Predictors of Longitudinal Outcomes for Children Using Long-term Non-invasive Ventilation

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Abstract

Background: Non-invasive ventilation (NIV) is a first-line therapy for sleep-related breathing disorders and chronic respiratory insufficiency. Evidence about predictors that may impact long-term NIV outcomes, however, is scarce. The aim of this study is to determine demographic, clinical, and technology-related predictors of long-term NIV outcomes. Methods: A ten-year multi-centred retrospective review of children started on long-term continuous or bilevel positive airway pressure (CPAP, BPAP) in Alberta. Demographic, technology-related, and longitudinal clinical data was collected. Long-term outcomes examined included ongoing NIV use, discontinuation due to improvement in underlying condition, switch to invasive mechanical ventilation (IMV) or death, patient/family therapy declination, transfer of services, and hospital admissions. Results: 622 children were included. Both younger age and CPAP use predicted higher likelihood for NIV discontinuation due to improvement in underlying conditions. Children with upper airway disorders or bronchopulmonary dysplasia were less likely to require NIV continuation while presence of central nervous system (CNS) disorders resulted in higher likelihood of hospitalizations and switch to IMV or death. The presence of obesity/metabolic syndrome and early NIV-associated complications predicted higher risk for NIV declination. Children with more co-morbidities or use of additional therapies required more hospitalizations and the latter also predicted higher risk to be switched to IMV or death. Conclusions: Demographic, clinical data, and NIV type impact long-term NIV outcomes and need to be considered during the initial discussions about therapy expectations with families. Knowledge of factors that may impact long-term NIV outcomes might help to better monitor at-risk patients and minimize adverse outcomes.

INTRODUCTION

Long-term non-invasive ventilation (NIV) has become a modality of choice for treating chronic sleep and respiratory disorders in children with conditions leading to upper airway obstruction, abnormal drive to breath, muscle weakness or abnormal lung gas exchange[1]. Continuous positive airway pressure (CPAP) and bi-level positive airway pressure (BPAP) therapies both allow children to maintain airway patency throughout the breathing cycle, and increase lung recruitment at the end of the expiration[2]. BPAP therapies can also increase alveolar ventilation by supporting the inspiratory part of the breathing cycle and setting a mandatory respiratory rate. Home NIV therapies are indicated in patients who require breathing support intermittently, most commonly during sleep, and allow individuals to be off the machine during most or part of the day[3,4].

Prior studies have shown NIV to be an efficacious therapy for improving breathing during sleep in children with a variety of underlying conditions[1,5]. NIV improves outcomes in conditions such as obstructive sleep apnea (OSA)[6] and respiratory insufficiency/failure due to lung and neuromuscular disease in children[7-10]. However, apart from predictors for NIV adherence[11,12], very few studies have examined how baseline clinical characteristics and technology-related factors may impact the benefit and success of NIV in children[13]. For example, it is known that some children using NIV will discontinue therapy due to improvements in their underlying condition[14]; however, it is unknown what underlying clinical and technological characteristics may impact this improvement. Factors impacting children who are at risk for NIV failure (i.e. their breathing is

not adequately supported by NIV leading to a switch to invasive mechanical ventilation (IMV) or because they die despite using NIV) are also less understood[15]. In addition, although patient/family declination of NIV therapy has been described in up to 15% of children who start NIV, the factors that may impact this decision are not clear[16]. Understanding the factors that may contribute to these outcomes will have a direct impact on clinical practice by discussing expectations with families prior to NIV initiation and anticipating potential challenges that might influence NIV use.

With an increasing shift towards the use of home NIV therapies in children that are time, socially, and financially demanding for families and the health care system[17], there is a need to understand factors that are easily identifiable in clinical practice that might influence long-term NIV outcomes. This information will inform clinical practice to allow for early interventions and close monitoring of patients at risk to decline NIV or to have adverse outcomes. The aim of this study is to examine the impact of demographic, clinical, technology-related, and follow-up factors on long-term outcomes in a cohort of children using long-term NIV.

