1990 to 2015 [2]. Search terms included Continuous Positive Airway Pressure, CPAP, NCPAP, bilevel ventilation (BPAP/BiPAP), airway pressure release ventilation, APRV, noninvasive ventilation, NIV, NPPV, NIPPV or

NIAV with a validated child and adolescent search filter. The search provided 4,564 additional titles between 2016 and September 2019. After excluding case reports, abstracts, non-English articles, papers on acute noninvasive ventilation in the intensive care setting, studies in adults, respiratory support < 3 months, and exclusive diurnal respiratory support), 140 references were selected to prepare the current document in addition to the references included in the review by Castro-Codesal et al. [2] (**Figure 1** and Online Table 1). The final statement was reviewed by caregivers of different countries who gave their input and participated to the research priorities.

1. Disorders that may benefit from CPAP/NIV

1.1 Disorders that may benefit from CPAP

Literature review (Online Table 2.1)

Severe persistent obstructive sleep apnea (OSA) after adenotonsillectomy or upper airway surgery is the main indication for CPAP [3]. Numerous studies have reported the use of CPAP in children with "complex" OSA, such as craniosynostosis [4-14], congenital bone disease (achondroplasia [15-20], pycnodysostosis [21], osteogenesis imperfecta [22]), laryngo-tracheo-bronchomalacia or stenosis [13, 23-29], pharyngomalacia [30], vocal cord paralysis [11, 31], Pierre Robin Sequence [13, 32-36], CHARGE syndrome [37], Down syndrome [27, 38-43], storage disease (mucopolysaccharidosis (MPS) [40] and Morquio-A syndrome [44], mucolipidosis [45]), Prader Willi syndrome [13, 46, 47], and OSA associated with obesity [9, 10, 13, 14, 48]. CPAP has also been used to overcome intrinsic positive end expiratory pressure (PEEP) in infants with bronchopulmonary dysplasia (BPD) [27]. A few studies reported the use of CPAP in children with central nervous disorders (tumors, malformations [49]), severe neurodisability [50], congenital cardiopathy [51], myelomeningocele [52], or Ehlers-Danlos syndrome [53].

Summary

- CPAP has been used in children with :
    - "Complex" OSA, defined as OSA associated with craniofacial or upper airway malformation, or OSA associated with morbid obesity (OSA type II) who present with severe OSA despite optimizing medical and surgical management, or when these aforementioned medical/surgical treatments are not feasible or indicated.
    - A high level of intrinsic PEEP, as observed in infants with BPD.
- CPAP has been successfully implemented at any age.

1.2 Disorders that may benefit from NIV

Literature review (Online Table 2.2)

Numerous studies reported the use of NIV in children with neuromuscular disease (NMD), such as spinal muscular atrophy (SMA) [54-68], Duchenne muscular dystrophy [69-71], juvenile Pompe disease [72, 73], COL6 myopathy (Ullrich congenital muscular dystrophy) [74-76], SEPN1-related myopathy [77-79], Fukuyama congenital muscular dystrophy [80], congenital myasthenic syndromes [81] and other NMD [69, 82-87]), diaphragmatic palsy [88], and severe thoracic deformity [85, 86]. NIV has also been used in children with storage disease (mucopolysaccharidosis [89], mucolipidosis [45]) or Prader Willi syndrome in case of nocturnal alveolar hypoventilation [46, 47, 86], rapid-onset obesity (RO) with hypothalamic dysregulation (H), hypoventilation (H), and autonomic dysregulation (AD) (ROHHAD) syndrome [90, 91], cystic fibrosis [92-95], congenital tracheal stenosis [29], or children with congenital central hypoventilation syndrome (CCHS) [96-99]. And finally, NIV may be proposed in children requiring or not tolerating high CPAP pressures, or in case of persistent hypercapnia despite optimized CPAP [100].

Summary

- The need for NIV is usually evaluated for all children with nocturnal alveolar hypoventilation associated with NMD, severe thoracic deformity, storage disease, Prader Willi syndrome, ROHHAD syndrome, morbid obesity, or children with CCHS.
- NIV is sometimes used as an alternative to CPAP in children with OSA in case of CPAP intolerance or when high CPAP pressure is required but not tolerated.
- Children with NMD are usually treated with NIV and not CPAP.
- NIV has been successfully implemented at any age.

1.3 **Longitudinal or cross-sectional national/regional/local studies**

Literature review (Online Table 2.3)

Long term NIV in children has been reported in countries with well-developed health care systems (USA [101], Canada [102-105], Australia [106, 107], France [108, 109], United Kingdom [86, 110-112], Ireland [113], Italy [114-116], Switzerland [117], Austria [118], the Netherlands [119], Portugal [120], Korea [121, 122], Hong Kong [123], Japan [124], Taiwan [125]) but also in other countries such as Turkey [126, 127], Serbia [128], Brazil [129], Chile [130], Argentina [91], South Africa [131], Thailand [132], Malaysia [133], Iran [134] and Nepal [135]). Most studies reported an increase in the number and respective percentages of children treated with CPAP/NIV over time as compared to invasive ventilation [119].

Summary

- The feasibility of long term CPAP/NIV has been proven worldwide.

2. Initiation criteria, initiation location and recommended/optimal settings

2.1 Initiation criteria

Literature review (Online Table 3.1)

CPAP/NIV has been initiated in an acute/subacute (pediatric intensive care unit (PICU)) setting or electively (in a stable setting, after a sleep study) [91, 102-105, 112, 124, 136, 137] or prior to elective surgery (such as arthrodesis [138]). CPAP/NIV may be initiated during an acute respiratory failure [102] in case of failure to wean from invasive ventilation (endotracheal tube or tracheotomy [102, 105, 118, 124, 137, 139]) or NIV [102, 136]. In an elective setting, CPAP/NIV has been initiated based on the following criteria: sleep-disordered breathing (SDB) symptoms [91, 109, 118, 126], recurrent pneumonia [118], failure to thrive [109, 118], anomalies in daytime arterial blood gases [104, 109, 112], nocturnal hypoxemia (low pulse oximetry (SpO_2)) ± hypercapnia (elevated transcutaneous carbon dioxide pressure ($PtcCO_2$)), nocturnal alveolar hypoventilation [104, 109, 112, 118, 124, 126, 133], lung function data (low forced vital capacity (FVC)) [102, 105, 109], echocardiographic data (right heart failure, pulmonary hypertension) [109, 126, 133], elevated apnea-hypopnea index (AHI) [91, 102, 104, 105, 109, 112], or "increase in work of breathing" [133]. However, the definitions of "hypoxemia", "hypercapnia", "alveolar hypoventilation" are rarely available and vary among studies. Severe persistent OSA in children with upper airway malformation, defined by an obstructive apnea-hypopnea index (OAHI) > 5 or 10 events/hour associated with abnormal nocturnal gas exchange (**Table 1**) after adenotonsillectomy or upper airway surgery, or as an alternative to surgical intervention, is the main indication for CPAP. In infants with SMA type 1, NIV has been initiated to prevent or limit thoracic deformity [58, 63]. Age- or disease-specific criteria are not available, except for infants with SMA and patients with Duchenne muscular dystrophy [54, 63, 140]. The efficacy and adherence with CPAP/NIV according to the initial setting (PICU or (sleep unit)-ward, i.e. acute vs elective), as well as initiation criteria have not been evaluated.

Summary

- CPAP/NIV initiation is usually based on objective criteria, after having explored all other alternative therapies.
- Nocturnal hypercapnia, defined by a $PtcCO_2$ > 50 mmHg during 2% or more of nocturnal sleep time or more than 5 consecutive minutes, has been used as a criterion to initiate NIV.
- Besides these criteria for CPAP/NIV, other criteria including the patient's respiratory status and disease, abnormal daytime and nocturnal gas exchange, sleep and/or lung function data or other parameters may also play a role.
- CPAP/NIV is usually initiated in an elective setting, which implies a pre-requisite screening of patients at risk for severe OSA and/or nocturnal alveolar hypoventilation.
- Long term CPAP/NIV may follow an admission to the PICU for acute respiratory failure. In this situation, long term CPAP/NIV has been justified by unsuccessful weaning from invasive ventilation or CPAP/NIV in the PICU.

2.2 Ineligibility criteria for CPAP/NIV

Literature review

CPAP/NIV may be difficult, impossible, or not indicated in the following situations: impossibility to correct OSA and/or alveolar hypoventilation, inability to protect the upper airways due to bulbar dysfunction and/or copious respiratory secretions, lack of cooperation of the patient and/or the family, uncontrolled gastro-oesophageal reflux or severe aerophagia, anatomical facial abnormalities, recent facial surgery or complications related to the interface, and high ventilator dependence [1, 141-144].

Summary

- The above listed criteria should be checked or corrected before proposing CPAP/NIV.

2.3 Location of elective CPAP/NIV initiation

Literature review (Online Table 3.1)

CPAP/NIV is usually initiated in a hospital setting [103-105, 109, 112, 126, 133] and more rarely at home [105]. CPAP initiated in an out-patient setting may be as efficacious (as defined as correction of SDB and objective adherence) as during hospitalization (when associated with a therapeutic education program [145]) but this remains to be confirmed by more studies considering different health systems and social conditions.

Summary

- CPAP/NIV is most often initiated during a hospitalization with a recent tendency towards an out-patient or even home setting, depending on the underlying condition, team expertise and local facilities.
- CPAP/NIV initiation in an out-patient setting is possible but needs further validation..

2.4 Initial settings for CPAP/NIV

Literature review (Online Tables 3.2 and 3.3)

The American Academy of Sleep Medicine (AASM) recommends a titration polysomnography (PSG) to set the optimal CPAP level [100]. However, a CPAP level set on other criteria (symptoms, comfort, SpO_2, built-in software data, measurement of the oesogastric pressures) has also shown to correct SDB symptoms and the AHI [27, 145, 146]. Mean CPAP level to overcome respiratory events is usually achieved at 8 ± 3 cmH_2O following titration with a starting pressure of 4 cmH_2O [5, 10, 27, 112, 147-149]. A minimal CPAP level has not been validated. Some studies highlighted that optimal CPAP level is independent of age and underlying diagnosis [5, 10]. Auto-CPAP, which is a CPAP mode that automatically adjusts the level of pressure to the patient's requirements, is sometimes used in children whose weight is above the minimal weight recommended by the manufacturer. Auto-

CPAP has shown to be a safe and effective means of initiating CPAP in children but mean autoPAP pressure (AutoMean pressure) and average device pressure ≤ 90% of time (Auto90 pressure) are usually below treatment pressure determined by titration PSG [150]. Auto-CPAP and other "complex" CPAP modes have not shown to be associated with a greater efficacy (decrease of AHI), comfort, or adherence than constant CPAP [148, 149]. The specific indications, settings and subset of patients who might benefit from these CPAP modes have not been identified.

For NIV, the usual treatment IPAP after titration ranges between 10-14 cmH_2O with an EPAP between 4-6 cmH_2O with starting pressures of 4 cmH_2O for EPAP and 8 cmH_2O for IPAP [60, 73, 82]. Higher IPAP pressures (18 ± 6 cmH_2O) have been used in children [112]. Lower EPAP levels have been used in patients without airway obstruction but an optimal EPAP level (or a range) has not been validated. In the literature, the goal of CPAP/NIV settings is to achieve a tidal volume of 6-10 ml/kg ideal body weight. For this reason, volume guarantee modes have been developed. A back up rate is commonly used in children with NMD or impaired central drive and is usually set at 2 to 3 breaths below the patient's physiological or spontaneous breathing rate (12-18 breaths/min) [60, 82, 151]. For children with OSA, the AASM recommends a titration PSG to set the optimal IPAP and EPAP level [100]. No data is available on the usefulness of a ramp (for fixed CPAP) and humidification. For children with cystic fibrosis, high IPAP levels may be required [93]. A small study showed that the titration of NIV settings by means of the monitoring of oesogastric pressures was associated with optimal patient-ventilator synchronization and a decrease in work of breathing [93]. In the case of inappropriate inspiratory trigger (not sufficiently sensitive), the use of a back up rate has shown to be associated with a decrease in the work of breathing [152].

Summary

- CPAP is usually initiated either with the help of PSG or other objective assessment tools and titrated to the optimal pressure to overcome the increased work of breathing, upper airway obstruction and gas exchange abnormalities. Starting pressure is usually set at 4 cmH_2O with a mean treatment CPAP pressure of 8 ± 3 cmH_2O.
- Auto-CPAP has been used in selected patients but has not shown to be superior to fixed pressure CPAP.
- For NIV, starting inspiratory (IPAP) and expiratory pressures (EPAP) are usually set at 8 and 4 cmH_2O, respectively, with a final IPAP of 10-14 cmH_2O and EPAP of 4-6 cmH_2O. Higher IPAP levels may be necessary in selected patients, as patients with cystic fibrosis or obesity.
- A back up rate is commonly used for children with NMD and impaired central drive and is usually set 2-3 breaths below the child's physiological or spontaneous breathing rate.
- The AASM recommends using a titration PSG to set the optimal IPAP and EPAP level [100]. However, as PSG is not available in all centers, adequate titration may be achieved without a full PSG [93, 145, 153].
- For children with cystic fibrosis having difficulties to adapt to NIV, the titration of NIV settings by means of the monitoring of oesogastric pressures has shown to be associated with an optimal decrease in the work of breathing and a better patient-ventilator synchrony.

2.5 Which professionals may initiate CPAP/NIV?

Literature review

The qualifications of the staff members who initiate and follow children on long term CPAP/NIV are rarely reported [145]. In Europe, children on long term CPAP/NIV are managed by pediatricians (pediatric pulmonologists and/or intensivists) ± nurses trained in

CPAP/NIV ± technicians (for home visits) [145]. In the US and Canada, children on long term CPAP/NIV are managed by pediatricians (pediatric pulmonologists and/or intensivists), nurses trained in CPAP/NIV, physiotherapists, and respiratory therapists.

Summary

- Children treated with long term CPAP/NIV seem to benefit from qualified medical staff to initiate and follow up treatment, as mandated by local/regional/national regulations.

3 **Equipment**

3.1 **Interfaces**

*Literature review (**Table 2** and Online Tables 4.1 and 4.2)*

Nasal masks are the most used interface [86, 141, 153-156] with an adequate fitting of the interface having shown to be crucial for CPAP/NIV success [86, 141, 156, 157]. It may be difficult to find a well-fitted interface for children with facial deformity [141, 154]. Case series studies reported a successful use of a humidified high-flow nasal cannula (HFNC) with a regular CPAP device [158] or of the nasal RAM cannula [159] with a NIV device for children who did not tolerate a commercial interface. Recently, a nasal cloth mask has become available for children > 2 years of age who have plastic intolerance [160]. Mouthpiece is the only interface that may exclusively be used while awake for diurnal NIV. Complications from the interface are common and may be related to an inappropriate fitting (skin injury, leaks, mucosal drying or excessive skin hydration, conjunctivitis, corneal ulcers) [157, 160-162] or the pressure exerted by the interface (skin erythema or ulcer, facial deformity, maxillary retrusion) [96, 160, 161, 163] (Table 2).

Summary

- The appropriate choice of interface is of paramount importance for CPAP/NIV success.

- Nasal masks are the first-choice interface but other interfaces may be indicated in case of poor tolerance or side effects (for example, oronasal mask for patients with mouth leaks difficult to manage, nasal prongs for older children who do not tolerate nasal masks).
- Although commercial pediatric masks are nowadays widely available, custom-made masks or "alternative masks" may be an option in selected patients when commercially available interfaces do not fit properly.
- All different types of interfaces have their advantages and limitations (**Table 2**).
- Problems with the interface represent the most common cause of CPAP/NIV failure or intolerance.
- The main interface adverse effects are related to pressure (skin injury, facial deformity), or poor fitting (leaks, mucosal drying, corneal ulcers).
- Oronasal masks are associated with a risk of aspiration, especially in infants and children with limited upper limb movements such as patients with NMD and/or impaired swallow function.
- The importance of an appropriately fitted headgear should not be underestimated, especially in children with skull or cranial deformity.

3.2 **Ventilators**

Literature review (Online Table 4.3)

A review has listed the CPAP/NIV devices that can be used in children at home [164] and two reviews listed factors guiding the choice of a CPAP/NIV device, such as humidification, alarms, trigger sensitivity, and cost [86, 142]. The performance of ventilators is not always optimal for children, especially the trigger sensitivity [165].

Summary

- The choice of a device is based on the child's characteristics (weight, underlying disease, and ability to trigger the ventilator) and medical needs (clinical stability).
- Each make (of device) has been approved by the manufacturer for use in patients with certain minimal weight(s).
- Appropriate alarms and an internal and external battery are required for patients with limited respiratory autonomy.
- Patients with a high ventilator dependency (> 16 hours/24) should have a backup device.
- A double switch-off maneuver offers a security to avoid untimely switch-off of the ventilator.
- Humidification of inspired air seems associated with a greater comfort and less secretions problems.
- Passive humidification with Heat and Moisture Exchange (HME) filters has not been validated for CPAP/NIV devices.

4 **Follow-up**

4.1 **Follow-up procedures**

Literature review (Online Table 5.1)

Several studies showed the persistence of respiratory events and/or abnormal nocturnal gas exchange requiring an intervention during systematic follow up PSG/PG, performed 3 to 6 months after CPAP/NIV initiation, even in asymptomatic patients [5, 146, 147, 166-172]. Monitoring of nocturnal gas exchange during CPAP/NIV at home is feasible and informative for outpatient follow-up [167, 168]. For some devices, the built-in software may give useful information on the child's respiratory parameters (when the child's weight is ≥ to the minimal weight recommended by the manufacturer) but the scoring of the AHI by the device tends to overestimate the AHI scored on a simultaneous respiratory polygraphy (PG) [173, 174]. The

OSA-18 questionnaire scores sometimes improve when ventilator setting changes are implemented after a PSG/PG [170]. A follow up PSG/PG (with or without CPAP/NIV) is sometimes indicated to assess the improvement in SDB following an intervention (e.g. change in ventilatory settings, upper airway or maxillofacial surgery, orthodontics*)* [12, 13, 175]. Telemedicine is sometimes useful for the follow-up of adolescents with NMD on long term NIV [176, 177] and children with OSA treated with CPAP [178, 179]. Despite of the information noted above, there is a lack of validated CPAP/NIV follow up strategies and numerous questions remain unanswered:

- The most pertinent outcome measures or targets (such as normalization or level of improvement of AHI, SpO_2, and $PtcCO_2$) have not been validated
- The optimal timing for the checking of CPAP/NIV settings during follow up has not been validated.
- Should the optimal timing be tailored according to the age of the child and/or the underlying disease?
- How should CPAP/NIV settings be checked: PSG, PG and/or overnight gas exchange or SpO_2 alone?
- Should the CPAP/NIV settings be checked after each intervention aiming at improving SDB (upper airway or maxillofacial surgery or neurosurgery?) and what is the optimal time lag (according to the type of surgery)?
- On which criteria should the CPAP/NIV settings be changed: persistent respiratory events ± abnormal gas exchange ± SDB symptoms and/or comfort?
- What are the consequences of suboptimal CPAP/NIV settings (e.g. poor compliance, poor sleep quality, arousals, and/or neurocognitive outcome)?

Summary

- Analysis of built-in software and home monitoring of overnight gas exchange (SpO_2 ± $PtcCO_2$) may be useful for the follow up of stable children treated with domiciliary CPAP/NIV. Together with a clinical evaluation, the analysis of the ventilator built-in software data may constitute and practical and efficient way to check the patient's status during follow up visits. This may also reduce the need for hospital visits and increase the satisfaction of the families.
- A PSG or PG with CPAP/NIV is useful in case of suboptimal control of SDB with standard follow up visits.
- Follow up schedule depends on patient's age, diagnosis, local facilities, and family support. A planned visit 1 month after CPAP/NIV initiation followed by regular visits every 3 to 6 months is usually considered as a minimum. A follow up sleep study to check CPAP/NIV settings is useful after each intervention (e.g. change in ventilator settings, upper airway or maxillofacial surgery, orthodontics) that may affect the severity of SDB.
- An overnight recording of gas exchange (SpO_2 + $PtcCO_2$) at minimum every 6 months has shown to be informative.
- Telemonitoring is feasible and may improve CPAP/NIV adherence and limit side effects.

4.2 **Adherence**

Literature review (Online Table 5.2)

Adherence has mainly been evaluated for CPAP, and less so for NIV [153, 180]. Adherence is assessed on objective criteria (built-in software data) because children and caregivers tend to overestimate real adherence [148]. Adherence reported in the literature usually not covers the entire night and represents the greatest challenge for long term CPAP/NIV [14, 148, 181-188]. Numerous predictors of adherence have been identified: greater self-perceived improvement in SDB symptoms [180], developmental delay (lower

compliance in children with Down syndrome) [144, 189] and better adherence in children with other causes of developmental delay [190, 191]), gender [190], rapid acclimatization to treatment [180], technical issues [180], NIV vs CPAP [192], side effects [180], familiarity with medical treatments, understanding of the disease and its consequences [180], greater improvement in the AHI [188, 193], age [184], ethnicity [184], maternal education [184], family social support [180, 184], family structure [185], perception of CPAP benefits [185], family member using CPAP [14], caregiver self-reported efficacy [194], and internalizing problems [188]. Some strategies/tools may improve adherence: behavioral therapy [195], ABC Questionnaire for identifying patient-specific barriers [183], therapeutic education sessions by a respiratory therapist [186], token economy [196], medical hypnosis [197], and Shared Decision-Making Tools [198]. There is currently no data on new technologies to improve adherence (telemedicine, mobile phone applications).

Summary

- Poor adherence represents one of the most important challenges for long term CPAP/NIV. Although there is no validated definition of good/optimal adherence in children, optimal adherence is a priority: the use of CPAP/NIV during the entire sleep time is the goal.
- In children with high ventilator dependence, (e.g. in CCHS or severe NMD), optimal adherence is essential.
- Adherence is usually evaluated regularly based on objective data (built-in software data).
- Numerous factors related to the patient and the family may impact adherence.
- Individually adapted strategies may improve adherence.

4.3 **Benefits of CPAP**

Literature review (Online Table 5.3)

CPAP may be associated with an improvement in OSA:

- decrease in OSA symptoms: decrease in sleepiness [199]
- correction or improvement in OSA: decrease in AHI, improvement in SpO_2 [5, 145, 146, 148, 149, 199]
- increase in OSA-related quality of life (QoL) [199] and caregiver QoL [199]
- decrease in work of breathing/respiratory effort (oesophageal pressure) [25-27, 32]
- CPAP may allow decannulation in children with a tracheostomy and persistent OSA after decannulation [139].

CPAP may also be associated with an improvement in academic function and behavior

- attention, alertness, concentration [199-202]
- behavior [199, 200]
- school performance [201]
- EEG features of attention-deficit hyperactivity disorder [203].

CPAP may be associated with improvement in other functions:

- cardiac function in Down syndrome [41]
- blood pressure: decrease in systolic blood pressure [204]
- metabolic syndrome: contradictory results: improvement [205, 206], no effect [207], and improvement in liver injury [208].

The data above originate mostly from observational studies; there are no randomized controlled studies. Furthermore, there are no studies evaluating benefits of CPAP on neurobehavioral functioning in children with "complex" OSA.

Summary

- CPAP may be associated with a correction/improvement in OSA-related symptoms and PSG/PG parameters such as AHI, sleep architecture and sleep quality.
- CPAP may be associated with an improvement in neurocognitive dysfunction and behavior.

- Benefits of CPAP on blood pressure, cardiovascular stress and metabolic dysfunction are inconclusive.

4.4 **Benefits of NIV**

Literature review (Online Table 5.4)

Due to ethical constraints, the benefits on NIV have not been confirmed in randomized controlled trials and the published cohort studies mainly consist of a limited number of patients. NIV is associated with:

- an increase in survival in patients with SMA type 1 [57, 62, 65, 66, 209] and Duchenne muscular dystrophy [71, 210]
- fewer hospitalizations in patients with SMA type 1[57, 61, 62, 64, 209], and some NMD [211, 212]); but no change in hospitalizations in other children with NMD [213]
- improvement in SDB symptoms in patients with SMA type 2-3 [60], infantile Pompe disease [73], and other NMD [69, 82, 84]
- improvement in nocturnal and daytime gas exchange in patients with juvenile Pompe disease [72], and NMD [82]
- improvement in sleep quality/architecture and cyclic-alternating patterns in patients with SMA type 1-2 [60], SMA type 2 [214], and other NMD [69, 82]
- decrease in chest deformity in patients with SMA type 1 [58, 63], and SMA type 1-3 [61]
- transient improvement in predicted FVC and thoraco-abdominal asynchrony in patients with Duchenne muscular dystrophy [215]
- improvement in cardiac function in patients with Duchenne muscular dystrophy [216]

- improvement in QoL in children with NMD [217].

Summary

- In children with progressive NMD, NIV is associated with an improvement of sleep-related breathing disorder symptoms, nocturnal and daytime gas exchange, sleep quality and architecture, chest deformity, acute respiratory episodes, and survival with preservation of a child's QoL.
- The benefits of NIV depend on the progression and the prognosis of the underlying disease.

5 **Weaning**

5.1 **Disorders that are conducive for weaning**

Literature review (Online Table 6.1)

A significant number of children could be weaned from long term CPAP over time:

- infants with OSA [147, 218, 219],
- children with craniosynostosis [12, 220]
- children with Down syndrome [38]
- children with "complex OSA" [13, 175]
- children with OSA type I [221]

Weaning from long term NIV is less common (and less reported) than from CPAP [105, 112, 123, 175] and in children with NMD as compared to children treated with NIV for other conditions [102]. However, this may change with the development of innovative therapies, in particular for SMA. Weaning from CPAP or NIV may occur after spontaneous improvement with age [106, 124].

Summary

- 6 to 40% of children can be weaned from long term CPAP or NIV. Weaning may be possible due to spontaneous improvement with age (physiological growth) or after an intervention (orthodontic treatment, upper airway or maxillofacial or neurosurgery).
- Weaning is more common in infants as compared to older children.
- Weaning may be possible in case of OSA type I: after adenotonsillectomy or physiological growth; OSA type II: after weight loss; "complex" OSA: after surgery or physiological growth; lung disease (BPD), or more rarely in patients with NMD.

5.2 Weaning procedure

Literature review (Online Table 6.2)

- Only one study described a local weaning protocol with weaning criteria for CPAP/NIV (**Table 3**) [175]. There is no information on the optimal timing of a weaning trial: this may depend on the underlying disease (ex. Pierre Robin sequence) and/or the age of the patient, and/or additional treatments (e.g. surgery) [175]. There is no information on the optimal duration of CPAP/NIV withdrawal before a baseline PG/PSG without respiratory support. After successful weaning, recurrence of SDB or hypoventilation may occur, underlining the need for continued follow up, at least clinically, depending on the underlying condition [175].

