https://doi.org/10.5664/jcsm.9288

JCSM | Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Treatment usage patterns of oral appliances for obstructive sleep apnea over the first 60 days: a cluster analysis

Kate Sutherland, PhD[1,2]; Fernanda R. Almeida, PhD[3]; Taiyun Kim, MBiomedE[4]; Elizabeth C. Brown, PhD[5,6]; Fiona Knapman, BEng, BSc[5,7]; Joachim Ngiam, MSD[2]; Jean Yang, PhD[4]; Lynne E. Bilston, PhD[5,7]; Peter A. Cistulli, MD[1,2]

[1]Sleep Research Group, Charles Perkins Centre and Northern Clinical School, Faculty of Medicine and Health, University of Sydney, Camperdown, New South Wales, Australia; [2]Department of Respiratory and Sleep Medicine, Royal North Shore Hospital, St Leonards, New South Wales, Australia; [3]Department of Oral Health Sciences, Faculty of Dentistry, University of British Columbia, Vancouver, British Columbia, Canada; [4]Charles Perkins Centre and School of Mathematics and Statistics, University of Sydney, Sydney, New South Wales, Australia; [5]Neuroscience Research Australia, Randwick, New South Wales, Australia; [6]Prince of Wales Hospital, Sydney, New South Wales, Australia; [7]University of New South Wales, Sydney, New South Wales, Australia

Study Objectives: Oral appliance (OA) therapy usage can be objectively measured through temperature-sensing data chips embedded in the appliance. Initial reports of group data for short-term treatment usage suggest good nightly hours of usage. However, individual variability in treatment usage patterns has not been assessed. We aimed to identify OA treatment usage subtypes in the first 60 days and the earliest predictors of these usage patterns.

Methods: OSA patients were recruited for a study of OA therapy with an embedded compliance chip (DentiTrac, Braebon, Canada). Fifty-eight participants with 60 days of downloadable treatment usage data (5-minute readings) were analyzed. A hierarchical cluster analysis was used to group participants with similar usage patterns. A random forest classification model was used to identify the minimum number of days to predict usage subtype.

Results: Three user groups were identified and named: "Consistent Users" (48.3%), "Inconsistent Users," (32.8%) and "Non-Users" (19.0%). The first 20 days provided optimal data to predict the treatment usage group a patient would belong to at 60 days (90% accuracy). The strongest predictors of user group were downloaded usage data, average wear time, and number of days missed.

Conclusions: Granular analysis of OA usage data suggests the existence of treatment user subtypes (Consistent, Inconsistent, and Non-Users). Our data suggest that 60-day usage patterns can be identified in the first 20 days of treatment using downloaded treatment usage data. Understanding initial treatment usage patterns provide an opportunity for early intervention to improve long-term usage and outcomes.

Keywords: obstructive sleep apnea, oral appliance therapy, adherence, cluster analysis

Citation: Sutherland K, Almeida FR, Kim T, et al. Treatment usage patterns of oral appliances for obstructive sleep apnea over the first 60 days: a cluster analysis. *J Clin Sleep Med*. 2021;17(9):1785–1792.

BRIEF SUMMARY

Current Knowledge/Study Rationale: Oral appliance treatment usage measurement to date has only been published in a small number of studies as group data. We aimed to identify treatment usage patterns for oral appliance therapy in the initial treatment period.

Study Impact: We were able to identify 3 treatment usage groups (Consistent, Inconsistent, and Non-Users) that could be identified from treatment usage downloads, with greatest accuracy at 20-days post-implementation. The early identification of poor treatment users could provide opportunity for the clinician to provide intervention to improve long-term treatment adherence.

INTRODUCTION

Oral appliance (OA) therapy for obstructive sleep apnea (OSA) tends to be reserved for patients who fail continuous positive airway pressure (CPAP) therapy. One potential reason for this is recognition that average efficacy is lower with OA compared to CPAP.[1] However, at least over short-term treatment, there is evidence that health outcomes, like blood pressure and quality of life, do not differ between these therapies.[1–3] Patients with OSA often report preferring OA to CPAP after trialing both therapies,[4] and self-reported nightly usage hours for OA are greater than CPAP.[1] Greater adherence to OA therapy is one potential explanation for similar treatment effectiveness between the therapies, despite presence of residual OSA.[5] However, most information on OA treatment usage has been self-reported (diaries, questionnaires).

Objective adherence monitors for OA therapy are now available and they report usage time based on a temperature range recorded by small microsensors embedded it the appliance.[6] However, to date, OA therapy studies reporting objective adherence are relatively few. Initial usage in a cohort of ~50 patients with OSA unaware of the monitoring capabilities of their appliance showed average nightly usage of over 6-1/2 hours a night in > 80% of regular users (> 4 hours/night on 70% of nights) after 3 months.[7] Longer follow-up, out to 1 year, has shown relative maintenance of these average usage rates in 2 small studies.[8–10] Although initial reports of average daily usage of OA therapy suggest good treatment adherence, there is likely to be different

patterns of usage, and the therapy initiation and acclimatization period (~2 months) could provide opportunity for early intervention to improve long-term treatment trajectories. OA adherence monitors provide an opportunity for more granular analysis of treatment adherence patterns between individuals.

We aimed to identify usage patterns of OA therapy over the first 60 days and, secondarily, to identify predictors of 60-day usage patterns as well as the minimum time needed to do so. We hypothesized that there are different subtypes of treatment users that can be identified in the early period of therapy.

