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Demographics, sleep apnea and positive airway pressure (PAP) treatment-related characteristics associated with PAP adherence: A large retrospective community-based longitudinal observational study

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ABSTRACT

Objective/background: Despite many years of research, multiple factors have inconsistently shown to be associated with positive airway pressure (PAP) adherence. We conducted a retrospective observational study to evaluate the association between selected demographics, obstructive sleep apnea (OSA) - and generally available PAP treatment-related factors with objective PAP therapy adherence.
Patients/methods: We considered all consented individuals with OSA who purchased a PAP device from a registered vendor (Ottawa, Ontario) between 2011 and 2017 who had usage data available (n = 11,614). PAP adherence was measured objectively as PAP use for at least 4 h on at least 70% of days on treatment.
Results: In our cohort, 7147 (61.5%) participants were deemed adherent to PAP over a median of 214 days (IQR: 84–675). The median percentage of days PAP therapy was used was 82% (IQR: 48–97%), and the median number of days PAP therapy was used for greater than 4 h was 95 (IQR: 28–372).
In multivariable logistic regression considering all variables available, increased body mass index, older age, and lower minimum SaO_2 at baseline sleep study were significantly associated with increased PAP adherence. Individuals who were using PAP longer and with greater adherence during the first month were subsequently more adherent to therapy. We also found a different predictive ability of PAP adherence-related factors by age and sex.
Conclusions: In this retrospective community-based longitudinal observational study, we identified readily available demographics and OSA-related factors associated with PAP adherence. We also confirmed previous findings on age and sex disparities in adherence to PAP.

1. Background

Worldwide, an estimated 934 million adults aged 30–69 have at least mild obstructive sleep apnea (OSA), the most common breathing disorder of sleep, with prevalence rates in some countries above 50% [1]. OSA is an important modifiable risk factor for several chronic diseases, including cardiovascular disorders [2], diabetes [3], and it is associated with increased motor vehicle accidents and decreased work productivity [4]. These risks may be reduced with nightly usage of positive airway pressure (PAP) therapy, the treatment of choice for individuals with clinically significant OSA. Despite being the treatment of choice, long-term adherence to PAP has been poorly investigated. Studies assessing long-term adherence in the general adult population demonstrate adherence rates between 40 and 85%, depending on the definition, population and study design, as clinical trials tend to overestimate PAP adherence [5–11]. Despite many years of research, multiple factors have inconsistently shown to be associated with PAP adherence, including demographic characteristics and OSA severity

Abbreviations: Adaptive Support Ventilation, ASV; Apnea-hypopnea index, AHI; Auto-titrating positive airway pressure, APAP; Bilevel positive airway pressure, Bilevel; Body mass index, BMI; Confidence interval, CI; Continuous positive airway pressure, CPAP; Oxygen saturation, SaO2; Obstructive sleep apnea, OSA; Odds ratio, OR; Positive airway pressure, PAP; Respiratory disturbance index, RDI; Standard deviation, SD.

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[12,13]. Studies in the area have often been limited by small numbers of participants, use of a clinical population, and difficulty obtaining objective and longitudinal adherence data.

Our study aimed to evaluate if any treatment, demographic, or sleep apnea severity factors, generally available in clinic and research, could be used to identify individuals who were less likely to be adherent to PAP therapy. We also wanted to confirm recent findings on age and sex disparities in adherence to PAP [14].

2. Materials and methods

For this retrospective community-based longitudinal observational study, all consented adults located in the greater metropolitan area of Ottawa (Canada) diagnosed with OSA by a sleep physician who purchased a PAP device from a provincially registered vendor between 2011 and 2017 and whose data on PAP adherence since the purchase were transferred from their devices from the AirView™ patient management system (ResMed) [15] were considered for inclusion. Information on PAP therapy type, time on therapy, demographic data, and initial OSA severity were available. In 2017, the greater metropolitan area of Ottawa had a population of 1,476,008 people and was one of the six million-plus metropolitan areas in Canada. This study has been approved by the Ottawa Health Science Network Research Ethics Board and is consistent with the principles in the Declaration of Helsinki. Informed consent was obtained from all individual participants included in the study.

Our primary outcome, adherence to PAP treatment, was defined as utilizing PAP therapy for at least 4 h a day on at least 70% of days over time. Our secondary outcomes were: (i) the percentage of days PAP therapy was used for any amount of time and (ii) the number of days PAP therapy was used for a minimum of 4 h. All patients were followed from the date they purchased their device through to the end of 2017.

