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Mandibular Jaw Movement Automated Analysis for Oral Appliance Monitoring in Obstructive Sleep Apnea

A Prospective Cohort Study

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Abstract

Rationale: Oral appliances are second-line treatments after continuous positive airway pressure for obstructive sleep apnea (OSA) management. However, the need for oral appliance titration limits their use as a result of monitoring challenges to assess the treatment effect on OSA.

Objectives: To assess the validity of mandibular jaw movement (MJM) automated analysis compared with polysomnography (PSG) and polygraphy (PG) in evaluating the effect of oral appliance treatment and the effectiveness of MJM monitoring for oral appliance titration at home in patients with OSA.

Methods: This observational, prospective study included 135 patients with OSA eligible for oral appliance therapy. The primary outcome was the apnea-hypopnea index (AHI), measured through in-laboratory PSG/PG and MJM-based technology. Additionally, MJM monitoring at home was conducted at regular intervals during the titration process. The agreement between

PSG/PG and MJM automated analysis was reevaluated using Bland-Altman analysis. Changes in AHI during the home-based oral appliance titration process were evaluated using a generalized linear mixed model and a generalized estimating equation model.

Results: The automated MJM analysis demonstrated strong agreement with PG in assessing AHI at the end of titration, with a median bias of 0.24/h (limits of agreement, −11.2 to 12.8/h). The improvement of AHI from baseline in response to oral appliance treatment was consistent across three evaluation conditions: in-laboratory PG (−59.6%; 95% confidence interval, −59.8% to −59.5%), in-laboratory automated MJM analysis (−59.2%; −65.2% to −52.2%), and at-home automated MJM analysis (−59.7%; −67.4% to −50.2%).

Conclusions: Incorporating MJM automated analysis into the oral appliance titration process has the potential to optimize oral appliance therapy outcomes for OSA.

Keywords: mandibular advancement device; OSA; oral appliance titration; artificial intelligence; mandibular jaw movements

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Author Contributions: J.-L.P., J.-B.M., and N.-N.L.-D. designed the study. J.-L.P., J.-B.M., and E.C. conducted the research procedure and had full access to all study data. J.-L.P., J.-B.M., N.-N.L.-D., R.T., and S.B. performed data analysis. J.-L.P., J.-B.M., P.A.C., G.L., A.B., and A.M. have personally reviewed the data, verified the statistical methods employed for all analyses, and confirms an understanding of these analyses, that the methods are clearly described and that they are a fair way to report the results. J.-L.P., J.-B.M., and N.-N.L.-D. prepared the first draft of the manuscript. G.L., P.A.C., and A.B. reviewed and edited the final manuscript. All authors made the decision to submit the manuscript for publication and assume responsibility for the accuracy and completeness of the analyses and for the fidelity of this report to the study protocol.

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Obstructive sleep apnea (OSA) is a highly prevalent disorder that has deleterious health consequences for individuals (including cardiovascular and metabolic comorbidities) and imposes a high burden on the health system (1, 2). Continuous positive airway pressure (CPAP) therapy is the first-line treatment for moderate to severe OSA. However, long-term adherence to CPAP remains a challenge, with nearly 50% of individuals with OSA having stopped using CPAP at 3 years after therapy initiation (3). Oral appliances have traditionally been recommended for second-line therapy in individuals who are intolerant of or refuse CPAP (4). However, in many countries, the indication for these devices has been expanded to include primary therapy for symptomatic individuals with different levels of OSA severity who have a low comorbidity burden (5, 6).

Titratable two-piece custom-made mandibular advancement devices (MADs) prescribed and managed by dentists are widely accepted as the gold-standard oral appliance therapy. Although CPAP is more effective than MADs for reducing the apnea-hypopnea index (AHI) and oxygen desaturation index (ODI), MADs have shown comparable effects to CPAP on sleep structure and health outcomes (7, 8). Additionally, patient preference and adherence favor oral appliance therapy, thereby balancing the slightly lower efficacy (9). Nevertheless, practical limitations to the implementation and titration of MADs continue to limit the large-scale adoption of such therapy in clinical practice. Furthermore, complexities in the multidisciplinary care pathway can result in delays in treatment initiation associated with a high rate of loss to follow-up in the absence of sleep studies to assess MAD efficacy (10). Therefore, there is a need to design new care pathways that incorporate digital medicine solutions for MAD titration to achieve optimal efficacy of treatment.

Previous research has demonstrated the reliability of mandibular jaw movement (MJM) monitoring coupled with machine-learning analysis as a diagnostic tool for

OSA (11–15). This approach also allows home-based evaluations over multiple nights. However, further validation is required to establish the effectiveness and reliability of MJM analysis in individuals using custom-made MADs that position the mandible in a forward and downward direction because this could impact the accuracy of MJM monitoring.

