



ERS statement on paediatric long-term noninvasive respiratory support

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Long-term noninvasive ventilation (NIV) in children is increasing worldwide. There is lack of validated criteria for NIV initiation, follow-up, monitoring and weaning. Children are optimally managed by a paediatric multidisciplinary team. <https://bit.ly/3bVfNvz>

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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 paediatric multidisciplinary team. This statement written by experts in the field of paediatric long-term CPAP/NIV aims to emphasise the most recent scientific input and should open up new perspectives and research areas.

Introduction

Long-term noninvasive respiratory support consists of delivering 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) (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 cases of obstruction of the upper airways where the restoration of airway patency throughout the entire breathing cycle is sufficient to normalise 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 characterised 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±hypoxaemia, occurs. Hypoventilation may also be observed in case of an abnormal central drive. The aim of NIV is 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]. 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 European Respiratory Society (ERS) task force reviewed the literature on long-term CPAP/NIV in children and summarised 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 paediatric 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 summarising 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 (B. Fauroux and S. Verhulst) to answer the formulated questions. The MEDLINE, Embase, Wiley Cochrane, the Cumulative Index to Nursing and Allied Health Literature and Child Development & Adolescent Studies 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.* [2] on paediatric (0–18 years) long-term noninvasive respiratory support, which included references from 1990 to 2015. 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 4564 additional titles between 2016 and September 2019. After excluding case reports, abstracts, non-English articles, papers on acute NIV 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 supplementary table S1). The final statement was reviewed by caregivers from different countries who gave their input and participated in the research priorities.

Disorders that may benefit from CPAP/NIV

Disorders that may benefit from CPAP

Literature review

Disorders that may benefit from CPAP are listed in supplementary table S2.1. Severe persistent obstructive sleep apnoea (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], Morquio-A syndrome [44], mucopolidosis [45]), Prader–Willi syndrome [13, 46, 47] and OSA associated with obesity [9, 10, 13, 14, 48]. In addition, CPAP has 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 (tumours, malformations [49]), severe neurodisability [50], congenital cardiopathy [51], myelomeningocele [52] or Ehlers–Danlos syndrome [53].

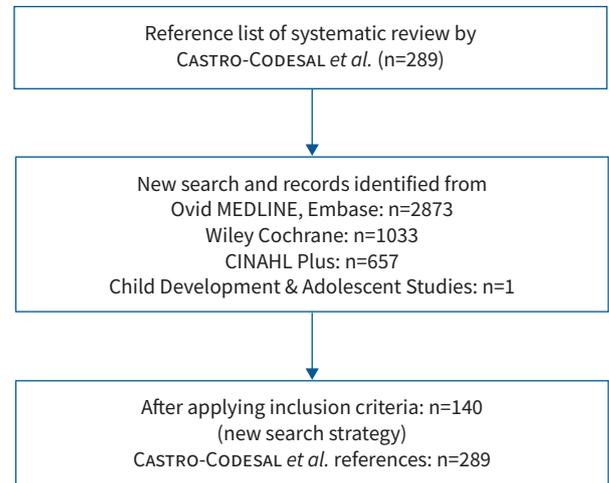


FIGURE 1 Reference search strategy. CINAHL: Cumulative Index to Nursing and Allied Health Literature.

Summary

- CPAP has been used in children with 1) complex OSA, defined as OSA associated with craniofacial or upper airway malformation, or OSA associated with morbid obesity (OSA type II) presenting with severe OSA despite optimising medical and surgical management, or when these aforementioned medical/surgical treatments are not feasible or indicated; and 2) a high level of intrinsic PEEP, as observed in infants with BPD.
- CPAP has been successfully implemented at any age.

Disorders that may benefit from NIV

Literature review

Disorders that may benefit from NIV are listed in supplementary table S2.2. 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 NMDs [69, 82–87]; diaphragmatic palsy [88]; and severe thoracic deformity [85, 86]. NIV has also been used in children with storage disease (mucopolysaccharidosis [89], mucopolidosis [45]) or Prader–Willi syndrome in case of nocturnal alveolar hypoventilation [46, 47, 86], rapid-onset obesity with hypothalamic dysregulation, hypoventilation and autonomic dysregulation (ROHHAD) syndrome [90, 91], cystic fibrosis [92–95], congenital tracheal stenosis [29] or congenital central hypoventilation syndrome (CCHS) [96–99]. Finally, NIV may be proposed in children requiring or not tolerating high CPAP pressures, or in case of persistent hypercapnia despite optimised 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 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.