Summary

- A significant proportion of children treated with long term CPAP, and lesser proportion of those on long term NIV, may be weaned from CPAP or NIV, respectively.
- Weaning trials are sometimes proposed in disorders/conditions associated with a potential physiological improvement or after an intervention/surgery aiming at improving SDB.

- Because of a possible need for a "wash-out" period, CPAP/NIV is usually withdrawn for a certain period before performing a sleep study for CPAP/NIV weaning. This wash-out period depends on the patient's status and can last from several days to several weeks.
- Table 3 shows weaning criteria that have been published in the literature.

6 **CPAP/NIV failure**

Literature review (Online Table 7)

HFNC may be an alternative to CPAP in children and adolescents with "complex" OSA non-adherent to CPAP [144, 222]. Management of OSA in infants with Pierre Robin Sequence is highly dependent on center's experience. In infants with Pierre Robin Sequence and severe OSA, Tubingen palatal plate [223], nasopharyngeal airway [224], mandibular distraction osteogenesis [35], glossopexy [225], and tracheostomy [36] have been used mostly as an alternative to CPAP, without a prior CPAP trial, and rarely in case of CPAP failure. In selected adolescents with Down syndrome non-adherent to CPAP, hypoglossal nerve stimulation may be an effective alternative to CPAP [226, 227]. The alternative approaches described above are mostly dependent on single center experience. To address the question of efficacy of various options, multi-centered-randomized controlled trials are needed. There is a lack of data about short- and long-term efficacy of CPAP alternatives (lack of comparative sleep studies). The existing literature has mainly focused on specific conditions with OSA with small series describing local experience on heterogeneous complex OSA patients. There is no (or few) data about management of NIV failure except tracheostomy. Tracheostomy represents the ultimate therapeutic option for all patients [228].

Summary

- There is heterogeneity in the literature about definition of *NIV/CPAP failure* - often used synonymously *with non-adherence of NIV/CPAP* which in itself lacks clarity of its definition in children.
- CPAP/NIV failure or non-(suboptimal/insufficient) adherence may be due to problems related to the equipment, the patient's underlying disease, cognitive status and cooperation, and/or the family or caregivers.
- It is important to address potential contributing factors to NIV/CPAP failure namely (1) technical issues which require checking of equipment and detection and correction of unintentional leaks and patient-ventilator asynchrony; (2) clinical ineffectiveness of treatment i.e. inability to correct SDB; in which case, dual pathology needs to be excluded; (3) behavioral and psychosocial issues; and (4) domestic environment and inadequate support.
- CPAP/NIV failure in a child with OSA is usually evaluated by a multidisciplinary team comprising a pediatric pulmonologist, an ENT surgeon, a maxillofacial surgeon, a neurosurgeon and an orthodontist.
- Behavioral therapy, token economy, and medical hypnosis sometimes increase CPAP adherence.
- HFNC and hypoglossal nerve stimulation offer alternative therapeutic options for selected children non-adherent to CPAP. Other treatments are sometimes effective in infants with Pierre Robin Sequence in specialist centers: Tubingen palatal plate, nasopharyngeal airway, tongue base adhesion (glossopexy), mandibular distraction osteogenesis, or lingual tonsillectomy in older children (mainly adolescents with Down syndrome).
- Tracheotomy represents the ultimate rescue therapy for children with severe OSA or with high NIV dependency.

7. Role of CPAP/NIV in palliative care

Literature review (Online Table 8)

CPAP or NIV has been used within the context of palliative care in few children with end-stage malignancies, musculo-skeletal disease or storage disease, mainly infants with SMA type I [63, 87, 229] but also with mucolipidosis [45] for comfort reasons. Use of NIV as a component of palliative care is limited by lack of experience, cost, unavailability in many hospitals, and lack of literature reporting experience and efficacy.

Summary

- Pediatric palliative care is a complex mosaic of activities that aim to relieve suffering and provide comfort to patients and their families, addressing their physical, psychological, spiritual, social, and ethical needs. It often spans over long time periods. The prevalence of SDB in children with life-limiting illness is underestimated; both pharmacological and noninvasive respiratory therapies are underused.
- Reports on CPAP/NIV as part of a palliative care program are scarce with no systematic information on indications (diseases, goals, symptoms to be controlled, modes, interfaces) or efficacy.
- Respiratory failure is common in children with terminal illness. CPAP/NIV is sometimes an alternative to invasive ventilation when it is not indicated/appropriate due to disease progression. Within this context, CPAP/NIV may contribute to symptom control and improvement in QoL.
- As other therapies within the context of palliative care, CPAP/NIV is sometimes integrated within a shared plan of care that involves the caregivers, health care staff, and children who are deemed competent.

8. CPAP/NIV in special populations

8.1 Children < 24 months

Literature review (Online Table 9.1)

Numerous infants with craniofacial malformations or anomalies of the upper airways may need long term CPAP:

- craniosynostosis [12]
- congenital bone disease: achondroplasia [230, 231], pycnodysostosis [21]
- Treacher Collins syndrome: [230]
- micrognathia: [147]
- choanal atresia : [147]
- cleft palate: [230]
- laryngo-tracheo-bronchomalacia: [26, 27]
- pharyngomalacia [30]
- laryngo-tracheal stenosis: [147]
- tracheal hypoplasia : [26]
- vocal cord paralysis: [31]
- Pierre Robin Sequence; [26, 27, 32, 36, 147, 230, 231]
- CHARGE syndrome: [37]
- macroglossia/Beckwith Wiedemann syndrome: [147]
- Down syndrome: [27, 38]
- storage disease: [230]
- chronic lung disease (BPD): [27]

Some infants are treated with long term NIV:

- SMA I b and c: [232]
- NMD: [87, 232]
- diaphragmatic paralysis: [87, 232]

- CCHS: [87, 232]
- myelomeningocele: [232]
- Down syndrome: [87, 232]
- chronic lung disease: [87]
- airway malacia: [87]
- pulmonary atresia: [87]
- OSA: [87]

Similar to the data on the larger population of long-term CPAP/NIV use in children, the data on the use of long-term CPAP/NIV in infants stems mostly from single center, retrospective studies with some prospective registries [209, 233, 234]. Given this low quality of evidence, strong conclusion with respect to long-term CPAP/NIV use must be made with caution. There is no data on the optimal timing to assess clinical improvement. Experience and use of long-term CPAP/NIV in infants appears to vary between centers with a range of criteria to determine the appropriateness of long-term CPAP/NIV use. Infants are included in many cohorts of the broader pediatric population of long-term CPAP/NIV users. Potential differences in the outcomes of long-term CPAP/NIV use in infants, relative to older children, support examining data related to infants as a distinct group to further understand these differences.

Summary

- Long term CPAP provides benefit across numerous anatomical and functional factors predisposing infants to upper airway obstruction with less risk than invasive ventilation. This, in addition to the high rate of resolution of underlying upper airway obstruction, even in infants with long term risk factors, sometimes supports the consideration of a trial of long-term CPAP/NIV before considering a tracheostomy in infants with upper airway obstruction.

- Given the diversity of disorders represented in the available literature for the use of long-term CPAP for upper airway obstruction, extrapolation of these results to conditions with similar pathophysiology is probably appropriate.
- Despite use in a broad range of NMD and central nervous systems disorders, the majority of data related to the use of long term NIV stems from data from infants with SMA type 1 and CCHS. Extrapolation of this data to other conditions may not be appropriate and should be done with caution.
- Close follow up should be performed due to the particularity of this population: interface side effects, need for specific equipment, regular interface assessment and follow-up visits (due to rapid growth) and weaning attempt.
- The risk of mid-face retrusion is particularly important and rapid in this age group and may limit the long term use of CPAP/NIV.
- With the exception of SMA type 1, mortality in infants using long-term NIV is rare.

8.2. Obese children

Literature review (Online Table 9.2)

The quality of research is low with mainly retrospective observational studies including a limited number of patients. Obese children requiring long term CPAP may present with:

- syndromic obesity: ROHHAD syndrome, Bardet Biedl syndrome, Prader Willi syndrome [47], Down syndrome or
- idiopathic obesity (OSA type II): [48]

Adenotonsillectomy was the first line therapy for OSA in obese children in a retrospective study on 19 children with 10 patients having residual OSA requiring CPAP after surgery [48]. Indeed, adenotonsillectomy is less likely to correct OSA in obese children as compared to non-obese children [185].

Specifics to children with OSA and obesity are:

- CPAP is sometimes withdrawn in case of sufficient weight loss but this is rarely observed.
- CPAP adherence is usually lower than that observed in non-obese children [14, 201, 208].
- Nocturnal hypoventilation is common in obese children with OSA, requiring NIV when hypoventilation is not controlled by optimized CPAP [207].
- Contradictory effects of CPAP on blood pressure and metabolic markers have been observed: no effect in a prospective study on 27 patients [207], benefit in a cross sectional prospective multicenter study on 113 patients, but only 6 treated with CPAP [206] and in a prospective study on 9 patients [208]).

An increase in academic performance and attention has been observed in a small group of CPAP-adherent adolescents with OSA and obesity [201]. A simulation cohort study performed in order to estimate the number of OSA related obesity cases among Indian children (1-14 y of age) and the number of cases of stroke, coronary heart disease (CHD) and type 2 diabetes, considered as main adverse outcomes of OSA related childhood obesity, showed that patients treated both with adenotonsillectomy and CPAP had a higher reduction in adverse outcomes [235].

Summary

- Obese children requiring long-term CPAP may suffer from syndromic obesity (ROHHAD syndrome, Bardet Biedl syndrome, Prader Willi syndrome, Down syndrome) or idiopathic obesity (OSA type II).
- All alternative therapies are explored in parallel or before starting CPAP in an obese child: weight loss, adeno-tonsillectomy, lingual tonsillectomy, orthodontic treatment, bariatric surgery, when possible.

- Barriers to CPAP/NIV adherence in children with obesity may differ from non-obese children; understanding potential differences may be important to tailor support for CPAP/NIV adherence.
- Data on the impact of CPAP/NIV on body mass index and metabolic parameters in children with obesity and OSA is encouraging; further work is needed to examine patient focused outcomes especially in adolescents.

8.3. Children with severe neurodisability

Literature review (Online Table 9.3)

Children with neurodisability may benefit from CPAP or NIV due to upper airway instability, reduction or dysfunction of central drive, and/or abnormal facial or upper airway anatomy. CPAP has been shown to be associated with an improvement of Epworth Sleepiness Scale score, total behavior score, OSA-specific score, and QoL in children with developmental delay [199, 236]. But, in general, there is a lack of data on health outcome changes attributable to CPAP/NIV in children with severe neurodisability [50]. The rate of NIV failure seems higher in children with neurodisability as compared to those without neurodisability [237]. Erratic sleep pattern, as well as concurrent comorbidities e.g. epilepsy, gastro-esophageal reflux, and uncontrolled secretions, may be risk factors for NIV failure.

Summary

- CPAP/NIV is sometimes a treatment option for SDB disorders in children with severe neurodisability (gross motor function classification system (GMFCS) level IV or V or equivalent) despite a potential high risk of failure to establish CPAP/NIV use and uncertain treatment outcomes.
- There is paucity of data on the usage, adherence, and tolerance of CPAP/NIV in these children.

- Although there is a high chance of failure in this group, if tolerated, CPAP/NIV has been associated with an improvement in OSA and QoL.

9. CPAP/NIV and quality of life in children and parents

Literature review (Online Table 10)

Few studies have evaluated QoL in children treated with long term CPAP or NIV and caregivers [238-249]. Several studies (cross-sectional control studies using questionnaires) reported sleep disturbance, poor sleep quality, and reduced sleep efficiency amongst caregivers, compared to controls [238, 242, 243]. Long term NIV in boys with Duchenne muscular dystrophy was associated with an improved sleep quality in mothers [238]. Youth adherent to CPAP had less sleep disturbance and caregivers were less concerned about health issues [241]. This study observed also significant improvement in OSA specific QoL and reduced carers concerns/anxieties among adherent CPAP users, compared to non-adherent users [241]. One cross sectional study used questionnaires to evaluate the anxiety and depression, family functioning and parental QoL and sleep quality of parents of children referred to a sleep lab and found frequent anxiety, poor sleep quality and daytime sleepiness in parents, irrespective of the age of the child, severity of SDB or use of CPAP/NIV [240].

One research study comparing the health related QoL of children with (1) gastrostomy, (2) gastrostomy and long-term ventilation, (3) or long term ventilation only, found the lowest score amongst gastrostomy group, followed by home ventilation and gastrostomy group and then home ventilation only group. This highlights the significant role of underlying conditions in the perception of QoL, rather than the technologies alone [242]. Also, parents of these children had a lower perception of QoL than parents of healthy children [242]. It has to be noted that parents quoted the QoL of their children lower than the children themselves [239, 247].

There is a lack of longitudinal data: most studies were cross sectional studies, with no or short follow up period (up to 3 months). And finally, the individual contribution of CPAP/NIV, the underlying disease, and use of other technologies to the impaired quality of sleep and/or other psychological factors in caregivers is unclear.

Summary

- Studies evaluating QoL in children treated with long term CPAP/NIV and their caregivers are scarce.
- Parents of children relying on NIV/CPAP reported poorer quality of sleep and health related QoL (including anxiety and daytime sleepiness), compared to parents of healthy children.
- Parental perception of health related QoL of children on long term home ventilation was lower compared to healthy children and other disease cohorts. Parents also reported a lower QoL of their children than the children themselves.
- Increased duration in NIV use (amongst Duchenne muscular dystrophy patients) was associated with better caregivers' sleep.
- CPAP adherence appeared to be associated with positive changes in OSA specific QoL.
- The QoL was highly dependent on the underlying disease and additional treatments/technologies.
- Caregivers and patient's input is crucial. **Table 4** gives a summary of the input of caregivers on the present Task Force.

10. Therapeutic education

Literature review (Online Table 11)

Studies describing therapeutic education tools or programs are scarce [55, 145, 250]. Only one study proposed a dedicated program with therapeutic education tools [145]. Training,

real-life scenario and on-going training seems to be of paramount importance [55]. The need for a variety (no details) of (multidisciplinary) health care professionals has been underscored for the appropriate training and education in the care of children on long term CPAP/NIV [250].

Summary

- Therapeutic education is of paramount importance for long-term home CPAP/NIV and should be performed in every center on a routine basis. This contrasts with limited available data on therapeutic education within the context of CPAP/NIV.
- The minimal requirements of an education program for CPAP/NIV include: information on the disease and rationale of CPAP/NIV; understanding of the goal and benefits of CPAP/NIV; adequate information on the appropriate use and cleaning of the interface, device and accessories (humidification); information on the problems and limitations of CPAP/NIV and how to deal with them; and information on the follow up and outcome of CPAP/NIV. This information is focused on the caregivers and the child (by means of an age-adapted program) and repeated during the entire follow up of the child.
- Therapeutic education is a continuous process and should be evaluated and reinforced if needed.

11. Transition

Literature review (Online Table 12)

Ten to 40% of adolescents on long term NIV (more than those on CPAP) are transitioned to adult units [91, 102, 103, 105, 107, 112, 123, 124, 251-253], with a number that tends to increase [105]. Transition facilitators and barriers have been identified [251, 253]. But in practice, the availability of a transition program is rarely specified [252].

Summary

- Transition to adult units is an integral part of care of children on long term CPAP/NIV.
- The transition program is usually adapted to the patient's decisional capacity, family condition, and local/regional/national organization and facilities.

12. Cost and resource use considerations of CPAP/NIV

Literature review (Online Table 13)

A limited number of studies have evaluated the costs and resources needed for long term CPAP or NIV in children. Cumulative expenditure for all care of a patient treated with CPAP or NIV at home are highly variable. Costs were shown to increase with longer ventilator dependency time and specific diagnostic group, like sleep apnea, with or without morbid obesity and congenital/genetic disorders [107, 254]. A study addressing additional caregivers "out-of-pocket" payments related to long term CPAP or NIV in children besides health insurance coverage found that such expenses may exceed 11% of the households' annual income. The large majority experienced at least moderate financial stress. Of note, in 89% of responders, one or more household members stopped or reduced work duties to take care for their child [255]. Several reports described successful use of long-term CPAP or NIV in low income or developing countries. Equipment was provided by family, sponsors or public sources. Cost estimates amounted to under 20.000 € annually [91, 133, 134].

Summary

- Long term CPAP/NIV is associated with considerable public and private expenses and may impose financial stress on caregivers or family.
- There is limited data on the impact of CPAP/NIV on health care savings (prevention of hospitalisations etc.).
- Long term CPAP/NIV is sometimes implemented in low income or developing countries.

Conclusion

There has been an exponential increase in the number of children receiving long term CPAP/NIV worldwide over the past three decades. In parallel, there is increasing complexities of children being considered for long term CPAP/NIV. The indications for CPAP/NIV are ever expanding; which are not matched by the level of evidence available for our clinical practice. These indications comprise children treated with CPAP for complex OSA, specific populations such as children with severe neurodisability and CPAP/NIV for palliative care. There have been improvements in equipment and interfaces, however, there is still a gap for a significant number of situations. There is a lack of validated criteria for CPAP/NIV initiation, optimal follow-up and monitoring, and weaning. Long term benefits of CPAP/NIV have not been evaluated. Therapeutic education of the caregivers and the patient is of paramount importance, as well as continuous support and assistance. CPAP/NIV success warrants optimal treatment adherence, which definition should be based on optimal treatment efficacy. The preservation or improvement of the QoL of the caregivers and the patients is a concern for all children treated with long term CPAP/NIV. Children on CPAP/NIV are optimally managed by a pediatric multidisciplinary and experienced team. Long term CPAP/NIV is expensive, yet it can be successfully implemented in low-resource settings. Healthcare planning based on up-to-date information on number of children receiving long term CPAP/NIV and their clinical information including health outcomes (e.g. in the form of registry) is much needed. A summary of research area for the future is given in **Table 5**.

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Figure 1: Search strategy

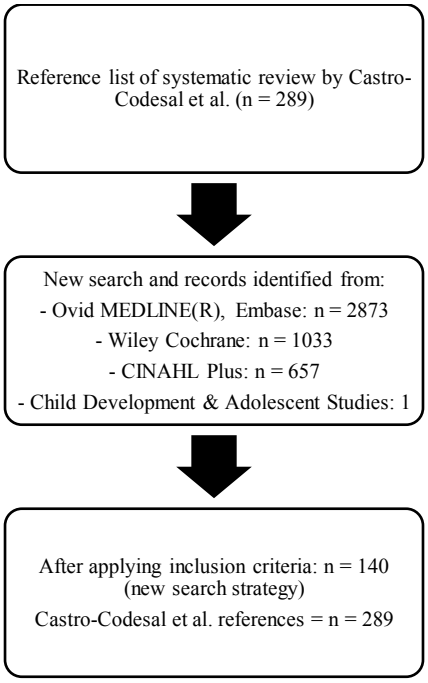

Table 1: Respiratory criteria that have been used for continuous positive pressure or noninvasive ventilation initiation [130].

1. Minimum SpO_2 < 90%
2. Maximal $PtcCO_2$ > 50 mmHg
3. Time spent with a SpO_2 < 90% ≥ 2% of recording time
4. Time spent with a $PtcCO_2$ > 50 mmHg ≥ 2% of recording time
5. 3% oxygen desaturation index > 1.4 events/h
6. AHI > 10 events/hour

Abbreviations: SpO_2: pulse oximetry, $PtcCO_2$: transcutaneous carbon dioxide pressure, AHI: apnea-hypopnea index.

Table 2: Interfaces for continuous positive pressure treatment or noninvasive ventilation.

Interface	Advantages	Disadvantages	Side effects
Nasal mask	Small volume Large choice of models and sizes Allows the use of a pacifier Allows speaking and eating (which provokes mouth leaks)	Not usable in cases of mouth leaks (unless a chin strap can be used concurrently)	Pressure sores (nasal bridge, face) Maxillary deformity (retrusion)
Oronasal mask	Prevents mouth leaks Less risk of midfacial hypoplasia	Large volume Not available for infants Risk of asphyxia (if can't be removed by the patient him/herself) Difficult to use with a pacifier Limits speaking and eating Limits secretion management	Pressure sores Risk of aspiration
Full face mask	Prevents mouth leaks Prevents maxillary deformity (retrusion)	Large volume Claustrophobia Risk of asphyxia (if can't be removed by the patient him/herself) Difficult to use with a pacifier Limits speaking and eating Limits secretion management	Pressure sores Risk of aspiration
Nasal prongs	Small, light No pressure sores Allows speaking and eating (which provokes mouth leaks)	Not available for infants Not usable in cases of mouth leaks	Nasal irritation and/or pain
Mouthpiece	Small, light, can be used on demand while awake	Cannot be used during sleep Difficult to be used by young children	None

Table 3: Respiratory criteria that have been used to allow discontinuation from continuous positive airway pressure (CPAP) or noninvasive ventilation (NIV): all 4 major criteria should be fulfilled with at least 2 minor criteria [169].

Major criteria	1) Resolution of nocturnal and daytime symptoms of sleep-disordered breathing after several nights sleeping without CPAP/NIV, such as snoring, sweating, arousals, laboured breathing, change in behaviour or attention, 2) Percentage of recording time spent with a $SpO_2 \leq 90\% < 2\%$, 3) Percentage of recording time spent with a $PtcCO_2 \geq 50$ mmHg $< 2\%$, 4) Obstructive apnea-hypopnea index < 10 events/h on a poly(somno)graphy
Minor criteria	1) Minimal $SpO_2 > 90\%$ 2) Maximal $PtcCO_2 < 50$ mmHg 3) 3% oxygen desaturation index ≤ 1.4 events/h.

Abbreviations: SpO_2: pulse oximetry, $PtcCO_2$: transcutaneous carbon dioxide pressure

Table 4: Summary of input and comments of our caregivers and patients panel

Section	Patient and caregiver input
General remarks	- Harmonization of practices among different countries. - The harmonization of the management of CPAP/NIV failure and intolerance is a priority to keep tracheostomy as a last treatment option.
2. Initiation	- Acclimatization to CPAP/NIV should be adapted to the individual patient, i.e. initial settings to facilitate acclimatization may differ between patients, as well as the time delay to obtain optimal compliance. - "Optimal compliance" e.g. during the entire sleep time, should be the goal
3. Equipment	- Regular check-ups including read-outs of the ventilator and the possibility of current ventilators (i.e. volume guarantee modes) to correct for changes in the patient's clinical conditions is reassuring for the caregivers. - Need for easy and immediate access to supplies when needed. - The availability of a back-up interface and circuit at home, prompt intervention in case of ventilator malfunctioning or breakdown, and a back-up ventilator in case of high ventilator dependency (patients with NMD)
4. Follow-up	- More research is needed on patient reported outcomes on the effects of CPAP/NIV. - It is critical that the patients and parents have understood and accepted the need for CPAP/NIV and get acquainted with the equipment, especially the interface, beforehand. - Definition/goals for subjective sleep quality under CPAP/NIV as this might differ according to the underlying condition and comorbidities. - Importance of 24/7 access to medical and technical back-up. - Side effects: • Who to manage gastric/abdominal distension? • How to prevent the risk vomiting/aspiration in patients who are unable to remove their mask? • How to prevent/manage CPAP/NIV craniofacial complications?
5. Weaning	- Harmonization of weaning criteria and procedures.
9. Quality of life	- Patients and caregivers QoL will increase after observing the positive effects of CPAP/NIV. - Importance of open and transparent communication with between caregivers and the medical team. - The effect of CPAP/NIV on neurocognitive functioning in children with underlying syndromes requires further study.
10. Therapeutic education	- Importance of continuous, age-appropriate education on the underlying condition, its evolution and consequences and the importance of CPAP/NIV as they grow older. - Importance of technical education on the different aspects and troubleshooting with machine and interface malfunctioning. - Education should include a patient and caregivers booklet which includes all practical information. - Tips and tricks for the cleaning and maintenance of the equipment.

	- In patients with neuromuscular diseases, education should also integrate airway clearance (which is not the scope of this statement).
11. Transition	- What are the goals in the transition procedure for our patients? - The transition process should be prepared/started early (during adolescence) - Patient's self-management should be promoted with psychological support addressing potential barriers. - Pediatric and adult teams should work closely together.

Abbreviations: CPAP: continuous positive airway pressure, NIV: noninvasive ventilation, NMD: neuromuscular disease.

Table 5: Future clinical and research priorities

1. Population	• Harmonization of the management of pediatric NIV patients across countries.
2. Initiation of CPAP/NIV	• The efficacy, benefit, and outcome of CPAP/NIV should be assessed according to the initiation criteria. • The most pertinent criteria to initiate CPAP/NIV according to the underlying disease or age should be identified. • Comparison of the efficacy and benefits according to the location of CPAP/NIV initiation. Definition of criteria for hospital or home initiation. • Comparison of the efficacy of "complex" CPAP modes vs constant CPAP. • Evaluation of the usefulness of additional settings (ramp for CPAP, humidification). • Larger scale studies on patients with BPAP to have better idea of settings used in a more comprehensive cohort of NIV patients.
3. Equipment	• Comparative data of interfaces with regard to tolerance and side effects and the usefulness of alternating different types on interfaces in a single child. • The long-term facial effects in older children. • Lack of data on the reversibility of the adverse effects after CPAP/NIV weaning or change of interface. • Lack of information on the importance of the headgear (suitability, skull deformity induced by the headgear). • Evaluation of the interest of complementary technologies (3 dimensional printing, pressure measurements) to guide the choice and positioning of the interface. • Development and validation of built-in software data for children, especially < 30kg. • Usefulness and benefit of new NIV modes (AVAPS, iVAPS).
4. Follow-up	*Follow-up procedures* • Evaluation of the optimal follow-up strategy in terms of timing and protocols. • Evaluation of the usefulness and limitations of telemonitoring for the follow up. *Adherence* • Usefulness of new technologies to improve adherence (telemedicine, mobile phone applications) • Investigating the link between adherence and relevant end-organ morbidity. *Benefits* • Benefits of CPAP on academic function and behavior in children with "complex" OSA. • Efficacy of NIV should also be assessed on the child's neurocognitive outcome, behavior and academic performance.
5. Weaning	• Development and validation of weaning criteria and protocols for CPAP and NIV.
6. CPAP/NIV failure	• Multi-centered-randomized controlled trials on alternative ventilation strategies
7. Palliative care	• Effects of NIV in palliative care (improvement in dyspnea, sleep quality, and QoL)
8. Special populations	*Infants* • Multi-centered studies investigating factors predicting greater benefit from long-term CPAP/NIV use with a focus on

	long-term outcome data. Studies looking at technical aspects concerning interfaces and ventilation modes are also warranted. *Obesity* • Studies assessing the long term follow-up of obese children treated with CPAP/NIV and differences comparing CPAP to NIV in obese children including differences in required pressures, adherence and health outcomes. • Additional sleep problems are common in children with obesity and may impact adherence to therapy; this has not been explored. *Severe neurodisability* • Prospective data collection focusing on QoL and changes in health outcomes in patient with severe neurodisability that is attributable to CPAP/NIV. • Prospective studies to assess the clinical benefit of CPAP/NIV in this patient group, comparing to alternative treatments, such as oxygen or nasopharyngeal airway, is needed.
9. Quality of life	• Longitudinal study investigating fluctuations and factors influencing the QoL of children on CPAP/NIV and their parents/caregivers, in conjunction with evolution of the underlying conditions, family functioning/coping strategies. • To examine the interaction between adherence and QoL outcomes for the patients and families.
10. Therapeutic education	• Development of therapeutic education tools and programs for CPAP/NIV with studies investigating their efficacy. • Which health care professionals should be involved in therapeutic education and should they receive a specific training?
11. Transition	• The efficacy of different transition programs evaluated on loss of follow up, optimal data, effect of the underlying disease, cognitive dysfunction or physical dependence, control of the disease, and patient satisfaction.
12. Costs	• Evaluation of health care cost savings thanks to CPAP/NIV (reduction of hospitalizations, health care use, etc.).