This study aimed to validate automated MJM analysis compared with in-laboratory polysomnography (PSG) and polygraphy (PG) in assessing the effectiveness of MAD treatment and to evaluate the suitability of automated MJM analysis for at-home monitoring of MAD treatment in individuals with OSA.

Methods

Study Design and Participants

This prospective cohort study included consecutive adults referred for assessment of suspected OSA at the sleep laboratory of Centre Hospitalier Universitaire Université Catholique de Louvain (CHU UCL) Hospital (Namur, Belgium). The protocol was approved by the Comité d'Éthique Hospitalo-Facultaire-Universitaire in Liège, Belgium (approval no. 00004890). All participants provided written informed consent.

Baseline Assessments and OSA Diagnosis

Baseline assessments included in-laboratory diagnostic PSG (Somnoscreen Plus; Somnomedics) with simultaneous MJM recording using Sunrise technology (*see* online data supplement for further details on this technology) (11–15) (Figure 1). PSG recordings were manually assessed using the American Academy of Sleep Medicine criteria (16, 17) by two experienced scorers who were unaware of treatment conditions (interobserver agreement, 92.1%; 95% confidence interval [CI], 89.1–94.2%) and the results of automated MJM analysis. Hypopnea events were defined as a $\geq 30\%$ decrease in flow signal amplitude for ≥ 10 seconds associated with a $\geq 3\%$ oxygen desaturation or an arousal. Apnea events

were defined as a decrease of $\geq 90\%$ of preevent baseline for ≥ 10 seconds (16, 17).

The OSA diagnosis was confirmed based on the International Classification of Sleep Disorders-3 criteria (18). OSA was defined as an AHI of $\geq 5/h$, with severity categorized as mild (AHI 5 to $< 15/h$), moderate (AHI 15 to $< 30/h$), or severe (AHI $\geq 30/h$).

Oral Appliance Therapy and Titration

Participants eligible for oral appliance treatment had a confirmed OSA diagnosis based on in-laboratory PSG. MAD therapy was offered to participants with OSA who did not have overt cardiovascular or metabolic comorbidities. However, MAD was not suitable for patients who exhibited severe sleepiness or for professional drivers and those with compromised stomatognathic situation (fewer than eight teeth per arch, temporomandibular disorder, periodontitis). The MAD used was a two-piece custom-made device (NOA; OrthoApnea) (19) (*see* data supplement for further details).

The titration protocol for oral appliance therapy was a dynamic process involving periodic evaluations and adjustments, with a total duration varying from 2 to 6 months. Continuous engagement was maintained with participants through weekly telephone consultations, focusing on evaluating the persistence or worsening of symptoms like snoring (as reported by the bedpartner), fatigue, or excessive daytime sleepiness. The titration began with a MAD set at 60% of the maximal voluntary advancement. Subsequently, the MAD was adjusted under the direction of the sleep physician, advancing in increments of 1 mm every few weeks as tolerated until it reached the maximum comfortable limit.

Treatment Assessment and Follow-up

There is a specific care pathway for ongoing reimbursement of MAD therapy in Belgium that requires objective demonstration of treatment benefit on PG within 6 months of starting MAD therapy. Therefore, all participants underwent in-laboratory PG at the completion of MAD titration, along with simultaneous MJM recording (Figure 1).

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This article has a related editorial.

A data supplement for this article is available via the Supplements tab at the top of the online article.

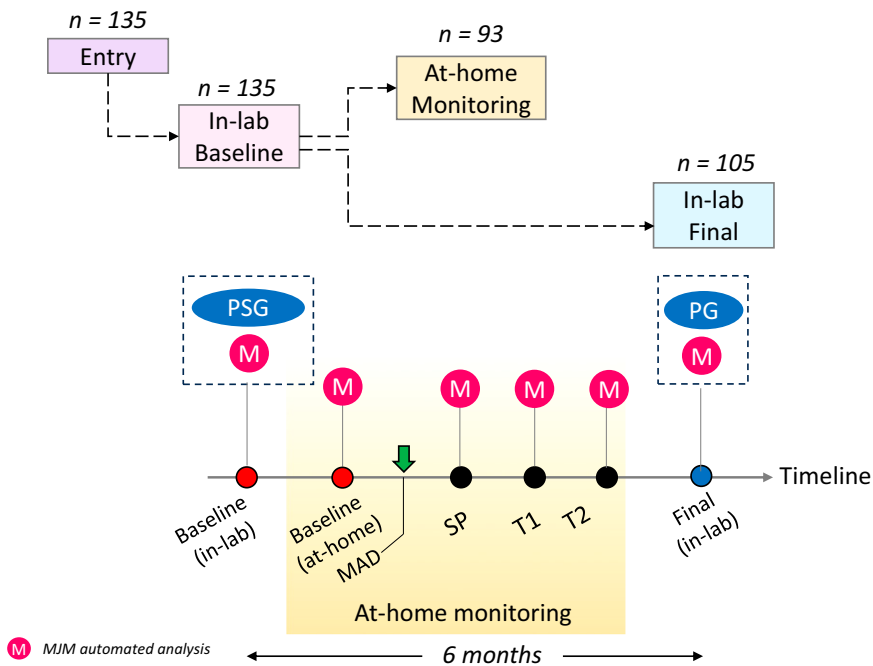


Figure 1. Study flow chart. MAD = mandibular advancement device; MJM = automated analysis of mandibular jaw movements; PG = polygraphy; PSG = polysomnography; SP = starting point of MAD titration; T1 = titration 1; T2 = titration 2.