Longitudinal or cross-sectional national/regional/local studies

Literature review

Longitudinal or cross-sectional studies are listed in supplementary table S2.3. Long-term NIV in children has been reported in countries with well-developed healthcare systems (USA [101], Canada [102–105], Australia [106, 107], France [108, 109], UK [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.

Initiation criteria, initiation location and recommended/optimal settings

Initiation criteria

Literature review

Initiation criteria are listed in supplementary table S3.1. CPAP/NIV has been initiated in an acute/subacute (paediatric 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 acute respiratory failure [102] in case of failure to wean from invasive ventilation (endotracheal tube or tracheostomy [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 hypoxaemia (low pulse oximetry (S_{pO_2}))± hypercapnia (elevated transcutaneous carbon dioxide pressure (P_{tcCO_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 apnoea–hypopnoea index (AHI) [91, 102, 104, 105, 109, 112] or “increase in work of breathing” [133]. However, the definitions of “hypoxaemia”, “hypercapnia” and “alveolar hypoventilation” are rarely available and vary between studies. Severe persistent OSA in children with upper airway malformation, defined by an obstructive AHI >5 or >10 events·h⁻¹ 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 I, 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]. Efficacy and adherence with CPAP/NIV according to the initial setting (PICU or (sleep unit) ward, *i.e.* acute *versus* 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 P_{tcCO_2} >50 mmHg during ≥2% or more of nocturnal sleep time or more than five 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 prerequisite screening of patients at risk of severe OSA and/or nocturnal alveolar hypoventilation.

TABLE 1 Respiratory criteria that have been used for initiation of continuous positive airway pressure or noninvasive ventilation [130]

Minimum S_{pO_2} <90%
Maximal P_{tcCO_2} >50 mmHg
≥2% of recording time spent with S_{pO_2} <90%
≥2% of recording time spent with P_{tcCO_2} >50 mmHg
3% oxygen desaturation index >1.4 events·h ⁻¹
AHI >10 events·h ⁻¹
S_{pO_2} : oxygen saturation measured by pulse oximetry; P_{tcCO_2} : transcutaneous carbon dioxide pressure; AHI: apnoea–hypopnoea index.

- 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.

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 ineligibility criteria should be checked or corrected before proposing CPAP/NIV.

Location of elective CPAP/NIV initiation

Literature review

Location criteria are listed in supplementary table S3.1. 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 outpatient setting may be as efficacious (as defined as correction of SDB and objective adherence) as during hospitalisation (when associated with a therapeutic education programme [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 hospitalisation with a recent tendency towards an outpatient or even home setting, depending on the underlying condition, team expertise and local facilities.
- CPAP/NIV initiation in an outpatient setting is possible, but needs further validation.

Initial settings for CPAP/NIV

Literature review

Initial and follow-up settings for CPAP and NIV are listed in supplementary tables S3.2 and S3.3, respectively. 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, S_{pO_2} , built-in software data, measurement of the oesogastric pressures) has also been shown to correct SDB symptoms and the AHI [27, 145, 146]. Mean CPAP level to overcome respiratory events is usually achieved at 8 ± 3 cmH₂O following titration with a starting pressure of 4 cmH₂O [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 $\leq 90\%$ 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 inspiratory positive airway pressure (IPAP) after titration ranges 10–14 cmH₂O with an expiratory positive airway pressure (EPAP) 4–6 cmH₂O with starting pressures of 4 cmH₂O for EPAP and 8 cmH₂O for IPAP [60, 73, 82]. Higher IPAP pressures (18 ± 6 cmH₂O) 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 $6\text{--}10$ mL·kg⁻¹ 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 two to three breaths below the patient's physiological or spontaneous breathing rate ($12\text{--}18$ breaths·min⁻¹) [60, 82, 151]. For children with OSA, the AASM recommends a titration PSG to set the optimal IPAP and EPAP levels [100]. No data are 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 synchronisation and a decrease in work of breathing [93]. In the case of an 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 cmH₂O with a mean treatment CPAP pressure of 8±3 cmH₂O.
- Auto-CPAP has been used in selected patients, but has not shown to be superior to fixed-pressure CPAP.
- For NIV, starting inspiratory and expiratory pressures are usually set at 8 and 4 cmH₂O, respectively, with a final IPAP of 10–14 cmH₂O and EPAP of 4–6 cmH₂O. Higher IPAP levels may be necessary in selected patients, such 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 two to three breaths below the child's physiological or spontaneous breathing rate.
- The AASM recommends using a titration PSG to set the optimal IPAP and EPAP levels [100]. However, as PSG is not available in all centres, 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.