Abbreviations: NIV: noninvasive ventilation, CPAP: continuous positive airway pressure, BPAP: bilevel positive airway pressure, AVAPS: average volume assured pressure support, iVAPS: intelligent volume assured pressure support, OSA: obstructive sleep apnea, QoL: quality of life.

On line Table 1: Final Search Strategy – Pediatric CPAP and NIV

Search date: September 29, 2019
Databases searched: Ovid MEDLINE(R), Embase, Wiley Cochrane; CINAHL, Child Development &Adolescent Health
Limits: Human, Children (0 – 18), English, 2016 to current
Excluded: Conference abstracts, letters, notes comments editorials, case reports

Note: This search was conducted from 2016 onwards to capture artcles published since the last update of the systematic search used for the following article: Sleep Med Rev. 2018 Feb;37:148-158. doi: 10.1016/j.smrv.2017.02.005. Epub 2017 Mar 2. The search strategy in this scoping review was not duplicated, as we focused on only CPAP and NIV.

Ovid MEDLINE: Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE® 1946-Present, Embase Classic+Embase 1947 to 2019 September 27

Ovid MEDLINE(R), Embase

#	Searches	Results
1	exp Continuous Positive Airway Pressure/ use ppez	6624
2	exp positive end expiratory pressure/ use emczd	54343
3	(cpap or ncpap or continuous positive airway pressure or aprv or airway pressure release ventilation*).ti,ab,kf,kw.	32750
4	exp Noninvasive Ventilation/	10445
5	((ventilat* or respirat*) adj2 (non-invasive or noninvasive)).ti,ab,kf,kw.	18860
6	(NIV or NPPV or NIPPV or NIAV).ti,ab,kf,kw.	11407
7	or/1-6	91100
8	exp adolescent/ or exp child/ or exp infant/ use ppez or exp adolescence/ use emczd or exp childhood disease/ use emczd or exp infant disease/ use emczd	8258030
9	(adoles* or teen* or boy* or girl* or minor or minors or puberty* or pubescen* or pediatric* or paediatric* or kindergar* or highschool*).ab,ti,kf,kw.	2459217
10	(infant* or infancy or newborn* or baby* or babies or child* or schoolchild* or school age or school ages or school aged or preschool* or kid or kids or toddler*).ab,ti,kf,kw.	4209639
11	(pediatric* or paediatric* or infan* or child* or adolescen* or young).jn,jw. or (pediatric* or paediatric* or infan* or child* or adolescen* or young).in.	3625222
12	exp Minors/ or exp Pediatrics/	173721
13	or/8-12	11047742
14	7 and 13	25564
15	animals/ not (humans/ and animals/)	5967853
16	14 not 15	25428

17	limit 16 to english language	23370
18	limit 17 to yr="2016 -Current"	7387
19	limit 18 to (case reports or comment or congress or editorial or letter or conference abstract or note) [Limit not valid in Ovid MEDLINE(R),Ovid MEDLINE(R) Daily Update,Ovid MEDLINE(R) In-Process,Ovid MEDLINE(R) Publisher,Embase; records were retained]	2378
20	Case Report/	4556630
21	18 not (19 or 20)	4009
22	remove duplicates from 21	2873

Wiley Cochrane

#1 MeSH descriptor: [Continuous Positive Airway Pressure] explode all trees 982
#2 (cpap or ncpap or continuous positive airway pressure or aprv or airway pressure release ventilation*):ti,ab 5116
#3 MeSH descriptor: [Noninvasive Ventilation] explode all trees 196
#4 ((ventilat* or respirat*) NEAR/2 (non-invasive or noninvasive)):ti,ab 2070
#5 (NIV or NPPV or NIPPV or NIAV):ti,ab 1378
#6 #1 or #2 or #3 or #4 or #5 7183
#7 MeSH descriptor: [Minors] explode all trees 8
#8 MeSH descriptor: [Child] explode all trees 1198
#9 MeSH descriptor: [Infant] explode all trees 15492
#10 MeSH descriptor: [Adolescent] explode all trees 100701
#11 (adoles* or teen* or boy* or girl* or minor or minors or puberty* or pubescen* or pediatric* or paediatric* or kindergar* or highschool*):ab,ti 73364
#12 (infant* or infancy or newborn* or baby* or babies or child* or schoolchild* or school age or school ages or school aged or preschool* or kid or kids or toddler*):ab,ti 151625
#13 #7 or #8 or #9 or #10 or #11 or #12 266932
#14 #6 and #13 with Cochrane Library publication date Between Jan 2016 and Dec 2019 1033

CINAHL Plus

#	Query	Limiters/Expanders	Last Run Via	Results
S18	S9 AND S15	Limiters - Published Date: 20160101-20191231 Expanders - Apply equivalent subjects Narrow by Language: - english Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus	657

			with Full Text	
S17	S9 AND S15	Limiters - Published Date: 20160101-20191231 Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	669
S16	S9 AND S15	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	1,929
S15	S10 OR S11 OR S12 OR S13 OR S14	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	849,991
S14	AB (infant* or infancy or newborn* or baby* or babies or child* or schoolchild* or school age or school ages or school aged or preschool* or kid or kids or toddler*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	371,352
S13	TI (infant* or infancy or newborn* or baby* or babies or child* or schoolchild* or school age or school ages or school aged or preschool* or kid or kids or toddler*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	327,023
S12	AB (adoles* or teen* or boy* or girl* or	Expanders - Apply	Interface -	215,329

	minor or minors or puberty* or pubescen* or pediatric* or paediatric* or kindergar* or highschool*)	equivalent subjects Search modes - Boolean/Phrase	EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	
S11	TI (adoles* or teen* or boy* or girl* or minor or minors or puberty* or pubescen* or pediatric* or paediatric* or kindergar* or highschool*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	171,403
S10	MH child OR MH infant OR MH adolescent OR MH minors OR MH pediatrics	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	489,951
S9	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	9,028
S8	AB (NIV or NPPV or NIPPV or NIAV)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	1,095
S7	TI (NIV or NPPV or NIPPV or NIAV)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases	118

			Search Screen - Advanced Search Database - CINAHL Plus with Full Text	
S6	AB ((ventilat* or respirat*) N2 (non-invasive or noninvasive))	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	2,363
S5	TI ((ventilat* or respirat*) N2 (non-invasive or noninvasive))	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	1,870
S4	MH Noninvasive Ventilation	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	0
S3	AB cpap or ncpap or continuous positive airway pressure or aprv or airway pressure release ventilation*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	3,127
S2	TI cpap or ncpap or continuous positive airway pressure or aprv or airway pressure release ventilation*)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database -	2,234

			CINAHL Plus with Full Text	
S1	MH Continuous Positive Airway Pressure	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	4,738

Child Development & Adolescent Studies

#	Query	Limiters/Expanders	Last Run Via	Results
S5	S1 OR S2 OR S3	Limiters - Publication Date: 20150101-20191231 Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Child Development & Adolescent Studies	1
S4	S1 OR S2 OR S3	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Child Development & Adolescent Studies	55
S3	TX (NIV or NPPV or NIPPV or NIAV)	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Child Development & Adolescent Studies	17
S2	TX ((ventilat* or respirat*) N2 (non-invasive or noninvasive))	Expanders - Apply equivalent subjects Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - Child Development & Adolescent Studies	14
S1	TX (cpap or ncpap or continuous	Expanders - Apply	Interface - EBSCOhost	31

	positive airway pressure or aprv or airway pressure release ventilation*)	equivalent subjects Search modes - Boolean/Phrase	Research Databases Search Screen - Advanced Search Database - Child Development & Adolescent Studies	

Online Table 2.1: Patients (pathologies) who may benefit from continuous positive airway pressure (CPAP).

Author	Country	Journal	Type of study	Number of patients	Ages	Pathologies	Comments
Afsharpaiman et al. [1]	Australia	Sleep & Breathing	Retrospective cohort	46 children 25 had OSA	3 m-14 yrs	Achondroplasia	9 treated with CPAP = 9.8% of those > 2 yrs and 28% of those < 2 yrs
Mogayzel et al. [2]	USA	J Pediatr	Prospective cohort	88 children	1 m-12.6 yrs	Achondroplasia	2 treated with CPAP
Schluter et al. [3]	Germany	Georgian Med News	Cohort study	22 + 2 children	1.3 m-15 yrs	22 achondroplasia + 2 hypochondroplasia	3 treated with CPAP or BPAP
Waters et al. [4]	Australia	Am J Med Gen	Cohort study	30 children	1-47.6 yrs	Achondroplasia	13 treated with CPAP
Julliand et al. [5]	France	Am J Med Gen	Retrospective cohort	30 children	0.4-17.1 yrs	Achondroplasia	1 treated with CPAP, 4 with BPAP
Tenconi et al. [6]	France	Am J Med Gen	Retrospective cohort	43 children	0.3-13.3 yrs	Achondroplasia	2 treated with CPAP
Fauroux et al. [7]	France	AJRCCM	Retrospective cohort	12 children	8 m-6.5 yrs	Laryngomalacia	12 treated with CPAP
Zwacka et al. [8]	Germany	Sleep & Breathing	Retrospective cohort	10 infants	1 to 5 m	Laryngomalacia	10 treated with CPAP
Essouri et al. [9]	France	Intensive Care Med	Prospective physiological + clinical study (Poeso + Pgas measures)	10 infants	3-18 m	5 laryngomalacia (1 + Down syndrome), 3 tracheomalacia (1 + Down syndrome), 1 tracheal hypoplasia, 1 Pierre Robin Sequence	BPAP associated with patient-ventilator asynchrony (trigger insufficiently sensitive)
Kawaguchi et al. [10]	USA	J Pediatr Surgery	Retrospective cohort	4 type III and 5 type IV	8 m-21 yrs	Tracheomalacia after laryngotracheal cleft	5 treated with CPAP

				laryngotracheal cleft		repair	
Pellen et al. [11]	Australia	Int J Pediatr Otorhinolaryngology	Retrospective cohort	16 infants (1 death)	0-9 m	Congenital tracheal stenosis	10/15 treated with CPAP
Shatz et al. [12]	Israel	Otol Rhinol Laryngol	Retrospective cohort	50 infants	1-18 m	Pharyngomalacia	9/50 treated with BPAP, 5/50 with CPAP
Lesnik et al. [13]	France	Laryngoscope	Retrospective cohort	26 children	<17 yrs	Bilateral vocal cord paralysis	8 treated with CPAP (< 10 yrs)
Nanaware et al. [14]	India	Indian J Pediatr	Retrospective cohort	56 children, 23 with sleep disordered breathing	<18 yrs	52% craniofacial anomaly, 17% NMD or skeletal disease, 1 vocal cord paralysis, 1 achondroplasia, 1 Bardet-Biedl, 1 Albright osteodystrophy	CPAP for 1 patient with bilateral vocal cord paralysis
Leboulanger et al. [15]	France	Pediatrics	Retrospective cohort	7 infants	1-10 m	Pierre Robin Sequence	5 treated with CPAP, 2 with BPAP
Amaddeo et al. [16]	France	Plastic Reconstructive Surgery	Prospective cohort	44 infants	0-2 m	Pierre Robin Sequence	9/44 treated with CPAP
Daniel et al. [17]	Australia	Int J Pediatr Otorhinola	Retrospective cohort	39 infants	> 12 m	Pierre Robin Sequence	18/39 treated with CPAP

		ryngology					
Filip et al. [18]	Norway	Cleft Palate Craniofacial Surgery	Retrospective national cohort 1980-2010	104 children	3.3-33.4 yrs	Pierre Robin Sequence	8 treated with CPAP (duration days to 1 yr), 8 nasopharyngeal tube, 2 oropharyngeal tube, 6 tracheotomy
Kam et al. [19]	Canada	Canadian Respir J	Retrospective cohort 2000-2010	139 patients	9 ± 14 m	139 Pierre Robin Sequence	20 treated with CPAP, 28 nasopharyngeal tube, 45 tong-lip adhesion, 5 mandibular distraction osteogenesis, 19 tracheotomy
Trider et al. [20]	Canada	Int J Pediatr Otorhinolaryngology	Prospective study	51 children	0-14 yrs	CHARGE syndrome	10/51 treated with CPAP
Girbal et al. [21]	Portugal	Rev Port Pneumol	Retrospective study	68 children	1-176 m	5 Pierre Robin Sequence 5 airway malacia 5 Down syndrome 6 Prader Willi syndrome 9 cerebral palsy 10 craniofacial malformation 5 mucopolysaccharidosis 6 metabolic diseases 3 obesity	CPAP (n=52) or NIV (n=16)

Marcus et al. [22]	USA	J Pediatr	Retrospective cohort	94 children	0-19 yrs	25 obesity 23 craniofacial malformation 17 idiopathic OSA 12 Down syndrome 5 cerebral palsy	
Guilleminault et al. [23]	USA	J Pediatr	Retrospective study	74 infants	< 12 m	Syndrome in 38/74: 9 Pierre Robin Sequence, 2 cleft palate, 2 Hunter, 3 achondroplasia, 7 cerebral palsy, 3 epilepsy, 2 hemiplegia, 1 hydrocephalus, 1 NMD	18 discontinued CPAP during follow up
Jarund et al. [24]	Sweden	Scandinavian J Plastic Reconstructive Surgery	Retrospective study	76 children with Apert (27), Crouzon (47), Pfeiffer (2)	23% < 13 yrs	76 children with Apert (27), Crouzon (47), Pfeiffer (2)	7 patients were treated with CPAP after craniofacial surgery
Jarund et al. [25]	Sweden	Scandinavian J Plastic Reconstructive Surgery	Retrospective stduy	13 children with craniofacial malformation, 13 had OSA		1 child had a tracheostomy, 10 of the 12 others accepted CPAP	
Padman et al. [26]	USA	Clinical Pediatr	Retrospective cohort	10 children	3-18 yrs	Obesity and craniofacial malformation	BPAP in 6 obesity 3 craniofacial

							malformation
Massa et al. [27]	UK	Arch Dis Childh	Retrospective cohort 1994-1999	66 children	0.1-19 yrs	24 craniofaciostenosis 6 isolated facial defect 4 osteochondrodysplasia 8 mucopolysaccharidosis, 4 NMD 4 obesity 2 Down syndrome, 2 cerebral palsy 3 airway malacia + other	42 accepted CPAP, 22 refused 3 patients could be weaned after craniofacial surgery
Gonsalez et al. [28]	UK	Childs Nervous System	Retrospective cohort	8 children	2.2-15 yrs	Craniofacial dysostosis	CPAP successful in 5/8
Bannink et al. [29]	The Netherlands	Inter J Oral Maxillofacial Surgery	Retrospective cohort	11 children	4.1-23.2 yrs	Syndromic craniofaciostenosis: 3 Apert, 6 Crouzon, 3 Pfeiffer	3 CPAP or nasopharyngeal tube before mid-face advancement, 3/11 needed CPAP after surgery
Shine et al. [30]	Australia	Arch Otolaryngology Head Neck Surgery	Retrospective cohort	19 children	2-18 yrs	Obesity	10 needed CPAP after AT
Beebe et al.	USA	PlosOne	Prospective	13 obese	14.8 ±	Obesity	

[31]			study	adolescents treated with CPAP for OSA	1.8 yrs	6 were compliant and 7 not	
Puri et al. [32]	USA	J Clin Sleep Med	Retrospective cohort	57 children	1.6 -18 yrs	37 obesity 3 craniofacial malformation	
Konstantinopoulou et al. [33]	USA	Sleep Med	Prospective study	23 children	8-19 yrs	Down syndrome (20 with OSA)	10 children with Down, syndrome were randomized to CPAP
Rosen et al. [34]	USA	Clinical Pediatr	Retrospective study	29 infants with Down syndrome, 16 had OSA	< 2 yrs	Down syndrome	6 treated with CPAP Spontaneous improvement in 3 infants after 5 to 10 m
Shete et al. [35]	USA	Int J Pediatr Otorhinolaryngology	Retrospective study	AT in 11 children with Down syndrome + 11 controls	mean age 8.5 yrs	Down syndrome	6 required CPAP or BPAP after AT
Esbensen et al. [36]	USA	J Dev Behav Pediatr	Retrospective study	954 children 455 (47.7%) had a PSG	5-25 yrs	Down syndrome 258 (27%) had OSA:	Patients with OSA: 18.6% treated with CPAP 82 (8.6%) had OSA + behavior disorder: 19.5% treated with CPAP
Dudoignon	France	Am J Med	Retrospective	57 T21	6.2 ± 5.9	Down syndrome	15/57 treated with CPAP

et al. [37]		Genetics Part A	study		yrs		for OSA 4/57 treated with NIV for hypoventilation
Amaddeo et al. [38]	France	Pediatr Pulmonol	Retrospective study	31 children started on CPAP in an out-patient setting	0.8 m-17.5 yrs	7 Down syndrome, 3 achondroplasia, 3 obesity and other	4 (3 Down syndrome) not compliant 3 patients weaned from CPAP
Sudarsan et al. [39]	India	Int J Pediatr Otorhinolaryngology	Prospective study, efficacy AT in mucopolysaccharidosis and Down syndrome	73 children	6-12 yrs	Mucopolysaccharidosis Down syndrome	17 mucopolysaccharidosis and 29 Down syndrome treated with CPAP
Tirosh et al. [40]	Israel	Acta Pediatr	Description of 4 patients	4 children with neurodisability	6 - 16 yrs	1 obesity + mental retardation, 1 attention-deficit/hyperactivity disorder, 1 epilepsy, 1 fragile X syndrome	CPAP possible in children with neurodisability
Al-Iede et al. [41]	Australia	Sleep Med	Retrospective study	148 children treated with CPAP for non-OSA	0.1-16.8 yrs (64% < 1yr)	47 chronic lung disease 37 congenital heart disease, 41 laryngomalacia, 16 tracheobronchomalacia,	

						5 congenital diaphragmatic hernia	
Kirk et al. [42]	Canada	Pediatr Pulmonol	Retrospective study	73 children	0-18 yrs	Myelomeningocele	30 OSA: CPAP success in 18/21 25 CSA: NIV required in 7
Khirani et al [43]	France	Crit Care	Prospective study	12 infants	2-22 m	5 BPD 4 laryngomalacia 1 OSA, 1 Down syndrome, 1 Pierre Robin Sequence	
Waters et al. [44]	Australia	AJRCCM	Retrospective study	80 children	5.7 ± 0.5 yrs	53% of children had a congenital syndrome or malformation	
Clift et al. [45]	UK	J Sleep Research	Retrospective study	17 children and young adults	?	Prader Willi syndrome	7/17 obese patients were treated with CPAP or BPAP (2 did not tolerate)
Pavone et al. [46]	Italy and France	Pediatr Pulmonol	Retrospective study	70 children (< 20 yrs) and 18 adults		Prader Willi syndrome	16/88 treated with CPAP or BPAP (> older patients)
Facchina et al. [47]	France	Am J Med Genetics Part A	Retrospective study	16 children	10.5 ± 4.2 yrs	Mucopolysaccharidosis type IVA (Morquio)	4/16 treated with CPAP (OSA) 2./16 treated with NIV (hypoventilation)
Tabone et	France	Am J Med	Retrospective	7 children	0.3-17.4	7 mucolipidosis	5 CPAP

al. [48]		Genetics	study		yrs	5 MLII, 1 type II-III, 1 type III: OSA in 6/7	1 NIV (hypoventilation)
Leotard et al. [49]	France	Ann Phys Rehabil Med	Retrospective study	15/188 patients with osteogenesis imperfecta had a PSG		12/15 patients with osteogenesis imperfecta had sleep disordered breathing:	2 patients treated with CPAP
Khirani et al. [50]	France	Am J Med Genetics Part A	Retrospective study	10 children	3.3-14.1 yrs	10 pycnodysostosis	9/10 treated with CPAP Weaning in 3 patients, 2 after surgery and 1 spontaneous
Rosen et al. [51]	USA	Supportive Care in Cancer	Retrospective study	70 children with cancer, PSG in 53, 9/20 severe OSA	6-21 yrs	Neoplasms of the CNS	9 treated with CPAP (6 success) and 3 with brainstem tumor treated with BPAP
Bunn et al. [52]	UK	Pediatr Cardiology	Retrospective study	4 children	3-34 m	Congenital cardiopathy and PHT	NIV for 13 – 19 m, correction of PHT with NIV
Domany et al. [53]	USA	J Clin Sleep Med	Retrospective study	65 children	< 18 yrs	Children with Ehlers Danlos referred to a sleep lab 17 OSA, 2 treated with CPAP (1 with mild OSA + somnolence and 1 with	No detailed information on CPAP

						moderate who refused AT)	

Abbreviations: m: months, yrs: years, OSA: obstructive sleep apnea, BPAP: bilevel positive airway pressure, NIV: noninvasive ventilation, Poeso: oesophageal pressure, Pgas: gastric pressure, NMD: neuromuscular disease, BPD: bronchopulmonary dysplasia, PSG: polysomnography, CNS: central nervous system, PHT: pulmonary hypertension, AT: adenotonsillectomy

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Online Table 2.2: Patients (pathologies) who may benefit from noninvasive ventilation (NIV).

Author	Country	Journal	Type of study	Disorders	Ages	NIV	Comments
Birnkrant et al. [1]	USA	Pediatr Neurology	Retrospective study	4 SMA I	2, 4, 7, and 7 m	NIV for 1, 3, 5, and 5 m	All died before 1 yr
Bach et al. [2]	USA	Chest	Retrospective study	11 SMA I	2 - 11 m	11 treated with NIV after ARF, 8 continued NIV during 15 to 59 m	
Bach et al. [3]	USA	Pediatr Pulmonol	Retrospective study	56 SMA I	Respiratory failure before 2 yrs	33 treated with NIV compared to 16 treated with tracheotomy	31/33 survived to 42 ± 26 m, fewer hospitalisations > 5 yrs as compared to tracheotomy
Bach et al. [4]	USA	Am J Phys Med Rehab	2 cases	2 SMA I	7 m, 3 yrs	2 “high span” NIV (NIV settings not specified)	No pectus excavatum, survival until 7 and 3 yrs with NIV 24h/24
Bach et al. [5]	USA	Am J Phys Med Rehab	Retrospective study	106 SMA I	?	Untreated died at 9.6 ± 4 m, 22 with tracheotomy survived at 70.5 ± 43.3 m, 47 treated with NIV, 29/47 were 65.2 ± 45.8 m, 8 died	Same survival with NIV as compared to tracheotomy but fewer hospitalisations with NIV
Lemoine et al [6]	USA	Pediatr Crit Care Med	Retrospective study	49 infants with SMA I	1 - 7 m	All treated with NIV	Longer survival in the proactive as

							compared to the supportive group
Chatwin et al. [7]	UK	Arch Dis Childh	Retrospective study	13 SMA I	4-24 m	All treated with NIV + MI-E, 5 died, duration of NIV not specified	NIV + MI-E associated with a decrease in chest deformity
Ottonello et al. [8]	Italy	Am J Phys Med Rehab	Retrospective study	16 infants with SMA I	< 3 yrs	All treated with NIV	NIV reduces ARF
Gregoretti et al. [9]	Italy	Pediatrics	Retrospective study 1999-2010	194 children with SMA I		121 (62%) no respiratory support, 42 (22%) IV, 31 (16%) NIV The choice of NIV increased from 8% in 1999-2004 to 23% in 2005-2010	Survival with NIV was 68% at 2 yrs and 45% at 4 yrs (95% and 89% with IV) Nearly all non treated patients died < 2 yrs of age
Pane et al. [10]	Italy	Neurology	Retrospective study	122 children with SMA I	3 - 266 m	Survival only possible with NIV > 16h/24 or tracheotomy + nutritional support after the age of 2 yrs	
Ioos et al. [11]	France	Chest	Retrospective cohort	33 SMA I, 35 SMA I-II 100 SMA II 12 SMA II	? (no access)	NIV for 43% SMA I-II 38% SMA II	
Mellies et al. [12]	Germany	Neuromuscul Disord	Prospective study	6 infants SMA I + 1 SMA II (+ 6 SMA controls without NIV)	6 -11 yrs	7 treated with NIV	6 – 12 m: improvement in sleep disordered breathing symptoms, sleep

							quality + architecture
Vasconcelos et al. [13]	Portugal	Revista Port Pneumol	Retrospective study	7 SMA I, 11 type II, 4 type III	6 m -26 yrs	17/22 treated with NIV	NIV associated with a decrease in thoracic deformity and ARF
Han et al. [14]	Korea	PlosOne	Retrospective study in one center (2000-2013)	Home mechanical ventilation in 57 children with child-onset NMD: 58% SMA, 51% SMA I		NIV in only 9/57 children	Decrease of hospitalisations after start of home mechanical ventilation but most children (48/57) were on IV
Kapur et al. [15]	Australia	Pediatr Pulmonol	Cross-sectional study	3 SMA type I, 15 SMA type II and 7 SMA type III	0 - 18 yrs	10 (40%) required NIV: 5 for sleep disordered breathing, 5 for lower respiratory tract infection in the pediatric intensive care unit	
Markstrom et al. [16]	Sweden	Acta Pediatr	Retrospective study	18 infants treated with NIV: 7 SMA intermediate, 3 CCHS, 2 Down syndrome, 2 NMD, 1 diaphragmatic paralysis, 1	1 - 12 m	All treated with NIV	NIV for hypoventilation in 12 and cough/recurrent infections in 6 SMA Duration of NIV 1 – 84 m NIV was discontinued in 6

				myelomening cele, 1 Leigh's sd			infants
Ishikawa et al. [17]	Japan	Neuromuscul Disord	Retrospective study	3 cohorts of Duchenne patients: untreated, tracheotomy, NIV		88 treated with NIV	Longer survival with NIV (mean 39.6 yrs)
Mellies et al. [18]	Germany	Eur Respir J	Retrospective study	5 Duchenne 9 muscular dystrophy 12 neuropathy 4 other NMD	6 - 19 yrs	All treated with NIV	NIV improves daytime and nocturnal gas exchange and sleep quality Re-appearance of sleep disordered breathing with NIV withdrawal
Mellies et al. [19]	Germany	Neurology	Retrospective study	7 juvenile Pompe disease	3 - 27 yrs	2/7 treated with NIV	NIV improves nocturnal and daytime gas exchange
Nabatame et al. [20]	Japan	Brain & Develop	Retrospective study	4 children juvenile Pompe disease	9 - 15 yrs	3 / 4 treated with NIV	No deaths and resumption sleep disordered breathing symptoms
Suresh et al. [21]	Australia	J Pediatr Child Health	Retrospective study	34 Duchenne	1 - 15 yrs	11 treated with NIV because of hypoventilation	