METHODS

Participants and treatment

This is a secondary analysis of a subset of participants recruited for a larger study of imaging biomarkers of OA therapeutic response. Inclusion criteria were OSA [apnea-hypopnea index (AHI) ≥ 10 events/h], suitability for OA therapy (eg, sufficient dentition, no accident risk from sleepiness), and no contraindications to magnetic resonance imaging (eg, claustrophobia, metallic foreign bodies, artifact-causing dental implants). Written informed consent was obtained from all participants, and the study was approved by the South Eastern Sydney Local Health District Human Research Ethics Committee (protocol number HRREC/13/POWH/688). Participants were provided with an OA (SomnoDent; SomnoMed Ltd, Crows Nest, Sydney, New South Wales, Australia) under supervision of the study dentist and instructed to self-titrate the level of mandibular advancement to the maximal comfortable limit. Following confirmation by the study dentist, participants used the optimized OA for 6 weeks before undergoing polysomnography with the OA in situ. The OA contained a compliance monitoring chip (DentiTrac, Braebon Medical Corporation, Kanata, Ottowa, Ontario, Canada). To be included in the current analysis participants needed to have an activated compliance chip in their appliance that was recording for a minimum period of 60 days (participants were included regardless of whether the participant had used the device on any of those 60 days or not). Additional details of the study data are available in the **Supplemental Material**. As the primary purpose of the study was to investigate imaging biomarkers related to treatment efficacy, factors that might relate to treatment adherence, such as occlusal status, side-effects, personality, and self-efficacy, were not systematically collected.

Data analysis

All computational and statistical analysis was carried out in R version 3.5.2. The overall framework of the analysis is described in **Figure S2** in the supplemental material. Raw daily device usage data (readings of in/out every 5 minutes) were obtained from each participant for the initial 60 days of treatment. Available clinical data included age, sex, body mass index, Epworth Sleepiness Scale (ESS) and AHI at baseline and after the treatment period. Cluster analysis is a statistical method that groups together individuals in a sample who are most similar to each other on a given set of characteristics and most different to individuals in other groups, hence revealing subtypes that may not have been hypothesized. Hierarchical cluster analysis was used to define major user groups based on device usage data and thus to find treatment usage subtypes. We compared resulting user groups on clinical characteristics (analysis of variance, or chi-squared test for categorical variables). We adjusted for multiple comparisons of these tests using the Holm procedure. Next, predictors of the resulting 60-day usage clusters and the minimum number of days of data needed for accurate prediction were assessed using decision trees in a random forest approach. A randomly selected 80% of the dataset was used as the training set, with validation in the remaining 20% of the dataset. This 80/20 split of the data is considered typical for training and testing.[11] Final validation of the model was performed using leave-one-out cross-validation (1 data point is removed to test the model constructed from all other data points, and this is repeated for all data points in the sample). Additional details on these analytical methods are provided in the **Supplemental Material**.

RESULTS

Participant characteristics

Treatment usage data for the first 60 days were available for 58 participants (74.1% male). Eighty-five participants (out of 110 recruited) completed the main trial (**Figure S1** in the supplemental material). Of our subset of 58 in the current analysis, 93.1% completed the trial. This subset of 58 did not differ in terms of baseline AHI or treatment changes, age, sex, ethnicity, or body mass index from the main trial completers, who were not included in this analysis (independent *t* test, **Table S1** in the supplemental material). There were a total 18 participants from the main trial who received an OA without a compliance chip and 1 chip was not activated. Of the study completers with chips eligible for the analysis, data were not readable for 4.2% at any attempt during a study visit. There were an additional 9.9% that were not readable due to issues with upgrading the software for the reading station, which was not necessarily a failure of the data chip. The additional missing 9.9% had insufficient data due to failure to return for the last visit for data download (**Figure S1**). Participant characteristics are shown in **Table 1**. Participants were on average middle-aged and overweight with moderate OSA. The sample was not particularly sleepy at baseline (average ESS 8.3 ± 4.5), but there was an improvement in self-reported sleepiness following treatment (ESS reduction –1.3 ± 2.9, $P = .003$). OA therapy halved the AHI on average ($P < .001$) with a complete response (AHI < 5 events/h on treatment) observed in 20.7% and a > 50% AHI reduction in 53.4% (**Table 1**).

Treatment usage over the first 60 days

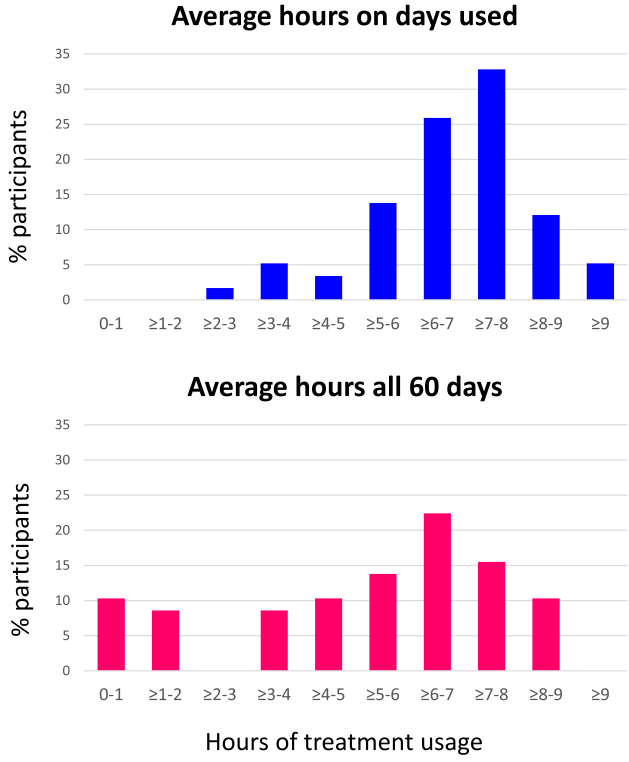
Descriptive statistics of treatment usage data downloaded from chips in the OA is shown in **Table 2**. The average nightly usage was 5.2 ± 2.5 hours across the 60 days of treatment. Individual nightly usage data showed an average standard deviation of 2.4 hours, indicating nightly variability in treatment usage. Over the 60-day period, the range of days the appliance was not used was 0% to 90% of the total 60 days across individuals; this represents an average of 26.2 ± 29.6% of days of non-use across the