Which professionals may initiate CPAP/NIV?

Literature review

The qualifications of the staff members who initiate and follow-up children on long-term CPAP/NIV are rarely reported [145]. In Europe, children on long-term CPAP/NIV are managed by paediatricians (paediatric pulmonologists and/or intensivists), nurses trained in CPAP/NIV and technicians (for home visits) [145]. In the United States and Canada, children on long-term CPAP/NIV are managed by paediatricians (paediatric 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.

Equipment

Interfaces

Literature review

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 an NIV device for children who did not tolerate a commercial interface. Recently, a nasal cloth mask has become available for children aged >2 years who have plastic intolerance [157]. A 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, 161] or the pressure exerted by the interface (skin erythema or ulcer, facial deformity, maxillary retrusion) [96, 157, 160, 162] (table 2 and supplementary tables S4.1 and S4.2).

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, an oronasal mask for patients with mouth leaks is difficult to manage, nasal prongs for older children who do not tolerate nasal masks).

TABLE 2 Interfaces for continuous positive pressure treatment or noninvasive ventilation

	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) 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) 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 Difficulty of use by young children	None

- Although commercial paediatric masks are 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.

Ventilators

Literature review

Ventilator studies are listed in supplementary table S4.3. A review has listed the CPAP/NIV devices that can be used in children at home [163] 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 [164].

Summary

- The choice of a device is based on the child's characteristics (weight, underlying disease, 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 h/24 h) should have a backup device.
- A double switch-off manoeuvre offers a security to avoid untimely switch-off of the ventilator.
- Humidification of inspired air seems associated with a greater comfort and less secretion problems.
- Passive humidification with heat and moisture exchange filters has not been validated for CPAP/NIV devices.

Follow-up

Follow-up procedures

Literature review

Several studies showed the persistence of respiratory events and/or abnormal nocturnal gas exchange requiring an intervention during systematic follow-up PSG/PG, performed 3–6 months after CPAP/NIV initiation, even in asymptomatic patients [5, 146, 147, 165–171] (supplementary table S5.1). Monitoring of nocturnal gas exchange during CPAP/NIV at home is feasible and informative for outpatient follow-up [166, 167]. For some devices, the built-in software may give useful information on the child's respiratory parameters (when the child's weight is equal to or greater than 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) [172, 173]. OSA-18 questionnaire scores sometimes improve when ventilator setting changes are implemented after a PSG/PG [169]. 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, 174]. Telemedicine is sometimes useful for the follow-up of adolescents with NMD on long-term NIV [175, 176] and children with OSA treated with CPAP [177, 178]. Despite the information noted herein, 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 normalisation or level of improvement of AHI, S_{pO_2} and P_{tCO_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 S_{pO_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 (S_{pO_2} ± P_{tCO_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 a 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 3–6 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 (S_{pO_2} ± P_{tCO_2}) at minimum every 6 months has been shown to be informative.
- Telemonitoring is feasible and may improve CPAP/NIV adherence and limit side-effects.

