



# Efficacy of Oral Appliance Therapy in the Treatment of Severe OSA in CPAP-Resistant Cases

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## Abstract

**Purposes** Continuous positive airway pressure (CPAP) is the current standard of care for the treatment of obstructive sleep apnea (OSA). It is known that there is a low rate of adherence in many patients. Oral appliance therapy (OAT) is effective in patients with mild-to-moderate OSA. The efficacy of OAT in severe patients is unknown. The aim of this study is to evaluate treatment using an in-laboratory titration method to determine whether OAT might be appropriate for patients with severe OSA.

**Methods** This is an IRB approved, retrospective study of 41 adults (mean age 51 years; 73% male) with severe OSA who were intolerant of CPAP therapy. All patients were treated with OAT (OASYS Oral–Nasal Airway System™). The sample was sub-divided into severe [Apnea–Hypopnea Index (AHI) > 30 < 50] and very severe (AHI > 50) groups. Informed consent was obtained from all patients included in the study. The device was custom fit by a dentist. After patients reported subjective symptom improvement, titration polysomnography was performed. If obstructive events were still noted after 90 min of the sleep study, an attending sleep technologist titrated the device in vivo in 1 mm increments for a maximum of 3 mm to optimize effectiveness.

**Results** For severe cases, almost half (46%) were resolved with a post-treatment AHI < 5, while two-thirds (66%) had an AHI < 10. For very severe cases, 43% were resolved with a post-treatment AHI < 5, while 64% had an AHI < 10. All findings were statistically significant ( $p < 0.001$ ).

**Conclusions** This preliminary study supports the notion that oral appliance therapy using the OASYS Oral–Nasal Airway System™ may be effective in severe cases of OSA.

**Keywords** Obstructive sleep apnea treatment · Mandibular advancement · Removable orthodontic appliances · Polysomnography

## Abbreviations

AHI Apnea–Hypopnea Index  
AASM American academy of sleep medicine

BMI Body mass index  
CPAP Continuous positive airway pressure  
ENT Ear nose throat  
ECG Electrocardiogram  
EEG Electroencephalogram  
EMG Electromyography  
EOG Electrooculogram  
FDA Food and drug administration  
OSA Obstructive sleep apnea  
OAT Oral appliance therapy  
PSG Polysomnography  
REM Rapid eye movement  
RDI Respiratory distress index

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Drs. John and Michael Bixby performed all the clinical work. All post-treatment sleep studies were performed at Sleep Dynamics—Center for Diagnosis of Sleep Disorders—An AASM Accredited Center. 2240 State Highway 33, Suite 114, Neptune City, NJ 07753.

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## 1 Introduction

Epidemiological studies have suggested a high prevalence of obstructive sleep apnea (OSA) in the general population [1–3]. Despite the availability of effective screening instruments and diagnostic testing, OSA remains underdiagnosed [4–8]. The severity of OSA is defined by the pre-treatment apnea–hypopnea index (AHI), which is the total number of apnea and hypopnea events that occur per hour of sleep. A higher AHI corresponds to more severe disease. At all levels of severity, OSA is associated with significant cardiovascular, neurocognitive, and metabolic morbidity [4–9]. In addition, OSA is independently associated with an increased likelihood of motor vehicle accidents, increased on-the-job accidents and other occupational hazards, and a diminished quality of life. Therefore, effective management of OSA is imperative to mitigate its sequelae and prevent long-term complications.

The currently recommended, first-line treatment of OSA is the use of continuous positive airway pressure (CPAP), which is highly efficacious. CPAP provides pneumatic splinting of the upper airway and prevents its collapse during inspiration [10]. In contrast, surgical management of OSA includes upper airway reconstruction and bypass procedures. The choice of surgical procedure depends on the severity of the condition and patient preference. On the other hand, oral appliances are the most accepted and clinically proven alternatives to CPAP. These appliances cover the upper and lower dental arches and are designed to keep the lower jaw in a protruded position during sleep [11]. Oral appliance therapy (OAT) that utilizes mandibular advancement, increases the pharyngeal airway space, and reduces upper airway collapsibility. In fact, results with OAT can be comparable to CPAP in some patients [12]. A recent 2-year follow-up study involving OAT suggested that mild-to-moderate cases could be effectively treated with an adjustable appliance, while severe OSA should be initially treated with CPAP [10]. However, it is known that there is a low rate of compliance in some patients being treated with CPAP [13–16]. Singh and Abramson [17] investigated the use of the OASYS Oral–Nasal Airway System™ for mild-to-moderate cases of OSA. Therefore, the aim of this study is to test the hypothesis that OAT using a novel in-laboratory titration method might be appropriate for patients with severe OSA that have been unable to tolerate CPAP therapy.