In addition, single-night home sleep studies using the MJM monitoring system were performed at regular intervals (Figure 1).

These tests were conducted at various stages: 1) before starting MAD therapy, 2) at the start of MAD titration (set at 60% of maximum active protrusion), 3) at an intermediate titration level (with mandibular advancement of +1 mm or +2 mm), and 4) at the final level of mandibular advancement (with an additional 1-mm protrusion compared with the intermediate level, i.e., +2 mm or +3 mm) (Figure 1). The tests were done under stabilized clinical conditions, ensuring that the advancement level was maintained consistently for ≥ 10 –15 days without any associated discomfort. Importantly, the results of these home sleep tests were not used as criteria for adjusting mandibular advancement levels and were kept undisclosed to the treating physician during the study. For each of the four aforementioned assessments, participants were required to complete digital surveys designed to collect information regarding device use, treatment effectiveness, OSA symptoms, as well as adverse events (in terms of frequency and intensity). Responses were measured on a scale of 0–10, whereby 0 indicated the absence of symptoms or side effects and 10 indicated severe symptoms or side

effects. For the primary analyses, all included patients adhered to the criteria of MAD therapy compliance, defined as using the device for ≥ 5 hours per night on $\geq 90\%$ of nights.

Outcomes

The primary endpoint was the change in AHI from baseline to the end of the titration protocol determined using PG or MJM automated analysis. Secondary endpoints included the change in ODI and subjective measurements of OSA-related symptoms (sleepiness, vigilance, fatigue), satisfaction with sleep quality, and the tolerability of MAD therapy.

Statistical Analysis

Based on the results of simulations (Figures E1 and E2 in the data supplement), it was determined that a sample of 90–100 participants would be sufficient to validate an absolute mean limit of agreement (LOA) measurement bias for an AHI of 5–14/h against the clinical acceptability threshold of 25/h and to detect a relative change in AHI of 40–70%, with a statistical power of 0.8 and type I error of 0.05 (see Figures E1 and E2 for full details).

Agreement between AHI measurements determined by in-laboratory PSG or PG and simultaneous MJM monitoring was

evaluated using Bland-Altman analysis, and analysis, with calculation of median bias and LOA values. A bias-corrected accelerated bootstrap process was used to determine the 95% CI of the results.

The average treatment effect of MAD therapy was determined by calculating the absolute and relative changes in the evaluated parameters between baseline and the final degree of MAD advancement. Estimation of the change in AHI between baseline and the final conditions was based on a generalized linear mixed model via the GAMLSS package (20) with an appropriate distribution law for the response variable (a γ -distribution for AHI and ODI, a negative binomial distribution for the occurring rate of apnea-hypopnea events, and an inflated β -distribution for normalized questionnaire scores) and included subject-specific random effects. The potential effect of total sleep time (TST) variation was adjusted using the same model framework with the number of apnea-hypopnea events as the outcome and TST included as a covariate. Change in AHI at home measured with MJM automated analysis in response to MAD titration was evaluated using a generalized estimating equation model (21) with γ -distribution. CIs for the marginal effects were determined by the delta method using the marginal effects package (22).

Data analysis was performed using the R programming language (<https://www.R-project.org/>). Statistical inferences were based on null hypothesis testing at a significance level of 0.005.

Results

Study Population

The study population included 135 individuals, 30 of whom were lost to follow-up (as a result of the impact of the coronavirus disease [COVID-19] pandemic [$n = 18$] or inadequate protocol compliance [$n = 12$]). Full data from home monitoring questionnaires were available for 93 participants. The study population was predominantly male, middle-aged, and overweight; snoring and daytime symptoms of OSA were common (Table 1). Baseline in-laboratory PSG showed altered sleep efficiency, sleep fragmentation, and moderate to severe OSA, with events occurring most frequently in the supine position. The mean duration of follow-up was 5.23 ± 0.40 months. Initial, intermediate, and final protrusion levels were $60.0 \pm 0.00\%$,

Table 1. Demographic and clinical characteristics of the study population and PSG findings at baseline ($N = 135$)