Adherence

Literature review

Adherence has mainly been evaluated for CPAP, and less so for NIV [153, 179] (supplementary table S5.2). Adherence is assessed on objective criteria (built-in software data) because children and caregivers tend to overestimate real adherence [148]. Usually, adherence reported in the literature does not cover the entire night and represents the greatest challenge for long-term CPAP/NIV [14, 148, 180–187]. Numerous predictors of adherence have been identified: greater self-perceived improvement in SDB symptoms [179], developmental delay (lower compliance in children with Down syndrome [144, 188] and better adherence in children with other causes of developmental delay [189, 190]), gender [189], rapid acclimatisation to treatment [179], technical issues [179], NIV versus CPAP [191], side-effects [179], familiarity with medical treatments, understanding of the disease and its consequences [179], greater improvement in AHI [187, 192], age [183], ethnicity [183], maternal education [183], family social support [179, 183], family structure [184], perception of CPAP benefits [184], family member using CPAP [14], caregiver

self-reported efficacy [193] and internalising problems [187]. Some strategies/tools may improve adherence: behavioural therapy [194], Adherence Barriers to CPAP questionnaire for identifying patient-specific barriers [182], therapeutic education sessions by a respiratory therapist [185], token economy [195], medical hypnosis [196] and shared decision-making tools [197]. There are 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.

Benefits of CPAP

Literature review

CPAP may be associated with an improvement in OSA:

- decrease in OSA symptoms: decrease in sleepiness [198]
- correction or improvement in OSA: decrease in AHI, improvement in S_{pO_2} [5, 145, 146, 148, 149, 198]
- increase in OSA-related quality of life (QoL) [198] and caregiver QoL [198]
- 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 behaviour:

- attention, alertness, concentration [198–201]
- behaviour [198, 199]
- school performance [200]
- electroencephalogram features of attention-deficit hyperactivity disorder [202].

CPAP may be associated with improvement in other functions:

- cardiac function in Down syndrome [41]
- blood pressure: decrease in systolic blood pressure [203]
- metabolic syndrome (contradictory results): improvement [204, 205], no effect [206] and improvement in liver injury [207].

These data originate mostly from observational studies; there are no randomised controlled studies. Furthermore, there are no studies evaluating benefits of CPAP on neurobehavioral functioning in children with complex OSA (supplementary table S5.3).

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

Benefits of NIV

Literature review

Due to ethical constraints, the benefits on NIV have not been confirmed in randomised controlled trials and the published cohort studies mainly consist of a limited number of patients (supplementary table S5.4). NIV is associated with:

- an increase in survival in patients with SMA type I [57, 62, 65, 66, 208] and Duchenne muscular dystrophy [71, 209]
- fewer hospitalisations in patients with SMA type I [57, 61, 62, 64, 208], and some NMD [210, 211]; but no change in hospitalisations in other children with NMD [212]
- improvement in SDB symptoms in patients with SMA type II–III [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 I–II [60], SMA type II [213] and other NMD [69, 82]
- decrease in chest deformity in patients with SMA type I [58, 63], and SMA type I–III [61]
- transient improvement in predicted FVC and thoraco-abdominal asynchrony in patients with Duchenne muscular dystrophy [214]
- improvement in cardiac function in patients with Duchenne muscular dystrophy [215]
- improvement in QoL in children with NMD [216].

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.

Weaning

Disorders that are conducive for weaning

Literature review

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

- infants with OSA [147, 217, 218]
- children with craniosynostosis [12, 219]
- children with Down syndrome [38]
- children with complex OSA [13, 174]
- children with OSA type I [220].

Weaning from long-term NIV is less common (and less reported) than from CPAP [104, 111, 122, 174] and in children with NMD as compared to children treated with NIV for other conditions [101] (supplementary table S6.1). 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 [105, 123].

Summary

- 6–40% 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.

Weaning procedure

Literature review

Only one study described a local weaning protocol with weaning criteria for CPAP/NIV (table 3) [174]. There is no information on the optimal timing of a weaning trial: this may depend on the underlying disease (*e.g.* Pierre Robin sequence) and/or the age of the patient, and/or additional treatments (*e.g.* surgery) [174]. There is no information on the optimal duration of CPAP/NIV withdrawal before a baseline PG/PSG without respiratory support (supplementary table S6.2). 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 [174].

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 washout period, CPAP/NIV is usually withdrawn for a certain period before performing a sleep study for CPAP/NIV weaning. This washout 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.