MATERIALS AND METHODS

Study Design

This study is a 10-year multi-centred retrospective review of all children who initiated long-term NIV in the province of Alberta, Canada, from January 2005 to December 2014, with patients followed until December 2015. Data were collected from the medical charts and sleep laboratory records of children at the Stollery Children's Hospital (Edmonton) and the Alberta Children's Hospital (Calgary). These two NIV programs provided care for the majority, if not all, of children using NIV in the province and the surrounding catchment area. The study was approved by the respective Health Research Ethics Boards at participating institutions.

Participants

NIV programs at the two participating hospitals were reviewed to identify the subjects. The inclusion criteria were children 0-18 years of age who have used NIV for a minimum of three months outside of an acute-care setting. We define NIV as any method of breathing support that provides positive airway pressure through an interface outside of the airway, including CPAP, and BPAP. As the goal included capturing information on long-term outcomes, patients who were recommended NIV but were not able to initiate it were excluded. No restrictions in terms of underlying conditions were applied to the inclusion criteria.

Data Collection

Demographic, clinical, and technology-related data were collected at: 1) the time of NIV initiation; 2) the initial follow-up visit within the first 12 months from NIV initiation; 3) the most recent follow-up visit after 12 months from NIV initiation (and a minimum of 3 months apart from the initial follow-up visit). Data was stored in an electronic REDCap database[18].

Baseline demographic data collection included age, sex, and site of NIV initiation. Clinical data collection included specific underlying disease conditions, co-morbidities (defined as any additional diagnosis aside from the primary underlying diagnosis as per previous definition)[19], additional technologies (e.g. oxygen therapy, V-P shunt, nasogastric/gastric-tube feeding, wheelchair), history of previous upper airway surgeries or/and additional major surgeries (e.g. heart surgery, neurosurgery, orthognathic surgery, spinal surgery). Technology-related data collected included NIV type (CPAP, BPAP or auto-PAP), mask type (nasal, oro-nasal, or other (total face mask or nasal pillow)), and trigger for NIV use (electively without polysomnography (PSG); electively with PSG; due to acute illness; other), date of NIV initiation and overall duration of NIV use. Follow-up data included the total number of NIV-related complications reported by patients/caregivers.

Outcome measures

Long-term outcomes, tracked at the most recent follow-up visit, included NIV continuation, reasons for NIV discontinuation (improvements in underlying condition, switch to IMV, death, patient or family declination, or transfer to other services including adult services, another NIV provider, or out-of-province care), and

hospital admissions tracked through the discharge summaries. Additional detail of the study design has been previously published[16].

Data Analysis

Summary statistics were reported as median (IQR) or frequencies (n, %) as appropriate. Logistic regression was used to perform a multivariate analyses of outcome measures and data from the multivariate analyses were reported as odds (Exp (B)) with the 95% confidence interval (CI). Demographic, clinical, technology-related and follow-up variables were initially included. Diagnostic category was included in the analysis to account for heterogeneity of the sample. Subjects were classified into five diagnostic categories according to their underlying condition (upper airway; central nervous system; musculoskeletal; cardiopulmonary; other category for those ones with characteristics of more than one category). Individual underlying disease conditions previously shown to influence long-term NIV outcomes[15] were also included in the initial multivariable analysis. We also included the time period in which NIV was initiated (Epoch 1, Jan 2005-Apr 2008; Epoch 2, May 2008-Aug 2011; Epoch 3, Sept 2011-Dec 2014).

Predictor variables that had a $p<0.20$ on univariate analysis for each outcome were tested in the respective logistic regression models. Co-variates considered clinically relevant, such as age, sex, diagnostic category, number of co-morbidities, number of additional therapies, and NIV type, were forced into multivariable analyses, regardless of their univariate significance. A stepwise purposeful addition and removal of covariates was performed until a best-fit model (using the Nagelkerke R-square) was produced. Analysis was performed using IBM SPSS Statistics version 26.0 (SPSS, Inc., Chicago, IL)[20]. Summary statistics were reported as median (IQR) or frequencies (n, %) as appropriate. A p-value of <0.05 on analysis was determined to be statistically significant.