Our factors of interest were treatment mode (auto-titrating positive airway pressure [APAP], bilevel positive airway pressure [Bilevel], continuous positive airway pressure [CPAP]), sex, self-reported height, weight, body mass index (BMI), and baseline OSA severity as measured by the apnea-hypopnea index (AHI), or if not available respiratory disturbance index (RDI), and the minimum oxygen saturation (SaO_2). PAP treatment length (days used) and PAP adherence during the first month were considered separately, given the high correlation and overlap in definitions with the outcome of interest.

Descriptive statistics were used as applicable to characterize our population of interest. For all outcomes, we performed both univariate and multivariate logistic or linear regressions as relevant. Beta coefficients and odds ratios were standardized using the standard deviation of the variable in question. Due to significant statistical interactions between some variables and sex and age, we stratified results for the primary outcome by sex and age subgroups (<50 years old; $\geq$ 50 years old). All analyses were performed in R version 3.6.3. Some of the results of these studies have been previously reported in the form of an abstract [16].

3. Results

Of 20,891 individuals associated with a CPAP vendor during the study period, 11,614 individuals were included in the analysis. 6799 (58.5%) were male, the median BMI was 31 (interquartile range [IQR]: 22–40), and the median age was 53 years (IQR: 34–72). The median minimum oxygen saturation was 85% (IQR: 76–94), and the median AHI was 21/hour (IQR: 0–51) during the baseline sleep study. Of 11,614 participants, 4542 (39.1%) were on CPAP, 4644 (40.0%) on APAP, 2291 (19.7%) on Bilevel and 66 (0.6%) on Adaptive support ventilation (ASV). Data on PAP adherence was available for a median of 214 days (IQR: 84–674.75); during this time, 706 (6.1%) have not initiated PAP (days PAP used = 0). In our cohort, 7147 (61.5%) participants were deemed adherent to PAP as per our primary definition. The median percentage of days PAP therapy was used was 82% (IQR: 48–97%) and remained stable over time while stratifying by year of PAP therapy initiation (results are not shown). The median number of days on any PAP therapy was 130 (IQR: 47–446); while the median number of days PAP therapy was used for greater than 4 h was 95 (IQR: 28–372).

For our primary outcome, using univariate logistic regression, we found increased adherence was significantly (p values $\leq$ 0.02) associated with male sex, increased BMI, older age, higher respiratory indices (AHI or RDI if AHI was unavailable), lower minimum SaO_2, and CPAP treatment mode (vs. APAP). In multivariable analysis considering all variables available, the effect of BMI, age, and minimum SaO_2 at baseline sleep study remained significantly associated with PAP adherence (Table 1). Controlling for all available covariates, individuals who were using PAP longer and with greater adherence during the first month were more adherent with the PAP. Adherence rates stratified by sex and age group are shown in Fig. 1. For the most part, PAP adherence was higher in males than females and increased with age.

Adaptive support ventilation, ASV; apnea-hypopnea index, AHI; auto-titrating positive airway pressure treatment, APAP; Bilevel positive airway pressure, Bilevel; body mass index, BMI; confidence interval, CI; continuous positive airway pressure, CPAP; oxygen saturation, SaO_2; respiratory disturbance index, RDI; standard deviation, SD.

Stratifying by sex, the effect of BMI remained significant in females but not in males, while the effect of age was significant in males, but not females (Table 1). Being on Bilevel therapy as compared to CPAP was associated with higher PAP adherence in females but not in males. Stratifying by age, the effect of BMI remained significant in younger individuals than in those 50 years and older; the same was noted for the effect of the PAP therapy mode (Table 1).

For secondary outcomes, male sex, increased BMI, older age, and more severe OSA were significantly (p values < 0.01) associated with a greater percentage of days participants used PAP therapy after adjusting for confounding using multivariate linear regression. An increase in BMI and OSA severity were also significantly (p values $\leq$ 0.03) associated with an increased number of days participants used PAP therapy for at least 4 h after adjusting for confounding.

4. Discussion

Our study is one of the larger studies investigating factors impacting PAP adherence measured objectively over a prolonged period, which importantly is also supplemented by information on OSA severity and BMI. Our study's adherence rate (61.5%) was consistent with other large retrospective database studies that used the same definition of adherence [14,17]; however, in contrast to those studies, ours was not limited by only 90 days of observation. Lower adherence rates were noted in clinical trials, such as the SAVE trial [18]; however, it may be due to differences in characteristics of the study groups as our study was not a recruited clinical trial population. It would be difficult to draw any conclusions about differences in adherence between our study and ADVENT-HF [19] and SERVE-HF [20] which were both clinical trials in patients with heart failure on ASV. RICCADSA [21] also differed from our study as this clinical trial selected non-sleepy individuals with coronary artery disease. We confirmed important differences in patterns and trajectories of PAP use by age and sex [14], as well as a different predictive ability of PAP

Table 1
The association between demographics, sleep apnea- and positive airway pressure (PAP) treatment-related characteristics and whether or not a patient was considered adherent (defined as PAP therapy used ≥70% of days for ≥4 h) estimated using multivariate[a] logistic regression analyses in the total sample and stratified by sex and age. Estimates are presented as odds ratio (ORs)[b] and 95% confidence intervals.