## 2 Materials and Methods

This retrospective, observational study was reviewed and approved by IRBco, an accredited organization which provides IRB oversight for studies. We included patients with severe levels of OSA who declined or were unsuccessful with CPAP therapy. The sample received treatment with an OASYS Oral–Nasal Airway System™ adjustable oral appliance (OAT). The OASYS Oral–Nasal Airway System™ is approved by the US Food and Drug Administration (FDA) as a mandibular advancement device (MAD). It is a custom-fabricated oral device (Fig. 1) used for the treatment of snoring, mild-to-moderate OSA, and upper airway resistance syndrome. In addition, the OASYS Oral–Nasal Airway System™ has been reviewed by the ENT division of the FDA, and has been approved as a nasal dilator for upper airway resistance. In view of these approvals, its use could be extended to treating severe cases of OSA. The device works by ameliorating obstruction in the posterior pharyngeal space as an MAD, but it also lowers nasal upper airway resistance by opening the nasal valves and stretching the nasolabial folds from within the mouth [18]. The device also incorporates an extension that projects to the root of the tongue (Fig. 1) to prevent the tongue from falling back by guiding it towards the palate.

This preliminary study comprised 41 subjects (30 men; 11 women) with severe OSA who were unable to tolerate CPAP therapy. The total sample was sub-divided into severe cases (AHI > 30 < 50) and very severe cases (AHI > 50). After obtaining informed consent from the patients in this study, a qualified dentist custom fit each device. All patients received the same custom-fitted device



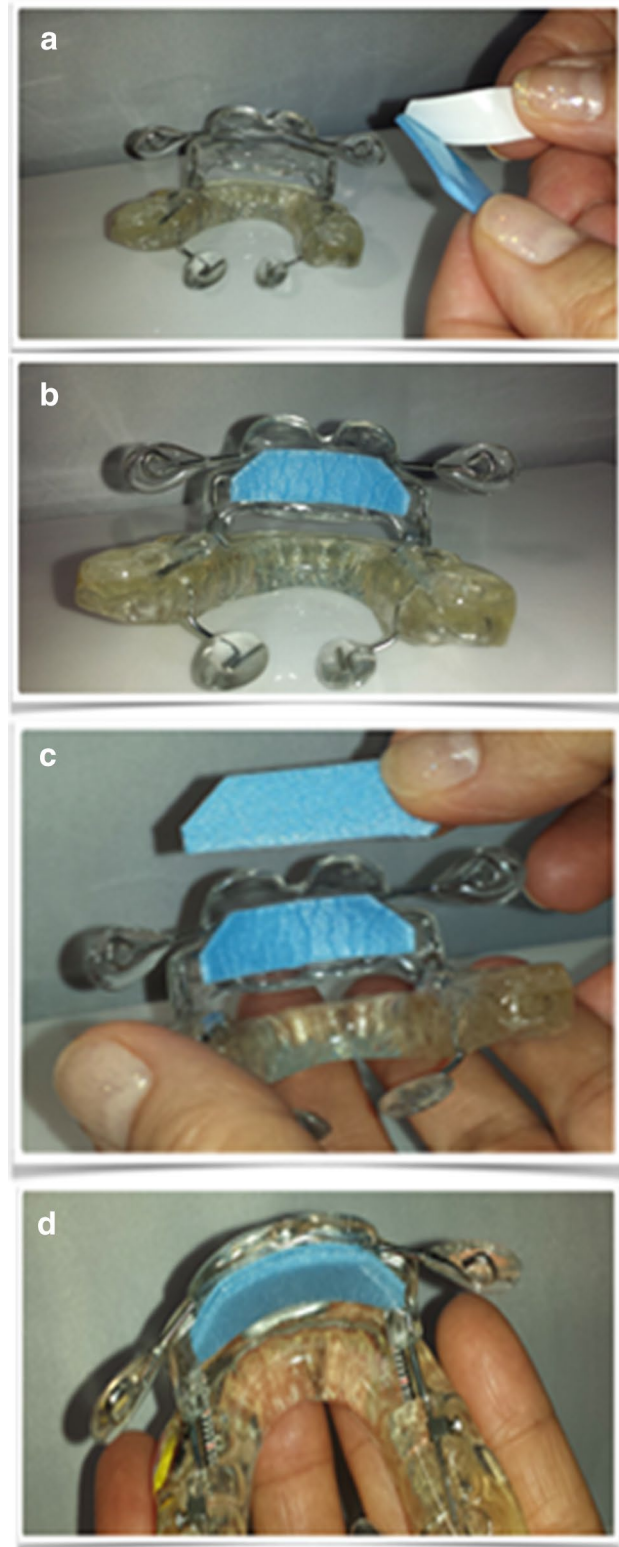
**Fig. 1** OASYS Oral–Nasal Airway System™. Note that the device incorporates an extension (arrowed) that projects to the root of the tongue to prevent it from falling back and guiding it towards the palate