Khan et al. [22]	UK	Arch Dis Childh	Retrospective study	8 children: 4 congenital myopathy 2 congenital muscular dystrophy 2 rigid spine	6 - 13 years	All treated with NIV	Decrease in sleep disordered breathing symptoms, decrease wake time, better SpO_2
Katz et al. [23]	Canada	Arch Dis Childh	Prospective study	49 children with progressive NMD	6 - 17 yrs	7 had nocturnal hypoventilation 6 were treated with NIV	After one yr of NIV: greater decrease in general percept-ion of health status on the Child Health Questionnaire (CHQ-PF50)
Kherani et al. [24]	Canada	Pediatr Pulmonol	Retrospective study	51 infants with NMD	< 1 yr	25/51 treated with NIV 56% NMD 7 /25 weaned from NIV 4 children NIV for palliative care	
Simonds et al. [25]	UK	Eur Respir J	Retrospective study	40 children with NMD or skeletal disease	9 m-16 yrs	38/40 tolerated NIV	Improvement in nighttime and daytime blood gases
Wallis et al. [26]	UK	Arch Dis Childh	Cross sectional survey	933 children on home ventilation	< 17 yrs	704 treated with NIV, 25 CCHS, 88 Duchenne, 10 SMA, 90 other NMD, 9	

			(questionnaire)			cyphoscoliosis, 58 Prader Willi syndrome/obesity	
Sato et al. [27]	Japan	Brain Development	Retrospective survey	48 patients with Fukuyama congenital muscular dystrophy	3.6-31.9 yrs	14 treated with NIV (mean age at NIV start 12 yrs)	
Nadeau et al. [28]	UK	Neurology	Retrospective study	13 patients with Ullrich congenital muscular dystrophy	> 15 yrs at last evaluation	9/13 started NIV at a mean age of 14.3 yrs	
Yonekawa et al. [29]	Japan	J Neurol, Neurosurg & Psychiatry	Cross sectional survey (questionnaire)	33 children + adults with Ullrich congenital muscular dystrophy		NIV started in 13 children, mean age 11.2 yrs	
Quijano-Roy et al. [30]	France	Neuromuscul Disord	Retrospective study	7 children with COL6 myopathy	6.7 ± 8.7 yrs	NIV in 2/7 patients	
Muntoni et al. [31]	UK	Eur J Pediatr Neurol	Retrospective study	5 patients with new form of muscular dystrophy with	< 11 yrs	3 on NIV (2 died)	

				secondary merosine deficiency			
Scoto et al. [32]	UK	Neurology	Retrospective survey	41 children and adults with SEPN1-related myopathy	1-60 yrs	Mean age of NIV start 13.9 yrs 1 child full-time NIV at 1 yr	
Schara et al. [33]	Germany	Eur J Pediatr Neurology	Retrospective survey	11 children with SEPN1-related myopathy	5-21 yrs	NIV in 4 children at a mean age of 11 yrs	
Caggiano et al. [34]	France	Neuromuscul Disord	Retrospective study	6 children with SEPN1-related myopathy (+1 adult)	1-18 yrs	5 treated with NIV (diaphragmatic dysfunction)	
Caggiano at al. [35]	France	Eur J Pediatr Neurology	Retrospective study	5 infants with congenital myasthenic syndrome	3, 6 and 24 mo	3/5 infants treated with NIV	
Payo et al [36]	Spain	Eur Spine J	Retrospective study	24 children severe scoliosis (17 NMD, 7 other)	9-19 yrs	8 children long term NIV (pre-operative)	
Kirk et al.	Canada	Pediatr	Retrospective	73 children with	0-18 yrs	25 central sleep apnea: 7 required NIV	

[37]		Pulmonol	study	myelomening ocele		30 with OSA: CPAP successful in 18/21	
Nashed et al. [38]	Canada	J Inherited Metabolic Dis	Retrospective study	11 children with mucopolysacc haridosis	08-17.8 yrs	4 treated with NIV	
Tibbals et al. [39]	Australia	Pediatr Pulmonol	Retrospective study	4 children with CCHS	6-16 yrs	4 treated with NIV	
Vanderlaan et al. [40]	USA	Pediatr Pulmonol	Cross-sectional survey (questionnaire)	196 patients with CCHS	0.4-38 yrs	55 treated with NIV, 5 with negative pressure ventilation, 17 with phrenic nerve pacing	
Hasegawa et al. [41]	Japan	Pediatr International	Cross sectional survey (questionnaire)	37 CCHS	4 m-34 yrs	14 treated with NIV + 1 with phrenic nerve pacing	
Diep et al. [42]	USA	Respiration	Retrospective study	18 CCHS	19.5 ± 10 yrs	3 prior NIV, 13 transitioned to phrenic nerve pacing with success, 1 failure due to upper airway obstruction	
Facchina et al. [43]	France	Am J Clin Gen Part A	Retrospective study	16 children with mucopolysacc haridosis type IVA	10.5 ± 4.2 yrs	2/16 treated with NIV 4./16 treated with CPAP (all > 11 yrs)	

				(Morquio)			
Tabone et al. [44]	France	Am J Med Gen Part A	Retrospective study	7 patients with mucolipidosis (5 type II, 1 II-III, 1 III)	0.3-17.4 yrs	5 treated with CPAP, 1 with NIV due to hypoventilation	
Dudoignon et al. [45]	France	Am J Med Gen Part A	Retrospective study	57 children with Down syndrome	6.2 ± 5.9 yrs	4/57 treated with NIV 15/57 treated with CPAP	
Clift et al. [46]	UK	J Sleep Research	Retrospective study	17 children with Prader Willi syndrome	?	7/17 treated with CPAP or BPAP (most obese, 2 did not tolerate)	
Pavone et al. [47]	Italy and France	Pediatr Pulmonol	Retrospective study	70 children and 18 adults with Prader Willi syndrome		16/88 treated with CPAP or BPAP (> older patients)	
Repucci et al. [48]	Canada	Orphanet J Rare Dis	Retrospective study	6 children with ROHHAD syndrome	4.7 - 10 yrs	1 died 5/6 treated with BPAP	
Padman et al. [49]	USA	Clin Pediatr	Retrospective study on effect of BPAP on sleep parameters	10 children with OSA	3 - 18 yrs	All treated with BPAP: 3 craniofacial malformation, 1 NMD, 6 obesity 8 continued BPAP	

Pellen et al. [50]	Australia	Int J Pediatr Otorhinolaryngol	Retrospective study	16 infants with congenital tracheal stenosis	0 – 9 m	All treated with NIV pre- post operative, age at start 1 – 6 m, duration 1 – 24 m, 2 (20%) discharged home on NIV	
Archangelidi et al. [51]	UK	J Cystic Fibrosis	Data from UK cystic fibrosis registry 2007-2015	1107/11079 (10%) patients with cystic fibrosis had at least on record with NIV	Children + adults	For children (only): Median age at NIV initiation 13.5 yrs	NIV associated with increased risk of death/transplant 16% of children with NIV died during follow up

Abbreviations: m: months, yrs: years, SMA: spinal muscular atrophy, ARF: acute respiratory failure, NIV: noninvasive ventilation, MI-E: mechanical insufflation-exsufflation, IV: invasive ventilation, NMD: neuromuscular disease, CCHS: congenital central hypoventilation syndrome, BPAP: bilevel positive airway pressure, ROHHAD syndrome: rapid-onset obesity with hypoventilation, hypothalamic dysfunction, and autonomic dysregulation (ROHHAD) syndrome, OSA: obstructive sleep apnea.

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Online Table 2.3: Longitudinal (local/regional/national) surveys

Author	Country	Journal	Study type & dates	Number of patients	Ages	Disorders	Comments
Fauroux et al. [1]	France	Eur Respir J	1992-1933	287 children treated at home with O2, IV or NIV	< 18 yrs	153 children treated with NIV (24 cystic fibrosis, 87 NMD, 21 thoracic deformity) 5 children treated with CPAP	
Jardine et al. [2]	UK	BMJ	Cross-sectional survey, 1997, questionnaires	141 children	< 16 yrs	NIV or IV home: 52 NMD, 13 CCHS, 10 spinal injury, 9 craniofacial syndrome, 1 BPD, 8 other	52/141 treated at home with NIV
Kamm et al. [3]	Switzerland	Swiss Medical Weekly	Postal questionnaires	32 children (7 centres)	< 16 yrs	41% CCHS, 41% NMD, 6% craniofacial	19 NIV, 2 phrenic nerve pacing
Resener et al. [4]	Brazil	J Pediatr (Rio J)	April 1997-June 1998	26 children	1-21 yrs	No detail on NIV: 15 NMD, 8 central sleep apnea, 3 obstructive lung disease	
Fauroux et al. [5]	France	Pediatr Pulmonol	Cross-sectional national study, July 2000	102 children	0-18 yrs	35 NMD, 31 OSA, 17 cystic fibrosis, 9 CCHS, 8 scoliosis, 2 spina bifida, 1 encephalopathy	Only NIV
Edwards et al. [6]	Australia	J Pediatr Child Health	Retrospective survey at 1 center 1991-2004	108 treated with CPAP and 47 with NIV	0-17 yrs	17 NMD, 6 CNS, 2 CCHS, 2 mucopolysaccharidosis, 39 OSA, 11 cyphoscoliosis, 10 obesity, 5 airway	108 treated with CPAP and 47 with NIV

						malacia, 2 cystic fibrosis, 2 BPD, 5 bronchiectasis, 2 achondroplasia, 2 Down syndrome, 1 craniofacial syndrome, 24 other	
Graham et al. [7]	USA	Pediatrics	Retrospective survey in 1995 in the Massachusetts	197 children having chronic ventilatory support	For NIV 10.3 ± 6.6 yrs	98 treated with CPAP or BPAP: 55 NMD or CNS, 2 spinal cord injury, 6 BPD, 21 upper airway, 9 other 2 treated with negative pressure	
Oktem et al. [8]	Turkey (Istanbul)	Respiration	Longitudinal (2001-2006),1 center in Istanbul	34 children	4 mo-17 yrs	For NIV: 18 BPD or airway problems, 3 NMD, (7 died)	23 NIV (11 IV)
Pekcan et al. [9]	Turkey	Turkish J Pediatr	Retrospective study in one center (4 yrs ?)	27 children on home MV: IV and NIV (no numbers)	0 - 15 yrs	16 NMD, 6 lung disease, 3 congenital heart disease, 2 storage disease No information on those on IV and NIV	
Tibbals et al. [10]	Australia	J Pediatr Child Health	Longitudinal (1979-2008), 1 center in Melbourne	168 children	3 w-19 yrs	No distinction IV vs NIV: 55 (32%) OSA, 42 NMD (25%), 23 (14%) tracheobronchomalacia, 20 (12%) cerebral palsy or scoliosis, 7 (4%) CCHS, 7 (4%) other central sleep apnea, +	58 CPAP, 50 BPAP, 48 tracheotomy, 5 phrenic nerve stimulation, 4 negative pressure, 3 nasopharyngeal tube

						other	
Goodwin et al. [11]	UK (SW)	Eur J Pediatr	Retrospective survey 1994-2009 South West of UK	106 children treated with home ventilation (IV and NIV)	< 18 yrs	63/106 treated with NIV:31 NMD, 21 upper airway, 9 CNS, 2 lung disease (no mention CPAP vs NIV)	
Racca et al. [12]	Italy	Pediatr Pulmonol	Postal questionnaires, NIV on January 2007	362 children	8-13 yrs	112 NMD, 52 BPD + upper airway, 17 encephalopathy, 19 central sleep apnea, 12 chest wall anomaly, 1 spinal cord injury	213 NIV
Wallis et al. [13]	UK	Arch Dis Child	Electronic based national questionnaire	933 children	< 17 yrs	25 CCHS, 47 other central sleep apnea, 6 cerebral palsy, 88 Duchenne, 69 SMA, 90 other NMD, 9 scoliosis, 14 BPD, 13 airway malacia, 58 Prader Will/obesity, 153 upper airway obstruction, 5 cystic fibrosis + other	704 (75%) NIV
Sovtic et al. [14]	Serbia	Pediatr Int	Longitudinal (2001-2011) in 1 center (Belgrade)	29 children	0.4-17.3 yrs	7 NMD, 4 cystic fibrosis, 5 OSA, 2 scoliosis or CCHS	18 NIV
Hsia et al. [15]	Taiwan	Pediatr Neonatol	Retrospective study in Taiwan	139 children	3m - 18 yrs	72% NMD, 14% airway/lung dysfunction, 12% metabolic/genetic	Only 3/139 children on NIV

						anomaly	
McDougall et al. [16]	Canada (Vancouver)	Arch Dis Child	Longitudinal (1995-2009), 1 center in Vancouver	144 children started on NIV	0-18 yrs	Decrease in NMD, increase in craniofacial/OSA	116 (81%) NIV, 22 CPAP, 94 BPAP, increase in NIV
Pavone et al. [17]	Italy (Rome)	Early Hum Development	1993-2012	Increase from 1 pt in 1993 to 100 in 2012	?	52 SMA, 26 other NMD, 15 cystic fibrosis, 30 obesity, 7 cerebral palsy, 21 Prader Willi syndrome, 17 encephalopathy, 6 CCHS + ROHHAD, 46 others	Only NIV
Amin et al. [18]	Canada (Toronto)	Pediatr Pulmonol	Longitudinal (1991-2011) in 1 center (Sick Kids Hospital)	379 children identified		35% musculoskeletal 36% respiratory disorders	313 NIV: increase 2x in IV, x10 in NIV
Preutthipan et al. [19]	Thailand	Curr Pediatr Rep	Retrospective data from 1 center	148 children	0-19 yrs	48% OSA, 15% NMD	64% NIV
Gupta et al. [20]	Nepal	J Nepal Pediatr Society	Longitudinal (2001-2012) in 1 center	24 children	?	?	4 NIV
Cancelinha et al. [21]	Portugal	Rev Port Pneumol	Retrospective data from 1 center	31 children	0 - 13 yrs	39% NMD, 23% metabolic disease, 19% central hypoventilation	NIV in 27 children
Han et al. [22]	Korea	PlosOne	Longitudinal (2001-2012) in 1 center (Seoul)	57 children with NMD		No diagnosis for the NIV patients	Only 9 NIV with 8 at home
Park et al. [23]	Korea	J Korean Med Sci	Data from the National	416 children	< 19 yrs, mean	IV: 202 (49%) NIV (51%): 146 NMD,	

			Health Insurance service in 2016	Prevalence 4.4/100000 children	age 6 yrs	46 CNS, 25 cardiopulmonary	
Chatwin et al. [24]	UK (London)	PlosOne	Longitudinal (1993-2011) in 1 center (Royal Brompton)	496 children started on home NIV	< 17 yrs 59 < 1 yr	56% NMD, 14% congenital syndrome, 9% upper airway anomaly, 5% BPD, 4% chest wall disease, 3% obesity, 3% central sleep apnea, 2% cardiac surgery, 4% other	Only NIV
Walsh et al. [25]	Ireland	Irish Med J	Questionnaires to pediatricians	Not available	??	Not available	Increase in NIV but no details
Rose et al. [26]	Canada	Respir Care	National web survey for home providers (2012-2013)	4334 ventilator-assisted patients	Adults and children, 425 (21%) < 18 yrs	Children: 30% muscular dystrophy, 30% central hypoventilation, 12% obesity, 10% chest wall, 6% neurological disease, 6% other	73% NIV
Weiss et al. [27]	Austria	Klin Pediatr	National cross-sectional study (questionnaire) on June 2013	143	143, 111 (78%) < 18 yrs	44% NMD, 19% other NMD, 9% central sleep apnea, 8% OSA, 8% thorax and spinal disease, 5% lung disease, 6% other	95/143 on NIV, 6% CPAP
Nathan et al. [28]	Malaysia	Pediatr Pulmonol	Longitudinal study in 1 center (2001-2014)	70 (2 pts in 2001 to 47 in 2014)	1.1 - 11 yrs for NIV	32 lung disease, 5 upper airway, 7 NMD, 4 chest/spine disease, 1 cardiac, 1 central sleep	60 patients on NIV: 30 CPAP + 30 BPAP

						apnea, 5 spinal cord injury	
Chau et al. [29]	Hong Kong	Respir Care	Longitudinal study in 1 center (1997-2015)	96 patients	< 21 yrs	NIV: 40 NMD, 13 upper airway anomaly, 6 BPD, 1 chest wall deformity, 11 central sleep apnea + metabolic + neurological + genetic disorder	71 NIV (34%): 16 CPAP, 55 BPAP
Van der Poel et al. [30]	South Africa	Pediatr Allergy Immunol Pulmonol	Retrospective study in 1 center	55 children	3 m - 18 yrs	60% NMD	16 (29%) NIV
Ikeda et al. [31]	Japan	Brain Development	Longitudinal study in 1 center (2001-2015)	53 patients	< 20 yrs	36 NMD, 23 congenital anomaly, 17 metabolic disease, 11 perinatal disorder, and other	All NIV
Castro-Codesal et al. [32]	Canada	PlosOne	Retrospective multicenter cohort (2005-2014) in Alberta: x6 increase	622 children	< 18 yrs	371 (60%) upper airway, 107 (17%) CNS, 93 (15%) musculoskeletal and NMD, 39 (6%) cardiorespiratory disease, 12 (2%) other	All NIV: 75% CPAP, 22% BPAP
Leske et al. [33]	Argentina	Pediatr Pulmonol	Longitudinal study in 1 center (2007-2018) Buenos Aires	244 children	3 - 14 yrs	No distinction IV vs NIV: 105 (43%) NMD, 56 (23%) genetic sd (achondroplasia, Prader Willi syndrome, craniostenosis, mucopolysaccharidosis, Down syndrome,	210 (86%) NIV: 21% CPAP

						Treacher Collins, 18 obesity, 11 CCHS 4 BPD, 4 ROHHAD, 17 other	
Hassani et al. [34]	Iran	Anestezjologia Intensywna Terapia	Retrospective study in 1 center	67 children	2 m – 15 yrs	45% lung disease, 31% NMD, 13% metabolic disease	62 (93%) NIV

Abbreviations: IV: invasive ventilation, NIV: noninvasive ventilation, CPAP: continuous positive airway pressure, BPAP: bilevel positive airway pressure, NMD: neuromuscular disease, SMA: spinal muscular atrophy, OSA: obstructive sleep apnea, CCHS: central congenital hypoventilation syndrome, BPD: bronchopulmonary dysplasia, CNS: central nervous system, ROHHAD syndrome: rapid-onset obesity with hypoventilation, hypothalamic dysfunction, and autonomic dysregulation syndrome.

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Online Table 3.1: Initiation criteria and location for CPAP or NIV initiation

Author	Country	Journal	Type of study	Number of patients	Ages	Initiation scenario/criteria	Location of CPAP/NIV initiation
Padman et al. [1]	USA	Pediatr Pulmonol	Retrospective study	15 children: 4 CF and 11 NMD	4 – 21 yrs	ARF in children with CRF: avoidance of intubation (1 failure in one patient with NMD) Duration of BPAP: 1 day to 21 mo	BPAP initiated in the ICU in all patients
Fauroux et al. [2]	France	Pediatr Pulmonol	Cross sectional national study in 1999 (questionnaire)	102 patients	< 18 yrs	Criteria (not exclusive, no details): 67% SDB symptoms 28% nocturnal hypoventilation 21% failure to thrive 18% other symptoms 82% nocturnal SpO_2 9% $PtcO_2$/$PtcCO_2$ 88% ABG 63% sleep study 56% lung function data 31% echocardiography data	All during a hospitalisation
Oktem et al. [3]	Turkey	Respiration	Retrospective study at 1 center 2001-2006	34	4 m-17 yrs	Criteria: 1) hypoventilation: hypoxemia + hypercapnia: daytime hypoxemia < 3 SD, nocturnal hypoxemia SpO_2 < 90% for >5% night, PHT, hypercapnia $PaCO_2$ > 45 mmHg. Indications for NIV: Symptoms of SDB or other symptoms (dyspnea, right heart failure, PHT, transition from tracheotomy) No details for the patients in the study	All during a hospitalisation, median duration 64 (3-180) days (due to delay to have the equipment)

McDougall et al. [4]	Canada	Arch Dis Child	Prospective longitudinal study in 1 center 1995-2009	144 children	< 18 yrs	28 failure to wean from ventilation 31 ARF 40 sleep study results (not specified) 23 SDB symptoms 9 vital capacity < 20% 10 other	Not specified
Amin et al. [5]	Canada	Pediatr Pulmonol	Retrospective study at 1 center 1991-2011	313 treated with NIV			27% in pediatric ICU 70% in sleep lab 3% in-patient ward
Rose et al. [6]	Canada	Respir Care	Web based questionnaire to home care providers 2012-2013	4334 adults & children	425 < 18 yrs	Considerable variation in criteria (adults + children): 57% nocturnal hypoventilation on PSG 38% daytime hypercapnia 32% nocturnal hypercapnia 31% never used daytime hypercapnia 11% never had PSG	All in hospital: sleep lab (38%), ICU (27%), in-patient units (21%)
Chatwin et al. [7]	UK	PlosOne	Retrospective study at 1 center 1993-2011	496 children started on NIV	< 17 yrs	NIV initiated if 1) chronic daytime $PaCO_2$ > 6.5 kPa (alone), 2) PSG: nocturnal $PtcCO_2$ > 6.5 kPa for > 50% night time CPAP initiated when normal PCO_2 with elevated AHI (not specified) 340 (76%) started as in-patients with 67 (15%) started in the pediatric ICU	340 (71%) started as in-patients with 67 (15%) being started in the pediatric ICU
Edwards et al. [8]	USA	Pediatr Crit Care Med	Retrospective cross-sectional analysis among 73 pediatric ICU 2009-2011	115437 PICU patients	?	381 (0.3%) initiated on long term NIV (16% on CPAP), 16% were discharged to a chronic care Disorders: 11% endocrinologic, 15% gastroenterologic, 11% metabolic, 31% epilepsy, 23% cerebral palsy, 34% NMD, 22% encephalopathy, 34%	

						scoliosis, 27% OSA	
Amaddeo et al. [9]	France	Pediatr Pulmonol	Retrospective study	76 children started on CPAP (64) or NIV 12) / 1 yr	0.3 -19.5 yrs	3 scenarios: acute (CPAP/NIV weaning failure in pediatric ICU, n=15), subacute on abnormal overnight gas exchange (n=18) or chronic on a sleep study (n=43)	5 Criteria: 1) min SpO_2 < 90%, 2) max $PtcCO_2$ > 50 mmHg, 3) time with SpO_2 < 90% ≥ 2%, 4) time with $PtcCO_2$ > 50 mmHg ≥ 2%, 5) ODI > 1.4/h, 6) AHI > 10/h. Subacute: most patients had ≥ 3 criteria, Chronic: most patients had ≥ 4 criteria
Weiss et al. [10]	Austria	Klin Padiatr	Cross-sectional survey by questionnaire on 2013	95 children CPAP 9/143 Other NIV		Signs and symptoms before onset: 68% nocturnal hypoxemia 70% nocturnal hypercapnia 29% ARF 28% recurrent pneumonias 17% failure to thrive 37% other symptoms	Not specified
Nathan et al. [11]	Malaysia	Pediatr Pulmonol	Retrospective study at 1 center 2001-2014	30 CPAP 30 BPAP 10 IV		Indications: 54% increase in work of breathing 31% hypoventilation 6% hypoxemia 9% heart failure 29/70 with additional oxygen	In hospital, median stay before discharge 59 (30-114) days
Ikeda et al. [12]	Japan	Brain & Development	Retrospective study at 1 center 2001-2015	53 children treated with NIV	< 20 yrs	Initiation criteria: Min SpO_2 < 92% or max $PtcCO_2$ > 50 mmHg (not specified day or night) 66% in an acute setting (= failure to withdraw NIV after an ARF) 34 % planned initiation (without details)	

						Especially in NMD 94% NIV only nocturnal 60% with additional oxygen (40% of NMD)	
Amaddeo et al. [13]	France	Pediatr Pulmonol	Retrospective study	31 children All on CPAP	0.8- 17.5 yrs	Outpatient program with setting criteria: OSA, age > 6 m, stable condition, living in the hospital area, agreement with regular follow up No pressures reported	All patients were started in an out-patient setting 4/31 non compliant (3 Down syndrome) Median compliance 8h21min/night, 25 nights/mo 3 pts weaned from CPAP
Castro-Codesal et al. [14]	Canada	PlosOne	Retrospective study in Alberta 2005-2014	622 children CPAP (75%) and BPAP (22%)	0-18 yrs	initiation 83% started electively after on PSG 16% acute illness 1%: vital capacity < 30% or transition from IV or palliative care	18% started in hospital 82% started at home
Kapur et al. [15]	Australia	Pediatr Pulmonol	Cross-sectional study	3 SMA type I, 15 SMA type II, 7 SMA type III	0-18 yrs	10/25 (40%) required NIV: 5 for SDB, 5 started during lower RTI (pediatric ICU)	Children requiring NIV were older (10.52 vs 5.67yrs), had a lower vital capacity and higher AHI (3.65 vs 0.08), 2/10 pts had a $PtcCO_2$ > 50mmHg > 2% of sleep time Initiation during RTI an indication? 3/5 had

							normal subsequent PSG
Leske et al. [16]	Argentina	Pediatr Pulmonol	Retrospective study at 1 center 2007-2018	244 children, mixed cohort NIV 210/244 (86%) IV 34/244 (14%) CPAP 51 patients of NIV group	0-18y	244 patients: initiation 48 (20%) acute illness 80 (33%) subacute 116 (48%) elective (without details) Initiation criteria: 79/244 (33%) on clinical status (71 without sleep study) 165/244 (67%) abnormal sleep study + SDB Where: General ward 204/244 (84%) Referral hospital 18/244 (7%) ICU 22/244 (9%) Modes: Pressure control 182/244 (74%) CPAP 51/244 (21%) BPAP 9/244 (4%)	All started in hospital

Abbreviations: m: months, yrs: years, OSA: obstructive sleep apnea, BPAP: bilevel positive airway pressure, NIV: noninvasive ventilation, ICU: intensive care unit, CF: cystic fibrosis, NMD: neuromuscular disease, SMA: spinal muscular atrophy, BPD: bronchopulmonary dysplasia, ARF: acute respiratory failure, CRF: chronic respiratory failure, RTI: respiratory tract infection, SDB: sleep disordered breathing, SpO_2 : pulse oximetry, $PtcO_2$: transcutaneous oxygen pressure, $PtcCO_2$: transcutaneous carbon dioxide pressure, ABG: arterial blood gases, PHT: pulmonary hypertension, PSG: polysomnography, AHI: apnea-hypopnea index, ODI: oxygen desaturation index, CNS: central nervous system.