Characteristics	Value
Age, yr	48.8 (33.7–64.1)
Male sex	100 (74%)
Body mass index, kg/m ²	27.4 (21.5–33.3)
Neck circumference, cm	40.0 (30.0–44.0)
ESS score	11 (4–19)
OSA subgroup	
Obstructive RDI <5/h with snoring	2 (1%)
Obstructive RDI 5–15/h with symptoms	21 (16%)
Positional OSA	32 (24%)
OSA severity	
Mild (AHI 5 to <15/h)	13 (10%)
Moderate (AHI 15 to <30/h)	75 (56%)
Severe (AHI ≥30/h)	47 (34%)
Symptoms	
Snoring	120 (89%)
Witnessed apneas	73 (54%)
Morning headache	82 (61%)
Morning fatigue	106 (79%)
Fatigue during the day	110 (81%)
Insomnia	58 (43%)
PSG data	
TST, h	7.1 (4.8–8.7)
Sleep efficiency, %	72.3 (51.4–91.5)
Arousal index, per hour	27.1 (13.7–49.2)
AHI, per hour	24.6 (13.4–58.0)
Supine AHI, per hour	23.8 (8.8–57.7)
Non-supine AHI, per hour	19.7 (6.1–57.7)
AHI during non-REM sleep, per hour	18.0 (8.0–41.0)
AHI during REM sleep, per hour	19.1 (1.3–49.5)
Obstructive AHI, per hour	18.8 (6.2–47.6)
Central AHI, per hour	4.5 (0.2–19.9)
RDI, per hour	29.4 (15.4–59.4)
Obstructive RDI, per hour	23.7 (8.4–49.1)
RERA index, per hour	2.8 (0.3–9.9)
ODI, per hour	17.2 (3.5–58.4)

Definition of abbreviations: AHI = apnea–hypopnea index; ESS = Epworth sleepiness scale; ODI = oxygen desaturation index; OSA = obstructive sleep apnea; PSG = polysomnography; RDI = respiratory disturbance index; REM = rapid eye movement; RERA = respiratory effort-related arousal; TST = total sleep time.

Data presented as median (5th percentile–95th percentile) where applicable.

68.15 ± 1.66%, and 76.56 ± 3.67% of the maximum active protrusion, respectively (Table E1).

AHI Estimation: Automated MJM Analysis versus PSG/PG

Visualization of the MJM biosignals with manually scored data from conventional PSG or PG showed a strong agreement between methods (i.e., MJM vs. either PSG or PG) (Figure E3). The AHI measurement bias was randomly and normally distributed at baseline and the final assessment, and the MJM automated analysis consistently replicated the same AHI distribution shape captured by PSG and PG across the entire measurement range (Figure 2). At baseline, the MJM automated analysis slightly underestimated the AHI compared with

in-laboratory PSG, with a median bias of –4.8/h (95% CI, –5.9 to –3.1/h). The LOA was –22.7 to 11.7/h. At the end of MAD titration, the median bias of MJM analysis was 0.2/h (95% CI, –1.4 to 2.1/h), which is clinically acceptable, and the LOA values had a narrower range (–11.2 to 12.8/h).

PSG/PG data showed a significant reduction in AHI from baseline to the end of MAD titration (absolute change, –15.6/h [95% CI, –15.6 to –15.5]; relative change, –55.6% [95% CI, –55.8 to –55.5]) (Figure 3 and Table 2). In the subgroup of participants who underwent in-laboratory PG and home-based MJM monitoring after MAD titration ($n = 93$), the average reduction in AHI measured with MJM analysis (–59.7% [95% CI, –67.4 to –50.2]) was very similar to that observed with

in-laboratory PG (–59.6% [95% CI, –59.8 to –59.5]) (Figure 3 and Table 2). By conducting a supplementary analysis that specifically examined the frequency of apnea–hypopnea events, incorporating TST as a covariate (Table E2), we substantiated that the changes in the observed AHI were not impacted by fluctuations in TST.

MJM-based Analysis for Evaluation of MAD Titration Efficacy and AHI Response at Home

At-home MJM-based monitoring showed a progressive and significant improvement in the AHI as the degree of protrusion increased during MAD titration (Figure 4 and Table E3). Even at the initial titration level (i.e., the starting point) set at 60% of the maximum active protrusion, there was a significant reduction in the AHI (–10.3/h, –47.7%; $P < 0.0001$) versus baseline. Further reductions in AHI were seen as MAD protrusion increased, with reductions of –12.7/h (–58.6%) from baseline to intermediate protrusion level and –13.0/h (–59.7%) from baseline to the final protrusion level (see Table E3).

Significantly, at the initial protrusion level (starting point), 47 of 93 participants (50.5%) had an AHI improvement of ≥50% versus baseline. The responder rates at the intermediate and final levels were 64.5% (60 of 93) and 65.6% (61 of 93), respectively. Furthermore, the responder rates associated with a normalized AHI (≤5 events/h) were 22.6% (21 of 93), 32.3% (30 of 93), and 46.2% (43 of 93) at the initial, intermediate, and final levels of advancement, respectively.