(OAT) to eliminate potential effects of variable appliance designs. Study participants were required to demonstrate that they tolerated and complied with the use of the device. After this assessment, when participants reported subjective improvement in symptoms, a PSG titration was performed in a sleep laboratory to fine-tune the appliance [19, 20] and establish the most accurate setting.

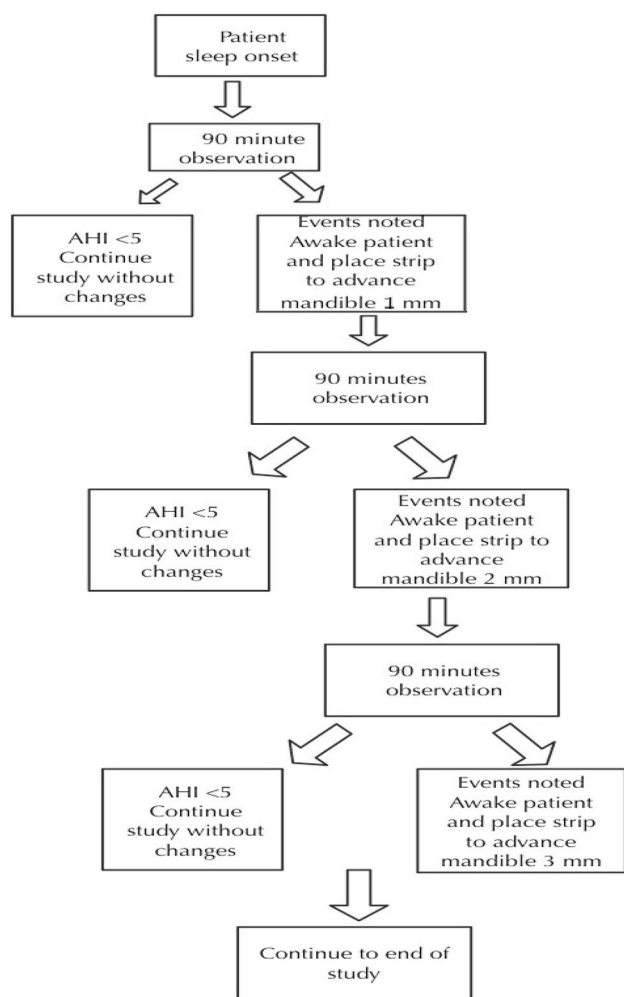
**Data Collection from Titration PSG:** a standard overnight PSG was performed using Phillips Respironics Alice 5 computerized monitoring software, with a sleep technologist in attendance. Measured parameters included: frontal EEG (F4–M1, F3–M2); central EEG (C4–M1, C3–M2); occipital EEG (O1–M2, O2–M1); left and right EOG; ECG; chin EMG; left and right anterior tibialis EMG; combined oral–nasal thermistor airflow, and nasal pressure. The equipment included abdominal and thoracic movement piezo-respiratory effort belts; a pulse oximeter and a transducer microphone to quantify snoring intensity. Body position was also monitored, as well as standard audio–video recording. The recorded signal tracings, including apneas and hypopneas, were scored using the American Academy of Sleep Medicine (AASM) scoring manual [21].

The sleep technologist used the protocol of CPAP titration as per AASM guidelines [21]. For example, titration was done by gradually adjusting the device to resolve any residual snoring, apneas, hypopneas, oxygen desaturations, and arousals. If obstructive events were still noted after 90 min of the PSG study, the attending sleep technologist titrated the device in vivo in 1 mm increments in a protrusive direction for maximum of 3 times or 3 mm, for optimal effect and to minimize sleep disturbance, using titration strips (Fig. 2). This procedure ensured that the appliance was effective in various body positions and during the different sleep stages. An attending dental sleep specialist also reviewed the data to determine the most appropriate position for the device. An attending board-certified sleep physician then interpreted the final PSG results, and determined the efficacy of the oral appliance according to AASM guidelines [21].

