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SCIENTIFIC INVESTIGATIONS

Defining the patterns of PAP adherence in pediatric obstructive sleep apnea: a clustering analysis using real-world data

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Study Objectives: The implementation of positive airway pressure (PAP) therapy to treat obstructive sleep apnea in children is a complex process. PAP therapy data are highly heterogeneous in pediatrics, and the clinical management cannot be generalized. We hypothesize that pediatric PAP users can be subgrouped via clustering analysis to guide tailored interventions.

Methods: PAP therapy data for 250 children with obstructive sleep apnea were retrospectively examined using unsupervised hierarchical cluster analysis based on (1) PAP tolerance (average hours on days used) and (2) consistency of PAP use (percentage of days used). Clinical features in each cluster were defined, and a tree decision analysis was generated for clinical implementation.

Results: We were able to subclassify all 250 children (median age = 11.5 years) into five clusters: A (13.6%), B (29.6%), C (17.6%), D (16.4%), and E (22.8%). The clusters showed significant differences in PAP use patterns (Kruskal-Wallis *P* value < 1e–16). The most consistent PAP use patterns were seen in clusters A, B, and C. Major differences across clusters included the prevalence of obesity, PAP setting, developmental delay, and adenotonsillectomy. We also identified important differences in mask acceptance, OSA severity, and individual responses to PAP therapy based on objective apnea-hypopnea reductions in PAP downloads.

Conclusions: A simple method to subset PAP use patterns in children can be implemented by analyzing cloud-based PAP therapy data. This novel approach may contribute to optimization of PAP therapy in children of all ages based on real-world evidence at the individual level.

Keywords: pediatric obstructive sleep apnea; CPAP; PAP; children; clusters; adherence

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BRIEF SUMMARY

Current Knowledge/Study Rationale: Positive airway pressure for treatment of obstructive sleep apnea in children is a complex process; multiple factors affect tolerance of this therapy. This study used cluster analysis with positive airway pressure therapy data to subgroup all children into five main groups according to patterns of use and identified clinical characteristics among each group.

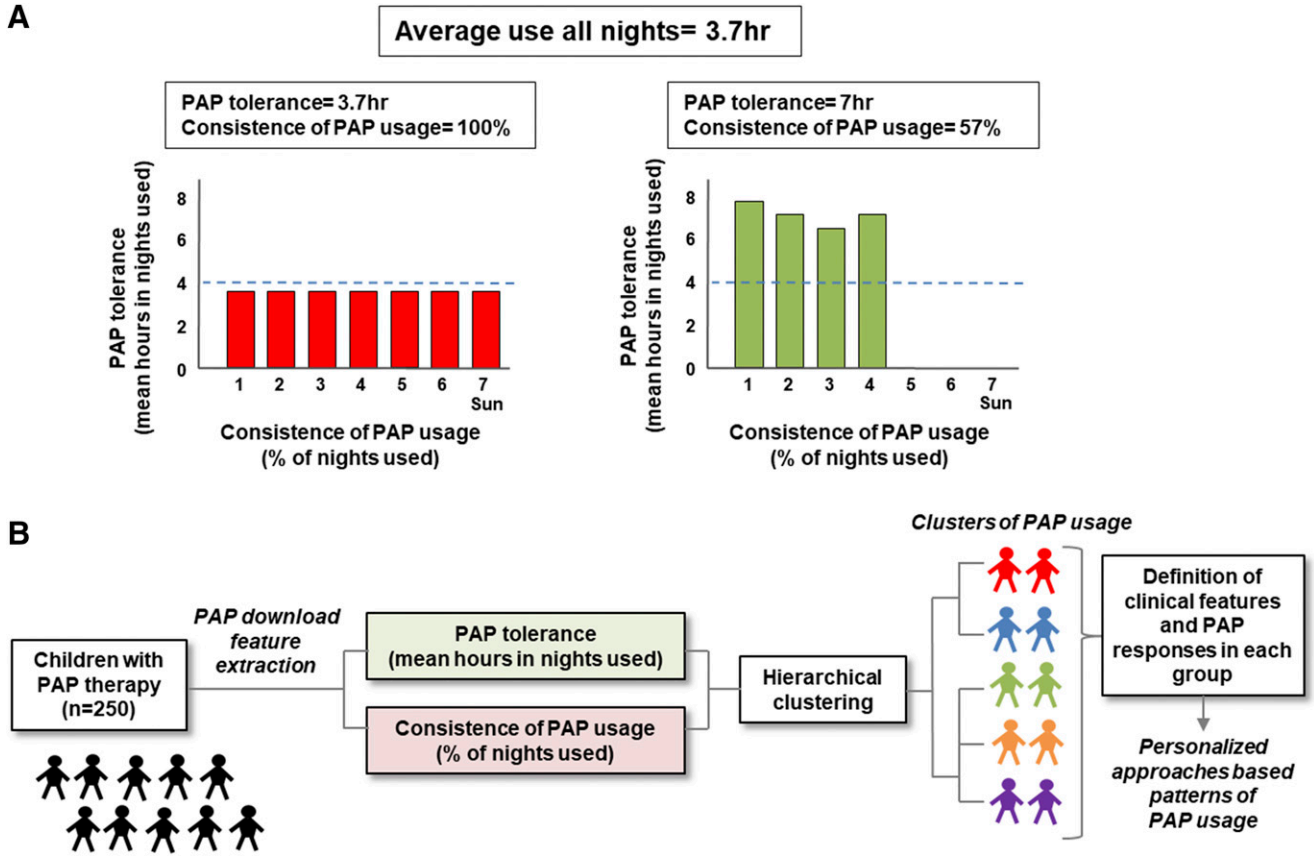
Study Impact: This method can help identify characteristics of different patterns of use to help guide personalized interventions. This novel approach may contribute to optimization of positive airway pressure in children of all ages based on real-world evidence at the individual level.