Table 1—Participant characteristics.

	n	Baseline	OA	Change OA
Age (years)	58	45.8 ± 12.1	—	—
Sex (% male)	58	74.1	—	—
BMI (kg/m^2)	58	29.1 ± 4.7	—	—
Epworth Sleepiness Scale	54	8.3 ± 4.5	6.9 ± 4.2	–1.3 ± 2.9*
AHI (events/h)	54	28.0 ± 16.4	13.9 ± 11.3	–13.3 ± 14.8**
Treatment response (% responders)				
Criteria 1: AHI < 5 + ≥ 50% AHI reduction	54	—	20.7	—
Criteria 2: AHI < 10 + ≥ 50% AHI reduction	54	—	36.2	—
Criteria 3: ≥ 50% AHI reduction	54	—	53.4	—

Paired *t* test, **P* < .01, ***P* < .001, baseline vs with OA. AHI = apnea-hypopnea index, BMI = body mass index, OA = oral appliance.

Figure 1—Histograms of average hours of oral appliance usage over the 60-day period.



The top histogram shows the average hours on days used over the 60 days. The bottom histogram shows the average hours, including days when no usage was recorded.

sample. We also looked at the amount of time that the OA was removed after it had been inserted at night. On average this occurred for 24 minutes during the night (periods of device removal during night, **Table 2**). Half of the participants (53%) took out the splint on average for more than 10 minutes a night. Histograms of average hours of usage over the 60-day period are shown in **Figure 1**. The proportion of patients who could be described as "regular users" (≥ 4 hours/night for ≥ 70% of nights) was 86.2% (**Table 3**).

Identification of subgroups according to treatment usage patterns

Hierarchical cluster analysis was used to identify patient subgroups based on objective treatment usage data. The cluster analysis identified 3 clusters, or subtypes, of patients. The clusters were examined for their treatment usage characteristics in order to name them "Consistent Users" (48.3%), "Inconsistent Users" (32.8%), and "Non-Users" (19.0%). A heat map of daily treatment usage time for individual patients within the subgroups is shown in **Figure 2**. The Consistent Users had high usage hours on most nights of treatment, the Inconsistent Users had moderate-to-high usage on some nights with irregular non-usage nights. The Non-Users mostly did not use the device at all; however, individuals did wear their devices on the occasional night throughout the 60-day period. **Figure 3** depicts a closer look at 1 individual in each of the 3 categories as examples of the 3 user subtypes.

Table 2—Treatment usage data across first 60 days of oral appliance therapy.

	Mean ± SD	Range
Mean daily usage (hours)	5.2 ± 2.5	0.2–8.9
Days with no usage (%)	26.2 ± 29.6	0–0
Periods of device removal during the night (hours)	0.4 ± 0.7	0.0–4.8

Descriptive summary of usage data from compliance chips in n = 58 participants. SD = standard deviation.

The 3 treatment usage groups did not differ in terms of patient characteristics of age, sex, body mass index, or OSA severity (AHI). The Non-Users were less sleepy at baseline as assessed by the ESS, although this did not reach the level of significance required to adjust for multiple comparisons ($P < .001$, **Table 4**). Reduction in AHI or treatment response did not differ between groups, and change in sleepiness was not statistically significant, although there appears to have been a trend toward a lesser improvement in ESS following treatment in the Non-Users compared to Consistent or Inconsistent Users ($P = .057$, **Table 4**).