There was also a significant ODI improvement between baseline and the final protrusion level, with an absolute change of –7.9/h (95% CI, –7.9 to –7.9/h) and a relative change of –41.0% (95% CI, –41.2 to –40.9%).

Effects of MAD on OSA Signs and Symptoms

The use of a MAD was associated with significant improvements in sleep quality, snoring, morning fatigue, headache, dry mouth, and daytime sleepiness (Table 3 and Table E4).

Tolerability

Patient-reported MAD-related adverse events indicated that the treatment was generally well tolerated, with a low burden of side effects (Table E5).

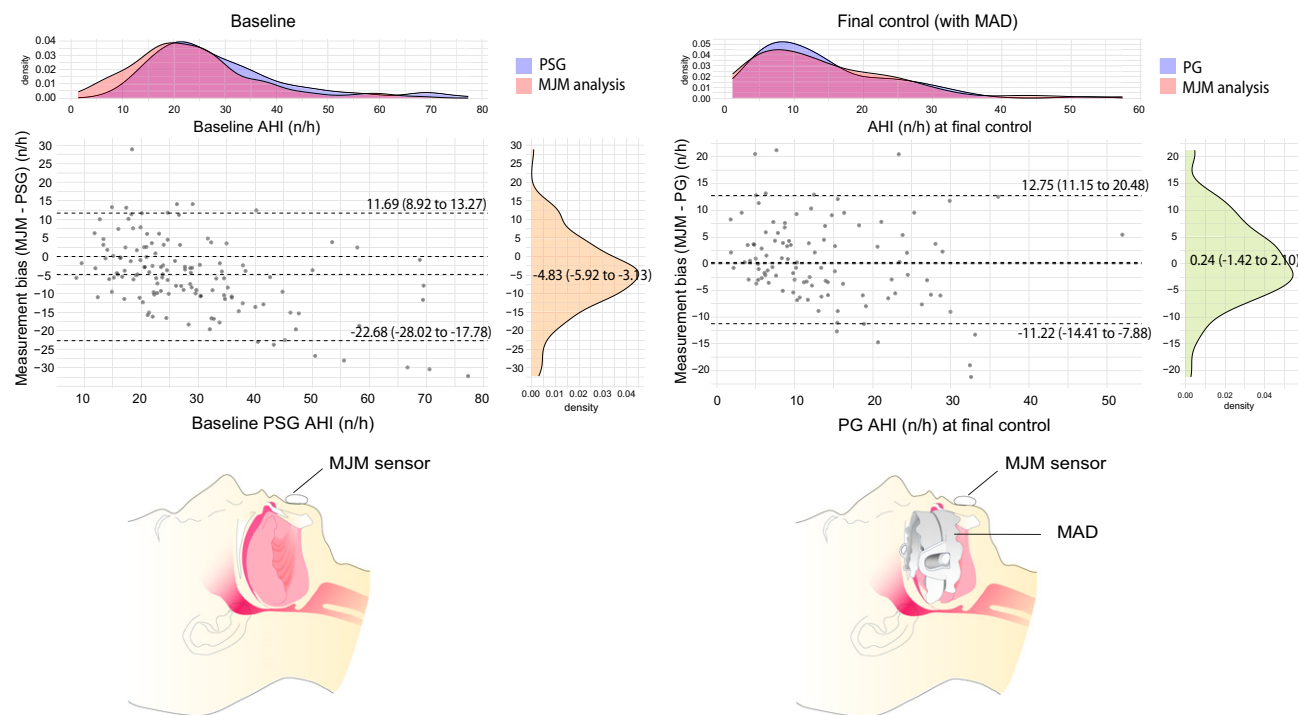


Figure 2. Agreement between polysomnography (PSG)/polygraphy (PG) and mandibular jaw movement (MJM) automated analysis for estimation of the apnea-hypopnea index (AHI). For each plot, the x-axis represents the reference scale for AHI estimated by in-laboratory PSG (baseline) or in-laboratory PG (final control), and the y-axis represents the scale of measurement bias between MJM analysis and PSG or PG. Each point on the scatter plot represents an individual patient; the three horizontal dotted lines indicate the median value and the upper (95th percentile) and lower (5th percentile) limits of the measurement bias. The density curves on the upper panel represent the distribution of MJM-derived AHI (red) and PSG/PG-derived AHI (blue). The vertical density curve on the right represents the distribution of measurement bias. MAD = mandibular advancement device.

Discussion

Our findings confirm that MJM monitoring is an accurate tool for diagnosing OSA and determining disease severity. Notably, this study demonstrated, for the first time to our knowledge, the excellent performance of MJM automated analysis in the home-based monitoring of MAD titration. Overall, measurement bias was consistent with previously reported LOAs of other U.S. Food and Drug Administration–approved machine learning–based sleep test solutions (23–26). Home sleep testing with MJM monitoring allowed effective visualization of the trajectories of AHI and improvements of OSA symptoms throughout MAD therapy.