INTRODUCTION

Obstructive sleep apnea (OSA) is a common disorder in children (prevalence: 1%–5%).[1,2] Adenotonsillectomy is the first line of treatment for pediatric OSA and is effective in about 79% of cases.[3] Children with residual OSA, or who are not candidates for adenotonsillectomy, may require positive airway pressure (PAP) therapy.[1–4] Continuous (CPAP) or bilevel PAP can be delivered via a mask interface securely attached to the head of children of all ages[4–7]; however, the implementation of PAP therapy in children is a complex process, and multiple factors (eg, mask fit, PAP setting, social factors, age) affect adherence.[4–7] How children and adolescents respond to PAP therapy is highly heterogeneous, and the clinical management cannot be generalized with a "one size fits all" approach. There is a critical need to develop personalized approaches to optimize PAP therapy for OSA in all age groups based on objective data at the individual level.[8]

One approach to examine objectively PAP use is monitoring cloud-based data, which is routinely available for most OSA patients with prescribed PAP therapy.[9] Indeed, residual OSA and mask leaks measured by cloud-based monitoring have been associated with poorer PAP adherence.[10] The growing need for telemedicine when in-person access is limited (eg, COVID-19 quarantine) promises further development of PAP monitoring technology[10–12]; however, the method for analyzing home-monitoring downloads from PAP therapy devices is still underdeveloped. Traditionally, PAP downloads have simply been used to define *compliance* based on a single cutoff parameter (eg > 4 hours per night). This approach is suboptimal in pediatrics and may lead to grouping together children with quite different causes of poor PAP therapy use (**Figure 1A**).

Figure 1—Study rationale and design.



(A) Example of two children with different PAP use patterns that can be easily separated after feature extraction (average hours per days used and % of days used). **(B)** Workflow of the study leading to clustering and potential cluster-specific tailored interventions. PAP = positive airway pressure.

The objective of this study was to subgroup pediatric PAP users via clustering analysis of their pattern of use. For this purpose, we integrated two common parameters available to clinicians in PAP downloads: (1) the average hours of PAP use on days used (PAP tolerance) and (2) the percentage of days used during the recording period (consistence of PAP use). With this novel approach, we were able to subgroup all children into five main groups with different patterns of PAP use. We also identified consistent clinical characteristics in each subset to guide personalized interventions that may optimize PAP therapy in the pediatric population.

METHODS

Study population

The study included children and adolescents (1 month to 18 years of age) treated with PAP therapy between 2015 to 2019 at the Sleep Medicine Program at Children's National Hospital in Washington, DC. We included only patients treated with PAP therapy who had home monitoring data. Subjects were included independently of the type of PAP therapy (CPAP or bilevel PAP) or underlying comorbidities, such as coexisting hypoventilation or central apnea. We excluded individuals without confirmed diagnosis of OSA and other sleep-breathing disorders in overnight polysomnogram (PSG) as these data were used to examine differences according to PAP use clusters. We collected demographics, clinical variables, mask type, in-office tolerance, and PSG parameters for all study participants. The Institutional Review Board of Children's National Hospital approved the study (Pro00007207) and granted a waiver of informed consent given that this research involved materials (data, documents, records, or specimens) collected solely for nonresearch purposes (clinical indications).

Variables and cluster analysis

We retrieved monitoring data from the PAP downloads, including use, apnea-hypopnea indexes (AHI), and PAP settings. We also recorded standard parameters during the initial PSG (obstructive AHI [OAHI], AHI) and sleep-stage–specific obstructive event indexes. PSG scoring was conducted in our sleep laboratory according to the pediatric American Academy of Sleep Medicine criteria.[13] OAHI included obstructive apneas, hypopneas, and mixed apneas. AHI included the preceding as well as central apneas. PSG was considered diagnostic of OSA if OAHI was ≥1.5 events/h. We calculated the individual response to PAP therapy as the percentage of AHI reduction comparing the AHI in the initial PSG with the mean AHI provided by the download of PAP devices.

The workflow for cluster analysis is illustrated in **Figure 1**. Two major features were used as core variables: (1) *PAP tolerance*, quantified as the average hours of PAP use over the days in which the device was used (average hours/day used) and (2) *consistence of PAP use*, quantified as the percentage of days the PAP device was used during the recording period (% of days used). These variables were used to perform the Ward's minimum-variance hierarchical clustering method using an agglomerative (bottom-up) approach and Ward's linkage. Normalization of variables (*z*-scores) was performed before clustering, and Euclidean distance was selected for cluster generation. At each generation of clusters, samples were merged into larger clusters to minimize the within-cluster sum of squares or to maximize the between-cluster sum of squares. A tree analysis was performed using cutoffs of our core variables to assess classification of the participants into the correct cluster. Discriminant analysis with K-fold cross-validation was performed to validate the results.

Statistical analysis

Minitab Statistical Package V.19.1. (Minitab, Inc., State College, Pennsylvania) was used for statistical and clustering analyses. Continuous variables in two groups were compared using the *t* test or the Mann-Whitney *U* test, as appropriate. To compare differences between clusters, we used analysis of variance or Kruskal-Wallis for parametric or nonparametric continuous variables, respectively. Associations between categorical variables were analyzed using the chi-square test. Significance level used was $P < .05$ and adjusted by multiple comparisons when appropriate.