Predicting treatment usage group based on early usage data

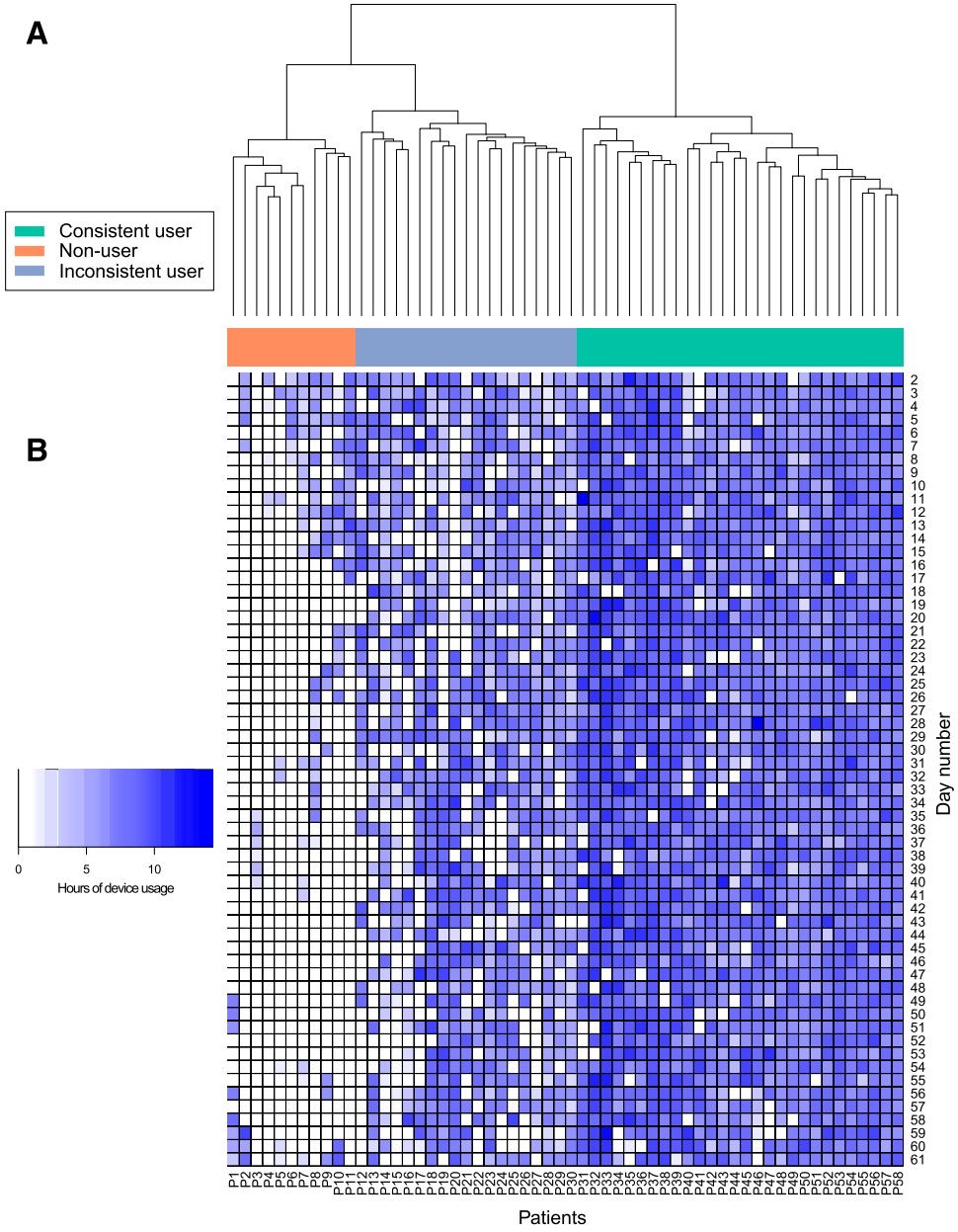
After identifying 3 patterns of OA treatment usage, we looked at whether these patterns could be predicted from initial usage and how many days of data would be needed to make an accurate prediction (accuracy by day is shown in **Figure S3** in the supplemental material). We observed that the accuracy plateaued at 20 days with

Table 3—Common compliance criteria.

	Definition	Meeting Criteria
Compliant User	Mean usage ≥ 4 h/night	72.4%
Regular User	≥ 4 h/night on ≥ 70% across all days	86.2%
Frequent User	≥ 4 h/night on ≥ 5 days/week, across all days	53.4%

Criteria commonly used to define adequate usage for CPAP treatment[10] based on a threshold of 4 hours nightly usage were applied for the objective oral appliance usage data (n = 58). The average usage was obtained from all days, regardless of whether treatment usage was attempted or not.

Figure 2—An overview of individual patient's device usage behavior over the 60-day period.



(A) A dendrogram of patients clustered by their device usage patterns. Three major clusters are identified as "Consistent user," "Non-user," and "Inconsistent user." **(B)** A heatmap representing each patient's daily device usage across the 60-day period studied. For each patient, the *x*-axis represents patient identification, and the *y*-axis represents the day number from the day patient was given the appliance. Each tile color represents the hours of device usage per day.

Table 4—Comparison of identified treatment usage groups (Consistent User, Non-User, and Inconsistent User) across clinical characteristics, OSA severity, and symptom changes with treatment.

Variable	Treatment Usage Groups			Statistical Test	*P*
	Consistent Users	Inconsistent Users	Non-Users		
n (%)	28 (48.3)	19 (32.8)	11 (19.0)	—	
Treatment usage data: daily usage (hours)	7.3 ± 0.8	4.6 ± 0.8	1.0 ± 0.6	—	
Baseline characteristics					
Age (years)	45.8 ± 12.4	47.1 ± 12.0	43.7 ± 12.1	Welch's one-way ANOVA	.78
BMI (kg/m^2)	28.7 ± 4.8	29.6 ± 4.3	29.3 ± 5.5	Welch's one-way ANOVA	.79
Sex [male n (%)]	19 (67.9)	15 (25.9)	9 (47.4)	Chi-squared test	.62
Ethnicity (% Caucasian)	64.3	54.5	63.2	Chi-squared test	.80
AHI (events/h)	32.3 ± 18.5	26.1 ± 14.5	20.2 ± 10.4	Welch's one-way ANOVA	.088
ESS	7.7 ± 4.6	10.3 ± 4.4	6.1 ± 2.1	Welch's one-way ANOVA	.0092
Treatment changes					
ΔAHI	17.7 ± 17.1	11.2 ± 12.6	10.0 ± 10.0	Welch's one-way ANOVA	.54
ΔESS	1.8 ± 2.5	1.9 ± 3.1	0.9 ± 2.7	Welch's one-way ANOVA	.057

Data are presented as mean ± SD. No *P* values are significant at the level adjusted for multiple comparisons (Holm procedure, $P < .001$ for ESS). AHI = apnea-hypopnea index, ANOVA = analysis of variance, BMI = body mass index, ESS = Epworth Sleepiness Scale, OSA = obstructive sleep apnea.

final accuracy of 0.88 (**Table 5**). Our model suggests descriptive statistics of patient's average wearing hours, median of wearing hours, and percent of days without the device as the top 3 important variables in prediction of user subgroup membership (**Figure S4** in the supplemental material). Overall, these data suggest we are able to accurately predict most patients' usage subtype (Consistent, Inconsistent, or Non-User) in the first 20 days of treatment.