TABLE 3 Respiratory criteria that have been used to allow discontinuation of continuous positive airway pressure (CPAP) or noninvasive ventilation (NIV): all four major criteria should be fulfilled with at least two minor criteria [168]

Major criteria	<ul style="list-style-type: none"> • 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% of recording time spent with $S_{pO_2} \leq 90\%$ • <2% of recording time spent with $P_{tcCO_2} \geq 50$ mmHg • Obstructive apnoea–hypopnoea index <10 events·h⁻¹ on poly(somno)graphy
Minor criteria	<ul style="list-style-type: none"> • Minimal $S_{pO_2} >90\%$ • Maximal $P_{tcCO_2} <50$ mmHg • 3% oxygen desaturation index ≤ 1.4 events·h⁻¹

S_{pO_2} : oxygen saturation measured by pulse oximetry; P_{tcCO_2} : transcutaneous carbon dioxide pressure.

CPAP/NIV failure

Literature review

HFNC may be an alternative to CPAP in children and adolescents with complex OSA nonadherent to CPAP [143, 221]. Management of OSA in infants with Pierre Robin sequence is highly dependent on centre experience. In infants with Pierre Robin sequence and severe OSA, Tübingen palatal plate [222], nasopharyngeal airway [223], mandibular distraction osteogenesis [35], glossopexy [224] 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 nonadherent to CPAP, hypoglossal nerve stimulation may be an effective alternative to CPAP [225, 226]. The alternative approaches described are mostly dependent on single-centre experience. To address the question of efficacy of various options, multicentred randomised 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 (supplementary table S7). There are no (or few) data about management of NIV failure except tracheostomy. Tracheostomy represents the ultimate therapeutic option for all patients [227].

Summary

- There is heterogeneity in the literature about definition of NIV/CPAP failure: it is often used synonymously with nonadherence 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 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) behavioural 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 paediatric pulmonologist, an ear, nose and throat surgeon, a maxillofacial surgeon, a neurosurgeon and an orthodontist.
- Behavioural therapy, token economy and medical hypnosis sometimes increase CPAP adherence.
- HFNC and hypoglossal nerve stimulation offer alternative therapeutic options for selected children nonadherent to CPAP. Other treatments are sometimes effective in infants with Pierre Robin sequence in specialist centres: Tübingen palatal plate, nasopharyngeal airway, tongue base adhesion (glossopexy), mandibular distraction osteogenesis or lingual tonsillectomy in older children (mainly adolescents with Down syndrome).
- Tracheostomy represents the ultimate rescue therapy for children with severe OSA or with high NIV dependency.

Role of CPAP/NIV in palliative care

Literature review

CPAP or NIV has been used within the context of palliative care in few children with end-stage malignancies, musculoskeletal disease or storage disease; mainly infants with SMA type I [63, 87, 228], but also with mucopolipidosis [45], for comfort reasons (supplementary table S8). 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

- Paediatric 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 programme 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, healthcare staff and children who are deemed competent.

CPAP/NIV in special populations

Children aged <24 months

Literature review

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

- craniosynostosis [12]
- congenital bone disease: achondroplasia [229, 230], pycnodysostosis [21]
- Treacher Collins syndrome [229]
- micrognathia [147]
- choanal atresia [147]
- cleft palate [229]
- 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, 229, 230]
- CHARGE syndrome [37]
- macroglossia/Beckwith–Wiedemann syndrome [147]
- Down syndrome [27, 38]
- storage disease [229]
- chronic lung disease (BPD) [27].

Some infants are treated with long-term NIV:

- SMA Ib and Ic [231]
- NMD [87, 231]
- diaphragmatic paralysis [87, 231]
- CCHS [87, 231]
- myelomeningocele [231]
- Down syndrome [87, 231]
- 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 stem mostly from single-centre, retrospective studies with some prospective registries [208, 232, 233] (supplementary table S9.1). Given this low quality of evidence, strong conclusions with respect to long-term CPAP/NIV use must be made with caution. There are no data on the optimal timing to assess clinical improvement. Experience and use of long-term CPAP/NIV in infants appears to vary between centres with a range of criteria to determine the appropriateness of long-term CPAP/NIV use. Infants are included in many cohorts of the broader paediatric 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 I and CCHS. Extrapolation of these 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 I, mortality in infants using long-term NIV is rare.

Obese children

Literature review

The quality of research is low with mainly retrospective observational studies including a limited number of patients (supplementary table S9.2). Obese children requiring long-term CPAP may present with

- syndromic obesity: ROHHAD syndrome, Bardet–Biedl syndrome, Prader–Willi syndrome [47] or 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 nonobese children [184].