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Online Table 3.2: Initial and follow up settings for CPAP

Author	Country	Journal	Type of study	Number of patients	Ages	CPAP mode	CPAP level	Follow up
Marcus et al. [1]	USA	J Pediatr	Retrospective study (written questionnaire)	94 children with obesity (27%), craniofacial malformation (25%), OSA type I (idiopathic post AT) (17%), Down syndrome (13%)	0-19 yrs	Constant CPAP-titration with PSG	Available for 70 patients Median CPAP =8 (range 4-20), CPAP were independent of age and diagnosis	Every 4 to 12 months Follow up: 22% required modification of CPAP level during follow up
McNamara et al. [2]	Australia	Chest	Prospective study	24 infants on long term CPAP	1-51 weeks old	Constant CPAP - Titration with PSG	Initial setting 3.7 to 6 cmH_2O Increments of 0.3 until obstruction overcome on PSG 5 infants with upper airway anomalies required up to 10 cmH_2O	CPAP discontinued in 13 infants ; CPAP level was increased in the 5 other infants (6 drop off due to non-compliance/adherence)
Massa et al. [3]	UK	Arch Dis Child	Retrospective study	42/66 children on long term CPAP (17 (26%) failed trials and alternative treatment)	0-19 yrs	Data on 42 children who ended up succesfully	Start at 4 cmH_2O then increments of 2 cm to overcome OSA and desaturation on PSG Mean CPAP 8.5 ±	Side effect: skin irritation/nasal dryness Up to 3 trials to achieve adherence

						adhering to CPAP	3.2 cmH_2O (4-16)	
Marcus et al. [4]	USA	Pediatrics	Prospective randomized study: CPAP or BPAP	29 children (13 CPAP 16 BPAP) 19 patients completed the study – of note 19 obese patients	2-16 yrs	CPAP vs BPAP	CPAP started at 3 cmH_2O then 4 then increments of 2 to overcome OSA on PSG BPAP aim to have 6 differential starting 4/3, 6/3, 8/3, 10/4,12/6,14/8,16/10 CPAP 8 ± 3 (4-12) BPAP 11 ± 4 (4-16) and 5 ± 3 (3-10)	CPAP vs BPAP no effect on drop outs, same mean compliance at 6 m: 5.3 ± 2.5 h/night
Tan et al. [5]	Australia	J Pediatr Child Health	Retrospective study over 1 yr	61 sleep studies in 45 children 33% PSG, 33% polygraphy and 33% with autoCPAP	0.4-18.6 yrs (median 8.3 yrs)		64% CPAP - 31% BPAP Changes to improve OSA or ventilation where any persistent apnoea, hypopnoea or hypoventilation	Changes recommended in 66%: 12 CPAP increase, 12 BPAP increase, 1 CPAP decrease, 4 BPAP decrease, 2 CPAP withdrawal
Marcus et al. [6]	USA	J Clin Sleep Med	Prospective double blind randomized study	56 children	2-16 yrs	CPAP vs BiFlex	At 3 m: CPAP 10 ± 3 BiFlex 14 ± 3 and 8 ± 2	At 3 m: same efficacy on AHI and daytime sleepiness and compliance: 24 vs 22 nights/m and 201 vs 185 min/night for CPAP vs

								BiFlex
Khirani et al. [7]	France	Crit Care	Prospective physiological study: oesogastric pressures measures vs clinical parameters, single centre	12 infants, 5 BPD and 7 UAO (3 laryngomalacia, 1 OSA, 1 Down syndrome, 1 Pierre Robin Sequence, 1 Prader Willi syndrome)	2-22 m 3.6-10.3 kg	Constant CPAP, different ventilators	CPAP level set on clinical signs: 8 cmH_2O CPAP level set on oesogastric pressures: 10 cmH_2O Physiological data superior to clinical. Patients discharged home with CPAP level determined by physiological data	Follow up program not specified. Improved gas exchange and weight gain. All patients weaned from CPAP (6 m – 3 yo) after improved clinical status
Widger et al. [8]	Australia	Sleep & Breathing	Retrospective study of all patients on respiratory support (CPAP + BPAP) 2007-2012 Single centre	42 children (25 CPAP + 17 BPAP) had 71 PSG	11 ± 6 yrs	CPAP + BPAP	CPAP titration 1-2 cm upwards or downwards based on presence/absence of apnoeas/hypopnoeas on PSG, special protocol for adjustment of BPAP	Annual titration PSGs. Changes recommended in 27/41 studies with CPAP and 11/30 studies with NIV – overall recommended in 53% of studies Full or partial changes implemented in 90% improvement in OSA symptoms on questionnaire in 50% when changes were implemented
Chatwin et al. [9]	UK	PlosOne	Retrospective descriptive study of	449 children started on home NIV,	< 17 yrs 13%<1	CPAP (12%) + BPAP	CPAP settings 8 ± 1.3 cmH_2O	PSG 3 m after initiation of respiratory support, then 3 m again and if

			outcomes at 1 center 1993-2011	565 with NMD	y, age at initiation 8.7 ±6 y			stable, once a year
Amaddeo et al. [10]	France	Sleep Med	Retrospective study using PGs of consecutive patients between 2011-2014, single centre	29 control PGs in 26 stable children treated with CPAP at home	7.8 ± 6.2 yrs	CPAP in 23 patients and Auto-CPAP in 3	Mean CPAP 7.7 ±1.5cm H_2O at time of PGs	Median respiratory events index: 1.4/h (range 0-34), > obstructive events often associated with desaturations/arousal; 50% unintentional leaks but with no desaturations. PGs resulted in 7 CPAP changes in settings or interface: 3 increase, 1 decrease, 1 to auto-CPAP, 1 to NIV and 1 interface change
Mihai et al. [11]	Australia	J Clin Sleep Med	Retrospective review on prospective collected data on children initially treated with auto-CPAP before switching to fixed CPAP (2013-2015)	26 children treated with auto-CPAP	11.9 ± 3.4 yrs	Auto-CPAP	Median CPAP level on titration PSG (9 (7-10)) comparable to median 90°percentile CPAP level on auto-CPAP (8.1 (7.1-9.5)) and higher than mean auto-CPAP (6.3 (5.3-7.5))	90° percentile CPAP is useful but does not completely eliminate the need for titration PSG when determining optimal CPAP level. Mean CPAP level downloaded from Auto-CPAP machine can be used to effectively shorten the PSG titration study

Al-Saleh et al. [12]	Canada	J Clin Sleep Med	Retrospective study 2009/2013 Single centre Review of PSGs for technology titration in patients with CPAP, BPAP or IV Major change: changes in mode, pressure/ rate and/or mask Minor change: inspiratory time, rise time, trigger or cycle setting	623 titration PSG in 166 children treated with BPAP and 83 children treated with CPAP and 25 children with IV 50% respiratory disorders, 28% NMD and 22% CNS	10.5 ± 5.1 yrs	CPAP BPAP IV	CPAP titration from 4, increase 1-2, max 15 cmH_2O Switch to BPAP if CPAP failure BPAP: Start spontaneous/timed mode, titrate from 8/4 cmH_2O, back-up rate 8 bpm, increase inspiratory / expiratory pressures by 1-2 cmH_2O, minimum difference 4 cmH_2O	Major outcome: clinical predictors of changes at follow-up PSG: age at PSG, CNS or NMD diagnosis, BPAP and shorter time between start of therapy and PSG had higher likelihood of a change in settings. 62% major change, 11% minor change, 27% no change, 4% mask change, 3% mode change. First titration study should be done no more than a year after treatment initiation

Abbreviations: m: months, yrs: years, OSA: obstructive sleep apnea, BPAP: bilevel positive airway pressure, NIV: noninvasive ventilation, IV: invasive ventilation, NMD: neuromuscular disease, PSG: polysomnography, PG: respiratory polygraphy, AHI: apnea-hypopnea index, , CNS: central nervous system.

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Online Table 3.3: Initial and follow up settings for NIV

Author	Country	Journal	Type of study	Number of patients	Ages	NIV mode	NIV settings
Khan et al. [1]	UK	Arch Dis Child	Retrospective study	8 children with NMD: 4 congenital myopathy, 2 congenital muscular dystrophy, 2 rigid spine	6-13 yrs	All treated with NIV	IPAP 10-14 cmH_2O BUR 12-18/min
Nabatame et al. [2]	Japan	Brain Dev	Retrospective study	4 children juvenile Pompe disease	9-15 yrs	3 treated with NIV	IPAP 10-12 cmH_2O EPAP 3-4 cmH_2O
Mellies et al. [3]	Germany	Neuromuscul Disord	Prospective study	6 infants with SMA I and 1 with SMA II (+ 6 SMA controls without NIV)	6 – 11 yrs	7 treated with NIV	IPAP 10.5 cmH_2O EPAP 3.7 cmH_2O BUR 16/min
Fauroux et al. [4]	France	Crit Care Med	Prospective physiological study oesogastric pressure measures	8 children with CF	11-17 yrs	Comparison volume/targeted vs pressure-targeted mode	Similar efficacy of the 2 modes but greater decrease of the work of breathing when the patients adopted a controlled mode (+ greater subjective comfort by VAS)
Fauroux et al. [5]	France	Eur Respir J	Prospective physiological study: oesogastric pressure measures	10 children with CF	10-21 yrs	Pressure support	Better setting with oesogastric pressure measures: IPAP 12-20 cmH_2O (mean 16), high peak insp flow, sensitive inspiratory trigger, expiratory trigger 25-50%), less asynchrony

Abbreviations: yrs: years, NIV: noninvasive ventilation, ICU: intensive care unit, IPAP: inspiratory pressure, EPAP: expiratory pressure, BUR: back up rate, CF: cystic fibrosis, NMD: neuromuscular disease.

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Online Table 4.1: Description of interfaces

Author	Country	Journal	Number of patients	Ages	Type of study	Results
Castro-Codesal et al. [1]	Canada	Paediatr Respir Rev			Review of the mask interfaces for home NIV in infants and children	The selection of the mask interface for NIV is recognized to be an essential part for therapy success. Careful mask selection, a well-fitting headgear and time investment for mask desensitization are some important recommendations for adequate mask adaptation in children. Investing in selection of the mask interface is an important first step in the initiation of long-term NIV.
De Jesus Rojas et al. [2]	USA	The Open Respir Med J	18 children 7 chest wall weakness, 6 CNS, 3 obstructive lung disease, 2 restrictive lung disease	4 m - 19 yrs (average 7 yrs)	Retrospective case series	Indications for Nasal NIV/RAM Cannula initiation included: CPAP/BPAP masks intolerability (11%), dyspnea secondary to chest wall weakness (38%) and tracheostomy avoidance (50%). All patients used a Nasal NIV/RAM Cannula with a portable mechanical ventilator. NIV modes were: BPAP (66%) and CPAP (23%) followed by Synchronized Intermittent Mandatory Ventilation – Pressure Control (SIMV-PC) (11%). Nasal NIV/Ram Cannula was successful in 94%. Analysis of PCO_2 levels showed a significantly lower PCO_2 levels after Nasal NIV/RAM Cannula initiation.
Overbergh et al. [3]	Belgium	Sleep Med	9 tracheobroncho malacia, Down syndrome, cerebral palsy, Trisomy 9	7 m - 15 yrs	Case series	These pilot data suggest that the Optiflow™ interface may be used for chronic CPAP use in infants and children. However, it should not be used for children who require BPAP because of insufficient triggering.
Ramirez et al. [4]	France	Sleep Med	62 children 51 OSA, 6	2-18 yrs mean age	Retrospective study	Most patients (61%) were ventilated with a nasal mask; these patients were significantly younger than

			NMD, 5 lung diseases	10 ± 5 yrs		the patients ventilated with a facial mask or nasal cannula. CPAP and NIV adherence was not affected by the type of the interface. The mean level of unintentional leaks was not different between patients using a nasal mask or a facial mask (not available for patients using nasal cannula).
Ramirez et al. [5]	France	Intensive Care Med	97 children started on CPAP/NIV:35 NMD or scoliosis, 32 craniofacial malformation, OSA without facial malformation, 9 lung disease	1 m to 18 years old	Retrospective study	All 25 children ≤ 2 yrs + 4 older children needed custom made nasal masks. In other patients, an industrial nasal mask, a facial mask, or nasal prongs were used in 50%, 16%, and 2% of pts. Industrial masks without and with manufacturer leaks were used in 35 (36%) and 33 (34%) patients, respectively.
Norregaard et al. [6]	Denmark	Eur Respir J			Review	Nasal masks seem to be the preferred type. Appropriate headgear should be a concern, and in small children custom-made versions are often preferable. Oral leaks can be reduced using a pacifier, or in older children, a chin strap.
Wallis et al. [7]	UK	Paediatr Respir Rev	76 children (survey) 34 craniofacial malformation, 6 mucopolysaccharidosis, 8 NMD, 2 achondroplasia,	0.3-16 years old	Review + results of a survey (home CPAP via nasal mask for OSA: The Great Ormond Street Experience	The greatest cause of failure in the long-term tolerance of NIV is the ill-fitting mask. In children with specific facial deformities such as Crouzon disease or mucopolysaccharidosis, the hospital dental department may assist with custom made masks. In small children and infants, caution is required in the use of the full face mask.

			26 other		1994–1998)	

Abbreviations: m: months, yrs: years, NIV: noninvasive ventilation, NMD: neuromuscular disease, CNS: central nervous system, CPAP: continuous positive airway pressure, BPAP: bilevel positive airway pressure, OSA: obstructive sleep apnea.

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Online Table 4.2: Side effects of interfaces

Author	Country	Journal	Number of patients	Ages	Type of study	Results
Ramirez et al. [1]	France	Intensive Care Med	97 children started on CPAP/NIV:35 NMD or scoliosis, 32 craniofacial malformation, OSA without facial malformation, 9 lung disease	0 - 18 yrs	Descriptive study	All 25 children ≤ 2 yrs + 4 older children needed custom made nasal masks. In other patients, an industrial nasal mask, a facial mask, or nasal prongs were used in 50%, 16%, and 2% of pts. Industrial masks without and with manufacturer leaks were used in 35 (36%) and 33 (34%) pts, respectively. The interface had to be changed in 20 (21%) patients because of discomfort (n=16), leaks (n=4), facial growth (n=3), skin injury (n=2), or change of ventilatory mode (n=2). A second or third mask change was necessary in 9 and 4 patients, respectively (> maxillofacial pts)
Kushida et al. [2]	USA	J Clin Sleep Med	16	2.4 - 7.7 yrs	Comparison of the Pixi mask with other masks	Pixi mask rated as more comfortable by parents (less restful sleep, trouble getting asleep and staying asleep), fewer skin side effects (marks on upper lip and under the ear) and easier to remove than previous mask Compliance with Pixi 7.1 ± 2.5h/night vs 8.2 ± 2.1h/night with previous mask (not significant)), PSG results comparable
Acorda et al. [3]	USA	J Ped Nursing	?	?	Descriptive study In hospital BPAP (in fact CPAP) treatment	Decrease of number and severity of skin pressure related ulcers after protocolized management (no numbers)
Visscher et al. [4]	USA	Respir Care	50	0.1-32.5 yrs	Prospective study: 3-dimensional face	Stage I ulcers most common, nose bridge most common, high skin hydratation was associated with skin ulcers, areas of high contact were associate with

					imaging and measure of skin hydratation	skin erythema and pressure ulcers. A cloth mask was associated with the best skin tolerance.
Fauroux et al. [5]	France	Intensive Care Med	40	0.2-17 yrs	Descriptive study	47% skin injury, predictors: age > 10 yrs + commercial mask 37% maxillary retrusion, predictor: longer daily use
Roberts et al. [6]	USA	J Clin Sleep Med	50 CPAP compliant compared to 50 non-compliant	Children with craniofacial conditions, mean age 10.4 yrs	Retrospective study, serial cephalographic images	Greater mean retrusion of mid-face in compliant pts + counterclockwise rotation of the palatal plane + upper incisor flaring
Tibbals et al. [7]	Australia	Pediatr Pulmonol	4 children with CCHS	6-16 yrs	Descriptive study	All treated with NIV, 3 transitioned to negative pressure ventilation due to mid-face hypoplasia
Castro-Codesal et al. [8]	Canada	Paediatr Respir Rev			Review of the mask interfaces for home NIV in infants and children	Interface-related problems are common and, if not recognized, have the potential to cause serious damage, jeopardize the use of the therapy, or lead to poor adherence. Frequent mask-related complications include nasal symptoms, unintentional leak, mask displacement, skin injury, and midface hypoplasia. Close monitoring and a pro-active approach may help to minimize complications and promote the optimal use of home NIV.
De Jesus Rojas et al. [9]	USA	The Open Respir Med J	18 children 7 chest wall disease, 6 central control abnormalities, 3 obstructive lung disease,	4 m -19 yrs (average 7 yrs)	Retrospective case series	Complications associated with Nasal NIV/RAM Cannula were negligible in our study population. A minimal nasal rub on the nasal columella was reported as an adverse side effect in one patient.

			and 2 restrictive lung disease.			
Norregaard [10]	Denmark	Eur Respir J			Review	Adverse effects are generally minor, although in the chronic setting the effect of the interface on facial bony structures should be monitored closely.
Wallis [11]	UK	Paediatr Respir Rev	76 children (survey)	0.3-16 yrs	Review + results of a survey (home CPAP via nasal mask for obstructive sleep apnoea: The Great Ormond Street Experience 1994–1998)	The mask should not be fitted tightly onto the face, but secured by straps that maintain a gentle pressure equally around the mask. Mask ventilation is safe and major complications have not been reported frequently. Masks need individual adjustment and the level of pressure support requires regular evaluation to ensure adequate gas exchange. Minor problems occasionally arise.

Abbreviations: m: months, yrs: years, OSA: obstructive sleep apnea, CPAP: continuous positive airway pressure, BPAP: bilevel positive airway pressure, NIV: noninvasive ventilation, NMD: neuromuscular disease, CCHS : congenital central hypoventilation.

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Online Table 4.3: Ventilators for CPAP and NIV

Author	Country	Journal	Type of study	Design	Results
Parmar et al. [1]	Canada	Paediatr Respir Rev	Review of CPAP devices for pediatric OSA		A wide variety of CPAP and BPAP devices are commercially available, each with unique capabilities and proprietary algorithms used to measure the phases of the respiratory cycle and airflow resistance. There are two distinct trademark comfort features in CPAP and APAP: ramp/delay and pressure reduction during exhalation. Many devices have the ability to wirelessly transfer data via cellular or Wi-Fi, from the device to a cloud-based software program on a daily basis.
Khirani et al. [2]	France	Clin Respir J	Bench and prospective clinical study	A classical inspiratory trigger (ITc) and an improved IT (NIV + IT) were tested on a bench with 6 pediatric profiles and 6 young patients requiring long-term NIV: fascioscapulohumeral myopathy, DMD, chronic obstructive pulmonary disease, Kenny–Caffey syndrome, SMA, congenital myopathy Age 9.9–16.5 yrs (mean 14.1 ± 2.7 yrs)	On the bench, trigger time delays (ΔT) and trigger pressures (ΔP) were significantly reduced with the NIV + IT as compared with the ITc. The clinical study confirmed the significant decrease in ΔT and ΔP.
Norregaa	Denm	Eur Respir	Review		When applying respiratory assist, the trigger function,

rd [3]	ark	J			usually sensed as either pressure or flow changes in the system, is of fundamental importance. In the case of a small or weak child, inspiratory flows generated by the child may be insufficient to activate the trigger. If supplemental oxygen is added, this is usually via the single hose system or via the mask. Heated humidifiers are much more efficient than passover humidifiers. The addition of a humidifier will add to the resistance of the circuit, and will tend to interfere with triggering and possibly pressure delivery. Complications related to NIV in paediatric ventilator users are: nasal and pharyngeal dryness, vasomotor rhinitis, air leaks, gastric distension, air flow-induced arousals, possible increase in work of breathing due to dyssynchrony/compromised triggering, carbon dioxide retention associated with large dead space.
Wallis [4]	UK	Paediatr Respir Rev	Review + results of a survey (home CPAP via nasal mask for OSA: The Great Ormond Street Experience 1994–1998)	76 children (survey) 34 craniofacial anomalies, 6 mucopolysaccharidosis, 8 NMD, 2 achondroplasia, 26 other 0.3-16 yrs	Factors determining the choice of a home device: cost, noise, alarms, trigger sensitivity, portability and adaptability, pressure vs. volume.

Khirani et al. [5]	France	Sleep Med	Prospective study	Comparison of AHI scoring on the built-in software and a PG in 15 children treated with CPAP aged 1.5-18.6 yrs	Comparison of scoring of AHI on -built-in software of a CPAP device (Resmed) + integrated SpO_2: automatic analysis and manual scoring on a breath-by breath analysis -PG during CPAP in hospital Strong correlation between the AHI scored on a manual analysis of built-in software and a PG: useful for cheap and simple follow up

Abbreviations: yrs: years, CPAP: continuous positive airway pressure, NIV: noninvasive ventilation, Vt: tidal volume, PEEP: positive end-expiratory pressure, SMA: spinal muscular atrophy, DMD: Duchenne muscular dystrophy, NMD: neuromuscular disease, OSA: obstructive sleep apnea, PG: respiratory polygraphy, AHI: apnea-hypopnea index.

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Online Table 5.1: Follow up of CPAP and NIV

Author	Country	Journal	Type of study	Number of patients	Ages	Follow up and outcome
Tan et al. [1]	Australia	J Pediatr Child Health	Retrospective study	61 sleep studies in 45 children: 29 CPAP, 14 BPAP, 2 tracheotomy	0.4 - 18.6 yrs	Children on CPAP/NIV > 3 m, stable condition, 1/3 PSG, 2/3 PG 51% of children had a sleep study in the previous 6 m 40 (61%) studies resulted in a change of setting: 12 increase in CPAP, 12 increase in BPAP, 1 decrease in CPAP, 4 decrease in BPAP, 2 discontinuation of CPAP, 8 need to continue CPAP (no weaning) Necessity of systematic PSG/PG in children treated with CPAP/NIV
Paiva et al. [2]	France	Intensive Care Med	Retrospective study	50 children treated with NIV (40) or CPAP (10): 23 NMD, 2 lung, 23 upper airway disease	8.5 ± 5.2 yrs	Routine follow up, none of the patients had SDB symptoms Overnight SpO_2 + $PtcCO_2$ with CPAP/NIV: 21 (42%) had a nocturnal $PtcCO_2 \geq 50$ mmHg ≥ 10% recording time or ≥ 5 continuous min, 18/21 had normal daytime PCO_2, and all had a nocturnal $SpO_2 > 90\%$ Necessity of systematic overnight $PtcCO_2$ recording during CPAP/NIV
Felemban et al. [3]	France	Pediatr Pulmonol	Prospective study	24 children treated with NIV: 11 NMD, 3 lung disease, 9 upper airway anomaly, 1 central hypoventilation	4 -19 yrs	29 pairs of home/hospital overnight SpO_2 + $PtcCO_2$ recordings/24 pts Feasibility: 1 SpO_2 failure in hospital Results similar between home vs hospital at lower cost Value of a home overnight SpO_2 + $PtcCO_2$ recording during NIV with trained technicians (home care provider)
Griffon et al. [4]	France	Respir Care	Retrospective study	79 children treated with NIV/CPAP/HFNC	1.5-14 yrs	Routine follow up, none of the patients had SDB symptoms Overnight SpO_2 + $PtcCO_2$ with NIV (n=52, 47%), CPAP (n=43, 39%), HFNC (n=2, 2%) or spontaneous breathing (n=13, 12%) Quality of recording excellent in 81%, more $PtcCO_2$ failures > SpO_2 failures

						11 abnormal recordings in 11 patients: 6 hypercapnia, 3 hypocapnia, 2 hypoxemia, corrected by change in settings/equipment Value of a home overnight SpO_2 + $PtcCO_2$ recording during NIV follow up with trained technicians (home care provider)
Caldarelli et al. [5]	France	Intensive Care Med	Prospective study	39 children treated with NIV: 13 NMD, 15 OSA and 11 lung disease	1 – 18 yrs	Systematic PG during NIV in stable NIV patients Unintentional leaks, patient ventilator asynchronies, decrease in ventilatory drive, upper airway obstruction with or without reduction of ventilatory drive, and mixed events were observed in 27%, 33%, 10%, 11%, 12%, and 3% of the patients, respectively. A predominant respiratory event was observed in all patients. Mean duration spent with respiratory events was 32±30% (range 3 to 96%) of total recording time. Unintentional leaks were the most frequently associated with AA whereas patient ventilator asynchronies were rarely associated with AA or 3% desaturation.
Widger et al. [6]		Sleep & Breathing	Retrospective study	25 children on CPAP, 17 on BPAP	11 ± 6 yrs	2 pairs of titration studies: 41 CPAP + 30 BPAP Changes in settings recommended in 27/41 (65%) of CPAP studies and 11/30 (36%) BPAP studies Changes were implemented by physicians in 55% of cases Titration studies led frequently to changes in settings
Amaddeo et al. [7]	France	Sleep Med	Prospective study	26 children treated with CPAP	7.8±6.2 yrs	Systematic PG during CPAP (use 10.6±14.4 m) in stable patients. Median index of total respiratory events 1.4/h (range 0-34). Mean number of different types of respiratory events per PG was 2±1 (range 0-4), with always a predominant event. Partial or total upper airway obstruction without decrease in ventilatory drive was the most frequent event and was the most frequently associated with an oxygen desaturation (in 30% of the events) and an AA (in 55% of the events).
Khirani et al. [8]	France	Sleep Med	Comparison of AHI scoring	15 children treated with CPAP	1.5-18.6 yrs	Comparison of scoring of AHI on -built-in software of a CPAP device (Resmed) + integrated SpO_2: automatic analysis and manual scoring on a breath-by breath analysis

			on the built-in software and a PG			-PG during CPAP in hospital Strong correlation between the AHI scored on a manual analysis of built-in software and a PG: useful for cheap and simple follow up
Al Iede et al. [9]	Australia	Sleep Med	Retrospective study	148 children started on CPAP	1 week-16.8 yrs	65 primary airway disease, 33 chronic lung disease (18 BPD), 20 CHD, 12 CHD + airway anomaly, 5 congenital diaphragmatic hernia, 4 interstitial lung disease Mean CPAP 7.3 cmH_2O Follow up: telephone call, cardiorespiratory monitoring (?) at 2 weeks, CPAP titration PSG after 3-6 m 30% stopped CPAP during a 15 m follow up (various reasons)
Liu et al. [10]	China	Sleep & Breathing	3 case reports	3 children	2 m - 5 yrs	1 OSA + PHT (CPAP), 1 Pierre Robin Sequence (BPAP), 1 laryngomalacia Home monitoring with TELETREK: home base remote monitoring system via telephone that records SpO_2, heart rate, CPAP use, leaks
Zhou et al. [11]	China	Int J Pediatr Otorhinolaryngol	Retrospective study 2009 - 2011	17 patients:	1 m - 12 yrs	TM: no details on what data is transmitted: ventilator data (pressure, leaks). Remote monitoring system activated by parents. Parents uploaded the data on 93.3% of days. No system or device failure Less time to upload the data (5.7 ± 3.1 min) compared to the travel time to hospital (371 ± 182 min) Cost was 59% lower than a hospital visit System convenient and easy to use for > 80% of parents
Trucco et al. [12]	Italy	J Telemed Telecare	2-year longitudinal multicentre TM trial	48 children with NMD + controls without TM	median 16.4 yrs (8.9-22.1)	TM trial protocol: patients' weekly overnight home-recording of SpO_2, heart rate and ventilation with transmission to each TM centre the following morning. Overnight data were reviewed by non-physicians and calls to families made to assess clinical condition. If necessary, unscheduled transmissions or calls were activated and managed by non-physicians or medical team according to severity Exacerbations in TM patients did not differ (59 versus 53; $p = 0.15$)

						from controls. Hospitalisations were reduced in TM patients when compared with those prior to TM (11 versus 24, $p = 0.04$) and to controls (11 versus 21, $p = 0.03$). Median hospitalisation length was lower in TM patients than controls (6 versus 7 days, $p = 0.03$). Caregivers satisfaction was excellent with no changes in Caregiver Burden Inventory
Casavant et al. [13]	USA	J Telemed and Telecare	9-m prospective study	14 patients (children and adults) with BIPAP or ventilated through tracheostomy: NMD, lung diseases + other	16 m - 35 yrs	Families completed questionnaires about clinical management before the addition of TM and 2–3 months after they had used TM Families reported higher confidence in clinical care with TM compared to telephone. The TM encounters supported clinical decision-making, especially in patients with active clinical problems or when the patient was acutely ill. The TM encounters prevented the need for 23 clinic visits, 3 emergency room visits, and probably 1 hospital admission.
Perrem et al. [14]	Canada	Pediatr Pulmonol	Review of the NIV device data reports to guide clinical care			This review provides a structured approach to the interpretation of CPAP/NIV device data reports to augment the clinical management of pediatric sleep-disordered breathing. It provided an overview of the data available from devices and their interpretation such as: check the settings, adherence and usage patterns, leak, treatment efficacy; for BPAP only: check that the back-up-rate is optimized; whether the inspiratory time settings are optimized for comfort and efficacy; BPAP is synchronous with patient respiratory effort; adherence and AHI in presence of optional pressure relief setting.