RESULTS

Study participants and generation of PAP use clusters

We included 250 children aged 1 month to 18 years (median age = 11.4 years). Of these, 61% were male and 60% were African American. The mean duration of adherence data used in the study was 65 days (standard deviation = 49.9 days), CPAP was the most common PAP therapy (CPAP n = 232, 93%; bilevel PAP n = 18, 7%), and about half of the children had pressures determined in a titration study (n = 132, 52.8%). **Table 1** and **Table 2** show the characteristics of all study participants, including type of PAP therapy, initial OSA symptoms, and PSG parameters. Using the cluster approach outlined in *Methods*, a dendrogram was generated, and five clusters (A–E) were identified **(Figure 2A).** Overall differences among clusters regarding PAP tolerance (average hours/day used) and consistence of PAP use (% of days used) can be visualized in the companion scattered plot **(Figure 2B**). Formal statistical testing confirmed significant differences across the clusters generated **(Figure 2C** and **Figure 2D).** Overall, there were no significant differences in age, sex, race, and OSA symptoms in the five clusters (**Table 1** and **Table 2**). Specific characteristics of the five clusters are summarized below.

PAP use, clusters A, B, and C

About 14% of the participants (n = 34) were grouped into cluster A. This cluster had the best PAP tolerance (median = 8.8 h/day used) and consistence use pattern (median use = 99% of days). Features of cluster A included (1) the lowest body mass index (BMI) across all clusters (median BMI = 23.1 kg/m^2); (2) the highest median REM OAHI index (58.8 events/h); (3) the highest median PAP setting (8 cmH_2O); and (4) the largest portion of individuals with history of adenotonsillectomy (77%), which was greater than in other clusters but not significant after Bonferroni adjustment (cluster D = 54%, $P < .03$ vs cluster A; and cluster E = 54%, $P < .02$ vs cluster A). Remaining features can be found in **Table 1**.

Thirty percent of the participants (n = 74) were grouped into cluster B, making this the largest cluster. Cluster B was characterized by acceptable PAP tolerance (median 6.2 hours/day used) and a consistent use pattern (median use = 89.3% of days). Cluster B had a median PAP setting of 7 cmH_2O, which was greater than in cluster E (**Table 2**); 95% of children in cluster B tolerated mask placement in the office, and 45% reported mask removal overnight at home (**Table 1**). Remaining features of cluster B can be found in **Table 1**.

Eighteen percent of the participants (n = 44) were grouped into cluster C. This cluster had poor tolerance to PAP therapy (median 2.2 h/day used) but a relatively consistent pattern of PAP use (median use 70% of days). The median PAP setting was 5.5 cmH_2O, which was significantly lower than in cluster A (**Table 1**). Cluster C had a larger number of individuals who reported mask removal overnight at home (89%), but 83% of these children tolerated mask placement in the office (**Table 1**). Remaining features of cluster C can be found in **Table 1**.

PAP use, cluster D and E

Sixteen percent of the participants (n = 41) were grouped into cluster D. This cluster had acceptable PAP tolerance (median = 5.2 h/day used) and inconsistent PAP use pattern (median use = 26.1% of days). Cluster D features included (1) the lowest proportion of children with developmental delays (22%); (2) the highest rate of mask tolerance in the office (97%); (3) the highest proportion of individuals with large leaks (29.3%); (4) lower OSA severity indexes, including the lowest median rapid eye movement OAHI (27.3 events/h); and (5) an elevated BMI (median = 34 kg/m^2).

Twenty-three percent of the participants (n = 57) were grouped into cluster E. This cluster had poor PAP tolerance (median = 0.3 h/day used) and inconsistent PAP use pattern (median use 11% of days). These children had the highest median BMI values (37.4 kg/m^2), the lowest tolerance to mask placement in the office (74%), and the lowest median PAP settings (5 cmH_2O).

Differential responses to PAP therapy according to clusters of use

We next examined whether the individual responses to PAP therapy were linked to a distinct cluster of use. We used two parameters to evaluate PAP response: the residual AHI on PAP downloads and the AHI reduction relative to the initial PSG. Overall, we found appropriate responses to PAP therapy across the different study groups (85% AHI reduction, **Table 3**). The best response to PAP therapy was seen in cluster A (88.3% AHI reduction), and clusters A and D had the lowest residual AHI

Table 1—Demographics and positive airway pressure therapy characteristics in each cluster.