DISCUSSION

In a novel analysis of objective treatment usage data from OA, we have identified 3 treatment user subtypes across the first 60 days of therapy, namely, Consistent Users, Inconsistent Users, and Non-Users. Effective OSA therapy comprises dual components of treatment efficacy and adherence.[5] Better adherence to OA therapy relative to CPAP therapy could be an explanation for equivalent short-term health outcomes, despite the common presence of residual OSA on OA compared to CPAP. Although initial group data suggest that objective adherence to OA therapy could be higher than reports for CPAP therapy,[10,12] our study demonstrates substantial variation between individuals. Suboptimal users of OA therapy are unlikely to achieve optimal health outcomes, of which hours of nightly usage are an important determinant.[2,13] Early recognition of those who are not adherent to OA treatment could provide an important opportunity for intervention to improve long-term adherence. Our data suggest that 60-day usage patterns can be detected after 20 days of therapy. This suggests that the initial 20 days after an OSA patient receives an OA is an important period for clinical monitoring and intervention to improve adherence.

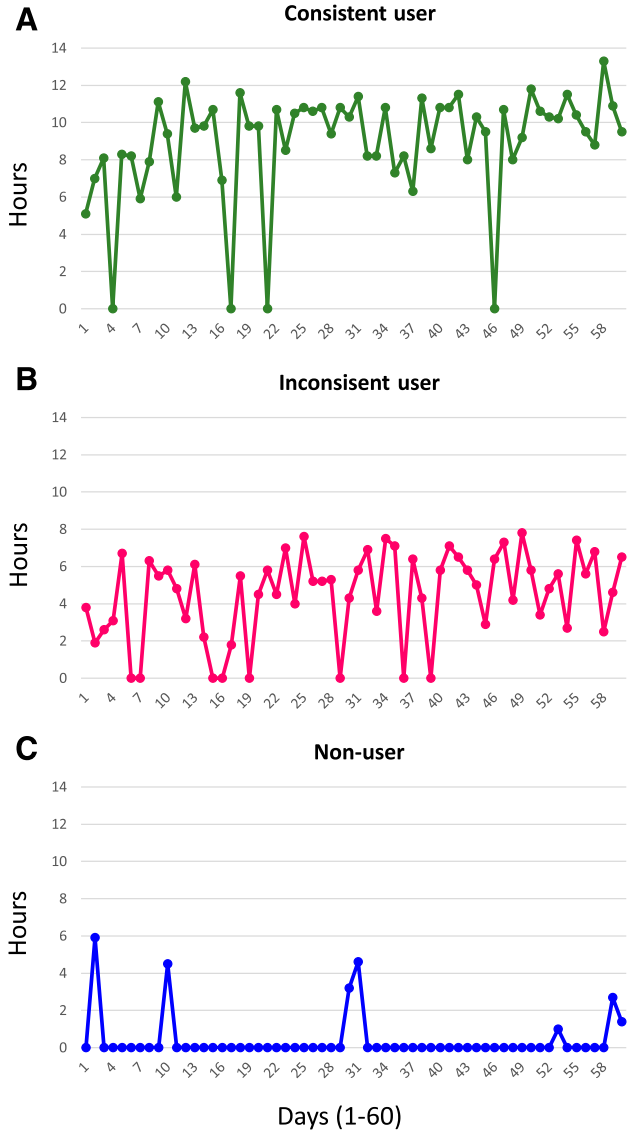
There are currently a limited number of studies reporting objective OA compliance,[7,8,10,14,15] although several commercially available monitoring systems have been validated for accuracy.[6] Our average data found 5.2 hours per day usage, which is slightly lower than some previous reports.[7] Our analysis provides more detailed information of treatment usage subtypes, with nearly half of our sample being designated Consistent Users (48.3%) with average usage > 7 hours/night, in line with previous studies. Non-Users were a minority of the sample (19.0%), with average ~1 hour/night usage. Although a minority of participants fall into this category, it is important to be able to identify them, with the aim of intervening to improve their treatment trajectory. This is particularly important after the manufacture of a customized device, in which identification of those who are showing early signs of being intolerant of therapy could benefit from additional efforts to improve adherence.

Table 5—Performance of the random forest model with summary of 20 days data to predict treatment user group.

	Consistent User	Non-User	Inconsistent User
Sensitivity	0.93	0.82	0.84
Specificity	0.93	0.96	0.92
Balanced accuracy*	0.93	0.89	0.88
Correctly classified	0.88		

*Normalized value of true positive rate and true negative rate for each class.

Figure 3—Individual treatment usage traces from examples of the 3 treatment usage subtypes.



These figures show daily usage hours for 3 study participants who were classified into 1 of the 3 user groups identified by the cluster analysis: **(A)** Consistent user, **(B)** Inconsistent user, and **(C)** Non-user. The Consistent user showed high nightly usage with minimal skipped days over the 60-day period. The Inconsistent user showed more skipped days with more days with more variable usage, including days with < 4 hours. This Non-user had no usage on the majority of days although sporadically attempted treatment throughout the 60-day period. In **Figure 2**, these examples are Non-user P5, Inconsistent user P28, and Consistent user P33.