After completion of the titration PSG, the oral appliance was returned to its original position by removing the titration strips. The final summary report included the supervising and interpreting physician's assessments and any significant observations, such as REM-dominant OSA, snoring, or any other events that occurred during sleep. In addition, the summary included tabulated data from each titration, post-titration AHI, REM sleep duration, and oxygen saturation. After receiving the summary report, the referring dentist determined the final mandibular position of the device, and adjusted it to the position determined by the results of the PSG study. The dentist continued to follow up with periodic examinations for about 4 months as recommended by the Clinical Practice Guideline for the Treatment of OSA and



**Fig. 2** a–d In-laboratory titration strips. These were used to gradually adjust the device to resolve any residual respiratory events. If events were still noted after 90 min of the PSG study, the attending sleep technologist titrated the device in vivo in 1 mm increments, using the titration strips



**Fig. 3** Flow chart summarizing the in-laboratory PSG titration technique. Note that if obstructive events were noted after 90 min of the PSG study, the attending technologist titrated the device in 1 mm increments in a protrusive direction for maximum of 3 times, using titration strips

Snoring with Oral Appliance Therapy Update 2015 [22]. Figure 3 summarizes the workflow.

The attending physician was responsible for the overall decisions regarding the need for supplemental oxygen therapy, central sleep apnea management, and any other implicating conditions discovered during the titration PSG. Finally, the physician determined whether the OSA had been adequately treated according to the AASM criteria.

Statistical analysis was performed on the PSG data using matched, paired *t* tests (SAS University Edition).

### 3 Results

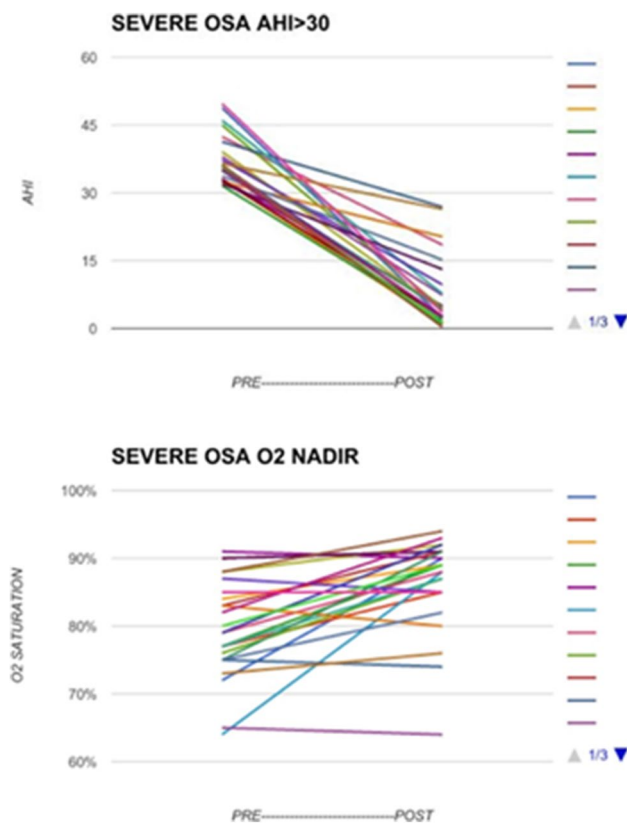
The mean treatment time of the study was 4 months. No significant side effects were reported either during the overnight titration PSG or during the study period. The total sample was sub-divided into severe cases (AHI > 30 < 50;  $n = 25$ ) and very severe cases (AHI > 50;  $n = 16$ ). The average age of the severe cases was 50.5 years (37–73) and average age of the very severe cases was 46.8 years (21–62). The average BMI of the severe cases was 32.2 (21.8–46.4) and 34.6 (27–43) for the very severe cases. Table 1 summarizes these results.

Treatment success was determined by a resolution of symptoms as defined by AASM criteria [23]. Indeed, the PSG data showed significant improvements for the major measures of OSA. For the severe cases, the average baseline AHI was  $37.5 \text{ h}^{-1}$  (31.6–49.7), while it was  $73.4 \text{ h}^{-1}$  (51.9–120.3) in very severe case. Specifically, for the severe subjects (18 males and 7 females), optimum resolution with an AHI of < 5 was achieved for 16 of the 25 subjects. Thus, 64% of the severe OSA sub-sample showed optimal resolution. For this sub-sample, the average AHI fell from  $37.5 \text{ h}^{-1}$  (31.6–49.7) to  $7.5 \text{ h}^{-1}$  (1.0–26.9) ( $p < 0.001$ ), while the  $\text{SpO}_2$  nadir improved from 80 to 88% ( $p < 0.001$ ). Similarly, the percentage of sleep time with  $\text{SpO}_2$  saturation < 90% improved from about 40–21% of the night. These findings are summarized in Table 1 and Fig. 4.