At the end of the MAD titration process, the AHI measured was similar between manual PG scoring and MJM automated analysis recorded the same night at a sleep clinic. These findings show that the reliability of MJM analysis is not impacted in individuals who use oral appliances protruding the mandible forward. The MJM analysis replicated the same AHI distribution

as determined by PG and captured the global trend of AHI changes with a high level of agreement. In addition to providing accurate data on the change in AHI between two time points (as obtained using PSG and PG), at-home MJM monitoring provides the opportunity for continuous monitoring of a progressive AHI response, allowing real-time adjustment of mandibular protrusion, ensuring that the MAD is optimized for each individual (9, 27).

The present study also recorded enhancements in OSA symptoms with MAD therapy, encompassing improvements in sleep quality, reduced snoring, decreased morning fatigue, alleviated headaches, diminished dry mouth, and reduced daytime sleepiness. Additionally, MAD treatment demonstrated good tolerability. Although they were gathered through specific visits or calls in the present study, in clinical application, these data could be acquired using the patient app of the MJM monitoring system. This approach would enable the collection of pertinent data and the seamless transmission of information to the clinician.

The accuracy of MJM monitoring for OSA diagnosis has previously been validated against PSG in the sleep laboratory and at home (11, 15). However, there are limited data on whether this accuracy compared with PSG/PG is preserved during MAD therapy. Only one previous study has investigated the use of MJM analysis to determine the effectiveness of oral appliance therapy in OSA (28). That study used a different MAD, but also successfully used MJM analysis to document the reduction in AHI during MAD therapy.

The sensitivity of the MJM monitoring technology is due to two important factors. First, the biosignal itself is highly robust and well-preserved, even during rapid eye movement sleep, because of the crucial leverage role the lower jaw plays in maintaining pharyngeal patency. This ensures accurate and consistent data collection. Second, the use of inertial units in the capturing technology contributes to its robustness. These units are extensively used in fields like aviation and smartphones, highlighting their proven reliability and

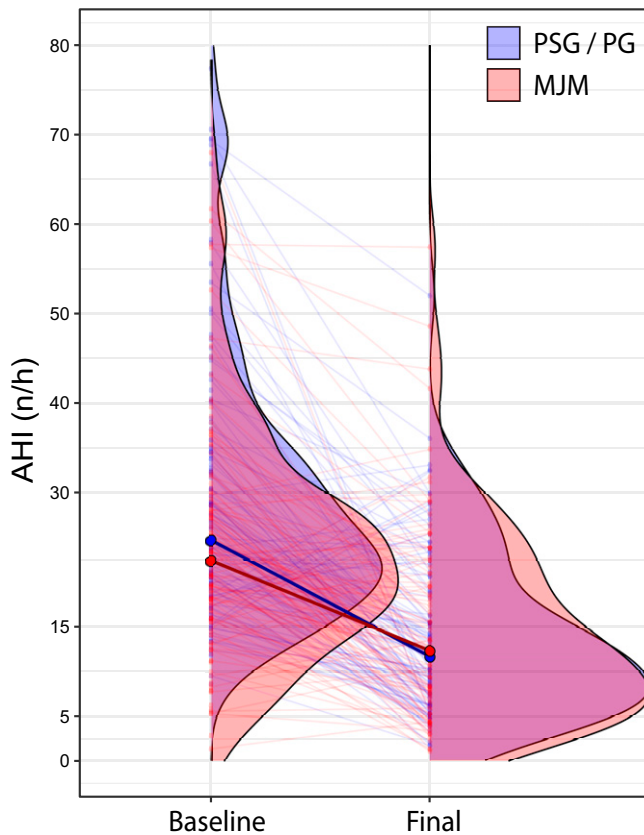


Figure 3. Apnea–hypopnea index (AHI) distribution before and after mandibular advancement device therapy based on polysomnography/polygraphy (PSG/PG) or mandibular jaw movement (MJM) automated analysis. The figure consists of two layers: the front layer shows the distribution of AHI values at baseline and the end of the titration process. The larger dots indicate the median AHI value at each time point, and the bold line connecting these dots indicates the trend of AHI change at the population level. In the background, a combination of dots and line plots shows individual changes in AHI from baseline to the end of treatment. For all graphical elements, blue indicates AHI assessment by PSG/PG and red indicates AHI assessment using MJM automated analysis. MJM = mandibular jaw movements; PG = polygraphy; PSG = polysomnography.

suitability for precise data acquisition in the scope of MJM technology.