Usage patterns have previously been explored for CPAP treatment. Aloia and colleagues used time series analysis to identify usage patterns across 1 year of CPAP therapy.[16] In this study of 71 OSA patients, usage patterns were visually grouped into different categories based on usage and slope over time. Seven different categories were identified and named "Good Users" (24%), "Slow Improvers" (13%), "Slow Decliners" (14%), "Variable Users" (17%), "Occasional Attempters" (8%), "Early Drop-Outs" (13%), and "Non-Users" (11%).[16] This work was extended to use cluster analysis based on mean daily usage over 180 days of treatment in 161 OSA patients.[17] The cluster analysis revealed 4 usage groups: "Great Users," "Good Users," "Low Users," and "Slow Decliners."[17] To the best of our knowledge, our study is the first such analysis in OA therapy. Our analysis revealed 3 groups of OA usage patterns, although some of our usage patterns (**Figure 3**) may have similar traits to CPAP good users, occasional attempters, and non-users. It is possible that additional treatment usage patterns may be identified in larger samples; for example, inconsistent users may consist of those who skip treatment nights altogether vs those who only use a portion of the night, which could require different approaches to improving adherence. Unfortunately, we do not have the sample size in the current study to be able to ascertain this (data not shown). It will be important to validate and extend this work in larger samples and over longer periods of OA therapy and to compare to CPAP usage patterns.

Initial CPAP compliance has been shown to relate to the effect on intimacy with partners, race, and OSA severity.[18] Treatment adherence to CPAP therapy is complex and is influenced by multiple factors ranging from the interface/mask, characteristic patient disease severity, side-effects, psychological factors, and the method of initiation.[19] There are few studies to date that have assessed factors related to short-term objective compliance to OA therapy. Two studies have shown some relationship with OA side-effect frequency and severity and objective usage time.[20,21] Improved snoring, but not self-reported daytime sleepiness, was associated with greater objective usage hours in the short-term.[20] In this study we did not collect side-effect information, but Non-Users did have less sleepiness at baseline compared to the Inconsistent or Consistent Users, and lack of OSA-related symptoms could relate to their low adherence to OSA therapy. Greater sleepiness, measured by the ESS, has also been found to indicate longer-term adherence to CPAP therapy.[22] Additionally, we did observe a trend toward less improvement in ESS following therapy in the Non-Users compared to the Consistent or Inconsistent User groups, which may relate to their lower level of sleepiness at baseline or lack of usage of the treatment. The lack of statistical significance on this outcome may reflect a sample-size issue. We additionally did not collect other lifestyle information, including marital status/bed partner, which could influence adherence. Sex and ethnicity did not relate to treatment user patterns in our sample. Future studies of OA could look at a broader range of factors, including dental occlusal status and appliance factors such as degree of mandibular advancement and side-effects. However, analysis based on data from the recording chip was able to robustly predict the type of user after the first 20 days of treatment. This suggests that objective adherence monitoring could have an important clinical role in early identification of Non-Users, even without knowledge of other factors. Objective adherence monitoring for OA has not been widely adopted in clinical practice, but this analysis suggests there may be value for early detection of Non-Users in the acclimatization phase.

We have found that 20 days of initial usage provided the best prediction of treatment usage subtype after 60 days of therapy (**Figure S2** in the supplemental material). This is broadly consistent with studies of CPAP adherence, where early adherence

predicts longer-term adherence, although the time points used for early prediction in CPAP studies have varied from 3 days to 3 months.[22–24] Moreover, most CPAP adherence studies have used predetermined fixed time points for measuring early adherence, in contrast with our method, by which we assessed the accuracy of prediction at each day post–treatment initiation. We determined 20 days to be optimal in that it provided nearly 90% accuracy, with relatively minor increases in accuracy beyond this. However, our data after 1 week indicated nearly 70% accuracy, which increased to nearly 80% accuracy after 2 weeks. A recent analysis of predictors of long-term adherence to CPAP in a cardiovascular disease cohort (from the SAVE trial) reported a stronger association with adherence over the first month compared to the titration week in multivariate analysis, also supporting that a slightly longer assessment of initial usage may add value for prediction of long-term usage.[25]

The need for precision medicine in the management of OSA is increasingly recognized.[26–30] One approach is to achieve more personalized care through recognition of different disease phenotypes. Cluster analysis is one method to identify subtypes based on specific sets of characteristics without presetting boundaries for what groups may be found. There have been recent examples of cluster analysis revealing OSA subtypes based on symptoms and polysomnographic data,[31,32] with these subtypes demonstrated to have clinical meaning in terms of cardiovascular risk.[33] We have applied similar cluster analysis approaches to treatment usage data downloaded from oral appliances. Understanding treatment usage behavior is another aspect to precision sleep medicine and provides opportunity to improve adherence for better health outcomes. This study provides an important step in utilizing objective adherence monitoring to identify clinically useful patterns from the data itself. Success with OA therapy involves a complex interaction of efficacy (with known variability in AHI reduction) and patient acceptance and ongoing usage. Predicting OSA patients who will respond to OA therapy in terms of AHI reduction has been the subject of much research, although reliable clinical prediction models remain elusive to date.[34] Continued efforts in this direction will hopefully enable preselection of candidates who will experience adequate efficacy with OA therapy. Both the initial selection of those suited to OA therapy and optimizing adherence once the appliance is made are important elements of successful therapy and complementary aspects of a precision approach to OA therapy.