Abbreviations: m: months, NIV: noninvasive ventilation, CPAP: continuous positive airway pressure, BPAP: bilevel positive airway pressure, HFNC: high flow nasal cannula, NMD: neuromuscular disease, OSA: obstructive sleep apnea, CHD: congenital heart disease, BPD: bronchopulmonary dysplasia, PSG: polysomnography, PG: respiratory polygraphy, AHI: apnea-hypopnea index, AA: autonomic arousal, SDB: sleep disordered breathing, SpO_2: pulse oximetry, $PtcCO_2$: transcutaneous carbon dioxide pressure, TM: telemonitoring.

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Online Table 5.2: CPAP/NIV adherence

Author	Country	Journal	Type of study	Number of patients	Ages	CPAP / NIV adherence results	Determinants of adherence
Waters et al. [1]	Australia	AJRCCM	Retrospective study	children with CPAP	< 15 yrs	63 (86%) continued to use CPAP after 6 m	Not specified
Marcus et al. [2]	USA	J Pediatr	Retrospective survey by questionnaires send to centers	94 children	1 – 19 yrs	Good adherence defined by a use > 50% of prescribed hours CPAP unsuccessful in 1 patient 12/ 94 not adherent, in 50% attributed to the parents	
Massa et al. [3]	UK	Arch Dis Child	Retrospective study	49 children on long term CPAP	0- 19 yrs	Data on 42/49 children: Good adherence (use every night during whole night by parents) in 68%	Not specified
Koontz et al. [4]	USA	Sleep	Retrospective study in CPAP non adherent children	12 Behavior therapy (BT) 6 Behavior consultation (BC) 3 None (refusal)	1-15 yrs	Significant improvement in adherence in the BT (8.55h/night) and BS (8.58h/night) groups vs the None group (0.67h/night)	Behavior therapy improves adherence
Marcus et al. [5]	USA	Pediatrics	Prospective study, CPAP vs BPAP	29 children	2-16 yrs	1/3 dropped out < 6 m Mean adherence at 6 m 5.3 ± 2.5h/night	No difference between CPAP and BPAP
O'Donnelle et al. [6]	Canada	Sleep	Retrospective study	Data on 50/71 children treated with CPAP	10 ± 5 yrs	Mean use 4.7h/night Mean use on night with CPAP 6.3h/night	
Uong et al. [7]	USA	Pediatrics	Retrospective study	46 children, data available for 27 (59%)	7-19 yrs	Mean adherence7 h/night, 73% of week 85% used CPAP > 4h/night	Greater improvement in AHI associated with a better adherence No difference CPAP vs BPAP

Nixon et al. [8]	USA	J Pediatr	Retrospective study	32 children	9.1 ± 5.3 yrs	Mean CPAP use 4.7 ± 2.7h/night Consistent users defined by CPAP use > 1h on > 6 nights/week: 10 (33%)	The number of hours of CPAP use during the 2nd night (and 1st week) was predictive of the use at 2 and 3 m
Beebe et al. [9]	USA	Plos One	Prospective study	13 obese adolescents	14.8 ± 1.8 yrs	Adherence defined by a night use > 21% of sleep time 6 were adherent, 7 not	Improved attention and academic function in the adherent vs the non-adherent patients
Marcus et al. [10]	USA	J Clin Sleep Med	Prospective study	56 children randomized to CPAP or BPAP	12 ± 4 yrs	No difference in adherence between CPAP and BPAP: 24 ± 6 vs 22 ± 9 nights/m and 201 ± 135 vs 185 ±165 min/night	No difference in adherence between CPAP and BPAP
Marcus et al. [11]	USA	AJRCCM	Prospective study	52 children with OSA	12 ± 4 yrs	Mean use 170 ± 145 min/night at M3	
Simon et al. [12]	USA	Sleep Med	Prospective study	51 children treated with CPAP (46%), BPAP (6%), auto-CPAP (48%)	8-17 yrs	Mean adherence 3.4 ± 2.8 h/night, 41% of nights with a use > 4h	The usefulness of the ABCQ (Adherence Barriers to CPAP Questionnaire) questionnaire is demonstrated: useful clinic-based tool for identifying patient-specific issues with CPAP-adherence
DiFeo et al. [13]	USA	J Clin Sleep Med	Prospective study	56 children and parents completed a questionnaire before CPAP initiation	?	Mean use 3 ± 3h/night	Greatest predictor of adherence: maternal education Adherence lower in Afro-Americans Inverse correlation with age Correlation with family social support
Nathan et al. [14]	Singapore	Singapore Med J	Retrospective study	51 children on home CPAP/BPAP	Median age 11.5 yrs	Adherence defined by a reported use ≥ 4 nights/week 21/51 (41%) were compliant	Predictors of adherence (by logistic regression): female gender, presence of asthma
Prashad et	USA	J Clin	Semi-	21 adolescents	12-18 yrs	7 good adherence (381 ±	Predictors of adherence: degree

al. [15]		Sleep Med	structured interviews ado and caregivers	and 20 caregivers (17 mothers)		80min/night), 7 low use (30 ± 24min/night) and 7 no use	of structure at home, social reactions, mode of communication among family members, perception of CPAP benefits
Jambhekar et al. [16]	USA	Respir Care	Prospective study: adherence at baseline and after a respiratory therapist intervention	46 children	11-18 yrs	12 (26%) baseline adherence 0%, 12 (26%) baseline adherence 0-50% of nights, 22 (48%) baseline adherence > 50% of nights (> 4 hours/night) Significant improvement (+22-24%) in adherence in children using CPAP < 50% of nights	An (1) extensive therapeutic education session performed by a skilled respiratory therapist in pediatric CPAP improves the objective adherence in children using CPAP < 50% of nights.
Ramirez et al. [17]	France	Sleep Med	Retrospective study	62 children treated with CPAP or NIV	2-18 yrs	Mean adherence 8h17 ± 2h30/night, 72% used CPAP/NIV > 8h/night, Mean number of nights with use 26 ± 5 nights/m	No effect of mode (CPAP vs NIV), age, interface, duration of CPAP/NIV
Ennis et al. [18]	Canada	J Clin Sleep Med	Semi-structured interviews in children and caregivers	7 dyads of youth-caregiver (4 NMD, 3 obesity) + 2 caregivers	> 12 yrs	Children treated with BPAP: mean use 6.04 ± 3.47min/night (range 0.53-11.10min/night)	Better adherence when: previous encouraging experiences with therapy, subjective symptom improvement, familiarity with medical treatments, understanding of nocturnal hypoventilation and its consequences, family and health-care team support, early adaptation to treatment Poorer adherence when: previous negative experiences with therapy, negative attitude towards therapy, difficulty

							adapting, lack of support from family and health-care team, fear-embarrassment regarding treatment, technical issues, side effects, lack of subjective symptom improvement
Hawkins et al. [19]	USA	J Clin Seep Med	Retrospective analysis of objective adherence over 1 yr	140 children	12 ± 5.7 yrs	Good adherence: > 4h/nights > 70% nights. 69/140 (49%) good adherence: 7.4 ± 1.9h/night, 94 ± 0.8% of nights	Adherence is poor: female sex and developmental delay are associated with a better compliance No effect of AHI, residual AHI, CPAP pressure, age; ethnicity, insurance status
Adeleye et al. [20]	Canada	Canadian Respir J	Retrospective study	92 infants < 12 m with PSG, 49 were prescribed CPAP	1-12 m	Objective adherence in 20/49: 25% of days with > 4h/use per night	Of the 92 infants (no details on those treated with CPAP), 35 Down syndrome, 9 prematurity, 9 Pierre Robin Sequence, 3 pulmonary hypertension, 6 achondroplasia, 2 Prader Willi syndrome, 2 genetic disease + 25 other
Machaalani et al. [21]	Australia	Sleep & Breathing	Routine clinical care over 2 yrs	55 children treated with CPAP and 44 with BPAP	0.4-18 yrs	Adequate adherence > 4h/night > 70% of nights Adequate adherence in 75% of CPAP and 91% of BPAP users	Better adherence with BPAP than CPAP, adherence maintained over time
Puri et al. [22]	USA	J Clin Sleep Med	Retrospective chart review	56 children treated with CPAP	1.6-18 yrs	Mean adherence at 3 m: 2.8 ± 2.4h/night	Better adherence in children with a family member using CPAP (3.6 ± 0.6h/night on all nights and 4.8 ± 0.6 on nights used)
Xanthopoulos et al.	USA	Sleep	Prospective study	Questionnaire given at CPAP	4 m-18 yrs	Pediatric modification of the Self-Efficacy Measure for Sleep	Adherence correlated to caregiver-reported self-efficacy

[23]				initiation to 59 children and 138 caregivers		Apnea questionnaire given to children treated with CPAP and their caregiver	(p=0.007)
Ai-Iede et al. [24]	Australia	Sleep Med	Retrospective study	148 children using CPAP at home for non OSA		Adherence 116/130 (89%) > 4h/night	65 primary airway disease 33 chronic lung disease, 32 congenital heart disease, 5 congenital diaphragmatic hernia, 4 interstitial lung disease No details on those < 24 m Mean CPAP 7.3 cmH2O Follow up: telephone call, cardiorespiratory monitoring (?) at 2 weeks, CPAP titration PSG after 3-6 m 30% stopped CPAP during a 15 m follow up (various reasons)
Amaddeo et al. [25]	France	Pediatr Pulmonol	Retrospective study	31 children started on CPAP in an out-patient setting	0.8 -16.8 yrs	4 (3 T21) not adherent, for the others: median compliance 8h21min/night, median of 25 nights/m	3 patients weaned from CPAP
Trucco et al. [26]	UK	Pediatr Pulmonol	Retrospective study	60 children with Down syndrome, 42 had SDB, 18 started on CPAP + 7 on NIV, rest on oxygen	0.7 -5.3 yrs	After 1.9 yrs, 11/24 had satisfactory adherence to CPAP/NIV (average 8h/night)	2 children weaned form CPAP and 1 switched to NIV
Perriol et al. [27]	France	Sleep & Breathi	Observational cohort	78 children with OSA type I on home	10.4 ± 3.4 yrs	Mean CPAP adherence at 1, 3, 6, 12, 24 m was 6.1 ± 2.8h, 6.2 ± 2.6h, 6.2 ± 2.8h, 6.3 ± 2.8h, and	No significant predictor of adherence

		ng		CPAP		7.0 ± 2.7 h	
Pascoe et al. [28]	USA	Pediatr Pulmonol		42 boys with Duchenne muscular dystrophy	mean age 15.1 ± 20.2 yrs	% days NIV use: 56 ± 39% % days with a use > 4h: 46 ± 41% Average use 5.6 ± 4.2h/night	Better compliance with high AHI at baseline and change vital capacity from baseline Adherence barriers: internalizing problems (anxiety, depression)
Mendoza-Ruiz et al. [29]	France	Sleep Med	Prospective study	6 CPAP non-adherent children	5 ± 5 yrs	Use of a table based on token economy, adherence evaluated after 1 month	Mean adherence improved from 1 ± 0.33h/night to 4h31 ± 1h12 at 1 m A token economy table is effective
Bergeron et al. [30]	USA	Laryngoscope	Prospective single-blind randomized controlled trial	Shared Decision-Making Tools given at CPAP start to 24 families + 26 controls	6.9-10.6 yrs	Adequate adherence = > 4h/night	Use of SDMT associated with a better adherence 57% for study patients vs 27% of controls.
Kang et al. [31]	USA	J Clin Sleep Med	Retrospective study	103 children with developmental disability (DD) and 137 typically developing (TD) children treated with CPAP	¨3.2-16.1 yrs	% of nights use was higher in DD children at 3 m (86.7 vs 62.9) and 6 m (90 vs 70.7) vs TD Hours of usage at night was similar: (5 vs 4.6) at 3 m and at 6 m (6.4 vs 5.7) for DD vs TD, respectively	% of nights use was higher in DD children at 3 and 6 m Hours of usage on nights used at 3 and 6 m were similar Adherence improved in both groups over time Higher income and titration at or before 6 m were associated with a better adherence

Abbreviations: m: months, yrs: years, CPAP: continuous positive airway pressure, BPAP: bilevel positive airway pressure, NIV: noninvasive ventilation, OSA: obstructive sleep apnea, NMD: neuromuscular disease, SDB: sleep disordered breathing, AHI: apnea-hypopnea index.

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Online Table 5.3: Benefits of CPAP (except decrease in AHI)

Author	Country	Journal	Study design	Number of patients	Ages	Benefits
Rains et al. [1]	USA	Clin Pediatr	Descriptive study	4 children: Down syndrome, Hurler disease, Hunter disease, Treacher Collins syndrome	3 - 12 yrs	Clinical observation of improved alertness, attention/concentration, and behavior/temperament in all 4 children
Johnstone et al. [2]	Australia	Sleep Med	Prospective study	19 children with ADHD and SDB	7 – 15 yrs	EEG before and after 6 m of CPAP 13/19 compliant with CPAP (use 6- 10h/night): IAH 1.4 - 4.2/h Children treated with CPAP had a decrease in slow wave (delta and theta) and an increase in fast wave (beta) EEG activity In children with ADHD and SDB, CPAP is associated with some improvement in the typical EEG features of ADHD
Beebe et al. [3]	USA	Plos One	Prospective study	13 obese children with OSA + 15 obese controls without OSA	10-16 yrs	13 obese with OSA all treated with CPAP: 6 CPAP users + 7 CPAP non-adherent Academic function: self-report on grades + parent and self-report on scholastic functioning on PedQL 4.0 Generic Attention: age-normed Total Corrected z-score on the computerized Gordon Diagnostic System Non-adherent: worsening functioning over time CPAP-adherent: improved attention and academic function
Marcus et al. [4]	USA	AJRCCM	Prospective study	52 children after 3 m of CPAP	12 ± 4 yrs	Neurobehavioral assessment before and at 3 m of CPAP Significant improvement in attention deficits (ADHD by Connors Abbreviated Symptoms Questionnaire + Attention Problems subscale on the Child Behavior Checklist: CBCL), sleepiness, behavior (on CBCL) and caregiver and child-reported QoL (on PedQL) and on OSAS-related symptoms and disease-specific QoL (on OSAS-18)

						Positive correlation between adherence and decrease in sleepiness but not with behavioral outcomes
Brooks et al. [5]	USA	Sleep & Breathing	Prospective study	23 children with Down syndrome, 10 had an AHI > 5/h	7.2-18.7 yrs	7 children treated with CPAP: CPAP effective in 5 Improvement in attention (Connors Hyperactivity test) in all 5 ($p< 0.05$)
Konstantinopoulou et al. [6]	USA	Sleep Med	Prospective randomized study	23 children with Down syndrome, 20 had OSA	8-19 yrs	9 patients randomized to CPAP, 11 to sham-CPAP (2 cmH_2O) Median CPAP use: 116 (70-139) min/night Duration of CPAP use: Negatively correlated with E/e' mitral lateral (reflects left ventricular (LV) diastolic dysfunction, higher index reflects greater dysfunction) Positively correlated with LV mass z-score
Katz et al. [7]	USA	J Clin Sleep Med	Prospective multicenter study	27 obese children treated with CPAP	8-16 yrs	At baseline: 10/25 (40%) had HOMA-IR (homeostasis model assessment of insuline resistance > 97° perc. 10/23 (44%) hypertension, 16/23 (70%) loss of nocturnal blood pressure dip, high sensitive-CRP was elevated in 16/27 (64%) No change in any outcome at 3 and 6 m between CPAP-adherent and non-adherent
Delrosso et al. [8]	USA	J Pediatr	Retrospective chart review	3 groups of 25 children: snorers, untreated OSA, CPAP-treated OSA	7-17 yrs	OSA: AHI between 4.3-22/h CPAP patients had higher body mass index than snorers and non-CPAP OSA patients Systolic blood pressure was higher in the 2 OSA groups vs snorers Systolic blood pressure decreased in the CPAP group after 6 m of CPAP

Abbreviations: m: months, yrs: years, ADHD: attention-deficit hyperactivity disorder, EEG: electroencephalography, CPAP: continuous positive airway pressure, NIV: noninvasive ventilation, SDB: sleep-disordered breathing, OSA: obstructive sleep apnea, AHI: apnea-hypopnea index.

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Online Table 5.4: Benefits of NIV (except decrease in AHI)

Author	Country	Journal	Study design	Number of patients	Ages	Benefits
Bach et al. [1]	USA	Pediatr Pulmonol	Retrospective study	56 SMA I	RF before 2 yrs	33 treated with NIV vs 16 treated with tracheotomy 31/33 survived to 42 ± 26 m, fewer hospitalisations > 5 yrs with NIV vs tracheotomy
Bach et al. [2]	USA	Am J Phys Med Rehab	2 cases	2 SMA I	7 m, 3 yrs	No pectus excavatum, survival until 7 and 3 yrs with NIV 24h/24
Mellies et al. [3]	Germany	Neuromuscul Disord	Prospective study	7 infants SMA I (6) and SMA II (1) (+ 6 SMA controls without NIV)	6-11 yrs	After 6-12 m of NIV: improvement in SDB symptoms, sleep quality and architecture vs no improvement in controls
Bach et al. [4]	USA	Am J Phys Med Rehab	Retrospective study	106 SMA I	?	Untreated died at 9.6 ± 4 m, 22 with tracheotomy survived at 70.5 ± 43.3 m, 47 treated with NIV, 29/47 reached 65.2 ± 45.8 m, 8 died Same survival with NIV and tracheotomy but fewer hospitalisations with NIV
Vasconcelos et al. [5]	Portugal	Revista Port Pneumol	Retrospective study	7 SMA I, 11 SMA II, 4 SMA III	6 m – 26 yrs	17/22 treated with NIV NIV associated with a decrease in chest deformity and ARF episodes

Chatwin et al. [6]	UK	Arch Dis Child	Retrospective study	13 SMA I	4 – 24 m	All treated with NIV + MI-E, 5 died, duration of NIV not specified NIV + MI-E associated with a decrease in chest deformity
Ottonello et al. [7]	Italy	Am J Phys Med Rehab	Retrospective study	16 infants with SMA I	< 3 yrs	All treated with NIV NIV associated with a reduction in ARF episodes
Lemoine et al. [8]	USA	Pediatr Crit Care Med	Retrospective study	49 infants with SMA I	1 – 7 m	All treated with NIV Longer survival in the pro-active (n=26, BPAP + MI-E) vs supportive group (n=23, suctioning ± O_2)
Gregoretti et al. [9]	Italy	Pediatrics	Retrospective study 1999-2010	194 infants with SMA I		31 (16%) treated with NIV Nearly all non treated patients died < 2 yrs Survival at 24 m: 95% for IV vs 68% with NIV Survival et 48 m: 89% for IV and 45% with NIV Longer survival with NIV as compared to no respiratory support
Verrillo et al. [10]	Italy	Sleep Med	Prospective study	9 children with SMA II + 15 healthy controls	2.2 - 8.1 yrs	PSG during before and with NIV (after a mean of 2 yrs of NIV) NIV associated with a decrease in awakenings + increase in >% of N2 sleep satge NIV associated with a decrease in cyclic-alternating pattern A1 duration and an increase in A3 index
Ishikawa et al. [11]	Japan	Neuromuscul Disord	Retrospective study	3 cohorts of Duchenne: untreated, tracheotomy, NIV		88 treated with NIV Longer survival with NIV (mean 39.6 yrs)

Eagle et al. [12]	UK	Neuromuscul Disord	Retrospective study 1 center 1967-2002	197 patients with Duchenne		Improvement in survival 1960s: mean age of death = 14.4 yrs In 1990 with NIV: 25.3 yrs
Lee et al. [13]	Korea	Korean J Pediatr	Retrospective study at one center 2010-2016	54 patients with Duchenne, 24 treated with NIV	NIV treated: mean 16.3 ± 1.9 yrs	Improved cardiac function in the NIV patients As compared to the no-NIV group, the NIV group had (better): Lower early ventricular filling velocity (VFV)/late VFV Higher tissue Doppler systolic S' (i.e. better LV systolic function)
LoMauro et al. [14]	Italy	Eur Respir J	7 yr retrospective study	115 patients with Duchenne	6-24 yrs	28/115 treated with NIV NIV associated with a transient (2 yrs) increase in % vital capacity and contribution of the abdomen to the vital volume (VAB%VT) before coming comparable to the no-NIV pts
Mellies et al. [15]	Germany	Neurology	Retrospective study	7 patients with juvenile Pompe disease	3 – 27 yrs	2/7 treated with NIV NIV improves nocturnal and daytime gas exchange
Nabatame et al. [16]	Japan	Brain Dev	Retrospective study	4 juvenile Pompe disease	9 – 15 yrs	3/4 treated with NIV With NIV: no ARF and resumption of SDB symptoms
Khan et al. [17]	UK	Arch Dis Child	Retrospective study	4 congenital myopathy, 2 congenital	6 – 13 yrs	All treated with NIV NIV improves SDB symptoms, decreases WASO, increases SpO_2

				muscular dystrophy, 2 rigid spine		
Simonds et al. [18]	UK	Eur Respir J	Retrospective study	40 children with NMD or skeletal disease	9 mo 16 yrs	38/40 tolerated NIV NIV associated with an improvement in nocturnal $PtcCO_2$ and SpO_2 and daytime blood gases
Mellies et al. [19]	Germany	Eur Respir J	Prospective study	30 children with progressive NMD	12.3 ± 4.1 yrs	NIV normalized daytime and nocturnal gas exchange, improved RDI + arousal index, decreased nocturnal heart rate, decreased light sleep, and increased slow wave sleep. 10 patients were also studied with and after 3 nights without NIV: NIV withdrawal was associated with a prompt deterioration of SDB and gas exchange back to baseline but resolved immediately after resumption of NIV
Dohna-Schwake et al. [20]	Germany	Pediatr Pulmonol	Retrospective study	12 children with NMD treated with NIV > 5 yrs		As compared with the yr before NIV, after NIV: decrease in the number of GP consultations for RTI; number of antibiotic treatments and number of hospital admissions due to RTI
Katz et al. [21]	Canada	Arch Dis Child	Prospective cohort study	46 children with progressive NMD	6 - 17 yrs	7/46 had nocturnal hypoventilation (NH: increase in $PetCO_2$ > 10 mmHg ± decrease in SpO_2 > 5% for > 10 min): 6 treated with NIV After one year of NIV (5 patients): greater decrease in the general perception of health status of the Child Health Questionnaire (CHQ-PF50) as compared to the

						children without NH
Zaman-Haque et al. [22]	Canada	Child Neurol Open	Retrospective study	7 children with NMD and 7 with CNS disease		CNS: Trisomy 18, Prader Willi syndrome, Leigh sd, cerebral palsy No change in the number of pneumonias 2 yrs before and after the start of NIV
Padman et al. [23]	USA	Pediatr Pulmonol	Retrospective study	15 children with ARF treated with BPAP: 4 CF and 11 NMD	4 - 21 yrs	1 BPAP failure (1 patient with NMD) In other patients: duration of BPAP 1 day to 21 m Decrease in the number of hospitalisation days in the yr after BPAP initiation vs the yr before: 6 vs 36 days/yr
Fauroux et al. [24]	France	Pediatr Crit Care	Retrospective study	15 children who were decannulated and had a relapse OSA	2 – 12 yrs	Pathologies: upper airway obstruction (n=13), congenital diaphragmatic hypoplasia (n=1) or lung disease (n=1) In 9 patients, NIV was started after recurrence of obstructive symptoms after a delay of 1 to 48 m following a successful immediate decannulation. NIV was anticipated in 6 patients who failed repeated decannulation trials because of poor clinical tolerance of tracheal tube removal or tube closure during sleep NIV avoids re-cannulation in case of relapse of OSA

Abbreviations: m: months, yrs: years, SMA: spinal muscular atrophy, RF: respiratory failure, ARF: acute respiratory failure, NIV: noninvasive ventilation, MI-E: mechanical insufflation-exsufflation, IV: invasive ventilation, NMD: neuromuscular disease, CNS: central nervous system, CF: cystic fibrosis, BPAP: bilevel positive airway pressure,O_2: oxygen, OSA: obstructive sleep apnea, GP: general practitioner, PSG: polysomnography, WASO: wake after sleep onset, SpO_2 :pulse oximetry, RDI: respiratory disturbance index, RTI respiratory tract infection.

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Online Table 6.1: Which patients may benefit from a weaning trial ?