	Total	Cluster A	Cluster B	Cluster C	Cluster D	Cluster E
No. of participants	250	34	74	44	41	57
Age at enrollment, median years*	11.5 (7)	9.7 (8)	11.4 (6)	11.5 (9)	12.3 (6)	12.8 (7)
Significant between-group difference†		—	—	—	—	—
Male sex, (%)	61	62	68	55	49	67
Significant between-group difference†		—	—	—	—	—
Race (%) White/African American/other	14/60/26	18/53/29	14/54/32	23/55/22	10/71/19	7/68/25
Significant between-group difference†		—	—	—	—	—
Household annual median income (US dollars)	94,061	86,809	100,337	90,473	81,829	101,805
Significant between-group difference†		—	—	—	—	—
BMI, median kg/m^2*	29.3 (19)	23.1 (17)	28.4 (14)	27.1 (20)	34.1 (17)	37.4 (28)
Significant between-group difference†		D, E	D, E	E	A, B	A, B, C
BMI Z-score (standard deviation)	—	–0.4 (0.9)	–0.2 (0.8)	–0.2 (0.9)	0.2 (0.9)	0.48 (1.2)
Significant between-group difference†		D, E	D, E	E	A, B	A, B, C
Type of PAP, (%) CPAP/bilevel PAP/APAP	90/7/3	91/9/0	86/11/3	84/9/7	93/2/5	95/4/2
Significant between-group difference†		—	—	—	—	—
PAP use, average h/day (all days)*	2.1 (5.3)	8.4 (1)	5.3 (2)	1.2 (1)	1.2 (2)	0.03 (0)
Significant between-group difference†		B, C, D, E	A, C, D, E	A, B, E	A, B, E	A, B, C, D
PAP therapy tolerance, average h/day (days used*)	4.4 (5.8)	8.8 (1)	6.2 (2)	2.2 (1)	5.2 (2)	0.3 (1)
Significant between-group difference†		B, C, D, E	A, C, D, E	A, B, D, E	A, B, C, E	A, B, C, D
PAP use consistence, % of days used	65.8 (68)	99 (5)	89.3 (25)	70 (34)	26.1 (23)	11 (20)
Significant between-group difference†		B, C, D, E	A, C, D, E	A, B, D, E	A, B, C, E	A, B, C, D
PAP setting median cm H_2O‡ *	6 (5)	8 (5)	7 (5)	5.5 (4)	7 (5)	5 (4)
Significant between-group difference†		C, E	E	A	E	A, B, D
PAP mask, (%) using nasal/other	80/20	79/21	76/24	82/18	76/24	92/8
Significant between-group difference†		—	—	—	—	—
High leak on PAP therapy, (%)#	14.8	11.8	9.5	18.2	29.3	10.5
Significant between-group difference†		D	D	—	A, B, E	D
Tolerated mask application in office (%)	89	93	95	83	97	74
Significant between-group difference†			E		E	B, D
Report mask removed at home (%)	62	17	45	89	71	95
Significant between-group difference†		B, C, D, E	A, C, D, E	A, B	A, B	A, B
PAP comfort, ramp time (min)*	15 (30)	20 (3)	7.5 (20)	20 (20)	15 (30)	20 (30)
Significant between-group difference†		—	—	—	—	—
PAP comfort, exhalation relief (1–3 level)*	2 (2)	2 (2)	2 (2)	2 (2)	2 (1)	2 (2)
Significant between-group difference†		—	—	—	—	—

*Numeric data are expressed as median and interquartile range. †$P < .05$ for each pairwise comparison (vs the group indicated) by one-way analysis of variance with Bonferroni correction for multiple comparisons across the five groups (10 comparisons) for continuous variables and by the chi-square test for categorical variables. ‡CPAP, average APAP or IPAP in bilevel PAP. #High PAP leak defined as a mean of > 24 liters/min or > 5% large leak according to device manufacturer's instructions. APAP = autotitrating PAP, BMI = body mass index, IPAP = inspiratory PAP, PAP = positive airway pressure.

(2.7 and 2.4 events/h, respectively). Cluster C showed significantly less response to PAP therapy (79.2% AHI reduction; *P* value .001 vs cluster A) and the highest residual AHI (4.8 events/h, **Table 3**).

Discriminant analysis and tree diagram

We generated a tree analysis to subgroup all pediatric PAP users according to our core variables **(Figure 3).** We used cutoffs of ≥ 8 hours, ≥ 4 hours, and ≥ 2 hours for PAP tolerance (average hours/days used) and ≥ 50% as cutoff for the consistency of PAP use (% of days used). We found that 90.8% of the participants were assigned to the appropriatester using this simplified appcluster using this simplified approach (**Figure 3B**). The results of the discriminant analysis, cross-validation and companion cluster-specific clinical correlations are shown in **Figure 3**.

Table 2—OSA clinical and PSG characteristics in each cluster.

	Total	Cluster A	Cluster B	Cluster C	Cluster D	Cluster E
No. of participants	250	34	74	44	41	57
Snoring at OSA presentation (%)	95.2	97	92	95	95	98
Significant between-group difference†		—	—	—	—	—
EDS at OSA presentation (%)	47	48	44	50	44	47
Significant between-group difference†		—	—	—	—	—
AT before enrollment (%)	60	77	59	63	54	54
Significant between-group difference†		—	—	—	—	—
Trisomy 21 (%)	15	9	15	25	7	16
Significant between-group difference†		—	—	—	—	—
Developmental delay (%)	38	45	42	50	22	30
Significant between-group difference†		—	—	D	C	—
AHI, median events/h*	22.8 (28)	30.2 (35)	23.9 (34)	22.5 (26)	17.3 (23)	23.4 (30)
Significant between-group difference†		—	—	—	—	—
OAHI, median events/h*	21.3 (27)	29.5 (35)	20.9 (30)	19.4 (25)	16.6 (21)	21.8 (28)
Significant between-group difference†		—	—	—	—	—
OAHI in REM, median events/h*	40 (49)	58.8 (72)	46 (57)	34.3 (78)	27.3 (32)	37.3 (36)
Significant between-group difference†		D	—	—	A	—
OAHI in NREM, median events/h*	17.8 (28)	16.2 (26)	19.6 (35)	16.7 (27)	17.6 (24)	19.5 (27)
Significant between-group difference†		—	—	—	—	—
Central apnea index, median events/h*	0.3 (1.5)	0.3 (1)	0.5 (2)	0.6 (2)	0.2 (1)	0.3 (1)
Significant between-group difference†		—	—	—	—	—
SpO_2 nadir, median %*	80 (15)	82 (19)	85 (10)	85 (10)	84 (11)	80 (15)
Significant between-group difference†		—	—	—	—	—