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 nonobese children [14, 200, 207]
- nocturnal hypoventilation is common in obese children with OSA, requiring NIV when hypoventilation is not controlled by optimised CPAP [206]
- contradictory effects of CPAP on blood pressure and metabolic markers have been observed: no effect in a prospective study on 27 patients [206], benefit in a cross-sectional prospective multicentre study on 113 patients, but only six were treated with CPAP [205] and in a prospective study on nine patients [207]).

An increase in academic performance and attention has been observed in a small group of CPAP-adherent adolescents with OSA and obesity [200]. A simulation cohort study performed in order to estimate the number of OSA-related obesity cases among Indian children (age 1–14 years) and the number of cases of stroke, coronary heart disease and type 2 diabetes, considered as the main adverse outcomes of OSA-related childhood obesity, showed that patients treated both with adenotonsillectomy and CPAP had a higher reduction in adverse outcomes [234].

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).
- When possible, all alternative therapies are explored in parallel or before starting CPAP in an obese child: weight loss, adenotonsillectomy, lingual tonsillectomy, orthodontic treatment, bariatric surgery.
- Barriers to CPAP/NIV adherence in children with obesity may differ from nonobese 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.

Children with severe neurodisability

Literature review

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 behaviour score, OSA-specific score and QoL in children with developmental delay [198, 235] (supplementary table S9.3). 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 [236]. Erratic sleep pattern, as well as concurrent comorbidities, *e.g.* epilepsy, gastro-oesophageal 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 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.

CPAP/NIV and quality of life in children and parents

Literature review

Few studies have evaluated QoL in children treated with long-term CPAP or NIV and caregivers [237–248] (supplementary table S10). Several studies (cross-sectional control studies using questionnaires) reported sleep disturbance, poor sleep quality and reduced sleep efficiency among caregivers, compared to controls [237, 241, 242]. Long-term NIV in boys with Duchenne muscular dystrophy was associated with an improved sleep quality in mothers [237]. Youths adherent to CPAP had less sleep disturbance and caregivers were less concerned about health issues [240]. In addition, this study observed significant improvement in OSA-specific QoL and reduced carer concerns/anxieties among adherent CPAP users, compared to nonadherent users [240]. One cross-sectional study used questionnaires to evaluate 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 [239].

One research study comparing the health-related QoL of children with 1) gastrostomy, 2) gastrostomy and long-term ventilation or 3) long-term ventilation only, found the lowest score among the gastrostomy group, followed by the home ventilation and gastrostomy group and then the home ventilation only group. This highlights the significant role of underlying conditions in the perception of QoL, rather than the technologies alone [241]. Additionally, parents of these children had a lower perception of QoL than parents of healthy children [241]. It has to be noted that parents quoted the QoL of their children lower than the children themselves [238, 246].

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 (among 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.
- Caregiver and patient input is crucial. Table 4 gives a summary of the input of caregivers on the present task force.

Therapeutic education

Literature review

Studies describing therapeutic education tools or programmes are scarce [55, 145, 249] (supplementary table S11). Only one study proposed a dedicated programme with therapeutic education tools [145].

TABLE 4 Summary of input and comments of the caregivers and patients panel

Section	Patient and caregiver input
General remarks	Harmonisation of practices among different countries The harmonisation of the management of CPAP/NIV failure and intolerance is a priority to keep tracheostomy as a last treatment option
Initiation	Acclimatisation to CPAP/NIV should be adapted to the individual patient, <i>i.e.</i> initial settings to facilitate acclimatisation may differ between patients, as well as the time delay to obtain optimal compliance “Optimal compliance”, <i>e.g.</i> during the entire sleep time, should be the goal
Equipment	Regular check-ups including read-outs of the ventilator and the possibility of current ventilators (<i>i.e.</i> 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)
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: <ul style="list-style-type: none"> • who to manage gastric/abdominal distension? • how to prevent the risk of vomiting/aspiration in patients who are unable to remove their mask? • how to prevent/manage CPAP/NIV craniofacial complications?
Weaning	Harmonisation of weaning criteria and procedures
Quality of life	Patient and caregiver 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
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 caregiver 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)
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 Paediatric and adult teams should work closely together

CPAP: continuous positive airway pressure; NIV: noninvasive ventilation; NMD: neuromuscular disease; QoL: quality of life.