RESULTS

A total of 622 children were initiated on long-term NIV in the province of Alberta over the study period. The median age for NIV initiation 7.8 (IQR 9.2) years and 61% were males (Table 1). The most common diagnostic category was upper airway disorders, followed by disorders of the central nervous system (CNS; specific underlying disorders specified in Table 2). A quarter of children were using a technology in addition to NIV therapy (Table 1). CPAP was used by 75% of children and the most common mask type was a nasal mask (62%). 73% of children were initiated electively after a PSG study while 18% started NIV during a hospital admission. Forty-six percent of children continued NIV, 39% discontinued, 14% were transferred to adult services, and 1% were lost to follow-up. Of the children who discontinued NIV, 16% of the total discontinued due to improvements in the underlying conditions, 15% of patients/family declined continuing NIV therapy, 5% died, and 1% switched to IMV. Follow up data were available for 97% of children for the initial follow-up visit and 61% had sufficient data for inclusion at the most current visit. A total of 93% of children reported at least one NIV-related complication during the initial follow-up visit and 90% in the most current follow-up visit.

Univariate analysis

On univariate analysis, age, NIV type, and the epoch that children started NIV had a significant impact on most of the long-term NIV outcomes (Table 3). Other co-variates such as the overall diagnostic category, parameters of medical complexity, and presence of NIV complications had outcome specific significance.

Demographic predictors

Of the 622 children using long-term NIV, 620 (99.7%) had available baseline and long-term follow-up data to be included in the multivariate analysis. Age was a significant predictor of NIV outcomes. Younger kids were more likely to discontinue NIV due to improvement in the underlying condition, with the odds of discontinuing NIV decreasing 5.6% for every one-year increase in age [0.944 (95% CI 0.893 to 0.999), Figure 1]. The odds of switching to IMV/death, or need for hospitalization, decreased with increasing age. As expected, older children were more likely to transition to adult services or out-of-province care [1.314 (95% CI 1.228 to 1.387)]. Sex was not a predictor of NIV outcomes in our cohort.

Clinical predictors

Diagnostic categories were also significant predictors of NIV outcomes. Overall, children with upper airway disorders were less likely to discontinue NIV compared to the other diagnostic categories (0.581 (95% CI 0.348 to 0.971, Figure 1). Children with CNS disorders had 3.3 times higher odds of being hospitalized while using NIV. Specific underlying conditions that were predictors of different NIV outcomes included children with bronchopulmonary dysplasia, who had higher odds of improving their breathing status and discontinuing NIV [4.707 (95% CI 1.306 to 16.962)], and children with obesity/metabolic syndrome who had higher odds of declining NIV therapy [2.077 (95% CI 1.110 to 3.888)].

Parameters of medical complexity including use of other medical technology, number of co-morbidities, and previous surgeries were also significant predictors of long-term NIV outcomes. Children requiring any technology in addition to NIV use had 3.3 (95% CI 2.051 to 5.387) times higher odds of NIV failure (switch to IMV or death) and 2.6 (95% CI 1.526 to 4.340) times higher odds of hospitalization for each added technology (Figure 1). They were also less likely to decline NIV, with a 0.417 (95% CI 0.202 to 0.859) reduction in odds ratio for each additional technology. The presence of comorbidities increased the odds for hospital admissions by 1.2 (95% CI 1.022 to 1.440) times but was not a predictor for NIV failure or any other long-term NIV outcomes. Children who had received a previous adenotonsillectomy surgery had 3.7 times less odds of NIV failure (switching to IMV or dying) compared to children who did not. The presence of previous major surgeries was not a significant predictor of long-term outcomes.