The determination of the optimal level of mandibular advancement is currently not standardized. However, a potential approach

to fine-tuning mandibular advancement involves monitoring the AHI and subjective OSA symptoms during treatment. Although this approach has been explored, previous studies have not specifically examined

individual responses at home in relation to the titration level as a percentage of the maximal protrusion (29). Some success has been reported with the use of at-home PG, with a $\geq 50\%$ decrease in AHI reported in 72% of patients (26 of 36) after only minimal advancement (30). In the present study, we observed a similar optimal improvement rate of 50.5% right from the initial advancement level, as well as a cumulative normalization rate (AHI $\leq 5/h$) as the protrusion level increased. These results demonstrate the benefits of real-time treatment monitoring process at home.

A cost-effective digital medicine solution with minimal technical and human resource requirements that enables home monitoring over multiple nights, along with the collection of patient-reported outcome measures (PROMs) data, could offer a convenient approach for clinical practice and research. Providing patients with devices in advance and getting results via a digital platform within minutes of the test being done would streamline the process, reducing the need for extensive in-person visits while significantly enhancing the capture of objective data on MAD effectiveness. This approach could effectively address challenges related to sleep laboratory capacity, which particularly worsened during the COVID-19 pandemic, and provide a valuable resource for individuals living in remote and isolated areas with limited access to in-laboratory PSG services. Local healthcare providers in these regions could easily adopt the MJM monitoring at home, which would be a significant advancement in making OSA management more accessible.

In addition, personalized titration by remote monitoring of clinical symptoms and MJM would allow the prescription of the minimal level of advancement that is associated with sufficient reduction in AHI,

Table 2. Change in the average AHI from baseline to the end of titration based on different evaluation methods

Evaluation Method			Change in AHI vs. Baseline (95% CI)*	
Baseline	End of Titration	n	Absolute, per Hour	Relative, %
In-lab PSG	In-lab PG	105	-15.6 (-15.6 to -15.5)	-55.6 (-55.8 to -55.5)
In-lab PSG	In-lab PG	93	-16.7 (-16.7 to -16.6)	-59.6 (-59.8 to -59.5)
HST MJM	HST MJM	93	-13.0 (-15.5 to -10.4)	-59.7 (-67.4 to -50.2)
In-lab PSG	In-lab MJM	105	-15.2 (-18.0 to -12.4)	-54.2 (-59.6 to -48.2)
In-lab PSG	In-lab MJM	93	-16.6 (-20.1 to -13.1)	-59.2 (-65.2 to -52.2)

Definition of abbreviations: AHI = apnea–hypopnea index; CI = confidence interval; HST = home sleep test; MJM = mandibular jaw movements; PG = polygraphy; PSG = polysomnography.

*All changes in AHI vs. baseline were significant at $P < 0.0001$.

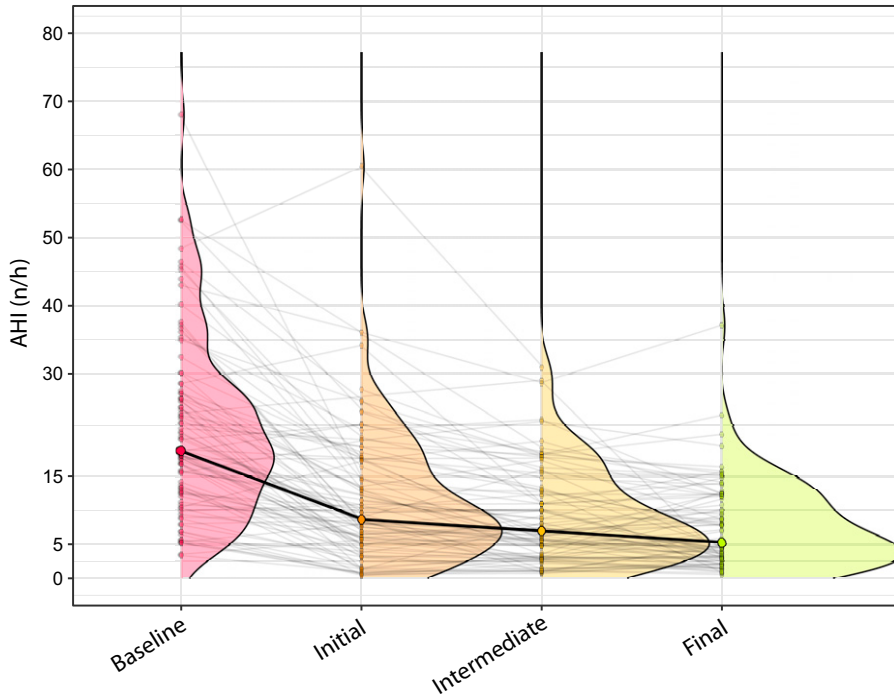


Figure 4. Change in the apnea-hypopnea index during mandibular advancement device therapy at home. This figure has the same structure as Figure 3. The x-axis shows the baseline and the three ascending levels of mandibular advancement device protrusion: initial protrusion was $60.00 \pm 0.00\%$, intermediate protrusion was $68.15 \pm 1.66\%$, and final protrusion was the final effective protrusion level achieved ($76.56 \pm 3.67\%$) of the maximum active protrusion. AHI = apnea-hypopnea index.

thus limiting the potential side effects associated with the use of oral appliances. By adopting such an approach and using a lower level of mandibular advancement, the potential risk of inducing discomfort in the temporomandibular structures could be reduced (31). This is highly relevant given

that the American Academy of Sleep Medicine guidelines acknowledge the development of temporomandibular disorders as the primary reason for discontinuing MAD therapy (32). There is also potential for such an approach to improve treatment compliance.