Training, real-life scenario and ongoing training seems to be of paramount importance [55]. The need for a variety (no details) of (multidisciplinary) healthcare professionals has been underscored for the appropriate training and education in the care of children on long-term CPAP/NIV [249].

Summary

- Therapeutic education is of paramount importance for long-term home CPAP/NIV and should be performed in every centre 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 programme 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 programme) and repeated during the entire follow-up of the child.
- Therapeutic education is a continuous process and should be evaluated and reinforced if needed.

Transition

Literature review

10–40% of adolescents on long-term NIV (more than those on CPAP) are transitioned to adult units [91, 102, 103, 105, 107, 112, 123, 124, 250–252], with a number that tends to increase [105]. Transition facilitators and barriers have been identified [250, 252]. But in practice, the availability of a transition programme is rarely specified [251] (supplementary table S12).

Summary

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

Cost and resource use considerations of CPAP/NIV

Literature review

A limited number of studies have evaluated the costs and resources needed for long-term CPAP or NIV in children (supplementary table S13). Cumulative expenditure for all care of a patient treated with CPAP or NIV at home is highly variable. Costs were shown to increase with longer ventilator-dependency time and specific diagnostic group, like sleep apnoea, with or without morbid obesity and congenital/genetic disorders [107, 253]. 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 [254]. 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 less than EUR 20 000 annually [91, 133, 134].

Summary

- Long-term CPAP/NIV is associated with considerable public and private expense and may impose financial stress on caregivers or family.
- There are limited data on the impact of CPAP/NIV on healthcare savings (prevention of hospitalisation, 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 are increasing complexities of paediatric conditions being considered for long-term CPAP/NIV. The indications for CPAP/NIV are ever expanding, and 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

TABLE 5 Future clinical and research priorities

Population	<ul style="list-style-type: none"> • Harmonisation of the management of paediatric NIV patients across countries
Initiation of CPAP/NIV	<ul style="list-style-type: none"> • 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 <i>versus</i> 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
Equipment	<ul style="list-style-type: none"> • 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 (three-dimensional printing, pressure measurements) to guide the choice and positioning of the interface • Development and validation of built-in software data for children, especially those weighing <30 kg • Usefulness and benefit of new NIV modes (AVAPS, iVAPS)
Follow-up	<p>Follow-up procedures:</p> <ul style="list-style-type: none"> • Evaluation of the optimal follow-up strategy in terms of timing and protocols • Evaluation of the usefulness and limitations of telemonitoring for follow-up <p>Adherence:</p> <ul style="list-style-type: none"> • Usefulness of new technologies to improve adherence (telemedicine, mobile phone applications) • Investigating the link between adherence and relevant end-organ morbidity <p>Benefits:</p> <ul style="list-style-type: none"> • Benefits of CPAP on academic function and behaviour in children with “complex” OSA • Efficacy of NIV should also be assessed on the child’s neurocognitive outcome, behaviour and academic performance
Weaning	<ul style="list-style-type: none"> • Development and validation of weaning criteria and protocols for CPAP and NIV
CPAP/NIV failure	<ul style="list-style-type: none"> • Multicentre randomised controlled trials on alternative ventilation strategies
Palliative care	<ul style="list-style-type: none"> • Effects of NIV in palliative care (improvement in dyspnoea, sleep quality and QoL)
Special populations	<p>Infants:</p> <ul style="list-style-type: none"> • Multicentre 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 <p>Obesity:</p> <ul style="list-style-type: none"> • 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 <p>Severe neurodisability:</p> <ul style="list-style-type: none"> • 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, are needed
QoL	<ul style="list-style-type: none"> • 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
Therapeutic education	<ul style="list-style-type: none"> • Development of therapeutic education tools and programs for CPAP/NIV with studies investigating their efficacy • Which healthcare professionals should be involved in therapeutic education, and should they receive specific training?
Transition	<ul style="list-style-type: none"> • The efficacy of different transition programmes 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
Costs	<ul style="list-style-type: none"> • Evaluation of healthcare cost savings thanks to CPAP/NIV (reduction of hospitalisations, healthcare use, <i>etc.</i>)

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

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 paediatric 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 areas for the future is given in table 5.

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