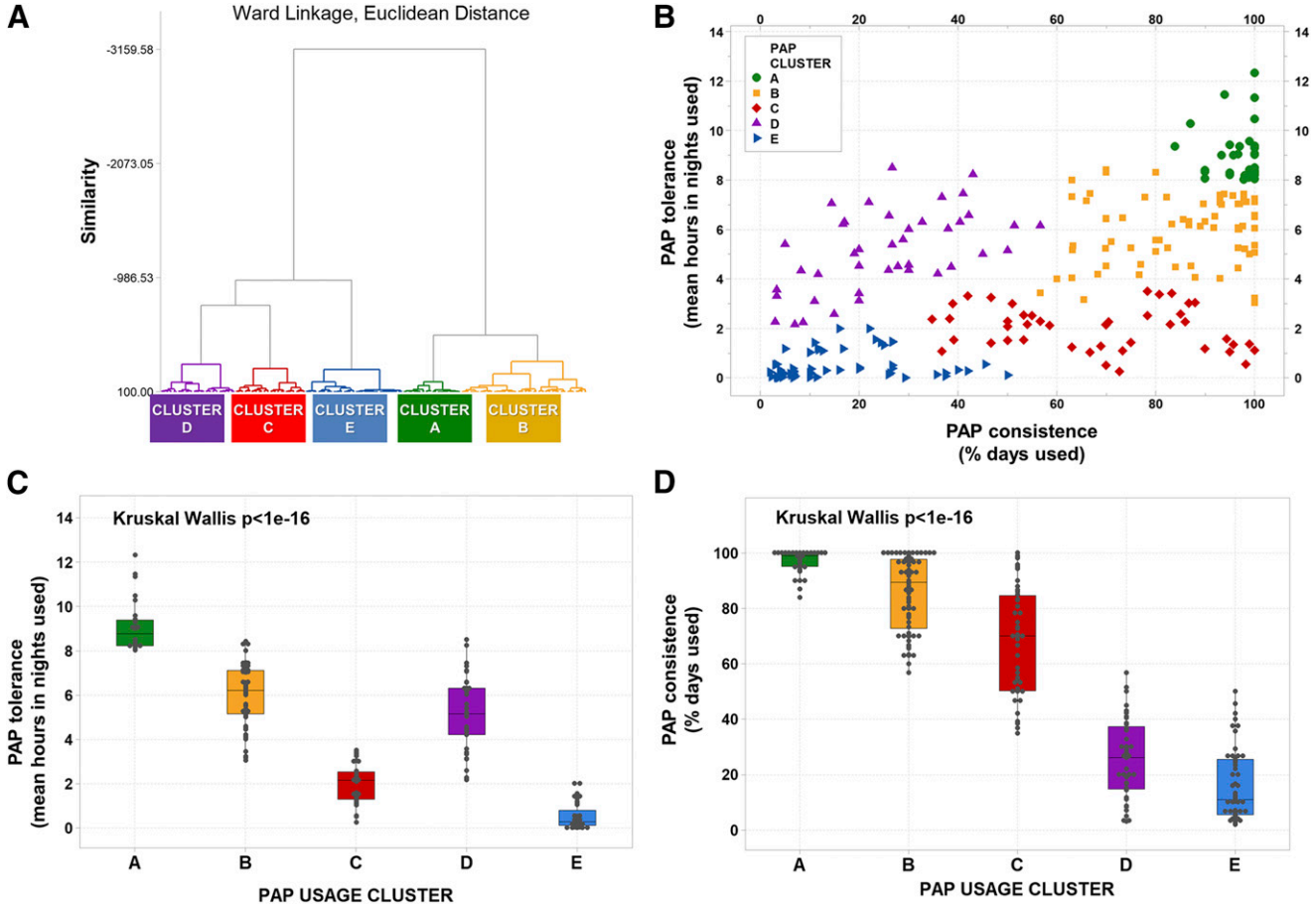
*Numeric data are expressed as median and interquartile range. †$P < .05$ for each pairwise comparison (vs the group indicated) by one-way analysis of variance with Bonferroni correction for multiple comparisons across the five groups (10 comparisons) for continuous variables and by the chi-square test for categorical variables. AHI = apnea-hypopnea index, AT = adenoidectomy and/or tonsillectomy, EDS = excessive daytime sleepiness, NREM = non-rapid eye movement, OAHI = obstructive apnea-hypopnea index, OSA = obstructive sleep apnea, SpO_2 = peripheral capillary oxygen saturation.

DISCUSSION

We have evaluated the patterns of PAP use in 250 children with OSA by clustering their cloud-based PAP therapy data. These analyses allowed us to define and characterize the main patterns of pediatric PAP use in a real-world setting. We identified five main clusters of PAP use with differences in the prevalence of obesity, PAP therapy settings, developmental delay, and history of adenotonsillectomy. We also identified important differences in mask acceptance, OSA severity, and the individual responses to PAP therapy as indicated by a reduction in the AHI while using the device. These new data may allow personalization of interventions to optimize PAP therapy adherence in the pediatric population.

PAP therapy tolerance has mostly been studied in the adult population. Initial studies reported an average PAP use of an average of 4.8 hours/day during 66%–68% of nights in adults.[14,15] More recently, Cistulli et al defined objective PAP use in individuals > 18 years old in a large cloud database of around two million patients.[9] The PAP tolerance rate was 75% using the US Center for Medicare and Medicaid Services definition (average of ≥ 4 h/day on 70% of days), and the mean PAP use was 6.0 hours per days.[9] Interestingly, our current results in children showed a very different pattern of PAP use. We found that pediatric patients overall had lower PAP tolerance rate with large variation in PAP tolerance and consistency (**Figure 2**). Prior studies have also shown lower PAP use rates in children,[4–8,16–19] which may be due to pediatric factors such as developmental stage and family dynamics.[20] PAP adherence in children is influenced by age (younger children are more adherent), maternal education (higher maternal education leads to better adherence), mask style (nasal mask is better tolerated), obesity (children with lower BMI have better adherence), and developmental delay (more adherence).[20,21] Social support and role modeling at home are also key determinants of PAP adherence in children.[7,22] Collectively, these data indicate that there is significant variability in PAP use patterns in children with OSA owing to multiple potentially modifiable factors. Extrapolating the US Center for Medicare and Medicaid Services definition of adult PAP compliance may not be appropriate for the heterogeneous population of children treated with PAP therapy. Developing better methods to objectively identify and characterize PAP use patterns are critically important to guide interventions in the pediatric population.