Author	Country	Journal	Type of study	Number of patients	Patients weaned
McNamara al. [1]	Australia	Chest	Prospective cohort	24 infants treated with CPAP	13/24 infants could be weaned form CPAP: 11 history of ALTE, 1 choanal atresia, 1 Smith-Lemli-Optiz sd after vascular ring surgery Parents reported decreased compliance in these infants
Downey et al. [2]	USA	Chest	Retrospective study at 1 center 1992-1999	18 infants < 2 yrs treated with CPAP	8/18 infants could be weaned from CPAP
Edwards et al. [3]	Australia	J Ped Child Health	Retrospective study at 1 center 1991-2004	108 children treated with CPAP + 47 NIV	61/108 improved after 3-52 m: airway malacia, CLD, neonatal diaphragmatic weakness, ARF with lung disease (no more details)
Nelson et al. [4]	USA	J Oral Maxillofacial Surgery	Retrospective study	25 children with syndromic bilateral coronal synostosis who had Lefort III distraction	6/9 patients treated with CPAP could discontinue CPAP after Lefort III
Bannink at al. [5]	The Netherlands	Int J Oral Maxillofacial Surgery	Retrospective study at 1 center	11 children treated with CPAP for craniofaciostenosis	After mid-face advancement, 6/11 patients could be weaned for CPAP (CPAP or tracheotomy was maintained in 5)
Rosen [6]	USA	Clin Pediatr	Retrospective cohort	29 infants < 2 yrs with Down syndrome, 6 treated with CPAP	3/6 had no OSA on a repeat PSG after 5, 5, and 110 m and could be weaned form CPAP
Tibbals et al. [7]	Australia	J Ped Child Health	Longitudinal study (1979-2008) in one center in	168 children, 58 (35%) CPAP, 50 (60%) BPAP	25 (15%) could be weaned from ventilatory support

			Melbourne		
McDougall et al. [8]	Canada	Arch Dis Child	Prospective study in one center / 15 yrs	144 children started on NIV	28/144 (19%) discontinued NIV: 7 NMD, 3 spinal injury, 5 abnormal ventilatory control, 5 craniofacial malformation, 4 airway malacia, 4 other Weaning incidence at 5-yrs: 21%, 42% at 10 yrs Time to weaning: 1.9 (0.2-11.5) years Weaning less common in NMD
Girbal et al. [9]	Portugal	Revista Portuguesa Pneumologia	Retrospective cohort at 1 center 1997-2012	68 children with complex OSA, 52 on CPAP, 16 on BPAP	22/68 could be weaned: 17 spontaneous improvement, 5 after surgery Even patients with complex OSA may be weaned from CPAP by time
Chatwin et al. [10]	UK	Plos One	Retrospective cohort at 1 center	496 children on home NIV (follow up data on 449)	42/449 (9%) could be weaned form NIV: 2 chest wall, 1 obesity, 6 CLD, 4 congenital syndrome, 4 upper airway obstruction, 4 NMD, 5 other (+ 5 ventilator intolerance, 5 mask intolerance)
Chau et al. [11]	Hong Kong	Respir Care	Retrospective cohort study at 1 center 1997-2015	96 children < 21 yrs, 71 treated with NIV	7 (8%) children treated with NIV could be weaned due to "improvement of chronic lung disease or underlying airway problems"
Kherani et al. [12]	Canada	Pediatr Pulmonol	Retrospective study	25 infants < 12 m treated with NIV	2 CCHS, 1 other CNS, 14 NMD, 3 CLD, 2 airway malacia, 1 diaphragm paralysis, 1 pulmonary atresia, 1 OSA 7/28 (28%) could be weaned from NIV
Mastouri et al. [13]	France	Pediatr Pulmonol	Retrospective cohort at 1 center 2013-2016	58/213 (27%) could be weaned: 50 CPAP + 8 NIV	Description of major and minor weaning criteria. Diagnosis: 9 laryngeal anomaly, 6 Pierre Robin, 6 Prader Willi syndrome, 6 Treacher Collins syndrome, 4 CLD, 3 achondroplasia, 3 OSA, 2 craniofaciostenosis, 2 pycnodysostosis, 2 mucopolysaccharidosis, polymalformative syndrome, 2 mandibular hypoplasia, 2 lung disease + other
Ikeda et al. [14]	Japan	Brain Dev	Retrospective cohort study	63 children < 20 yrs	3 (6%) children could be weaned due to "improvement of respiration"

			at 1 center 2001-2015		
Castro-Codesal et al. [15]	Canada	Plos One	Retrospective cohort study in Alberta 2005-2014	622 children < 18 yrs	39% of children could be weaned after 3-105 m of NIV due to spontaneous improvement in 16%
Al-Iede et al. [16]	Australia	Sleep Med	Retrospective study	148 children treated with CPAP for cardiorespiratory disorder	6/148 could be weaned from CPAP / 15 m follow up due to improvement
Amaddeo et al. [17]	France	Pediatr Pulmonol	Retrospective study	31 children started on CPAP in an out-patient setting	3/31 children could be weaned from CPAP during a mean follow up of 12.3 m (2.2 - 258.2 m) 1 patient with mucopolysaccharidosis improved after mandibular distraction osteogenesis Spontaneous improvement in 1 patient with 22q11 and 1 patient with polymalformative syndrome
King et al. [18]	Australia	J Clin Sleep Med	Retrospective cohort at 1 center 2016-2017	24 children (1-10.5 yrs) could be weaned during a 2 yrs follow up	11 spontaneous improvement, 7 airway surgery, 2 decrease in body mass index, 4 low physician perceived benefit (no symptoms and normal PSG)
Perriol et al. [19]	France	Sleep & Breathing	Observational cohort over 2 yrs	78 children (10.4 ± 3.2 yrs) with OSA type I initiated on CPAP	Weaning: 6 at 3 m, 15 at 6 m, 23 at 12 m, 44 at 24 m thanks to rehabilitation programs, dentofacial orthopedics ± weight loss

Abbreviations: m: months, yrs: years, CPAP: continuous positive airway pressure, BPAP: bilevel positive airway pressure, NIV: noninvasive ventilation, ALTE: acute life-threatening event, ARF: acute respiratory failure, OSA: obstructive sleep apnea, PSG: polysomnography, NMD: neuromuscular disease, CNS: central nervous system, CCHS: central congenital hypoventilation syndrome, chronic lung disease.

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Online Table 6.2: Weaning from CPAP or NIV: optimal timing and requirements for a weaning trial and follow up ?

Author, year	Country	Journal	Type of study	Number of patients	Ages	Timing	Requirements	Follow up after weaning
Mastouri et al. [1]	France	Pediatr Pulmonol	Retrospective	58/213 (27%) children on long term CPAP or NIV	0-16.2 yrs	0.1 - 7.8 m after CPAP or NIV withdrawal	Requirement of all 4 major and at least 2 minor criteria Major criteria 1) disappearance of nocturnal and daytime symptoms of sleep-disordered breathing after several nights sleeping without CPAP/NIV, such as snoring, sweating, arousals, laboured breathing, change in behaviour or attention, 2) percentage of recording time spent with a $SpO_2 \leq 90\% < 2\%$, 3) percentage of recording time spent with a $PtcCO_2 \geq 50$ mmHg $< 2\%$, 4) obstructive apnea-hypopnea index < 10 events/h on a poly(somno)graphy Minor criteria 1) minimal $SpO_2 > 90\%$ 2) maximal $PtcCO_2 < 50$ mmHg 3) oxygen desaturation index ≤ 1.4 events/h.	7/35 patients with a follow up P(S)G had a relapse of OSA after 1 - 3 yrs 6/7 had CPAP resumption and 1/7 neurosurgery

Abbreviations: m: month, yrs: years, CPAP: continuous positive airway pressure, BPAP: bilevel positive airway pressure, NIV: noninvasive ventilation, SpO_2: pulse oximetry, $PtcCO_2$: transcutaneous carbon dioxide pressure, P(S)G: poly(somno)graphy, OSA: obstructive sleep apnea.

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Online Table 7: Which options when CPAP or NIV fails?

Author	Country	Journal	Type of study	Number of patients	Ages	Options	Efficacy
Koontz et al. [1]	USA	Sleep	Retrospective	20 children with syndromic OSA not compliant to BPAP	1-15 yrs	Behavioral analysis and then given the options of receiving recommendations or therapy	Improvement of compliance (= hours/night usage) in 75% of patients who received behavioral intervention (recommendation or behavioral therapy); benefit extended beyond the therapy period though follow up period not specified. Not clear what the referral criteria was in terms of non-compliance though at baseline, the usage ranged 0.77-3.3 hours/night - the significance of the duration of use may differ across age groups.
Slifer et al. [2]	USA	Behav Sleep Med	Descriptive case series	4 children prescribed BPAP for complex OSA or hypoventilation but all demonstrated refusal behavior	3-5 yrs	Behavioral therapy	Good use of the device (sleep age-appropriate time) with sustained benefit
Mendoza-Ruiz et al. [3]	France	Sleep Med	Prospective study	6 CPAP non-adherent (defined as <3 hours/night) children and 9 adherent children	2.2-14.1 yrs (non-adherent group); 0.9-8.6 yrs (adherent group)	Use of a table based on token economy, adherence evaluated after 1 mo	Mean adherence in non-adherent children improved from 1 ± 0.33h/night to 4h31 ± 1h12/night at 1 m, but still significantly lower than adherent children
Delord	Franc	Chest	Retrospe	9 children, in	2-15 yrs	Hypnosis	Acceptance of the NIV in all patients after 1

et al. [4]	e		ctive study	whom initiation of NIV was expected to be difficult or who refused CPAP/NIV by standard procedure (n=2)		Distraction in the 2-yrs old, (In)direct hypnotic suggestions in the other (n=8) older children	session, median of 3 sessions for a > 6h use/night Mean compliance at 6 m: 7.5h/night
Cheng et al. [5]	Austr alia	ANZ J of Surgery	Retrospe ctive study 2003-2008	20 infants with Pierre Robin Sequence	neonates	CPAP failed (failure to treat respiratory deterioration/distre ss due to obstruction) in 6 infants: successful management with MDO and glossopexy	MDO with glossopexy were effective for management of multilevel airway obstruction in infants who would otherwise be considered for tracheostomy following failed CPAP
Abel et al. [6]	UK	Arch Dis Child	Retrospe ctive cohort 2000-2010	104 patients with Pierre Robin Sequence	64/104 < 4 weeks of age	Conservative management in 27 patients, NPT in 63 patients, tracheotomy in 14 patients	PSG results improved in all patients with NPT No CPAP trial in any patient.
Kam et al. [7]	Canad a	Canadi an Respir J	Retrospe ctive cohort	139 patients with Pierre Robin Sequence	9 – 14 m	20 treated with CPAP, 28 NPT, 45 TLA, 5 MDO, 19 tracheotomy	No details on the protocol but 13/60 surgical patients had another intervention prior to surgery TLA was performed earlier than MDO and tracheotomy
Muller-Hagedor n et al.	Germ any	Head Face Med	Retrospe ctive study at	68 children with Pierre Robin Sequence	0-12 yrs	Palatal plate	5 patients did not tolerate PP, 2 laryngeal problems, 1 immediate tracheotomy Of the 56 patients who tolerated TPP, 1

[8]			1 center (2003-2009)	treated with PP			needed CPAP and 4 HFNC (with O_2)
Amaddeo et al. [9]	France	Plastic and Rec Surgery	Retrospective study 1 center (2014-2015)	44 children with Pierre Robin Sequence, 9 received CPAP in NICU	0-2 m	Tracheotomy in 4 out of 9 patients with severe upper airway obstruction and dependent on ventilation in the NICU Failure in CPAP = failure to wean non-invasive CPAP to usage during sleep time only in 1-2 weeks	No objective evaluation of tracheotomy efficacy (not clear if (1) polygraphy post tracheostomy insertion was performed to assess residual obstructive SDB (2) if any patient needed pressure support with tracheostomy in situ (3) no follow up on tracheotomy patients
Overbergh et al. [10]	Belgium	Sleep Med	Case series	9 children with complex OSA and CPAP intolerance	7 m - 15 yrs	Optiflow nasal cannula adapted to a life support ventilator	Median AHI reduction from 37 to 10/h. Drawback of the set up : cannot be used to deliver BPAP because of insufficient trigger
Joseph et al. [11]	Israel	J Clin Sleep Med	Case series	5 children with OSA	2m-15 yrs	High Flow Nasal Cannula	One child used HFNC at home for 23 mo
Amaddeo et al. [12]	France	Sleep Med	Prospective study	8 CPAP non-compliant children, 6 Down syndrome, 1 Pierre Robin Sequence, 1 Pfeiffer	0.1 17.3 yrs	High Flow Nasal Cannula	Success in 5; mean compliance 7h10 ± 0.36 min/night Refusal (failure) in the 3 oldest patients with Down syndrome:1 orthodontic treatment, 1 spontaneous improvement

				(one of the few studies with a clear definition of failed CPAP /non-adherence)			
Koncick et al. [13]	USA	Pediatr Pulmonol	Retrospective cohort on data from the Pediatric Health Information System (2007-2015)	3802 children with chronic respiratory failure (OSA excluded) discharged on NIV	< 21 yrs	Tracheotomy: 337 (8.9%) were transitioned to tracheotomy 58% had a neurologic disorders and 39% a NMD	Factors associated with a tracheotomy: younger age, anoxia/encephalopathy, quadriplegia
Diercks et al. [14]	USA	JAMA Otolaryngology Head Neck Surgery	Case series	6 Down syndrome adolescents not compliant to CPAP after upper airway surgery	12 - 18 yrs	Hypoglossal nerve stimulation	56% to 85% reduction in AHI and good use
Caloway et al. [15]	USA	Laryngoscope	Case series	20 Down syndrome non obese adolescents not compliant to CPAP after adenotonsillecto	10 - 21 yrs	Hypoglossal nerve stimulation	Median reduction in AHI of 85%, good use

				my			

Abbreviations: m: months, yrs: years, CPAP: continuous positive airway pressure, BPAP: bilevel positive airway pressure, NIV: noninvasive ventilation, NMD: neuromuscular disease, OSA: obstructive sleep apnea, MDO: mandibular distraction osteogenesis, NPT: nasopharyngeal tube, TLA: tongue-lip adhesion, PP: palatal plate, HFNC: high flow nasal cannula, AHI: apnea-hypopnea index, O2: oxygen, NICU: neonatal intensive care unit, BMI: body mass index.

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Online Table 8: Role of CPAP and NIV in palliative care

Author, year	Country	Journal	Type of study	Number of patients	Ages	Palliative care
Chatwin et al. [1]	UK	Arch Dis Child	Retrospective study	13 SMA I	4 – 24 m	All treated with NIV + MI-E NIV used for palliation of symptoms in 4 patients
Chong et al. [2]	Malaysia	Singapore Med J	Retrospective of children referred to a hospital inMalaysia for palliative care	137 patients 72% malignancies 80% died at home	2-250 m	CPAP in 5 children (without details on diseases)
Kherani et al [3]	Canada	Pediatr Pulmonol	Retrospective study on all infants < 1 yr treated with long term IV and NIV in Sick Kids (Toronto) between 1991-2014	51 infants 25 NIV: 14 musculosketal, 8 deaths	< 1 yr	8/25 deaths in the NIV patients, in 4 infants, NIV was used as a palliative treatment
Tabone et al. [4]	France	Am J Med Gen A	Retrospective study	7 children with mucolipidosis	0.3-17.4 yrs	All patients were treated with CPAP or NIV, one patient had NIV as part of palliative care (2 have died since)

Abbreviations: m: months, yrs: years, CPAP: continuous positive airway pressure, NIV: noninvasive ventilation, IV: invasive ventilation, SMA: spinal muscular atrophy, MI-E: mechanical insufflation-exsufflation

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Online Table 9.1: Special populations: CPAP and NIV in infants (< 24 m)

Author	Country	Journal	Type of study	Number of patients	Ages	Sample description/Outcomes
Adeleye et al. [1]	Canada	Canadian Respir J	Retrospective study	92 infants <12 m with PSG, 49 were prescribed CPAP	< 12 m	Of the 92 infants (not only the CPAP treated), 35 Down syndrome, 9 prematurity, 9 Pierre Robin Sequence, 3 PHT, 6 achondroplasia, 2 Prader Willi syndrome, 2 ALTE, 2 genetic disease and 23 others No details (diagnosis) on those treated with CPAP. No data on length of use.
Al-Iede et al. [2]	Australia	Sleep Med	Retrospective study; data not presented separately for infant group	148 children treated with nasal CPAP for "non-OSA", 130 included	18.6±33.6 m (1 wk to 16.8 y) 72% < 24 m, 26% < 6 m	65 (50%) primary airway disease [36 laryngomalacia, 17 airway malacia, 5 glottic stenosis, 5 vocal cord paralysis], 33 (25%) chronic lung disease [18 prematurity, 6 oncology, 5 CDH, 4 neonatal ILD], 20 (15%) CHD, 12 (9.2%) CHD + airway. No details on those < 24 m Compliance 116/130 (89%) > 4h/night Mean CPAP 7.3 cmH_2O Follow up: telephone call, cardiorespiratory monitoring (?) at 2 weeks, CPAP titration PSG after 3-6 m 30% stopped CPAP during a 15 m follow up (various reasons)
Amaddeo et al. [3]	France	J Plastic Reconstr Surgery	Retrospective study	9 (22%) of 44 neonates with Pierre Robin sequence treated with CPAP in 1 yr at single centre	0-2 m	4 initiation in PICU, 5 on pediatric ward, CPAP level 6-8 cmH_2O CPAP duration 1-5.5 m No failure, no death, no tracheotomy after CPAP CPAP adherence after 1 m at home >8h/24h Two remained on CPAP at 4 m, 7 ceased CPAP with normal polygraphy or gas exchange between 1-5.5 m
Bach et al.	USA	Pediatr Pulmono	Retrospective	33 using	10.9±6.8	SMA type 1; from birth to 3rd birthday, NIV had more hospitalizations than IV with no difference in hospitalizations

[4]		l	comparison of SMA1 managed with NIV vs IV vs supportive care	NIV	m	beyond 3rd birthday; 2 died at home; 24 evaluated for gastro-oesophageal reflux, 13 underwent fundoplication
Bach et al. [5]	USA	Am J Phys Med Rehabil	Retrospective cohort, single centre, 1993-2006	47 (51%) of 92 with typical, severe SMA type 1	10.6±5.7 mo	SMA type 1; 32 (68%) used BPAP only during sleep, 6 (13%) more than 16h/d, 9 (19%) continuously. 34 (72%) could communicate verbally (cf 22% of IV group). 5 (17%) died at 61±26 m, 45 (96%) underwent gastrostomy, 13 (28%) underwent fundoplication, follow-up to 65±46 m. NIV and tracheostomy can both prolong survival for SMA type 1 patients, but the latter results in continuous ventilator dependence and speech does not develop.
Bedi et al. [6]	Canada	Canadian J Respir, Crit Care Sleep Med	Retrospective study	120 infants using CPAP or BPAP in the province of Alberta over 10 yrs, matched 1 :2 with older children	9.0 m (IQR 12.0 m)	All infants using CPAP or BPAP in the province of Alberta over 10 yrs (55% upper airway, 22% CNS, 15% NMD, 16% cardiorespiratory, 2% other). Average of comorbidities 4 (IQR 3), 51% with 2 or more comorbidities. In comparison with older children (2-17 yrs), infants had more comorbidities, similar efficacy of NIV in improving sleep and respiratory parameters on sleep studies, greater use of BPAP, a higher rate of discontinuation of NIV because of improvement or switch to IV and similar adherence.
Chatwin et al. [7]	UK	Arch Dis Child	Retrospective case registry after 1993	13	4-24 m	SMA type1 & 2 (11 SMA1, 2 borderline SMA type I/II); 5 (38%) died, 2 before 1 yr; tracheotomy discussed but declined in all patients. All NIV was BPAP, S/T mode, nasal mask in 11 (85%)

						12 (92%) required enteral nutrition, none had problems with feeding overnight during NIV. No infant given NIV subsequently developed pectus excavatum. Parents of those who died report more comfortable breathing with NIV, allowed family time at home. One family reported that NIV gave them time at home to come to terms with the diagnosis and prognosis.
Downey et al. [8]	USA	Chest	Retrospective	10	< 2 yrs; 11 were <1 yr	OSA diagnosed on PSG who consented to CPAP use; 3 laryngomalacia, 2 post adenotonsillectomy with residual OSA, 1 BPD, 1 Down syndrome, 1 CHD, 1 Pierre Robin Sequence. CPAP 6-9 cmH_2O, 5 with O_2 2 with tracheotomy used CPAP; 1 used CPAP until OSA resolved, 1 used CPAP for 1 yr then elected tracheotomy as long-term treatment. 2 with residual OSA post adenotonsillectomy used CPAP until OSA revolved 6 used CPAP until OSA resolution; 1-5 y Awakenings, apnea index, obstructive apnea index, hypopnea index, longest apnea, minimal SpO_2, SaO_2<90% all improved from baseline PSG on titration PSG
Essouri et al. [9]	France	Intensive Care Med	Prospective physiological and clinical study (oesogastric pressure measures)	10 infants	9.5 m (3-18 m)	5 laryngomalacia (1 + Down syndrome), 3 tracheomalacia (1 + T21), 1 tracheal hypoplasia, 1 Pierre Robin Sequence CPAP level 8-12, mean 11 ± 2 cmH_2O BPAP associated with patient-ventilator asynchrony (trigger not sufficiently sensitive) CPAP resulted in approximayely 7% reduction in all indices of respiratory effort. There was no correlation between optimal level of CPAP, age, cause of upper airway obstruction, or oesophageal or transdiaphragmatic pressure swing during spontaneous breathing.

						BPAP improved breathing pattern and respiratory effort similar to that observed with CPAP
Gregoretti et al. [10]	Italy	Pediatrics	Retrospective; 1992-2010; NIV not available until 1999	31 infants with SMA type i	age of first respiratory failure: 12.6±14.4 m (0-42 m to start NIV)	BPAP; 14 (45%) died at median age 28.6 m (means age 32±21 m, IQR 12.8-41.4 m). NIV used increased from 8% (1999-2004) to 23% (2005-2010). Follow-up 38±21 m. Survival at 24 and 48 m higher in IV than NIV group: 24 m - 95 (95%CI 82-99)% vs 68 (95%CI 47-82)%; 48 m – 89% vs 45%. Hospitalization rate lower in IV vs NIV: 0.023 vs 0.006 episodes/patient/y. Hours/day on ventilation less for NIV vs IV. 7 (22%) eventually tracheostomized.
Guilleminault et al. [11]	USA	J Pediatr	Retrospective study	74 infants with CPAP at home	< 12 m	Reasons for referral: ALTE (23%), failure to thrive (11%), abnormal sleeping patterns with growth retardation (50%) or without growth retardation (16%). 57 (77%) had craniofacial anomalies. 45 (60%) were below the 20% for weight and 40% for height. Follow-up period between 5 m to 12 yrs with mean 35±21 m. 72 infants successful treated at home with CPAP, 28 eventually discontinued CPAP, 7 were lost to follow-up, 37 continued CPAP. Complications: major problems were related to mask selection. Treatment failure: 1 infant with Down syndrome, extensive cardiac procedures; 1 infant with Pierre Robin Sequence, BPAP tried for 3 weeks, new cardiorespiratory complications, child died at 6 weeks.
Kam et al. [12]	Canada		Retrospective; comparison of surgical and non-surgical treatment	20 infants with Pierre Robin Sequence	9±14 m	CPAP; 14 (70%) isolated, 6 (30%) syndromic. PICU stay 16±23 days (cf tracheotomy 37±34 days), hospital admission 66±46 days (cf tracheotomy 138±76 days). Duration of CPAP use: 6±6 m

Kherani et al. [13]	Canada	Pediatr Pulmonol	Retrospective study	25 children treated with NIV between 1991 and 2013	0.6 (IQR 0.4-0.7) yrs	Underlying disease: CNS n=3 (2 CCHS, 1 other central cause), NMD n=14 (3 SMA 1, 2 congenital myopathy, 2 congenital dystrophy, 3 NMD), respiratory disease n=8 (3 CLD, 2 airway malacia, 1 diaphragmatic paresis, 1 pulmonary atresia, 1 OSA). Location of NIV start: 72% PICU, 21% hospital ward, 13% sleep lab. Outcomes: 32% continuing on NIV, 28% improved (no longer require NIV), mortality 32% (age at death 1.1 [IQR 0.9-1.4] y), treatment failure 8% Main complications: mid face hypoplasia 8%, dermatographism 8%
Shatz et al. [14]	Israel	Oto Rhinol Laryngol	Retrospective study	50 infants with pharyngomalacia	1-18 m	9/50 treated with BPAP, 5/50 treated with CPAP, spontaneous weaning from respiratory support before the age of 36 m
Khirani et al. [15]	France	Crit Care	Prospective physiological study (oesogastric pressure measures)	12 infants treated with CPAP for OSA	2-22 m	5 BPD, 1 Pierre Robin Sequence, 1 Prader Willi syndrome, 3 laryngomalacia and 1 laryngomalacia + Down syndrome + 1 OSA
Leboulanger et al. [16]	France	Pediatrics	Prospective physiological and clinical study (oesogastric pressure measures)	7 infants with Pierre Robin Sequence	2 m (1-10 m)	4 required enteral nutrition. Respiratory effort, assessed by oesogastric pressure measures, decreased significantly during NIV (CPAP, BPAP). Time spent with SpO_2 <90% was reduced (14% to 2%) as was mean and maximal $PtcCO_2$ values and proportion of time with $PtcCO_2$>50 mmHg. Objective compliance was excellent at >8h/day. No tracheotomy or death, 6 of 7 infants weaned from nutritional support. No facial side effects attributable to NIV. CPAP/BPAP duration 16.7±12.2 m (3-39 m) Custom-molded nasal mask for all patients

						Multidisciplinary hospital/home care approach
Lemoine et al. [17]	USA	Pediatr Crit Care Med	Retrospective, intention to treat, Jan 2002 to May 2009, Proactive respiratory care vs supportive care	23 with SMA type I (3 with tracheotomy so 20 with NIV)	Age at diagnosis: 136 (IQR 54-196) d; days after diagnosis to BPAP: 44 (IQR 22-93) days	BPAP; proactive respiratory care (including NIV and tracheotomy), as opposed to supportive care, was associated with fewer days to first episode of respiratory insufficiency, similar frequency of acute life threatening events, higher rates of in-patient care for respiratory insufficiency, longer survival. Adherence to treatment protocols was associated with a trend for longer adjusted survival.
Leonardis et al. [18]	USA	JAMA Otolaryngo Head Neck Surgery	126 infants with OSA on PSG	18/126 treated with CPAP/BPAP	16 mos	No details on those treated with CPAP/BPAP 46/(129) 126 had congenital malfomration or craniofacial syndrome (10 Down syndrome, 9 cleft palate, 6 Pierre Robin Sequence, 6 achondroplasia) and 36 laryngomalacia For those with pre and post-intervention PSG, CPAP showed the highest mean percentage decrease in AHI (67.2% decrease) followed by tracheotomy (67.0%), observation (65.6%), and suprglottoplasty (65.3%). CPAP proved to be the most objectively efficacious intervention.
Markstrom et al. [19]	Sweden	Acta Pediatr	Retrospective study	18 infants treated with NIV	4 m (1-12 m)	Reason for initiation of NIV: hypoventilation in 12 and reduced cough/recurrent infections in 6 infants. Diagnoses: 7 intermediate SMA, 3 CCHS, 2 diaphragmatic paralysis, 2 Down syndrome, 1 centronuclear myopathy, 1 nemaline myopathy,1 Leigh syndrome, 1 myelomeningocele. Initiation of NIV resulted in significant improvements in $PtcCO_2$ and PtcO2. Location of initiation: PICU 44%, ward with special training in NIV 28%, electively on ordinary children's ward 28%.