Technology-related predictors

Technology type was a strong predictor of long-term outcomes: children using CPAP had 23 (95% CI 3.017 to 79.482) times higher odds of improving their underlying condition and discontinuing therapy, whereas children on BPAP had 4.7 (95% CI 2.481 to 8.822) times the odds of needing ongoing NIV (Figure 1). BPAP was also a predictor of NIV failure, with children on BPAP having 2.3 (95% CI 1.069 to 5.063) times the odds of switching to IMV or dying compared to children on CPAP. Mask type and triggers for NIV therapy did not significantly impact long-term NIV outcomes. The period children were initiated on NIV was also a significant predictor of NIV outcomes. Children who started NIV in the most recent epoch (2011-2014) had 3.6 (95% CI 2.044 to 6.277) times the odds of continuing NIV compared to those in the previous epochs. In contrast, children starting NIV in the second epoch (2008-2011) had 2.6 (95% CI 1.229 to 5.552) times the odds of being switched to IMV or dying compared to the third epoch. Expectedly, children who started NIV in the first epoch (2005 – 2008) and the second epoch (2008 – 2011) were more likely to be transferred to other services (i.e. adult services) compared to those who started NIV in the most recent epoch [5.812 (95% CI 2.799 to 12.07) and 3.491 (95% CI 1.845 to 6.605) respectively].

Follow-up predictors

Early and late NIV-related complications detected during the initial and follow-up visit significantly predicted long-term outcomes. For each additional complication reported, the odds that the patient/family would decline NIV increased 1.3 (95% CI 1.034 to 1.642) and 1.4 (95% CI 1.052 to 1.854) times at the initial and most recent follow-up visit respectively (Figure 1). In addition, as the number of complications increased, the odds of continuing NIV decreased by 8.7% for each added complication in the most recent follow up visit.

Discussion

This multicenter study focuses on the impact of commonly available demographic, clinical and technology-related parameters on the outcomes of long-term NIV therapies in children. As children may improve over time, particularly younger children, periodic evaluation of the need for NIV is recommended. The presence of a CNS disorder implies worse prognosis despite NIV use, with higher risk for hospitalization and ongoing need for NIV use in the long-term while children with upper airway abnormalities and children with bronchopulmonary dysplasia were more likely to be able to discontinue NIV in the long-term. Higher medical complexity, including higher number of co-morbidities and additional technology use, predicts an

increased risk for NIV failure (switch to IMV or death), requiring a proactive approach during periodic clinical evaluations and discussion with patients and families. The technology type also has an impact on long-term outcomes with children requiring BPAP generally showing more technology dependence in the long-term and worse outcomes despite NIV. Finally, children using NIV during the most recent period were more successful at maintaining NIV in the long-term and prevent need for IMV or death than in previous epochs, suggesting a positive learning curve of the medical team with improved counselling, patient's monitoring, and treatment strategies.

As a significant number of children discontinued NIV therapies due to improvement of their underlying condition (16%), periodic re-evaluation of their underlying sleep-related breathing disorder with polysomnography should be warranted. According to our data, this is especially relevant in younger children and children with upper airway disorders, as they are more likely to improve and not require NIV in the long-term. These results adds on previous data from our group showing higher likelihood of NIV discontinuation due to improvement in underlying condition (OR 2.04 (1.04 to 4.03)) in a study comparing NIV outcomes in infants (<2 years of age) versus older children[13]. These data are comparable with a previous study describing NIV (CPAP and BPAP) discontinuation rates of 27% of their overall cohort based on symptoms improvement and normalization of gas exchange (oxygen and/or carbon dioxide levels)[14]. In this study, children tend to be younger (median age 1.4 years) at NIV discontinuation and the most frequently weaned children had upper airway anomalies (40%), Prader Willi syndrome (10%) and bronchopulmonary dysplasia (7%). Other cohorts, however, showed lower rates of NIV discontinuation and no differences by diagnostic category[21-23], suggesting differences in the population of children receiving NIV at different centers. While it is clear from the results of this study that re-evaluation of the underlying sleep-related breathing disorder and need for NIV support is needed in young children and children with upper airway abnormalities or bronchopulmonary dysplasia, this study does not analyze the periodicity of such evaluations, for which further studies might be required.