In addition, there were 16 subjects with very severe OSA (AHI > 50): 12 males and 4 females. An optimum resolution with AHI of < 5 was achieved for 10 of the 16 subjects. Thus, 63% of the very severe OSA sub-sample showed optimal resolution. For this sub-sample, the average AHI fell from  $73.4 \text{ h}^{-1}$  (51.9–120.3) to  $13.4 \text{ h}^{-1}$  (0.5–55.3) ( $p < 0.001$ ), while the  $\text{SpO}_2$  nadir improved from 76 to 85% ( $p < 0.001$ ). Similarly, the percentage of sleep time with  $\text{SpO}_2$  saturation < 90% improved from about 40% (0.0–82) to 21% (0.0–100) of the night. These findings are summarized in Table 1 and Fig. 5.

**Table 1** Summary of parameters used in this study

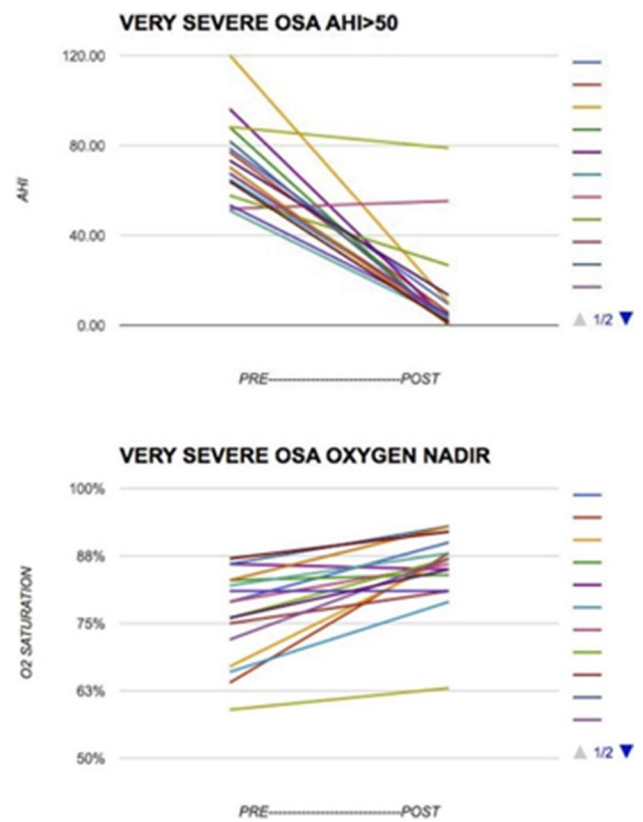
	Average age	Average BMI	Males–females	Pre-treatment AHI	Post-treatment AHI	Pre-treatment $\text{O}_2$ nadir < 90%	Post-treatment $\text{O}_2$ nadir < 90%
Severe OSA AHI > 30 < 50	50.5	32.2	18–7	37.5	7.5	80% –37.9 min	88% –20 min
Very severe OSA AHI > 50	46.8	34.6	12–4	73.4	13.4	76% –47.2 min	85% –10.6 min



**Fig. 4** Plots showing changes in the AHI and SpO<sub>2</sub> nadir for the severe OSA group. For this sub-sample, the average AHI fell from 37.5 h<sup>-1</sup> (31.6–49.7) to 7.5 h<sup>-1</sup> (1.0–26.9) ( $p < 0.001$ ), while the SpO<sub>2</sub> nadir improved from 80 to 88% ( $p < 0.001$ )

## 4 Discussion

The current treatment of choice in patients diagnosed with OSA is continuous positive airway pressure (CPAP). However, this approach is prone to intolerance, and compliance is sometimes less than optimal [24]. Indeed, although some cases of OSA are thought to be disorders of craniofacial anatomy, oral appliance therapy (OAT) is not typically recommended for severe or very severe cases of OSA unless the patient is refractory to CPAP [25]. However, in some preliminary studies, OAT has been used to treat cases of severe OSA [25, 26] without an overnight titration PSG. Our present study suggests that a follow-up titration PSG is an effective method of demonstrating the efficacy of OAT in the treatment of severe OSA. Just as CPAP devices are titrated to find the best pressure setting for the subject, oral appliances can be titrated in the sleep laboratory to find the most efficacious setting and position of the mandible. A titration PSG study involves fine-tuning the device in vivo to ensure maximum resolution of OSA. In our study, a nighttime attending technologist performed the adjustments, while the subject slept wearing the customized and adjustable oral appliance.