Although this study used a novel analytical approach to provide new insights about objective treatment usage patterns with OA therapy for OSA, there are important limitations. This study included 58 people on OA treatment: Although this is a relatively small sample and we advocate assessment in other and larger samples, the sample size is larger than most objective OA usage data samples published to date. The primary study was not designed to look specifically at treatment adherence, and therefore there were some variables that were not collected that could have been useful to an understanding of the contributors to these patterns, such as information on OSA symptoms (beyond self-reported sleepiness), self-efficacy, dental occlusal status, side-effects, degree of mandibular advancement, and other potential reasons for non-usage. We did not look at final mandibular advancement level in relation to usage groups, as data was primarily gathered in the titration period when advancement level was changing. However, a more detailed exploration of titration methods and usage in future studies would be warranted. Regardless, a potential advantage is that treatment usage in this study was not influenced by participants knowing they were in a study of treatment adherence, and hence the data likely reflect real world usage patterns. Our inclusion criteria included a requirement for 60 days of recording data. Therefore, participants who could not tolerate therapy and abandoned it earlier were not included in our summary. The results would therefore underestimate numbers of people not tolerating OA therapy. We do not have information on sleep time related to hours of usage, so we are unable to confirm whether compliant users were using the appliance for their entire sleep time. Given our slightly lower average usage times compared to previous studies, it would have been advantageous to know whether sleep time truly reflected less usage or shorter sleep times in our sample. We experienced technical issues accessing data from the chips in some cases (both due to chip read failure and software issues); of our total study sample with data chips in their OA, only around two-thirds had the first 60 days of data available for analysis. Temperature data loggers and reading systems are likely to improve further when demand and usage of these devices increases. Finally, the data reported here relate to a single OA design, and it is unknown whether the results can be generalized across other OA designs, although it has been shown previously that OA device does not relate to compliance in a self-report study.[35]

CONCLUSIONS

Our initial work suggests the first 20 days is a key window in the treatment period in which there may be a role for intervention strategies in patients predicted to be on a poor adherence trajectory. However, longer periods could now be studied for usage patterns and in relation to other factors that affect adherence, including personality types,[9] side-effects, and symptomatic improvements.[20] The relationship between long-term treatment usage patterns and health outcomes is also important. This study is the first to combine objective OA treatment usage data and cluster analysis methods to identify patterns in the data. Understanding these individualized treatment patterns is an important step toward precision medicine in OSA and OA therapy.

ABRREVIATIONS

AHI, apnea-hypopnea index
CPAP, continuous positive airway pressure
ESS, Epworth Sleepiness Scale
OA, oral appliance
OSA, obstructive sleep apnea

REFERENCES

1. Schwartz M, Acosta L, Hung YL, Padilla M, Enciso R. Effects of CPAP and mandibular advancement device treatment in obstructive sleep apnea patients: a systematic review and meta-analysis. *Sleep Breath.* 2018;22(3):555–568.