Given the constraints of our observational study, our findings support the utility of MJM analysis as a monitoring tool but could not establish a causal link with treatment efficacy. Nonetheless, these findings suggest that at-home MJM analysis is valuable for remote MAD titration optimization.

Simplifying the MAD titration procedure remains a significant unmet requirement that restricts the broader adoption of oral appliance therapy. The efficacy of this therapeutic strategy is currently largely unpredictable before titration. Respiratory/sleep physicians frequently overlook oral appliance therapy as a viable option because of the intricate nature of the multidisciplinary care pathway, necessitating them to closely collaborate with dental specialists for comprehensive patient management. The use of MJM monitoring alongside digital medicine strategies could simplify this process. In addition, there is a need to better define the roles of stakeholders in MAD titration and follow-up to avoid inefficiency and redundancy in the management pathway and reimbursement models. The development of multidisciplinary digital medicine platforms shared between dentists and sleep specialists might represent a step forward for easy access, better therapy implementation, and optimized treatment effectiveness (in terms of objective data and PROMs).

Future studies should explore the long-term efficacy, the impact on the titration time, and the cost-effectiveness of the MJM-based digital medicine approach compared with traditional MAD titration methods.

Table 3. Impact of mandibular advancement device therapy on patient-reported outcome measures

Measure	Baseline	End of Titration	Change from Baseline (95% CI)*	
			Absolute, per Hour	Relative, %
Global satisfaction with sleep quality [†]	3.4 ± 1.7	6.2 ± 2.0	2.2 (2.0 to 2.5)	62.3 (52.1 to 73.3)
Snoring [‡]	7.9 ± 2.2	2.2 ± 2.0	-3.8 (-4.0 to -3.5)	-60.4 (-63.4 to -57.3)
Morning fatigue [‡]	6.1 ± 2.1	4.4 ± 2.2	-1.2 (-1.7 to -0.7)	-21.5 (-29.1 to -13.1)
Headache [‡]	3.2 ± 2.2	0.8 ± 1.8	-0.9 (-1.1 to -0.7)	-22.1 (-26.7 to -17.1)
Dry mouth [‡]	4.6 ± 2.7	2.2 ± 2.0	-2.1 (-2.4 to -1.7)	-44.3 (-49.4 to -38.7)
ESS score [§]	11.1 ± 4.3	8.5 ± 4.4	-2.7 (-3.4 to -2.0)	-24.5 (-30.0 to -18.6)
Pichot Fatigue Scale score [§]	12.3 ± 6.7	8.0 ± 7.4	-3.2 (-4.5 to -2.0)	-27.3 (-35.5 to -18.0)

Definition of abbreviations: CI = confidence interval; ESS = Epworth sleepiness scale. Baseline and end of titration values are mean ± standard deviation.

*All changes vs. baseline were significant at $P < 0.0001$.

[†]Rated on a scale from 0 to 10, whereby higher scores indicate higher levels of satisfaction.

[‡]Self-reported OSA symptoms were rated on a scale from 0 to 10, whereby a higher score indicates a higher rate of that symptom.

[§]The ESS and Pichot Fatigue Scale were scored from 0 to 24 and from 0 to 32, respectively; data were converted into a standard continuous scale to be compatible with the statistical inference that implied a generalized linear mixed model with beta-distribution.

Conclusions

The results of this study showed the effectiveness and reliability of MJM monitoring coupled with an automated analysis by machine learning as a digital solution for MAD titration. The MJM-based method demonstrated a strong agreement with conventional in-laboratory PSG and PG in estimating AHI and evaluating the MAD treatment effect. Furthermore, the results of at-home MJM analysis revealed its potential

for remote monitoring and optimization of MAD titration. Coupled with digital surveys, its capability would include continuous monitoring of the evolving AHI response and OSA-related symptoms, enabling real-time mandibular protrusion adjustments to ensure that the MAD is tailored optimally to each patient. These findings help overcome several significant obstacles to the widespread clinical integration of MAD therapy for OSA. They also support the use

of MJM automated analysis as a valuable tool to enhance accessibility to MAD therapy and improve treatment effectiveness and patient outcomes. ■

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