The presence of high medical complexity seems to influence ongoing need for NIV as well as higher risk for NIV failure resulting in escalation to IMV or death and higher need for hospitalization despite NIV use. Medically complex children have been defined as those having multiple underlying conditions, impairment of daily functioning, and/or technology dependence[24,25]. While previous research have shown higher risk for escalation to IMV or death in children with certain underlying conditions who are more prone to have high medical complexity (neurologic, neuromuscular and cardiac conditions)[15], to our knowledge, the impact of specific parameters of medical complexity in long-term NIV outcomes have not been studied before. Although only a small proportion of children using NIV in our cohort required switch to IMV or died in our cohort (1% and 5% respectively), in alignment with data from previous studies[15,22,23,26-29], this study adds on critical information about which patients are at higher risk for adverse outcomes, allowing stakeholders to better plan for the care of children with ongoing high medical needs after NIV initiation. Further these results provide guidance to clinicians and families of medically complex children regarding long-term expectations for NIV and counselling for overall goals of care.

A frequent concern for clinicians caring for children using NIV is the patient/family decision to discontinue NIV therapy (15% in our cohort), particularly in children with OSA[30]. Although patient/family-reported reasons for NIV declination were not analyzed in this study, interesting data arose from these results. Unexpectedly, no specific diagnostic category predicted the patient/family decision to stop NIV therapy. The presence of OSA per se did not predict patient/family NIV declination while children with obesity/metabolic syndrome using NIV were more likely decline NIV. The reasons for these findings are unclear. As highlighted in a previous qualitative study, these children may have a different perception of their health and need of NIV as well as psychological, social and health barriers for NIV continuation[31]. The presence of NIV-related complications was, not surprisingly, a significant predictor for NIV declination. This has previously been examined in studies looking at predictors of NIV adherence[32]. We, however, could not find studies describing factors influencing the patient/family decision to fully discontinue NIV. Knowing this information will allow clinicians to anticipate which patients are more likely to stop NIV over time and work with children and families to prevent dropouts. In addition, this information highlights the need for ongoing close monitoring

of children using NIV to detect technology-related complications and implement early interventions that mitigate such events and prevent therapy declination.

The outcomes of long-term NIV use appear more promising for children using NIV in the most recent epoch period. While more children continue using NIV therapy lately suggesting less patient/family NIV declination, escalation to IMV or death has decreased compared to the previous epochs. These findings are not surprising, as previous reports have demonstrated similar learning curves resulting in higher long-term adherence rates[33,34]. These improvements might be due to changes that have taken place in our pediatric NIV programs over time, including closer monitoring of children requiring NIV therapies and early detection of NIV-related complications, barriers to NIV initiation, family support and counselling, and larger availability of mask interfaces for pediatric ages and more customization options available, although these changes have not been included in this study analysis[33,35,36]. This information is encouraging to continue investing resources and time in the care of this group of children.

There were some limitations to our study. There are likely to be more co-variates that influence the outcomes we have examined; however, as our study is a retrospective chart review, data collection was limited to the information present in the patient's medical records. In addition, the data reported in the second follow-up visit (i.e. number of NIV related complications) was only available in 61% of our cohort. To account for this bias, we ran the statistics with and without the second follow-up variable. Since the models did not significantly change with the addition of this co-variate, we decided to include it into our regression analysis.

Conclusion

The results of this study reflect the influence of demographic, clinical characteristics and technology of the children receiving NIV on long-term therapy outcomes particularly age, diagnostic category and specific underlying conditions, added comorbidities and technologies in use and technology type. These results are important for clinicians, as they can use available information to discuss goals and expectations of NIV with children and families even prior to NIV initiation and optimize resources to ensure adequate follow up management and improve the success children may achieve using NIV therapy.