2. Bratton DJ, Gaisl T, Wons AM, Kohler M. CPAP vs mandibular advancement devices and blood pressure in patients with obstructive sleep apnea: a systematic review and meta-analysis. *JAMA.* 2015;314(21):2280–2293.
3. Phillips CL, Grunstein RR, Darendeliler MA, et al. Health outcomes of continuous positive airway pressure vs oral appliance treatment for obstructive sleep apnea: a randomized controlled trial. *Am J Respir Crit Care Med.* 187(8):879–887.
4. Sutherland K, Vanderveken OM, Tsuda H, et al. Oral appliance treatment for obstructive sleep apnea: an update. *J Clin Sleep Med.* 2014;10(2):215–227.
5. Sutherland K, Phillips CL, Cistulli PA. Efficacy vs effectiveness in the treatment of obstructive sleep apnea: CPAP and oral appliances. *J Dent Sleep Med.* 2015;2(4): 175–181.
6. Kirshenblatt S, Chen H, Dieltjens M, Pliska B, Almeida FR. Accuracy of thermo-sensitive microsensors intended to monitor patient use of removable oral appliances. *J Can Dent Assoc.* 2018;84:i2.
7. Vanderveken OM, Dieltjens M, Wouters K, De Backer WA, Van de Heyning PH, Braem MJ. Objective measurement of compliance during oral appliance therapy for sleep-disordered breathing. *Thorax.* 2013;68(1):91–96.
8. de Vries GE, Hoekema A, Claessen JQPJ, et al. Long-term objective adherence to mandibular advancement device therapy versus continuous positive airway pressure in patients with moderate obstructive sleep apnea. *J Clin Sleep Med.* 2019;15(11): 1655–1663.
9. Dieltjens M, Vanderveken OM, Van den Bosch D, et al. Impact of type D personality on adherence to oral appliance therapy for sleep-disordered breathing. *Sleep Breath.* 2013;17(3):985–991.
10. Dieltjens M, Braem MJ, Vroegop AVMT, et al. Objectively measured vs self-reported compliance during oral appliance therapy for sleep-disordered breathing. *Chest.* 2013;144(5):1495–1502.
11. Lever J, Krzywinski M, Altman N. Model selection and overfitting. *Nature Methods.* 2016;13(9):703–704.
12. Rotenberg BW, Murariu D, Pang KP. Trends in CPAP adherence over twenty years of data collection: a flattened curve. *J Otolaryngol Head Neck Surg.* 2016;45(1):43.
13. Weaver TE, Maislin G, Dinges DF, et al. Relationship between hours of CPAP use and achieving normal levels of sleepiness and daily functioning. *Sleep.* 2007;30(6): 711–719.
14. Inoko Y, Yoshimura K, Kato C, Morita O, Kohno M. Efficacy and safety of temperature data loggers in measuring compliance with the use of oral appliances. *Sleep Biol Rhythms.* 2009;7(3):188–192.
15. Lowe AA, Sjöholm TT, Ryan CF, Fleetham JA, Ferguson KA, Remmers JE. Treatment, airway and compliance effects of a titratable oral appliance. *Sleep.* 2000;23 (Suppl 4):S172–S178.
16. Aloia MS, Goodwin MS, Velicer WF, et al. Time series analysis of treatment adherence patterns in individuals with obstructive sleep apnea. *Ann Behav Med.* 2008;36 (1):44–53.
17. Babbin SF, Velicer WF, Aloia MS, Kushida CA. Identifying longitudinal patterns for individuals and subgroups: an example with adherence to treatment for obstructive sleep apnea. *Multivariate Behav Res.* 2015;50(1):91–108.
18. Ye L, Pack AI, Maislin G, et al. Predictors of continuous positive airway pressure use during the first week of treatment. *J Sleep Res.* 2012;21(4):419–426.
19. Weaver TE, Grunstein RR. Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. *Proc Am Thorac Soc.* 2008;5(2): 173–178.
20. Dieltjens M, Verbruggen AE, Braem MJ, et al. Determinants of objective compliance during oral appliance therapy in patients with sleep-disordered breathing: a prospective clinical trial. *JAMA Otolaryngol Head Neck Surg.* 2015;141(10): 894–900.
21. Mullane S, Loke W. Influence of short-term side effects on oral sleep appliance compliance among CPAP-intolerant patients: an objective monitoring of compliance. *J Oral Rehabil.* 2019;46(8):715–722.
22. McArdle N, Devereux G, Heidarnejad H, Engleman HM, Mackay TW, Douglas NJ. Long-term use of CPAP therapy for sleep apnea/hypopnea syndrome. *Am J Respir Crit Care Med.* 1999;159(4):1108–1114.
23. Popescu G, Latham M, Allgar V, Elliott MW. Continuous positive airway pressure for sleep apnoea/hypopnoea syndrome: usefulness of a 2 week trial to identify factors associated with long term use. *Thorax.* 2001;56(9):727–733.
24. Budhiraja R, Parthasarathy S, Drake CL, et al. Early CPAP use identifies subsequent adherence to CPAP therapy. *Sleep.* 2007;30(3):320–324.
25. Van Ryswyk E, Anderson CS, Antic NA, et al. Predictors of long-term adherence to continuous positive airway pressure in patients with obstructive sleep apnea and cardiovascular disease. *Sleep.* 2019;42(10):zsz152.
26. Bonsignore MR, Suarez Giron MC, Marrone O, Castrogiovanni A, Montserrat JM. Personalised medicine in sleep respiratory disorders: focus on obstructive sleep apnoea diagnosis and treatment. *Eur Respir Rev.* 2017;26(146):170069.
27. Lim DC, Sutherland K, Cistulli PA, Pack AI. P4 medicine approach to obstructive sleep apnoea. *Respirology.* 2017;22(5):849–860.
28. Martinez-Garcia MA, Campos-Rodriguez F, Barbé F, Gozal D, Agustí A. Precision medicine in obstructive sleep apnoea. *Lancet Respir Med.* 2019;7(5):456–464.
29. Zinchuk AV, Gentry MJ, Concato J, Yaggi HK. Phenotypes in obstructive sleep apnea: a definition, examples and evolution of approaches. *Sleep Med Rev.* 2017;35:113–123.
30. Carberry JC, Amatoury J, Eckert DJ. Personalized management approach for OSA. *Chest.* 2018;153(3):744–755.
31. Ye L, Pien GW, Ratcliffe SJ, et al. The different clinical faces of obstructive sleep apnoea: a cluster analysis. *Eur Respir J.* 2014;44(6):1600–1607.
32. Zinchuk AV, Jeon S, Koo BB, et al. Polysomnographic phenotypes and their cardiovascular implications in obstructive sleep apnoea. *Thorax.* 2018;73(5):472–480.
33. Mazzotti DR, Keenan BT, Lim DC, Gottlieb DJ, Kim J, Pack AI. Symptom subtypes of obstructive sleep apnea predict incidence of cardiovascular outcomes. *Am J Respir Crit Care Med.* 2019;200(4):493–506.
34. Sutherland K, Kairaitis K, Yee BJ, Cistulli PA. From CPAP to tailored therapy for obstructive sleep apnoea. *Multidiscip Respir Med.* 2018;13:44.
35. Saglam-Aydinatay B, Taner T. Oral appliance therapy in obstructive sleep apnea: long-term adherence and patients experiences. *Med Oral Patol Oral Cir Bucal.* 2018; 23(1):e72–e77.

ACKNOWLEDGMENTS

The authors thank the study participants and sleep technologists involved in the study and SomnoMed Australia for their donation of appliances for this research.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication September 7, 2020
Submitted in final revised form March 22, 2021
Accepted for publication March 22, 2021
Address correspondence to: Peter A. Cistulli, MD, Department of Respiratory and Sleep Medicine, 8A, Acute Services Building, Royal North Shore Hospital, Reserve Road, St. Leonards NSW 2065; Email: peter.cistulli@sydney.edu.au

DISCLOSURE STATEMENT

All authors have seen and approved the manuscript. This work was performed in the Department of Respiratory Medicine, Royal North Shore Hospital, and Neuroscience Research Australia, Sydney, NSW, Australia. This study was funded by a National Health and Medical Research Council of Australia (NHMRC) project grant (GNT1082364). The oral appliances and compliance chips were provided to the study by SomnoMed, Australia. P.A.C. has an appointment to an endowed academic chair at the University of Sydney that was created from ResMed funding. He receives no personal fees, and this relationship is managed by an oversight committee of the university. He has received research support from ResMed, SomnoMed, Zephyr Sleep Technologies, and Bayer. He is a consultant/adviser to Zephyr Sleep Technologies, ResMed, SomnoMed, and Signifier Medical Technologies. He has a pecuniary interest in SomnoMed related to a previous role in R&D (2004). All other authors report no conflicts of interest.