	Total sample	Male	Female	Age ≥50[c]	Age <50
	(n = 11,614)	(n = 6799)	(n = 4608)	(n = 7021)	(n = 4593)
Demographics at positive airway pressure (PAP) therapy start date (self-reported)					
↑BMI, per SD (7.7 kg/m^2)	**1.16 (1.05–1.29), 0.003**	1.13 (0.99–1.30), 0.07	**1.20 (1.03–1.41), 0.02**	1.10 (0.97–1.25), 0.13	**1.21 (1.04–1.43), 0.02**
↑Age (years), per SD (14.3 years)	**1.16 (1.06–1.27), 0.001**	**1.23 (1.09–1.39), 0.001**	1.09 (0.95–1.25), 0.22	–	
Male vs. Female (reference group)	1.10 (0.92–1.30), 0.34	–		1.20 (0.96–1.50), 0.10	0.96 (0.72–1.27), 0.77
Baseline obstructive sleep apnea severity					
↑Respiratory index: AHI or RDI (if AHI unavailable), per SD (25.7/hour)	1.08 (0.97–1.20), 0.18	1.12 (0.97–1.30), 0.12	1.01 (0.87–1.18), 0.86	1.09 (0.95–1.25), 0.20	1.10 (0.93–1.43), 0.25
↑Minimum SaO_2 (%), per SD (7.8%)	**0.89 (0.80–0.99), 0.03**	0.88 (0.76–1.02), 0.08	0.89 (0.76–1.04), 0.16	0.88 (0.77–1.00), 0.06	0.91 (0.75–1.08), 0.29
Type of PAP treatment (reference group: individuals on CPAP)					
APAP vs. CPAP	0.91 (0.76–1.09), 0.49	1.18 (0.92–1.52), 0.20	1.02 (0.78–1.34), 0.88	1.04 (0.82–1.31), 0.78	1.23 (0.92–1.63), 0.16
Bilevel (combined with ASV) vs. CPAP	1.13 (0.89–1.43), 0.40	0.98 (0.71–1.36), 0.91	**1.65 (1.15–2.37), 0.01**	1.08 (0.80–1.48), 0.61	**1.47 (1.01–2.15), 0.04**
Treatment length (considered in a separate statistical model adjusting for covariates listed above)					
Days PAP was used since treatment initiation, per SD (372.9 days)	**3.11 (2.69–3.63), <0.001**	**2.97 (2.33–3.40), <0.001**	**3.67 (2.41–4.75), <0.001**	**4.12 (3.30–5.24), <0.001**	**2.35 (1.95–2.86), <0.001**
PAP adherence during the first month (each variable was considered in a separate statistical model adjusting for covariates listed above)					
Days PAP was used for any amount of time, per SD (8.3 days)	**10.8 (8.83–13.47), <0.001**	**10.52 (7.97–14.18), <0.001**	**30.46 (20.01–39.42), <0.001**	**9.73 (7.58–12.73), <0.001**	**12.19 (8.72–17.57), <0.001**
Days PAP was used for a minimum of 4 h, per SD (10.3 days)	**24.10 (18.71–31.4), <0.001**	**20.84 (15.19–29.51), <0.001**	**24.32 (13.70–36.49), <0.001**	**21.27 (15.61–29.86), <0.001**	**27.25 (18.08–43.25), <0.001**
PAP therapy used ≥70% of days for ≥4 h, Yes vs. No	**191.13 (121.86–318.51), <0.001**	**137.26 (80.81–252.60), <0.001**	**348.94 (155.24–999.48), <0.001**	**180.07 (105.99–331.48), <0.001**	**230.88 (103.10–659.58), <0.001**

In bold – statistically significant association: $p < 0.05$.
[a] Variables included in the statistical model: age, sex, BMI, respiratory index, minimum SaO2, and type of PAP treatment. n missing for sex variable = 207 (1.8%).
[b] ORs were standardized using the standard deviation of the variable in question.
[c] The threshold for stratification was chosen because it is close to the median age of 53 years.