Figure 2—PAP use clusters in pediatric OSA.



(A) Dendrogram and **(B)** scattered plots showing the five different clusters of PAP use patterns. Formal statistical testing (Kruskal-Wallis) showed significant differences between the clusters in terms of **(C)** PAP hours per night in days used and **(D)** PAP consistency defined as % of days used. All pairwise comparisons are significant after Bonferroni correction for multiple comparisons across the five groups ($P < .005$). Data are presented as box plots (boxes represent the median and interquartile range). OSA = obstructive sleep apnea, PAP = positive airway pressure.

In this study, we used cluster analysis as an unsupervised modeling approach to identify major PAP therapy patterns of use in children. It is important to clarify that unbiased clustering was used to examine the heterogeneity of real-life PAP utilization patterns in the entire population of children without selecting factors that may influence PAP use (eg, age groups or developmental delays); however, these factors were considered in our analyses after clustering generation (**Table 1** and **Table 2**). Using this clustering approach, we defined five groups of pediatric participants who differed in their PAP tolerance (average h/day used) and PAP consistency (% days used). Demographic factors (age, sex, race) were comparable among the clusters, but the clinical features of each group showed important differences. Children in cluster A had optimal PAP use (median = 8.8 hours/day used and use 99% of days) and can serve as a benchmark for the design of interventions. These individuals had the highest rapid eye movement OAHI values, the lowest prevalence of obesity, the highest rates of adenotonsillectomy before PAP initiation (77%), the highest PAP pressures (median = 8 cmH_2O), and the best responses to PAP therapy (88% AHI reduction). Individuals in clusters B and C showed acceptable PAP use consistency (median = 89% and 70% of days, respectively) but a much lower PAP use per night relative to cluster A (**Figure 2**). Thus, it is reasonable to assume that parents and children in clusters B and C have adequate motivation and self-efficacy but may benefit from interventions tailored at optimizing their PAP responses (eg, weight reduction, adenotonsillectomy, and PAP titration), which may optimize PAP tolerance as seen in cluster A. This is particularly relevant to children in cluster C, who had the lowest PAP responses (79% AHI reduction), and poor tolerance with a median 1.2 hours/day used. Furthermore, children in cluster C had lower tolerance to mask placement in the office (**Table 1**). This suggests that some individuals in cluster C may also benefit from specialized pediatric programs aimed at mask desensitization, intensive education, and mask-fitting strategies to improve overnight tolerance to PAP.[23–25]

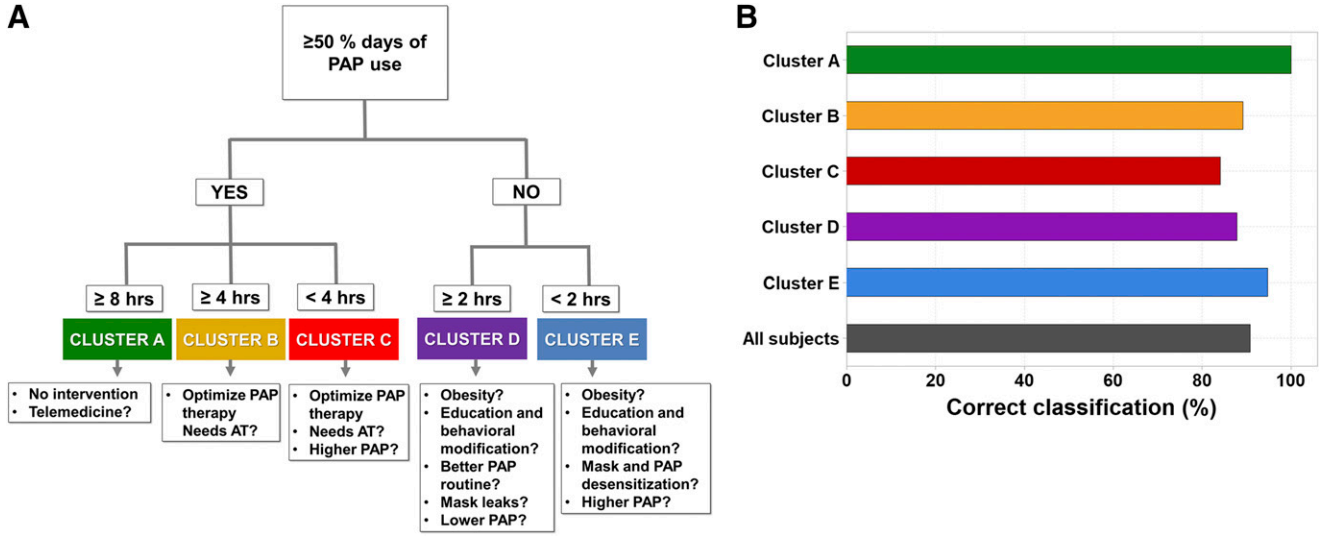
Children in clusters D and E had overall poor PAP therapy use (**Figure 2**), likely caused by other modifiable factors. Individuals in cluster D had acceptable tolerance to PAP (median = 5.2 h/day used), the highest rates of mask tolerance in the office (97%), elevated BMI values (34 kg/m^2), and the lowest rates of

Table 3—Differential responses to PAP therapy according to clusters of use.