						Duration of NIV: 3 (17%) CCHS on nocturnal only, 2 11%) diaphragmatic paralysis discontinued because of improvement, 7 (38%) still on NIV, 4 (22%) discontinued because of improvement, 2 (11%) tracheotomy, 1 (5%) died. Asynchrony associated only with leakage from the mask. Mid face hypoplasia of varying degree in CCHS and diaphragm paralysis; custom-made full face mask in 1 CCHS
McNamara et al. [20]	Australia	Chest	Retrospective study	8 infants with OSA treated with CPAP [compared to 8 control infants and 8 with OSA not treated with CPAP]	At diagnosis 10.8±1.3 weeks (6-18 weeks); At CPAP sleep study: 11.4±1.3 weeks	Referred for OSA investigation because of ALTE or family history. CPAP resulted in prevention of nearly all obstructive events during sleep with a significant reduction in central apnea. Each infant tolerated CPAP mask and CPAP well. Parents reported their infants sleeping well at home with the use of CPAP. Treatment with CPAP resulted in significant increase in the spontaneous arousals during rapid eye movement sleep which was similar to the spontaneous arousal index in control infants.
Pelen et al. [21]	Australia	Int J Ped Otorhinolaryngo	Retrospective study	19 infants with congenital tracheal stenosis	0 - 9 m	All treated with NIV pre and post-operative, age at start 0 – 6 m, duration NIV 1 – 24 m, 2 (20%) patients discharged home on NIV
Robison et al. [22]	USA	Laryngoscope	Retrospective study, treatment of OSA in infants	18 (6%) of 295 treated with CPAP or BPAP	15.6 m (3-29 m)	No data on medical comorbidities in those on NIV Mean age at CPAP/BPAP initiation 3 –29 m No information on diagnosis, settings, follow up Subjective intervention efficacy (-1 to 3) based on subjective parental response. Objective efficacy based on reduction in AHI: 84% (on tracheotomy 93%, supplemental O_2 60%, adenotonsillectomy 56%, observation 54%, adenoidectomy alone 18%, tonsillectomy alone increase of

						5%).
Rosen et al. [23]	USA	Clin Pediatr	Retrospective study, Down syndrome < 2 yrs, referred to sleep lab, Jan 2004-June 2009	6 (21%) of 29 treated with CPAP	< 2 yrs	3 (50%) of 6 infants treated with CPAP found at 5, 5, and 10 m to have no further evidence of OSA
Vasconcelos et al. [24]	Portugal	Retrospective study, 11 yrs		7	13 m (3 m to 3 yrs)	SMA type 1 on BPAP Duration: 29 m (16 m-3.5y) Deaths: 5 (71%), age 4 m (1 m-15 m) [At least one started NIV outside of infancy]

Abbreviations: m: months, yrs: years, OSA: obstructive sleep apnea, BPAP: bilevel positive airway pressure, NIV: noninvasive ventilation, IV: invasive ventilation, SMA: spinal muscular atrophy, NMD: neuromuscular disease, BPD: bronchopulmonary dysplasia, ALTE: acute life-threatening event, SIDS: sudden infant death syndrome, CDH: congenital diaphragmatic hernia, CHD: congenital heart disease, CLD: chronic lung disease, ILD: interstitial lung disease, CNS: central nervous system, CCHS: congenital central hypoventilation syndrome, BPD: bronchopulmonary dysplasia, PHT: pulmonary hypertension, AT: adenotonsillectomy, PSG: polysomnography, PICU: pediatric intensive care unit, O2: oxygen, SpO_2: pulse oximetry, $PtcO_2$: transcutaneous oxygen pressure, $PtcCO_2$: transcutaneous carbon dioxide pressure.

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Online Table 9.2: Special population: obese children

Author	Country	Journal	Study design	Number of patients	Ages	BMI	Evaluation	Conclusion
Shine et al. [1]	Australia	Arch Otolaryngol Head Neck Surgery	Retrospective cohort	19 obese (BMI >95th centile) children	2 - 18 yrs	Median BMI z-score (SD): 2.84 (0.94)	10 children needed CPAP after AT	AT improves sleep respiratory parameters in morbidly obese children with OSA but most patients have residual OSA requiring further treatment.
Beebe et al. [2]	USA	Plos One	Prospective study	13 obese patients treated with CPAP + 15 obese controls without OSA	14.8 ± 1.8 yrs	42.4 ± 6.1	Neurobehavioral evaluation (parent and self report questionnaire), academic grades and attention test done at baseline and > 4 m after CPAP initiation Adherence defined by a use > 21% of sleep time: 6 were adherent, 7 not	Improved attention and academic performance in the adherent patients Limitations: data not presented separately for those with obesity, no comparison of obese vs non-obese subjects.
Puri et al. [3]	USA	J Clin Sleep Med	Retrospective study	37 obese children treated with CPAP	1.6 – 18 yrs	BMI z-score 1.8±1.4 [full group], 65% obese	Overall group: mean use was 3.4 ± 2.7 h/night at 1 week, 2.8 ± 2.3 h/night at 1 m, 2.7 ± 2.4 h/night at 3 m Greater adherence when younger age, higher maternal education, household member using CPAP, and greater use at 1 week	Overall CPAP adherence was low Having a family member with OSA on CPAP therapy was associated with better adherence in the child. The cohort has a number of comorbidities (asthma, neurological condition, craniofacial conditions) that can affect CPAP adherence, and that is not specific for obese population. Limitation: data not presented or

								analyzed separately for subjects with obesity.
Katz et al. [4]	Canada	J Clin Sleep Med	Prospective multicenter	27	6-18 yrs	BMI z-score: mean 2.6 (2.3-2.8)	Evaluation of insuline resistance, 24h-BP, h-CRP at baseline and 6 and 12 m 14 CPAP, 13 BPAP 14 adherent (> 6h use/night)	CPAP/BPAP no effect on insulin resistance, 24h-BP, hs-CRP at 6 and 12 m However there were[3] clinically relevant improvements in insulin resistance and systolic BP load.
Alonso-Alvarez et al. [5]	Spain	Sleep Med	Cross sectional prospective multicenter	113 but only 6 treated with CPAP	11.3 ± 2.9 yrs	BMI z-scores: 1.34 ± 0.59	Only 6/113 children treated with CPAP for 1 yr	Significant univariate associations between BMI and CRP, insulin, and homeostasis model assessment of insulin resistance present at baseline and after 1 yr after CPAP initiation. With CPAP (n=6): decrease in glucose, CRP, cholesterol, LDL/HDL No information on compliance
Sudaram et al. [6]	USA	J Pediatrics	Prospective	9	11.5 ± 1.2 yrs	BMI z-score 2.2 ± 0.3	CPAP duration 89 ± 62 days Adherence 73 ± 24% of nights Mean use 296 ± 126 min/night	Improvement of biomarkers of non-alcoholic fatty liver disease, liver enzymes, oxidative stress and metabolic syndrome Of note: low baseline AHI : mean 7, max 11/h
Amini et al. [7]	USA	Children	Retrospective, single centre	18 (BMI≥85 %, AHI >1, treated with CPAP/BPAP)	11.8±3.4 y (full group)	BMI z-score 2.6±0.5	17 CPAP, 1 BPAP; 2 CPAP + 1 BPAP titrated in the lab, remainder (14) treated with auto-CPAP. Mean follow-up 19 m (median 12.5 m, range 3-46 m)	Decrease in total cholesterol, LDL cholesterol in CPAP/BPAP group No change in HDL cholesterol, triglycerides, fasting glucose, or BMI in either subgroup.
Baldi et al. [8]	India	Indian J Pediatr	Simulation cohort,	Not applicable	1-18 yrs	Not applicabl	Simulation of adverse outcomes of obesity in	Costs for adverse outcomes related to OSA (stroke, CHD, type 2 DM in

			based on 2011 Indian census			e	OSA children	adulthood) in patients only treated with AT are higher compared to those treated with both AT and CPAP; even if CPAP results are more expensive than AT, the two treatment together promote a greater reduction of obese subjects and a subsequent higher reduction in adverse outcomes resulting in an overall cost reduction compared to AT alone.
Carriere et al. [9]	Franc e	Acta Paediatr	Retrospect ive cohort, single centre, received care for obesity	128 children referred for overweigh t or obesity, 10 on CPAP	12.1 ± 3.2 yrs		Healthcare management offered; diagnostic and therapeutic impact of sleep consultation Time to set-up CPAP 1-9 m after consultation	PSG identified OSA in 24.2% of overall population. CPAP suggested for 17, prescribed for 10 and finally used by 8 (6.2% of the study population, 10% of those undergoing PSG).

Abbreviations: m: months, yrs: years, CPAP: continuous positive airway pressure, BPAP: bilevel positive airway pressure, NIV: noninvasive ventilation, OSA: obstructive sleep apnea, BMI: body mass index, AT: adenotonsillectomy, PSG: polysomnography, AHI: apnea-hypopnea index, DM: diabetes mellitus, BP: blood pressure, hs-CRP: high sensitivity C-Reactive Protein, LDL: low density lipoprotein, HDL: high density lipoprotein.

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Online Table 9.3: Special population: CPAP or NIV in children with neurodisability

Author, Year	Journal	Country	Study design	No of patients	Age of patients	Evaluation	Conclusion
Grychtol et al. [1]	Arch Dis Child	UK	Retrospective review of case series (2010-2016)	21 patients with severe CP (20 with GMFCS IV/V)	1.7-16.1 yrs	21 children with CP were moderate – severe SDB were initiated on NIV; Indication for NIV: mod-severe OSA ± hypoventilation, despite upper airway intervention. 11/21 (55%) patients failed to establish on NIV due to mask intolerance ± ventilation pressure at initial trial or poor adherence during follow up. Erratic sleep pattern may have contributed to intolerance of NIV and vice versa. Established NIV users showed good adherence with significant improvement in SDB	Challenging group of patients: success rate less than total NIV patient cohort. Decision to initiate should be based on benefit outweighing risk and burden
Marcus et al. [2]	AJRC CM	USA	Prospective study	52 children with OSA, 10 (19%) had neurodevelopmental disability	12 yr ± 4 yrs	Children treated with CPAP/BIPAP had significant improvement in attention deficit, sleepiness and quality of life. Behavioral factors improved in children with developmental delay.	Heterogeneous group – no subgroup analysis for children with neurodisability. Variable adherence, mean adherence was 3 hours/night.
Hsiao at al. [3]	Res Dev Disabil	New Zealand	Retrospective case control study:	Children with CP (GMCSF	3-18 yr	Treated patients (surgical or CPAP) showed improvement in OSA symptoms (sleep	Treatment of OSA in children with CP leads to significant benefit in aspects of health and QoL.

			comparison between adenotonsillectomy and NIV for OSA with a control group	V) Treatment group (n=10): 7 had AT; 3 on CPAP vs control group (n=9) who had no OSA or treatment		disturbance, daytime functioning, carer's concern)	Limited by small sample, retrospective design and lack of comparison between treatment options
Girbal et al. [4]	Rev Port Pneumol	Portugal	Restrospective cohort, single centre	9 CP (13% of cohort), 6 inborn error of metabolism (9% of cohort)	Age of start of NIV in patients with CP CP 168 m (IQR 89-173)		All patients with sustained NIV had clinical improvement as reported in clinic files. Limitations: complex OSA not defined, patients with CP not analyzed separately

Abbreviations: m: months, yrs: years, CPAP: continuous positive airway pressure, BPAP: bilevel positive airway pressure, NIV: noninvasive ventilation, GMFCS: gross motor function classification system, CP: cerebral palsy, OSA: obstructive sleep apnea, SDB: sleep-disordered breathing, AT: adenotonsillectomy, QoL: quality of life.

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Online Table 10: CPAP and NIV and quality of life for patients and families / caregivers

Author, year	Country	Journal	Type of study	Number of patients	Ages	QoL (family, child)
Nozoe et al. [1]	Brazil	Sleep & Breath	PSQI administered to mothers of Duchenne patients	32 caregiver mothers and 32 control mothers: 16 patients treated with NIV		Of the 16 NIV patients: 8 mothers had good sleep quality and 8 bad The longer the NIV use (months), the better mother sleep quality (=only sleep quality predictor)
Gonzalez et al. [2]	Spain	Eur J Pediatr	Cross-sectional study, interview (PedQoL)	41 patients (invasive and NIV) with 20 children treated with NIV	Median age of NIV patients: 10.1 yrs (7.1-13)	Lower QoL in patients and parents (compared to healthy children and their parents) Parents perceived lower QoL than the patients Importance of underlying disease (> 50% NMD) QoL scores were low in all age groups, mainly physical domain, scores are lower in children treated with NIV
Cadart et al. [3]	France	Acta Pediatr	Prospective	96 parents of 86 children with rare conditions and referred to a sleep lab for a P(S)G filled in questionnaires on anxiety, depression, family functioning, parents QoL, daytime sleepiness and sleep quality	0.3 - 18 yrs	27/86 children were treated with CPAP or NIV 19% of the parents of children on NIV/CPAP presented with moderate-to-severe anxiety; 8% presented with moderate-to-severe depression. The responses to all the questionnaires did not differ between parents of children treated or not treated with long term CPAP or NIV
Lynch et al. [4]	USA	Behavioral Sleep	OSA-specific QoL	42 youth-caregiver dyads: data from 25 youth-caregiver	8-16 yrs (exclusion 1. cognitive &	CPAP-adherent youth had decreased sleep disturbance + decreased caregiver concern

		Med	questionnaire given before and after 3 m of CPAP	dyads suitable for analysis	physical disabilities; 2. comorbid medical and neurological conditions; 3. on anti-psychotic drugs	No significantly different changes in overall QoL between CPAP adherent and non-adherent youths before CPAP and 3 m after initiation.
Redouane et al. [5]	Canada	Plos One	Single centre cross-sectional study on QoL of parents of children using G, IV or NIV, or both	39 using NIV, 8 using IV, 20 using G + NIV, and 8 G + IV	5-18 yrs	Parental perception of QoL was lower than those of parents with healthy children. QoL perception was lower in parents of children using G than IV/NIV; technologies do not have additive effect on QoL. No difference between children using IV or NIV: importance of underlying condition
Meltzer et al. [6]	USA	J Clin Sleep Med	Cross sectional prospective study comparing sleep patterns and Health releated QoL of parents of ventilated	42 families with ventilated children (30 IV and 12 NIV children) and 40 families of healthy children	4-17 yrs	Parents of children treated with IV or NIV showed significantly later bedtimes, shorter total sleep time, lower sleep efficiency. Many showed significant instability of their sleep, directly related to health related QoL.

			and healthy children			
Young et al. [7]	Australia	Neurology	Retrospective review of effect of NIV on clinical and QoL in children with severe NMD	14 children (SMA II, congenital myopathy, merosine deficient myopathy. myotonic dystrophy and Duchenne muscular dystrophy)	Median age 7.7 yrs (1.5-16 years)	Comparison before and after NIV initiation. Symptoms of daytime sleepiness (p=0.003) and headaches (p= 0.046) improved after initiation of NIV Sleep quality improved. QoL remained stable after NIV despite disease progression
Johannsen et al. [8]	Germany	Health and QoL outcomes	Questionnaire survey in 43 families of children with NMD	43 families returned questionnaire: 18 with ventilated children 25 non-ventilated children	Age of IV/NIV initiation 4.4 yrs ± 5.4	Compared to normative data, children with NMD and their families had a lower health-related-QoL and mental health. No additional negative influence on the overall health related QoL of ventilator use. IV/NIV per se is not responsible for the reduction of health related QoL and mental health
Baiardini I et al. [9]	Italy	J Child Neurology	Cross-sectional study using questionnaires (Child health questionnaire –parent form 30, Family	27 DMD children and their parents	Mean age of children 11.2 yrs Mean age of parents mean age 40 yrs	Out of 27 children, 4 were ventilator users. Children reported significantly lower scores than normative group in 10/15 children health questionnaire dimensions. Only the use of wheelchairs (p=0.02) and ventilators (p<0.001) was significantly associated to lower health related QoL. Family strain questionnaire scores were not influenced by children's characteristics.

			strain questionnaire			
Noyes J et al. [10]	UK	J Advanced Nursing	Cross sectional study using validated questionnaires	Comparison of ventilator dependent children reports of health related QoL with parents report and normative population 27 ventilated children (17 responded to questionnaires) 27 parents of ventilated children (15/27 on nocturnal NIV)	Age of children 4-18 yrs The underlying diagnosis were only classified into congenital/spinal injury/brain injury.	Ventilated patients report significantly lower overall health related QoL and significantly lower scores in all domains except about their friends, compared with healthy children and children with other chronic diseases. Parents reported significantly lower scores for their child's disease and relationships with friends. Positive correlation between children and parents in all areas apart from self-esteem and school. Parents are not necessarily accurate proxies for all aspects of their child's experience and perceptions.
Vuillerot C et al. [11]	France	J Adolescent Health	Cross sectional study using questionnaire to assess self perceived QoL correlating with impairment, disability	43 adolescents with NMD including DMD, SMA, congenital myopathy; congenital muscular dystrophy and fascioscapulo-humeral muscular dystrophy	mean age 13.8 ± 1.7 yrs	VSP-A (self-perceived health state in adolescents) assess perceived wellbeing in 10 domains. VSP-A scores in physically disabled adolescents were similar to those of non-disabled group with regard to vitality, body image, relationships with parents and friends, physical and psychological wellbeing. Adolescents with ventilatory support did not express lower scores than adolescents not requiring ventilatory support (p=0.39)

			and respiratory status			
Carneval e et al. [12]	Canada	Pediatr ics	A qualitative study using semistruct ured interview of 12 families with children on ventilatory support at home	12 families with children having: abnormal ventilatory control; NMD; spina bifida; craniofacial or airway abnormalities (4 tracheostomy invasive ventilation; 8 NIV) Fieldwork observations were carried out at home	Age not specified	6 principal themes were identified: 1. Confronting parental responsibilities – stressful for parents 2. Families seeking normality 3. Conflicting social values – parents feeling child's life devalued 4. Living in isolation 5. Voice of child often not heard 6. Questioning of moral order Despite difficulties described by families, they also reported deep enrichments and rewarding experiences that they could not imagine living without.

Abbreviations: m: months, yrs: years, QoL: quality of life, CPAP: continuous positive airway pressure, BPAP: bilevel positive airway pressure, NIV: noninvasive ventilation, IV: invasive ventilation, G: gastrostomy, PSQI: Pittsburgh Sleep Quality Index, PedQoL: Pediatric Quality of Life, NMD: neuromuscular disease, SMA: spinal muscular dystrophy, OSA: obstructive sleep apnea, P(S)G: poly(somno)graphy.

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Online Table 11: Therapeutic education programs for CPAP and NIV.

Author	Country	Journal	Type of study	Number of patients	Ages	Therapeutic education program	Evaluation, efficacy
Hewitt-Taylor [1]	UK	Intensive Crit Care Nursing	Survey questionnaire, descriptive study on local practice	21/35 centers responded	Not specified	Areas that were seen as important for children with complex diseases requiring CPAP or NIV are discussed Role of trained nurses A variety of health care professionals are needed	
Tibbals et al. [2]	Australia	J Ped Child Health	Longitudinal survey (1979-2008) in one center in Melbourne	168 patients	3 weeks – 19 yrs	Patients are considered early for discharge, condition must be stable, parents must be motivated. Nurses and technologists teach the parents/carers in the PICU and the ward. Social workers act as case managers in the home. Parents are trained to cope with predictable instability at home. A full set of equipment for ventilation, suctioning and monitoring (SpO_2) with disposable items is provided. Children requiring 24-h ventilation have a spare ventilator at home	No information on eventual discharge failures
Boroughs et al. [3]	USA	Children		11 children with SMA, 6 on BPAP	6 m-18 yrs	Evaluation of caregiver skills via simulated scenario, corrections with re-evaluation after 3 and 6 m.	Training beneficial for all participants Desire for real-life scenarios Value of an on-going training for caregivers
Amaddeo et al. [4]	France	Pediatric Pulmono	Prospective study:	31 children	0.8 - 17.5 yrs	Description of the therapeutiuc education program and tools: educational boards and	Compliance was excellent: mean

		l	outpatient program for CPAP initiation			cartoons, booklet, teddy bear, relaxation, distraction, follow up at home, home visits, etc.	use 8h21/night (5h45-12h20); % of night with use > 4h: 83 ± 17%, median nights use/m: 25 (18-30)

Abbreviations: m: months, yrs: years, BPAP: bilevel positive airway pressure, PICU: pediatric intensive care unit, SpO_2: pulse oximetry, SMA: spinal muscular atrophy.

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Online Table 12: Transition

Author	Country	Journal	Type of study	Number of patients	Ages	Transition	Transition program
Tibbals et al. [1]	Australia	J Ped Child Health	Longitudinal (1979-2008) in 1 center in Melbourne	168 children	3 weeks - 19 yrs	58 CPAP, 50 BPAP, 48 tracheotomy, 5 phrenic nerve, 4 negative pressure, 3 nasopharyngeal tube 27 (16%) were transferred to adult services (no more information)	
McDougall et al. [2]	Canada	Arch Dis Child	Retrospective study in 1 center 1995-2009	144 children (116 on NIV)	< 18 yrs	37/144 (26%) children (5 IV + 32 NIV) transitioned to adult services (increase over time) median age of transition 18 yrs (16.4-19.3)	?
Amin et al. [3]	Canada, 2014	Pediatr Pulmonol	Retrospective study in 1 center 1991-2011	313 children treated with NIV	2.9 - 13.9 yrs	106 transitioned to an adult service (of 379 IV and NIV)	?
Chatwin et al. [4]	UK	Plos One	Retrospective study in 1 center 1993-2011	496 children	< 17 yrs	181 (40%) transitioned to adult services	?
Dale et al. [5]	Canada	Pediatr Child Health	Semi-structured telephone interview	14 adolescents with NMD treated with NIV	17-21 yrs	Facilitators: early planning, written information material, joint pediatric-adult provider-family transition meetings Barriers: insufficient information, limited access to nursing and allied health providers, reduced funding or health services More difficulties if cognitive dysfunction or physical dependence	
Chau et al. [6]	Hong Kong	Respir Care	Retrospective study in 1 center 1997-2015	71 children treated with NIV	< 21 yrs	7/71 (10%) patients with NIV transitioned to adult services or other services because of geographical reasons	?
Castro-Codesal et al. [7]	Canada	Plos One	Retrospective study in Alberta 2005-2014	622 children	0-18 yrs	Increase in the number of children transitioned over time: median 4 (5-19)/yr between 2011-2014	?

Ikeda et al. [8]	Japan	Brain Dev	Retrospective study in 1 center 2015-2015	53 children		10 children transitioned to adult services (29% of the 34 continuing patients)	?
Onofri et al. [9]	Italy + UK	Italian J Pediatr	Retrospective study, comparison Brompton/Babino Gesu	Patients with NMD on NIV: 15 + 15	Ado > 15 yrs	Patients transitioned at a younger age in the Brompton Brompton has an adult unit in same hospital Care similar No analysis of quality of life.	Brompton has a transition program but not B Gesu
Dale et al. [10]	Canada	Pediatr Pulmonol	Prospective longitudinal interview of ado-caregiver dyads	18 ado 17-19 yrs	10 treated with NIV	Facilitators: early transition discussion, opportunity for patients to speak directly with home care providers, printed information about adult services, joint pediatric-adult team handover meeting Modifiable barriers: lack of other specialist referrals, insufficient information about homecare service funding, limited involvement of family doctors	
Leske et al. [11]	Argentina	Pediatr Pulmonol	Retrospective study in 1 center 2007-2018	244 children (210 NIV)		40/244 (16%) transitioned to adult services	?

Abbreviations: m: months, yrs: years, CPAP: continuous positive airway pressure, BPAP: bilevel positive airway pressure, NIV: noninvasive ventilation, IV: invasive ventilation.

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Online Table 13. Cost and resource use of CPAP or NIV.

Author	Country	Journal	Type of study	Number of patients	Ages	Cost and resources
Oktem et al. [1]	Turkey	Respiration	Longitudinal study in one center in Istanbul (2001-2006)	34 children, 23 on NIV	4 m -17 yrs	No information on the investigations that led to the prescription of NIV nor on health insurance Patients spent a median of 32 (3 - 270) days in hospital before discharge due to the delay in supplying home equipment Ventilator failure seen in 2 patients (NIV or IV ?) without any serious complication
Tibbals et al. [2]	Australia	J Ped Child Health	Longitudinal (1979-2008) in one center (Melbourne)	168 children	3 weeks - 19 yrs	58 CPAP, 50 BPAP, 48 tracheotomy + other Median annual cost of all care of a patient at home: 115 300 AUS dollar (range 82 000 - 200 000), no distinction IV-NIV
Nathan et al. [3]	Malaysia	Pediatr Pulmonol	Longitudinal study in one center (2001-2014)	70 patients, 60 on NIV (30 CPAP + 30 BPAP)	1.1 - 11 yrs (for NIV)	No information on the investigations that led to the prescription of NIV Lack of health insurance for children on NIV Equipment bought by family 24 (83%), or sponsor 5 (17%), borrowed 41 (57%) by medical social worker (35 (85%) or other source 6 (15%)
Leske et al. [4]	Argentina	Pediatr Pulmonol	Longitudinal study in one center in Buenos Aires (2007-2018)	244 children	3 - 14 yrs	Home ventilation (IV + NIV) possible in a low-income country, 210/244 (86%) used NIV, 84% had health insurance 173/244 (71%) had sleep studies, 147/173 (91%) PSG, and 13/173 (7.5%) nocturnal SpO_2 + $PtcCO_2$, and 2 diurnal ABG + nocturnal SpO_2 > 50% of patients lived > 100 km and 34% > 500 km from NIV center NIV was started electively in 116/244 (47.5%) patients, subacutely in 80/244 (32.8%) and acutely in 48/244 (19.7%).

Abbreviations: m: months, yrs: years, CPAP: continuous positive airway pressure, BPAP: bilevel positive airway pressure, NIV: noninvasive ventilation, IV: invasive ventilation, AUS: Australian dollar, PSG: polysomnography, SpO_2: pulse oximetry, $PtcCO_2$: transcutaneous carbon dioxide pressure, ABG: arterial blood gases.

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