**Fig. 5** Plots showing changes in the AHI and SpO<sub>2</sub> nadir for the very severe OSA group. For this sub-sample, the average AHI fell from 73.4 h<sup>-1</sup> (51.9–120.3) to 13.4 h<sup>-1</sup> (0.5–55.3) ( $p < 0.001$ ), while the SpO<sub>2</sub> nadir improved from 76 to 85% ( $p < 0.001$ )

Therefore, the goal of in-laboratory titration in this study was to optimize the efficacy of OAT. While the nighttime PSG technologist made every effort to eliminate obstructive events and airflow limitations to improve breathing during sleep, a board-certified sleep physician used AASM guidelines to interpret the PSG results, establish the efficacy of OAT, and prepare the summary report. The main variable used to determine the PSG titration outcomes in this study was the apnea hypopnea index (AHI).

We attempted to minimize selection bias in this study in a number of ways. First, all pre- and post-treatment polysomnographic studies were completed consecutively during the study period. Second, we only included patients who: strictly adhered to the OAT protocol; used a single type of appliance, and we required the use of expert sleep technologists to complete the titration PSG. Finally, all results, such as the AHI, were reviewed and interpreted by board-certified sleep specialists following established AASM guidelines. The AHI is the most accepted measurement at this time to determine effective titration during a PSG study [27], even though the Respiratory Distress Index (RDI) values are not included. Nevertheless, the

results of this present study showed robust improvements in both severe and very severe categories of OSA studied, and we found that most of the study subjects showed significant improvement in AHI.

Specifically, when the pre-treatment, baseline AHI was compared with the post-treatment AHI over a 4-month period (Figs. 5, 6), our analysis revealed a most remarkable effect in subjects with severe and very severe OSA (Table 1). Our findings are notable in that they demonstrated that the OASYS Oral–Nasal Airway System™ oral appliance was highly efficacious. We found little or no relationship between device efficacy and a range of confounding variables, such as gender, age, and BMI (data not shown). Interestingly, our results differ somewhat from other previously published data in the literature. For example, our data demonstrated significant improvement in OSA in older individuals, in contrast to data previously reported by Liu and Lowe, which suggested that OAT was restricted to younger patients [28]. Similarly, Otsuka and colleagues found that patients with lower BMIs were more likely to respond to OAT [29], which also contrasts with our findings. Importantly, however, we also found that OAT was effective in the treatment of both severe and very severe OSA (Table 1, Figs. 5, 6). These findings are in accord with a review by Hoffstein [30], which concluded that OAT constitutes a relatively heterogeneous group of devices for the treatment of OSA. This heterogeneity likely accounts for the variability in their benefit and side effects, at least in part, and supports our findings. Indeed, according to the current evidence, OAT successfully resolves mild-to-moderate OSA in 40–50% of patients, and significantly improves it in an additional 10–20% [30–32]. The results of our current study appear to extend this range into severe and very cases of OSA.

We also reviewed the changes in post-treatment SpO<sub>2</sub> nadir, using the oxygen saturation nadir as a surrogate marker of oxidative stress that perpetuates the detrimental process of atherosclerosis [33–35]. We found that the use of OAT significantly increased the lowest post-treatment SpO<sub>2</sub>, regardless of disease severity ( $p < 0.001$ ; Table 1; Figs. 5, 6). Moreover, a review of the desaturation data indicated that treatment significantly reduced the percentage of total oxygen desaturation sleep time by about – 7% ( $p < 0.001$ ; Table 1). Other studies have shown more variable results in improvement in the oxygen saturation, especially in cases of severe OSA [36]. Therefore, our results are encouraging, but are limited by the study's retrospective design and modest sample size. There is now a clear need for well-controlled, prospective trials with larger sample sizes to determine the overall efficacy of OAT with overnight PSG titration in the treatment of severe OSA. Future studies are also needed to evaluate the effect of nasal dilation in conjunction with mandibular advancement versus mandibular advancement alone.

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## Compliance with ethical standards

**Conflict of interest** This study did not receive any intra- or extramural financial support. There is no conflict of interest, off label or investigational use of any product or service discussed in this article.

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