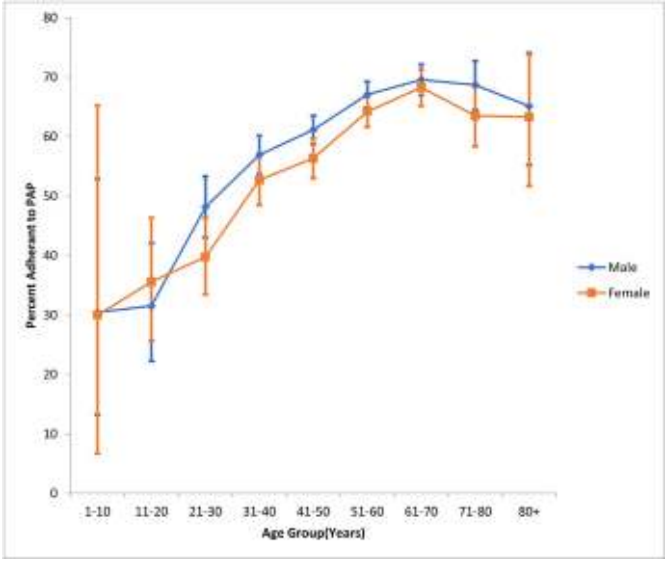

Fig. 1. Positive airway pressure (PAP) adherence rates by age and sex. The proportion of patients meeting criteria for PAP adherence (4 or more hours of use per night on 70% of nights of PAP trial) by age group for males and females. Error bars display 95% confidence intervals.

adherence-related factors. In our study, PAP adherence was generally higher in males than females and increased with age. Females tend to have lower severity of OSA assessed by the AHI and female-specific symptoms [14], which may explain lower PAP adherence compared to males. Older age, being a predictor of better PAP adherence, may be due to less social stigma surrounding PAP therapy because of an increased incidence of OSA at higher ages [22] and an increased incidence of both symptoms and comorbidities [23]. This has been documented previously [14]; however, the results were limited by a shorter time frame and individuals who required PAP adherence in order to maintain insurance coverage.

Consistent with published studies, we found that increased BMI [24] and lower SaO_2 [25] were other potential predictors of increased PAP adherence. This could be due to higher BMI associated with more severe and symptomatic sleep apnea [26] and an increased number of medical comorbidities [27]. PAP therapy may also be a requirement for individuals with moderate to severe OSA to qualify for bariatric surgery [28]. Oxygen saturation is also a marker of OSA severity; so, it is possible that patients with lower SaO_2 are more symptomatic [29] or more motivated by a sleep physician, consequently leading to greater treatment adherence.

Finally, we confirmed the importance of early and regular PAP use [30,31] to long-term adherence. Behavioral interventions

focusing on improving adaptation to PAP therapy initiated early in the treatment period may be an effective strategy to improve PAP adherence [32].

4.1. Strengths and limitations

Strengths of this study include a large sample size, an objective measure of PAP adherence, and long and complete follow-up due to remote data access. However, unmeasured confounders may bias effect estimates in this observational study as well as a limited number of characteristics available. For example, information on comorbidities, symptoms, mask type and leak, and income status were not available. Other limitations include potential measurement errors and recall bias associated with self-reported height and weight and limited generalizability due to being a single-vendor study design and the AirView™ availability. Finally, our study was not designed to investigate the pattern of PAP adherence over time, which is an important question to address in future studies.

5. Conclusion

Understanding factors and disparities associated with PAP adherence is essential to maximizing the benefits of PAP therapy. When prescribing PAP, we recommend using readily available variables to identify those who are less likely to use their device regularly, such as those younger, female, have a lower BMI, and who have higher minimum SaO_2 during the sleep study, by initiating targeted interventions to improve adherence.

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Conflicts of interest/Competing interests

None. T Kendzerska received a speaker honorarium from AstraZeneca Canada Inc. and is a Clinical Consultant at Pitolisant Medical Advisory Board (Paladin Labs Inc.).

Ethic's approval

This project has been approved by both the Ottawa Health Science Network Research Ethics Board and is consistent with the principles in the Declaration of Helsinki.

Consent to participate

Informed consent was obtained from all individual participants included in the study.

Consent for publication

The authors affirm that human research participants provided informed consent for publication.

Availability of data and material

The data that support the findings of this study are available from the corresponding author, TK, upon reasonable request and REB approvals.

CRediT authorship contribution statement

Jonathan Villa Alvarez: Study design, Formal analysis, and interpretation, drafting the manuscript. **Robert Dales:** Study conception and design, Formal analysis, and interpretation, critically important revisions. **Tetyana Kendzerska:** Study conception and design, Formal analysis, and interpretation, drafting the manuscript, critically important revisions. All of the above authors have approved this final version of the paper to be published and agree to be accountable for all aspects of the work.

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