References

1. Castro-Codesal ML, Dehaan K, Featherstone R, et al. Long-term non-invasive ventilation therapies in children: A scoping review.*Sleep medicine reviews.* 2018;37:148-158.

2. Amaddeo A, Frapin A, Fauroux B. Long-term non-invasive ventilation in children. *The Lancet Respiratory Medicine.* 2016;4(12):999-1008.

3. Marcus CL, Brooks LJ, Draper KA, et al. Diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics.*2012;130(3):e714-755.

4. Hull J, Aniapravan R, Chan E, et al. British Thoracic Society guideline for respiratory management of children with neuromuscular weakness. *Thorax.* 2012;67 Suppl 1:i1-40.

5. Castro-Codesal ML, Dehaan K, Bedi PK, et al. Long-term benefits in sleep, breathing and growth and changes in adherence and complications in children using noninvasive ventilation. *Canadian Journal of Respiratory, Critical Care, and Sleep Medicine.* 2020:1-9.

6. Marcus CL, Radcliffe J, Konstantinopoulou S, et al. Effects of positive airway pressure therapy on neurobehavioral outcomes in children with obstructive sleep apnea. *American journal of respiratory and critical care medicine.* 2012;185(9):998-1003.

7. Dohna-Schwake C, Podlewski P, Voit T, Mellies U. Non-invasive ventilation reduces respiratory tract infections in children with neuromuscular disorders. *Pediatric Pulmonology.* 2008;43(1):67-71.

8. Mellies U, Ragette R, Dohna Schwake C, Boehm H, Voit T, Teschler H. Long-term noninvasive ventilation in children and adolescents with neuromuscular disorders. *The European respiratory journal.*2003;22(4):631-636.

9. Winfield NR, Barker NJ, Turner ER, Quin GL. Non-pharmaceutical management of respiratory morbidity in children with severe global developmental delay. *The Cochrane database of systematic reviews.*2014;10.

10. Moran F, Bradley JM, Piper AJ. Non-invasive ventilation for cystic fibrosis. *Cochrane Database of Systematic Reviews.* 2017(2). http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002769.pub5/abstract.

11. DiFeo N, Meltzer LJ, Beck SE, et al. Predictors of positive airway pressure therapy adherence in children: a prospective study.*Journal of clinical sleep medicine : JCSM : official publication of the American Academy of Sleep Medicine.* 2012;8(3):279-286.

12. Machaalani R, Evans CA, Waters KA. Objective adherence to positive airway pressure therapy in an Australian paediatric cohort. *Sleep Breath.* 2016;20(4):1327-1336.

13. Bedi PK, Castro-Codesal M, DeHaan K, MacLean JE. Use and outcomes of long-term noninvasive ventilation for infants. *Canadian Journal of Respiratory, Critical Care, and Sleep Medicine.* 2018:1-8.

14. Mastouri M, Amaddeo A, Griffon L, et al. Weaning from long term continuous positive airway pressure or noninvasive ventilation in children. *Pediatric pulmonology.* 2017;52(10):1349-1354.

15. Koncicki ML, Zachariah P, Lucas AR, Edwards JD. A multi-institutional analysis of children on long-term non-invasive respiratory support and their outcomes. *Pediatric pulmonology.*2018;53(4):498-504.

16. Castro-Codesal ML, Dehaan K, Bedi PK, et al. Longitudinal changes in clinical characteristics and outcomes for children using long-term non-invasive ventilation. *PloS one.* 2018;13(1):e0192111.

17. Edwards EA, Nixon GM. Paediatric home ventilatory support: Changing milieu, proactive solutions. *Journal of Paediatrics and Child Health.* 2013;49(1):13-18.

18. Harris PA, Taylor R, Thielke R, Payne J, Gonzalez N, Conde JG. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform.* 2009;42(2):377-381.