	Total	Cluster A	Cluster B	Cluster C	Cluster D	Cluster E
No. of participants	241	34	69	42	41	55
AHI in PAP download events/h*	3.6 (6)	2.7 (4)	3.6 (4)	4.8 (10)	2.4 (4)	4.2 (15)
Significant between-group difference†		C	—	A, D	C	—
Reduction in AHI on PAP therapy (%)*	85 (26)	88.3 (11)	85.4 (26)	79.2 (33)	85.3 (12)	83.3 (70)
Significant between-group difference†		C	—	A	—	—

*Numeric data are expressed as median and interquartile range. †$P < .05$ for each pairwise comparison (vs the group indicated) by one-way analysis of variance with Bonferroni correction for multiple comparisons across the five groups (10 comparisons) for continuous variables and by the chi-square test for categorical variables. #Nine participants without available AHI on PAP were excluded. AHI = apnea-hypopnea index, PAP = positive airway pressure.

Figure 3—Clinical decision tree diagram for the PAP use clusters in pediatric OSA.



(A) Tree diagram generated with potential companion cluster-specific interventions. **(B)** Bars represent the results of discriminant analysis and K-fold cross-validation showing 90.8% correct cluster classification using the proposed clinical decision tree algorithm. OSA = obstructive sleep apnea, PAP = positive airway pressure.

developmental delay. Large PAP leaks were common in this group, suggesting that optimal mask fitting and education to ensure proper positioning of the mask at home are important in this group of individuals. Children in cluster D did not appear to need other interventions for PAP therapy optimization as they had the lowest residual AHI in PAP downloads (median AHI, 2.4 events/h). The major issue with cluster D was the inconsistent use pattern (median use = 26% of days). Individuals in cluster E had the highest BMI levels (37 kg/m^2) and inconsistent PAP use (median use 11% of days) and poor tolerance (median 0.3 hours/day used). The poor tolerance and use in clusters D and E are mostly likely due to multidimensional behavioral factors. It is possible that inconsistent PAP use is a manifestation of the lack of healthy routines and schedules, which may require increased parental involvement. Lack of parental and individual self-efficacy and/or motivation could be a driving factor for poor PAP use as well as obesity. Thus, individuals in cluster D and E may benefit from motivational programs directed at enhancing self-care. These types of cognitive and behavioral interventions have been successfully implemented in adults with OSA[26,27] and in obese individuals.[28,29] Peer supportive interventions such as telecommunicating may also be useful in these children and adolescents.[30–32] In addition, individuals in cluster E had poor tolerance to mask placement; thus, intensive education and mask desensitization may also be required to improve PAP use in this subset of children.

The main caveat of our current study is that it requires additional validation in larger longitudinal studies. In this cross-sectional study, we could not ascertain the exact timing of PAP prescription and initiation, which is important as use may change over time, particularly during the first 90 days.[6] We also do not know how the reported clusters will change with age, an issue particularly critical for children and adolescents undergoing developmental changes. The cross-sectional nature of the study also limits our conclusions, and the efficacy of the subsetting of PAP therapy in children still needs to be tested in clinical practice (eg, interventional trials). In addition, in our population, only half of individuals had titration studies, which could have been ideal to find optimal mask and pressures. The latter is relevant because the residual AHI reported by PAP devices may not be totally comparable to the indices reported by an in-lab titration study. We believe that future clustering

longitudinal studies may need to include other diagnostic evaluations increasingly conducted in children with OSA (eg, drug-induced sleep endoscopy) and alternative treatments in selected populations (eg rapid palatal expansion in maxillary insufficiency).[33,34] Lastly, we also must emphasize that this is a simplified clustering approach based only on PAP use parameters in downloads, and many clinical factors influencing PAP use and responses must be taken into account when deciding the most appropriate intervention to optimize PAP therapy in children. On the other hand, strengths of this study include a relatively large and diverse sample of children treated with PAP therapy and novel methods that may facilitate analysis of the patterns of PAP use in the pediatric population.

CONCLUSIONS

Our results indicate that a simple method to subset PAP use patterns can be implemented to subclassify all the pediatric OSA patients treated with PAP to guide cluster-specific interventions. Based on our results, we propose that PAP use patterns can be analyzed to optimize PAP therapy in children of all ages based on real-world evidence at the individual level.

ABBREVIATIONS

AHI, apnea-hypopnea index
BMI, body mass index
CPAP, continuous positive airway pressure
OAHI, obstructive apnea-hypopnea index
OSA, obstructive sleep apnea
PAP, positive airway pressure
PSG, polysomnography