19. Cohen E, Kuo DZ, Agrawal R, et al. Children with medical complexity: an emerging population for clinical and research initiatives.*Pediatrics.* 2011;127(3):529-538.

20. IBM Corp. Released 2019. IBM SPSS Statistics for Windows, Version 26.0. Armonk, NY: IBM Corp.

21. Chatwin M, Tan HL, Bush A, Rosenthal M, Simonds AK. Long term non-invasive ventilation in children: impact on survival and transition to adult care. *PloS one.* 2015;10(5):e0125839.

22. Goodwin S, Smith H, Langton Hewer S, et al. Increasing prevalence of domiciliary ventilation: changes in service demand and provision in the South West of the UK. *Eur J Pediatr.* 2011;170(9):1187-1192.

23. Edwards EA, Hsiao K, Nixon GM. Paediatric home ventilatory support: The Auckland experience. *Journal of Paediatrics and Child Health.*2005;41(12):652-658.

24. Cohen E, Kuo DZ, Agrawal R, et al. Children With Medical Complexity: An Emerging Population for Clinical and Research Initiatives.*Pediatrics.* 2011;127(3):529-538.

25. Srivastava R, Stone BL, Murphy NA. Hospitalist Care of the Medically Complex Child. *Pediatric Clinics of North America.*2005;52(4):1165-1187.

26. Amin R, Sayal P, Syed F, Chaves A, Moraes TJ, MacLusky I. Pediatric long-term home mechanical ventilation: Twenty years of follow-up from one Canadian center. *Pediatric pulmonology.* 2014;49(8):816-824.

27. Chatwin M, Bush A, Simonds AK. Outcome of goal-directed non-invasive ventilation and mechanical insufflation/exsufflation in spinal muscular atrophy type I. *Archives of disease in childhood.*2011;96(5):426-432.

28. McDougall CM, Adderley RJ, Wensley DF, Seear MD. Long-term ventilation in children: Longitudinal trends and outcomes.*Archives of disease in childhood.* 2013;98(9):660-665.

29. González Cortés R, Bustinza Arriortua A, Pons Ódena M, et al. Domiciliary mechanical ventilation in children: A spanish multicentre study. *An Pediatr (Barc).* 2013;78(4):227-233.

30. Tapia IE, Marcus CL. Fitting Positive Airway Pressure Adherence into Teenage Life: Don't Push It! *Annals of the American Thoracic Society.* 2018;15(1):22-23.

31. Ennis J, Rohde K, Chaput JP, Buchholz A, Katz SL. Facilitators and Barriers to Noninvasive Ventilation Adherence in Youth with Nocturnal Hypoventilation Secondary to Obesity or Neuromuscular Disease.*Journal of Clinical Sleep Medicine.* 2015;11(12):1409-1416.

32. Blinder H, Momoli F, Bokhaut J, et al. Predictors of adherence to positive airway pressure therapy in children: a systematic review and meta-analysis. *Sleep medicine.* 2020;69:19-33.

33. Harford K-L, Jambhekar S, Com G, et al. Behaviorally based adherence program for pediatric patients treated with positive airway pressure.*Clinical Child Psychology & Psychiatry.* 2013;18(1):151-163.

34. Koontz KL, Slifer KJ, Cataldo MD, Marcus CL. Improving pediatric compliance with positive airway pressure therapy: The impact of behavioral intervention. *Sleep.* 2003;26(8):1010-1015.

35. Castro-Codesal ML, Olmstead DL, MacLean JE. Mask interfaces for home non-invasive ventilation in infants and children. *Paediatric respiratory reviews.* 2019;32:66-72.

36. Lanza CRM, de Arruda JAA, Soares AM, et al. Fabrication of a custom pediatric nasal mask for noninvasive ventilation using a maxillofacial elastomer: A straightforward technique. *The Journal of Prosthetic Dentistry.* 2019;121(1):179-182.

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