REFERENCES

1. Marcus CL, Brooks LJ, Draper KA, et al. American Academy of Pediatrics. Diagnosis and management of childhood obstructive sleep apnea syndrome. *Pediatrics*. 2012;130(3):576–584.
2. Capdevila OS, Kheirandish-Gozal L, Dayyat E, Gozal D. Pediatric obstructive sleep apnea: complications, management, and long-term outcomes. *Proc Am Thorac Soc*. 2008;5(2):274–282.
3. Marcus CL, Moore RH, Rosen CL, et al. Childhood Adenotonsillectomy Trial (CHAT): arandomized trial of adenotonsillectomy for childhood sleep apnea. *N Engl J Med*. 2013;368(25):2366–2376.
4. Amaddeo A, Frapin A, Touil S, Khirani S, Griffon L, Fauroux B. Outpatient initiation of long-term continuous positive airway pressure in children. *Pediatr Pulmonol*. 2018;53(10):1422–1428.
5. Perriol MP, Jullian-Desayes I, Joyeux-Faure M, et al. Long-term adherence to ambulatory initiated continuous positive airway pressure in non-syndromic OSA children. *Sleep Breath*. 2019;23(2):575–578.
6. Kang EK, Xanthopoulos MS, Kim JY, et al. Adherence to positive airway pressure for the treatment of obstructive sleep apnea in children with developmental disabilities. *J Clin Sleep Med*. 2019;15(6):915–921.
7. DiFeo N, Meltzer LJ, Beck SE, et al. Predictors of positive airway pressure therapy adherence in children: a prospective study. *J Clin Sleep Med*. 2012;8(3):279–286.
8. Sunwoo BY, Light M, Malhotra A. Strategies to augment adherence in the management of sleep-disordered breathing. *Respirology*. 2020;25(4):363–371.
9. Cistulli PA, Armitstead J, Pepin JL, et al. Short-term CPAP adherence in obstructive sleep apnea: a big data analysis using real world data. *Sleep Med*. 2019;59:114–116.
10. Bhattacharjee R, Benjafield AV, Armitstead J, et al. Adherence in children using positive airway pressure therapy: a big-data analysis. *Lancet Digit Health*. 2020;2(2):e94–e101.
11. Grote L, McNicholas WT, Hedner J; ESADA collaborators. Sleep apnoea management in Europe during the COVID-19 pandemic: data from the European Sleep Apnoea Database (ESADA). *Eur Respir J*. 2020;55(6):2001323.
12. Johnson KG, Rapoport DM. Future of positive airway pressure technology. *Sleep Med Clin*. 2017;12(4):617–622.
13. Berry RB, Brooks R, Gamaldo C, et al. AASM Scoring Manual Updates for 2017 (Version 2.4). *J Clin Sleep Med*. 2017;13(5):665–666.
14. Kribbs NB, Pack AI, Kline LR, et al. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. *Am Rev Respir Dis*. 1993;147(4):887–895.
15. Engleman HM, Martin SE, Douglas NJ. Compliance with CPAP therapy in patients with the sleep apnoea/hypopnoea syndrome. *Thorax*. 1994;49(3):263–266.
16. Hawkins SM, Jensen EL, Simon SL, Friedman NR. Correlates of pediatric CPAP adherence. *J Clin Sleep Med*. 2016;12(6):879–884.
17. Ramirez A, Khirani S, Aloui S, et al. Continuous positive airway pressure and noninvasive ventilation adherence in children. *Sleep Med*. 2013;14(12):1290–1294.
18. 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.
19. O'Donnell AR, Bjornson CL, Bohn SG, Kirk VG. Compliance rates in children using noninvasive continuous positive airway pressure. *Sleep*. 2006;29(5):651–658.
20. Sawyer AM, Gooneratne NS, Marcus CL, Ofer D, Richards KC, Weaver TE. A systematic review of CPAP adherence across age groups: clinical and empiric insights for developing CPAP adherence interventions. *Sleep Med Rev*. 2011;15(6):343–356.
21. 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 Med*. 2020;69:19–33.
22. Puri P, Ross KR, Mehra R, et al. Pediatric positive airway pressure adherence in obstructive sleep apnea enhanced by family member positive airway pressure usage. *J Clin Sleep Med*. 2016;12(7):959–963.
23. Riley EB, Fieldston ES, Xanthopoulos MS, et al. Financial analysis of an intensive pediatric continuous positive airway pressure program. *Sleep*. 2017;40(2).
24. Xanthopoulos MS, Kim JY, Blechner M, et al. Self-efficacy and short-term adherence to continuous positive airway pressure treatment in children. *Sleep*. 2017;40(7).
25. Mendoza-Ruiz A, Dylgjeri S, Bour F, Damagnez F, Leroux K, Khirani S. Evaluation of the efficacy of a dedicated table to improve CPAP adherence in children: a pilot study. *Sleep Med*. 2019;53:60–64.
26. Sawyer AM, King TS, Weaver TE, et al. A tailored intervention for PAP adherence: The SCIP-PA Trial. *Behav Sleep Med*. 2019;17(1):49–69.
27. Lai AYK, Fong DYT, Lam JCM, Weaver TE, Ip MSM. The efficacy of a brief motivational enhancement education program on CPAP adherence in OSA: a randomized controlled trial. *Chest*. 2014;146(3):600–610.
28. Olsen S, Smith SS, Oei TP, Douglas J. Motivational interviewing (MINT) improves continuous positive airway pressure (CPAP) acceptance and adherence: a randomized controlled trial. *J Consult Clin Psychol*. 2012;80(1):151–163.
29. Pastor R, Tur JA. Effectiveness of interventions to promote healthy eating habits in children and adolescents at risk of poverty: systematic review and meta-analysis. *Nutrients*. 2020;12(6):1891.
30. Mayberry LS, Berg CA, Greevy RA, et al. Mixed-methods randomized evaluation of FAMS: a mobile phone-delivered intervention to improve family/friend involvement in adults' type 2 diabetes self-care [published online ahead of print, 2020 Jul 24]. *Ann Behav Med*. doi:10.1093/abm/kaaa041.

31. Browne S, Kechadi MT, O'Donnell S, et al. Mobile health apps in pediatric obesity treatment: process outcomes from a feasibility study of a multicomponent intervention. *J Med Internet Res*. 2020;8(7):16925.
32. Hamilton-Shield J, Goodred J, Powell L, et al. Changing eating behaviours to treat childhood obesity in the community using Mandolean: the Community Mandolean randomised controlled trial (ComMando)--a pilot study. *Health Technol Assess*. 2014;18(47):i–xxiii, 1-75.
33. Pirelli P, Saponara M, Guilleminault C. Rapid maxillary expansion in children with obstructive sleep apnea syndrome. *Sleep*. 2004;27(4):761–766.
34. Villa MP, Rizzoli A, Miano S, Malagola C. Efficacy of rapid maxillary expansion in children with obstructive sleep apnea syndrome: 36 months of follow-up. *Sleep Breath*. 2011;15(2):179–184.

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DISCLOSURE STATEMENT

All authors have seen and approved this manuscript. Work for this study was performed at the Sleep Medicine Program at Children's National Hospital in Washington, DC. The authors report no conflicts of interest.